DIFFERENTIATION OF DEEP VENOUS THROMBOSIS AMONG CHILDREN WITH OR WITHOUT ACUTE HEMATOGENOUS OSTEOMYELITIS TO FOSTER EARLY RECOGNITION AND EFFECTIVE MANAGEMENT

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Background

Children with osteomyelitis are at risk for deep venous thrombosis (DVT). This study evaluates the characteristics of DVT among children to differentiate between those with and without osteomyelitis.

Methods

Children with DVT of any cause were studied between 2008 and 2016. Children with DVT and osteomyelitis were compared to those with DVT without osteomyelitis. Another comparison cohort included children with osteomyelitis but without DVT. Comorbidities, severity of illness, and clinical course were compared between cohorts.

Results

DVT was identified in 224 children, a prevalence of 2.5 per 10,000 children. Among those with DVT, 28 (12.1%) had osteomyelitis. The DVT rate among 466 children with osteomyelitis was 6.0%. Children with osteomyelitis and DVT had greater severity of illness (9.1 vs 2.7), bacteremia rate (82.1% vs 38.4%), MRSA rate (89.3% vs. 21.2%), surgeries per child (2.1 vs 0.7), and ICU admission rate (67.9% vs 5.9%) than that of children without DVT (p<0.00001). Of 196 children who had DVT without osteomyelitis, 166 (84.7%) had comorbidities including defined hypercoagulability (27 or 13.8%). Children with DVT due to osteomyelitis were without comorbidities or hypercoagulability (p<0.00001). The rate of pulmonary embolism (PE) was similar for children with DVT with or without osteomyelitis (3 of 28, or 10.7% vs 18 of 196, or 9.2%).

Conclusions

Children with DVT and osteomyelitis differ substantially from other children with DVT by the absence of comorbidities or PTS. They also differ from children with osteomyelitis without DVT by higher severity of illness, MRSA rate, and occurrence of intensive care. Awareness of for the characteristics of DVT among children with osteomyelitis will reduce delay to diagnostic ultrasound and improve anticoagulation management which must be carefully coordinated given the high rate of surgery of these children.
Pneumococcal vaccines are powerful tools to protect patients from severe diseases. Until today more than 90 different serotypes of this capsule have been described, but only 23 serotypes are included in the available vaccines. Therefore serotyping of pneumococci is mandatory to monitor distribution of different serotypes. The traditional method of typing is the “Quellung” reaction, which is expensive and technically demanding to perform. Fourier transform infrared spectroscopy (FT-IR) is a technique with the potential to differentiate strains and closely related species. We used FT-IR to investigate its typing capabilities for the 23 serotypes included in the 23-valent vaccine.

Methods

We studied 112 isolates covering the 23 serotypes included in the 23-valent polysaccharide vaccine. Isolates were cultivated overnight on blood agar and homogenous suspensions of bacteria were dried on silicon plates as thin films. Infrared spectra were acquired with an FT-IR spectrometer (Tensor 27 with HTS-XT microplate reader) using OPUS software (Bruker Optics). In total three independent measurements per isolate with aspired 5 technical replicates summed up to 2060 infrared spectra. Second derivative spectra were truncated to wavenumbers 800-1300 /cm and vector-normalized. Then hierarchical cluster analysis of median spectra was performed.

Results

All isolates generated good spectra and the method was capable of distinguishing between serotypes/serogroups with an accuracy of >99%. To reliably distinguish between members of serogroup 6 more isolates have to be studied. The results for FTIR “sero”-typing were available the same day the pure culture was available. First results with clinical strains look promising.

Conclusions

FT-IR is a new and promising technology for “sero”-typing of pneumococci. It is faster and less laborious as conventional methods. The results are reliable and highly discriminatory.
Diphtheria outbreak in Rohingya refugee camps in Bangladesh 2017/18

Background

A rapid increase in the number of cases of diphtheria was reported in southern Bangladesh near the Myanmar border in November 2017. The World Health Organisation (WHO) responded to the potential epidemic by mass immunisation and a request for Emergency Medical Teams (EMT) to set up isolation facilities for cases and deliver diphtheria anti-toxin (DAT).

Case Presentation Summary

The UK responded to the request for an EMT in three densely populated camps. DAT is equine immunoglobulin. All were treated with antibiotics (penicillin or azithromycin) and immunised. MSF had previously sent almost 400 swabs from suspected cases for diphtheria toxin PCR. Of the cases described as having pseudomembrane, 25% were PCR negative. Of the ones without pseudomembrane, 30% were PCR positive. WHO set up further funding for 20 PCR and culture per day later in the outbreak as numbers were appearing to wane. At the end of the first UKEMT deployment over 3000 cases of diphtheria had been diagnosed and 30 deaths attributed to the disease. The UKEMT had administered DAT to 45 patients.

Learning Points/Discussion

The UKEMT demonstrated the capacity of a WHO coordinated response to a country's appeal for assistance with up to date currently employed health professionals to come at short notice.

Once seen the pseudomembrane of diphtheria is unmistakable but 'early' and 'gross' lymphadenopathy or 'Bull neck' are clinically difficult to be certain about.

Laboratory back up is essential to confirm cases so that resources could be allocated to those areas still seeing confirmed cases with intensive contact tracing, antibiotic prophylaxis and immunisation.
ASSOCIATION BETWEEN THE SAFE DELIVERY APP AND QUALITY OF CARE AND PERINATAL SURVIVAL IN ETHIOPIA: A RANDOMIZED CLINICAL TRIAL

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Background

Health apps in low-income countries are emerging tools with the potential to improve quality of health care services. We aimed to determine the effects of the safe delivery app (SDA) containing animated clinical instruction videos, on perinatal survival and on health care workers’ knowledge and skills in neonatal resuscitation.

Methods

In a cluster-randomized clinical trial in 5 rural districts of Ethiopia, 73 health care facilities were randomized to the mobile phone intervention or to standard care (control). 3601 women in active labor were included at admission and followed up until 7 days after delivery to record perinatal mortality. Knowledge and skills in neonatal resuscitation were assessed at baseline, 6 and 12 months after the intervention among 176 health care workers at the included facilities.

Results

The SDA was associated with a nonsignificant lower perinatal mortality of 14 per 1000 births in intervention clusters compared with 23 per 1000 births in control clusters (odds ratio, 0.76; 95% CI, 0.32-1.81). The skill scores of intervention health care workers increased significantly at 6 months (mean difference, 6.04; 95% CI, 4.26-7.82) and 12 months (mean difference, 8.79; 95% CI, 7.14-10.45) from baseline, corresponding to 80% and 107%, respectively, above the control level. Knowledge scores also significantly improved in the intervention group at 6 months (mean difference, 1.67; 95% CI, 1.02-2.32) and at 12 months (mean difference, 1.54; 95% CI, 0.98-2.09), corresponding to 39% and 38%, respectively, above the control level.

Conclusions

The SDA was an effective method to improve and sustain the health care workers’ knowledge and skills in neonatal resuscitation as long as 12 months after introduction. Perinatal mortality was nonsignificantly reduced after the intervention. The results are highly relevant for low-income countries.

Clinical Trial Registration (Please input N/A if not registered)

clinicaltrials.gov Identifier:NCT01945931
GENOME WIDE NETWORK ANALYSIS OF RNA-SEQ DATA REVEALS NOVEL PATHWAYS AND GENES RELATED TO MULTI-DRUG RESISTANCE DEVELOPMENT IN STAPHYLOCOCCUS AUREUS

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Background

The multidrug resistance (MDR) in *S. aureus* is a complicated problem and it is necessary to develop new strategies to overcome. Recent advances in sequencing technologies such as RNA-seq have aided the systematic identification of genes involved in antibiotic resistance. Yet the mechanistic aspects of multidrug resistance, its regulation and its effect on the phenotype are still not well defined.

Methods

We construct a global mRNA interactome of all known/predicted interactions in *S. aureus* and identify a module of genes that are involved in Multidrug Resistance Development (MRD) using a collection of RNA-seq profiles of resistant strain. Rather than focusing on the differentially expressed gene candidates or the hubs detected *prima facie*, we dwell further deep into the network and refine our search by considering the level of differential expression in their vicinity.

Results

A global interactome network was constructed with 2789 nodes and 29639 interactions. The interactions of 66 mRNAs which showed altered expressions on treating with four different antibiotics (Vancomycin, Ceftobiprole, Linezolid, Tigecyclin) were extracted from the interactome and designated as the MRD-module and further analysed.

Pathway relationship analysis identified the enrichment of two-component systems, *aromatic amino-acid biosynthesis* and *galactose metabolism* pathways with p-values<0.05 (FDR corrected) in the module.

A notable hub detected by neighborhood analysis was the hypothetical protein *SAOUHSC_02155* which on further analysis was found to be a probable GntR family transcriptional regulator, interconnected with many transporter proteins and nine genes were detected as strong candidates from this study.

Conclusions

Differential gene expression between treated and untreated resistant strains combined with neighborhood analysis of the interactome reveals novel candidate genes and regulatory interactions along with a number of previously known/validated candidates.

Clinical Trial Registration (Please input N/A if not registered)
Background

Tick-borne encephalitis (TBE) is a severe viral infection of the brain for which no treatment is available. TBE vaccines were first licensed more than 40 years ago solely based on immunological surrogate markers for protection. As there is no treatment currently available for TBE, vaccination is the only method of prevention in endemic areas; however the duration of protection is unknown.

Methods

Data presented here are from two follow-up studies in 486 healthy children, adolescents, and adults who had received primary immunizations and first boosters in previous trials. Both current studies followed subjects for TBE antibody persistence after the first booster with FSME-IMMUN (i.e. 4th dose administered 3 years after the third vaccination). Yearly blood draws were performed to assess seropersistence of TBE virus antibodies for up to 10 years.

Results

Antibody titers peaked roughly one month post-booster dose, then decreased to a plateau. From one month through 3 years post-first booster dose, seropositivity rates were 98.1% for subjects age 50-60 years and 100% for all other age groups as measured by neutralization test. After year 3, seropositivity rates began to decline for all but the 3-6 years age group, which remained 100% seropositive through year 9. The decline was most prominent in those age >60 years (Figure 1).
Conclusions

Although there were some differences between the age groups <60 years of age, an FSME-Immun booster interval of 5 years is believed to provide an ample safety buffer for all age groups. This long-term seropersistence data may support prolongation of the booster interval beyond the recommended 5 years for the second and subsequent boosters.

Clinical Trial Registration (Please input N/A if not registered)
Higher intake of coagulase-negative staphylococci from breast milk promotes gut colonization with meca-negative S. epidermidis in preterm neonates

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Background

In preterm neonates meca-positive S. epidermidis (MRSE) causes late-onset sepsis (LOS) potentially by translocation from gut. Gut colonization with meca-negative S. epidermidis (MSSE) instead of MRSE could contribute to prevention of LOS. We aimed to determine factors associated with gut colonization of preterm neonates with MSSE detected in breast milk (BM).

Methods

Weekly collected stool from BM-fed preterm neonates (n=49; median (IQR), gestational age 28 (25-30) weeks, birth weight 1.15 (0.81-1.56) kg) hospitalized in neonatal intensive care unit and mothers’ BM were cultured onto mannitol salt agar. S. epidermidis was identified by MALDI-TOF MS, meca by PCR, genetic similarity by multilocus variable-number tandem-repeat analysis (MLVA). BM-MSSE was defined as MSSE MLVA-type detected in ≥1 mother’s own BM sample.

Results

MSSE colonized gut of 26 (53.1%) preterm neonates, BM of 41 (83.7%) mothers. BM-MSSE colonized 20 (40.8%) preterm neonates at median (IQR) age of 15.5 (11-21) days. BM-MSSE colonized BM at median (IQR) 7 (0-12) days earlier than gut (p=0.012). Higher intake of coagulase-negative staphylococci from BM increased, and colonization of BM with MRSE decreased the probability of gut colonization with BM-MSSE (Table).

The proportion of MRSE among S. epidermidis in gut decreased during the first month of life in neonates colonized with BM-MSSE (from 86.7% to 40.7%; p<0.001), but not in those not colonized with BM-MSSE (from 98.5% to 94.3%). Smaller proportion of neonates colonized with BM-MSSE compared with those not colonized with BM-MSSE had LOS caused by coagulase-negative...
staphylococci (5% (1/20) vs 34.5% (10/29); p=0.017).

Table. Cox proportional hazards regression with Firth’s penalized likelihood of factors associated with gut colonization of preterm neonates with BM-MSSE

<table>
<thead>
<tr>
<th>Time-fixed variables</th>
<th>Univariate HR (95% CI)</th>
<th>p-value</th>
<th>Multivariate HR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational age (weeks)</td>
<td>1.04 (0.90-1.21)</td>
<td>0.60</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>BW (kg)</td>
<td>1.27 (0.54-2.54)</td>
<td>0.56</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Caesarean section</td>
<td>0.64 (0.24-1.68)</td>
<td>0.37</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Unit A</td>
<td>1.63 (0.62-4.31)</td>
<td>0.31</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Time-dependent variables</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospitalization in neonatal intensive care unit</td>
<td>0.39 (0.14-1.02)</td>
<td>0.055*</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Penicillin or ampicillin</td>
<td>0.98 (0.01-8.83)</td>
<td>0.99</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Other beta-lactams</td>
<td>0.11 (0.001-0.79)</td>
<td>0.023*</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>0.65 (0.01-4.88)</td>
<td>0.75</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>0.15 (0.001-1.15)</td>
<td>0.075*</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>BM (mL/kg BW)</td>
<td>1.01 (0.997-1.02)</td>
<td>0.18</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Formula (mL/kg BW)</td>
<td>1.01 (0.99-1.01)</td>
<td>0.27</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Enteral feeding (mL/kg BW)</td>
<td>1.01 (0.99996-1.03)</td>
<td>0.051*</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>BM of total enteral feeding (%)</td>
<td>0.89 (0.25-4.99)</td>
<td>0.87</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Count of CoNS in BM (log_{10} cfu/mL)</td>
<td>1.30 (0.76-2.38)</td>
<td>0.36</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Intake of CoNS from BM (log_{10} cfu/g BW)**</td>
<td>5.73 (1.03-37.12)</td>
<td>0.046*</td>
<td>9.14 (1.50-55.78)</td>
<td>0.017</td>
</tr>
<tr>
<td>Colonization of BM with MRSE</td>
<td>0.35 (0.12-0.98)</td>
<td>0.045*</td>
<td>0.26 (0.09-0.78)</td>
<td>0.016</td>
</tr>
</tbody>
</table>

BM – breast milk; BW – birth weight; CI – confidence interval; CoNS – coagulase-negative staphylococci; HR – hazard ratio; MRSE – mecA-positive S. epidermidis.

*Variables significant at a p-value <0.1 in univariate regression were further analysed in multivariate regression.

**Intake of CoNS from BM (log_{10} cfu/g BW) was calculated by multiplying count of CoNS in BM (log_{10} cfu/mL) with amount of BM (mL/g BW).

Conclusions

Larger proportion of BM in enteral feeding, not pasteurizing BM and prevention of BM colonization with MRSE promotes gut colonization with BM-MSSE in preterm neonates. This may reduce the abundance of MRSE in gut and prevent LOS.

Clinical Trial Registration (Please input N/A if not registered)

N/A
Background

The West African Ebola epidemic of 2013-2016 was the largest Ebola virus (EBOV) epidemic in history. The epidemic shed light on the plight of Ebola virus disease (EVD) survivors and the ongoing sequelae they may suffer. We sought to determine differences in post-Ebola sequelae between adult and child survivors and whether differences in Ebola virus antibody levels were indicative of further problems.

Methods

A cross sectional study determining the variety and severity of sequelae suffered by EVD survivors through interviews and serology testing. Conducted in twenty-four communities throughout Sierra Leone and encompassing both urban and rural settings, a detailed questionnaire and oral fluid sample were obtained from 504 Ebola survivors. Oral fluid samples were analysed for anti-EBOV IgG antibodies using the Kalon Diagnostics Ltd EBOV IgG capture Enzyme Immuno-sorbent Assay (EIA). Using a quantified antibody measurement, the antibody index, comparison of antibody levels and the incidence of post-Ebola sequelae was made between child and adult survivors.

Results

Of 504 EVD survivors, 448 were EBOV antibody positive. Of these, 20% were children under 19 years of age. Just over 48% of child and adolescent EVD survivors experienced ongoing problems following surviving the disease, compared with 71% of adult survivors (table 1). While numbers were small, proportionally children experienced more neurological sequelae (9.1%) than adults (1.6%). The antibody index did not vary significantly between child and adult survivors (p=0.11), but did vary based on the type of sequelae experienced.

Conclusions

Early data indicate that child EVD survivors are less likely to experience ongoing sequelae than adults, although those who do suffer sequelae are more likely to experience neurological sequelae than adult survivors. Differences in antibody index did not differ between adult and child survivors.
Clinical Trial Registration (Please input N/A if not registered)

N/A
PYRAZINAMIDE RESISTANCE MUTATIONS DETECTED IN MYCOBACTERIUM TUBERCULOSIS CLINICAL ISOLATES FROM THE UKRAINE

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Background

Multi-drug resistant Mycobacterium tuberculosis (MTB) in children often reflects drug resistance patterns in the adult population. In the Ukraine, MTB is becoming increasingly drug resistant. Pyrazinamide (PZA) is a critically important drug in first- and second-line tuberculosis (TB) treatment regimes. However, PZA drug susceptibility testing (DST) is both time consuming and technically challenging. Next-generation sequencing (NGS) of the \textit{pncA} gene could rapidly identify resistance conferring mutations and facilitate patient care and treatment. The present study used NGS to characterize PZA resistance mutations in clinical isolates and assess the prevalence among multi-drug resistant (MDR), and extensively-drug resistant (XDR)-TB patients.

Methods

Clinical isolates (\textit{N}=98) grown in Löwenstein–Jensen media were inactivated in molecular transport media, and shipped from Kharkiv, Ukraine to San Antonio, Texas. Whole-genome or targeted \textit{pncA} gene sequencing was carried out using Illumina MiSeq instrumentation, and a subset of isolates were analyzed and compared to DST.

Results

Mutations were noted in 65 of 98 (66%) clinical isolates comprising substitutions, insertions, and deletions along the \textit{pncA} coding region and upstream promoter region. Importantly, 16 novel mutations were identified, of which 15 did not have supporting resistance conferring DST. One novel clinical isolate (F-81-S) was confirmed resistant by DST. Eight isolates contained mixed bases; whereas six harbored doubled mutations, and one contained a triple mutation.

Conclusions

Several unique mutations were identified that have not been previously reported. Comparison of \textit{pncA} mutations with phenotypic DST will be important to validate mutations that confer resistance. NGS is a powerful tool for complete \textit{pncA} gene characterization including hetero-resistant mixed strains, and may be useful to guide PZA therapy particularly in children who are increasingly exposed to drug resistant MTB in their households and communities.

Clinical Trial Registration (Please input N/A if not registered)

N/A
ESPID SYMPOSIUM - GLOBAL CHILD HEALTH

HOW SHOULD NON-SEVERE UNCLASSIFIED FEVER AT THE COMMUNITY LEVEL BE HANDLED? UNIVERSAL VERSUS CONDITIONAL THREE-DAY FOLLOW-UP - A CLUSTER RANDOMIZED TRIAL IN ETHIOPIA


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Background

Declining malaria prevalence and improved use of malaria diagnostic tests have led to an increasing proportion of children in sub-Saharan Africa with fever of unknown origin. Children seen by community health workers (CHWs) with non-severe unclassified fever are, according to current guidelines, advised to return after two days for re-assessment. We compared the safety of conditional reassessment (only when symptoms do not resolve), with universal follow-up.

Methods

We undertook a two-arm cluster-randomised controlled non-inferiority trial in Southwest Ethiopia. 282 CHWs enrolled children aged 2-59 months with fever and without malaria, pneumonia, diarrhoea, or danger signs. Caregivers received advice to bring children on day three (universal follow-up arm), or to come back only if symptoms persisted (conditional follow-up arm). We conducted a per-protocol analysis using generalised linear models with a non-inferiority margin of 4% for treatment failure by day seven.

Results

From Dec 1, 2015, to Nov 30, 2016, the per protocol populations included 1,953 (95.0%) in the universal follow-up arm and 1,993 (93.8%) in the conditional follow-up arm. Overall, 2.7% had treatment failure by day seven: 0.8% in the conditional follow-up arm and 4.6% in the universal follow-up arm, with a difference of -3.8% (upper 95% CI limit of -0.65%). No deaths were recorded by day 28.

Conclusions

Conditional follow-up of children with non-severe unclassified fever in a low-malaria transmission setting in Ethiopia is non-inferior to universal follow-up advice for outcomes measured through day seven. Allowing CHWs to advise caregivers to bring children back only in case of continued symptoms might be more efficient in similar settings.

Clinical Trial Registration (Please input N/A if not registered)

clinicaltrials.gov (identifier NCT02926625)
SEROLOGICAL RESPONSE AND CLINICAL OUTCOMES OF CHILDREN EXPOSED TO ZIKA VIRUS DURING GESTATION: PRELIMINARY RESULTS OF A PROSPECTIVE PAEDIATRIC COHORT STUDY IN A NON-ENDEMIC COUNTRY

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Background

Zika virus (ZIKV) infection has been associated to microcephaly and other neuro-developmental abnormalities. An ongoing Spanish database of ZIKV-exposed mother-child pair was created in May 2016. Our aim was to describe the first preliminary clinical/serological outcomes of ZIKV-exposed children followed-up in the main referral paediatric tropical medicine centres of a non-endemic country.

Methods

Multicentric prospective observational cohort study of ZIKV-exposed mother-child pair (May 2016-January 2018). Children were recruited at birth and laboratory/clinical data from mothers obtained from gestational database. ZIKV-infected mothers were defined as confirmed or probable following national guidelines. Epidemiological, clinical and laboratory data were registered on a RedCAP® database. Statistical analysis was carried out through Stata®v13. Ethical approval was obtained from participating centres.

Results

Overall, 119 children (52.6% male) were included; median[IQR] gestational age at birth was 39[38-40] weeks. ZIKV-infected pregnant-women (n=113) were from South-America 34.5%(39/113), Dominican Republic 37.2%(42/113), Central-America 24.8%(28/113), and other countries 3.6%(4/113). A 1.7%(2/119, 95%CI:0.4-6.6%) of children presented at birth clinical/radiological signs of ZIKV Congenital Syndrome, up to 25% (95%CI:4.1-72.4%) for children born to ZIKV-confirmed mothers. Seven children showed audiological adverse outcomes (7/119, 8.1%; 95%CI:3.9-16.3%) with mild/moderate hearing loss, congenital cytomegalovirus infection was ruled out at birth. Among 12-m old children (n=39), serorreversion for IgG-ZIKV was achieved at a mean (SD) of 7.2 (3.7) months.
Conclusions

the largest series of prenatally ZIKV-exposed children in Europe estimated an overall ZIKV-congenital syndrome prevalence of 1.7% (95%CI:0.4-6.6%), up to 25% (95%CI: 4.1-72.4%) in the small group of children born to ZIKV-confirmed mothers. A considerable percentage of these children had adverse audiological outcomes 8.1%(95%CI:3.9-16.3%), and a IgG-ZIKV serorreversion was achieved at a mean of 7.2 months after birth.

Clinical Trial Registration (Please input N/A if not registered)

N/A
There is a paucity of data in Europe regarding the epidemiology, species distribution and outcomes of candidemia in children. We collected standardized data throughout Europe, to better understand the epidemiology of candidaemia among hospitalized neonates and children, to assess *Candida* species distribution and outcome.

**Methods**

A retrospective study was performed over the period 2005-2015. All first positive blood cultures (BC) collected from patients <18yrs of age with candidaemia were entered into the EUROCANDY REDCap database. Demographic, clinical characteristics, and *Candida* species were recorded.

**Results**

833 BC with *Candida* species (59% were males) were recorded from 17 hospitals in 8 European countries. 30% were obtained from neonates (<30d), 7% from infants (30d-1yr) and 59% from children >1yr. 58% of the patients were admitted to neonatal or paediatric ICUs. Overall, *Candida albicans* was isolated from 53.2%, *Candida parapsilosis* from 30.1%, and other *Candida* species from 16.7% of BC. Species distribution was clearly different per age group with *C. albicans* identified from 70.9% of neonates, 60.3% of infants and 43.8% of children >1yr. *C. parapsilosis* was most frequently isolated from children >1yr (35.2% versus 21.6% from neonates and 20.7% from infants). *C. krusei* and *C. glabrata* were detected in only 2.7% (7/255) and 5.5% (27/495) of BC from neonates and children >1yr, respectively; whereas, these species were not detected in infants. Between 2005-2010 and 2011-2015, no significant changes in species distribution were observed. Mortality rates for *C. albicans* and non-*albicans Candida* candidemia were 16% and 12.5%, respectively.

**Conclusions**

This is the first and largest multi-centre European dataset characterizing the epidemiology of candidaemia in paediatric patients. These data can be used to inform antifungal stewardship interventions and the development of evidence-based management guidelines.
ESP18-0396  
SCIENCE TRACK

ESPID SYMPOSIUM - SEVERE BACTERIAL INFECTIONS

INVASIVE GROUP A STREPTOCOCCUS (GAS) INFECTIONS IN CHILDREN IN SOUTHERN ISRAEL, BEFORE AND AFTER VARICELLA VACCINE INTRODUCTION

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²Ben-Gurion University of the Negev, Faculty of Health Sciences, Beer-Sheva, Israel  
³Israel Ministry of Health, Government Central Laboratories, Jerusalem, Israel  
⁴Soroka University Medical Center, Microbiology Laboratory, Beer-Sheva, Israel

Background

GAS is a leading cause of pharyngitis and invasive infections. Several countries have reported an increase in invasive GAS disease rates, possibly attributable to dynamics in bacterial virulence or host predisposing factors, such as concomitant varicella skin lesions. We assessed dynamics and clinical characteristics of childhood invasive GAS infections before and after varicella vaccine implementation.

Methods

A population-based surveillance of GAS bacteremia and other GAS invasive infections, conducted since January 1990 and 2005, respectively, both until December 2016, in children 0-18yrs in southern Israel. Varicella vaccine was introduced to the private market in 2003 and to the national immunization program in September 2008, with vaccine coverage of 30% and >90%, respectively. Clinical data were collected from the hospital's records. All isolates were sent to the Streptococcal National Reference Laboratory for typing.

Results

Overall, 264 invasive GAS isolates and 132 GAS bloodstream infections were identified. GAS bacteremia rates significantly declined post varicella vaccine introduction, from 2.43±0.8 (1995-2002) to 1.39±0.5 (2010-2016), P=0.04. Similarly, rates of varicella rash history and skin port of entry were significantly lower in the post-vaccine compared with the pre-vaccine periods, P=0.04.

The 264 invasive GAS isolates were isolated from: soft-tissue abscesses (57.0%), osteoarticular infections (20.2%), blood (17.3%), mastoid (3.0%), lung (1.8%) and central nervous system (0.7%). Of all GAS isolates, 3.0% and 4.1% were non-susceptible to macrolides and lincosamide, respectively. Dynamics of emm-typing distribution is presented in the Figure. Proportion of emm 1.0, the most common serotype, which was associated with bacteremia, increased post-varicella vaccine introduction.
Conclusions

GAS bacteremia rates significantly declined in children in southern Israel following varicella vaccine introduction, in correlation with the disappearance of varicella rash as a predisposing factor. Additionally, an increase in emm 1.0 was observed.
THIRTY EUROPEAN CASES OF ENTEROVIRUS-D68 ASSOCIATED ACUTE FLACCID MYELITIS IN 2016

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³Royal Hospital for Sick Children Edinburgh, Department of Paediatric Neurosciences, Edinburgh, United Kingdom
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Title of Case(s)

THIRTY EUROPEAN CASES OF ENTEROVIRUS-D68 ASSOCIATED ACUTE FLACCID MYELITIS IN 2016

Background

Enterovirus-D68 (EV-D68) is a respiratory picornavirus that has recently been associated with acute flaccid myelitis (AFM). In 2014, the first cases of EV-D68 related AFM were reported from Colorado, USA; concurrently, four cases were reported in Europe. In 2016, a European joint initiative of virologists, neurologists and pediatricians, identified 30 EV-D68 related AFM cases. We present the clinical and virological data of these cases to improve future case identification.

Case Presentation Summary

Cases were reported from twelve different countries, mostly in Western Europe. Twenty-seven were children (median age 3.9 years), three were adults. Gender was equally distributed. EV-D68 was detected in all 30 patients, in respiratory materials (n=28), feces (n=8) and cerebrospinal fluid (n=2). Asymmetric flaccid limb weakness, cranial nerve deficits and bulbar symptoms were most common. Ventilatory support was necessary in 19/30 patients. On magnetic resonance imaging, typical findings were hyperintensity of the spinal cord (n=20) and/or brain stem (n=16). Decreased amplitude of compound motor action potentials with normal conduction velocities were commonly seen on electromyography, compatible with anterior horn cell disease. Patients were treated with various regimens: 20 received intravenous immunoglobulins, 17 were treated with steroids, 14 with both. Five patients underwent plasmapheresis and one patient received fluoxetine. Follow-up ranged from two weeks to one year and most patients showed only partial recovery (n=24).

Learning Points/Discussion

Case identification is dependent on awareness amongst clinicians and on adequate viral diagnostics on respiratory samples. These 30 cases of EV-D68 related AFM are likely an underestimation of the true number of cases. International and multidisciplinary collaboration is the only way to improve...
diagnostics, treatment and prevention of EV-D68 related AFM, and reduce the associated burden.
MATERNAL PERTUSSIS VACCINATION ENABLES A DELAYED INFANT VACCINATION SCHEDULE

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¹National Institute for Public Health and the Environment RIVM, Centre for Infectious Disease Control, Bilthoven, The Netherlands
²Spaarne Gasthuis Hospital, Department of Pediatrics, Hoofddorp, The Netherlands

Background

Recently a resurgence of pertussis has been observed primarily in infants < 2 months of age with highest hospitalization and complication rates but who are too young to be protected by routine vaccination.

Maternal pertussis vaccination offers protection by transferring high antibody concentrations to these infants. We investigated the effect of Tdap vaccination during pregnancy on infant immune responses and the possibility to delay primary vaccination from two to the age of three months.

Methods

A randomised controlled trial was conducted in which pregnant women either received a Boostrix, (Tdap) vaccine during 30-32 weeks of pregnancy (maternal group), or within 48 hrs after giving birth (control group). All children were vaccinated with a DTaP-IPV-Hib-HepB and 10-valent-pneumococcal vaccine at age 3- and 5-months and with a booster vaccination at 11-months. Total pertussis specific IgG responses were determined in serum with a bead-based fluorescent multiplex immunoassay (MIA).

Results

118 pregnant women were enrolled; 58 women were randomized in the maternal group and 60 women in the control group. Three months old infants of vaccinated mothers had significantly higher GMCs of all anti pertussis antibodies compared to infants of the control group at 2- and 3-months of age. Maternal antibodies showed interference with the infants antibody response after primary and booster immunization for all pertussis antigens as well as DT toxoid.

Conclusions

We showed that after maternal immunization, pertussis specific GMCs at age of three months are still significantly higher than the levels of control infants at age 2 months, which supports a delay of the start of infant immunization to age three months. It has the advantage of later start of primary vaccination, less vaccine administrations and wider space between vaccinations.

Clinical Trial Registration (Please input N/A if not registered)

trialregister.nl NTR4314
Background

West Bohemian Region (currently Pilsen and Karlovy Vary Regions) is a high tick-borne encephalitis (TBE) endemic region in the Czech Republic. Between 1960 and 2017 there were 2,409 laboratory confirmed cases of TBE among inhabitants of West Bohemia (average population of 850,568).

Methods

During this period, the laboratory diagnostics were predominantly performed by the Department of Virology of the University Hospital in Pilsen. Epidemiological surveys were performed by the staff of local West-Bohemian RPHAs. Since 1991, once a year, vaccination centres and vaccinating GPs have been reporting the numbers of persons per age group that received the third dose of TBE vaccine. As statistical methods were used Spearman’s correlational coefficient and test of trends.

Results

Between 1960 and 2017, 498 cases of TBE in children and teenagers were confirmed by laboratory testing in Pilsen and Karlovy Vary Regions), i.e. 3.8 per 100,000 inhabitants p.a. The highest incidence rate for both male and female sexes (6.7 and 4.3 respectively) concerns the same age group 15-19 years. Of all the reported cases, one case was fatal (a 15-year-old boy, 0.2%). Tick bite was reported from 293 patients (58.8%). In 7.5% of cases, patient’s history showed data on the consumption of non-pasteurized milk or non-pasteurized diary products. As a result of the gradual infection season prolongation, the transmission can currently occur anytime between March and November. During the monitored period there was the altitude shift of infection transmission occurring in the higher altitudes. Based on officially available data, 27.0% of the Pilsen Region’s young population has been vaccinated, so far.

Conclusions

The low vaccination coverage may hardly influence the unfavorable tick-borne encephalitis epidemiological situation in West-Bohemian Region.
Congenital infections cause significant long-term morbidity. However, the incidence of the commonest congenital infections in England is not known. This is the first study to assess the long term trends in neonates with congenital infections and observe how rates may have changed with improved diagnostics.

Methods

We conducted a retrospective analysis of routinely collected hospital discharge records from English National Health Service Hospitals (1999 – 2016) to evaluate rates of hospital diagnoses for neonates with congenital cytomegalovirus (cCMV), herpes simplex virus (HSV), rubella and varicella zoster virus (VZV). All delivery and admission records were included.

Results

The annual incidence of cCMV per 100 000 infants increased from 4.56 discharges in 1999 to 10.01 in 2016.

The annual incidence of HSV per 100 000 increased from 3.71 discharges in 1999 to 14.65 in 2016. This coincided with a year-on-year increase in the number of cases of genital herpes during 2007 – 2016 reported to Public Health England.

The annual incidence of VZV per 100 000 increased from 7.26 in 1999 to 14.50 in 2016. Congenital rubella was rarely seen (annual incidence per 100 000 was 0 in 1999 and was 0.15 in 2016).

Conclusions

The increase in recorded congenital infections during the 17-year surveillance period is most likely due to the introduction of highly sensitive molecular diagnostic assays such as polymerase chain reaction (PCR).

Public health measures such as promoting antenatal behavioural and hygiene measures to prevent acquisition and transplacental transmission of infection should be prioritised. The implementation of routine screening for cCMV should be considered. Preventive measures through vaccination (e.g. developing a CMV vaccine, considering introduction of routine varicella vaccine and ensuring continued high uptake of MMR vaccine) are warranted.

Clinical Trial Registration (Please input N/A if not registered)
INCREASED INCIDENCE OF PEDIATRIC PNEUMOCOCCAL MENINGITIS IN FRANCE LINKED TO THE EMERGENCE OF SEROTYPE 24F, A TIME SERIES ANALYSIS OF A 16 YEARS NATIONAL REGISTRY

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⁴GPIP, Pediatric infectious disease research group, Paris, France

Background

Successive pneumococcal conjugate vaccines 7 and 13 (PCV) implementations have led to a significant reduction of pneumococcal disease burden including pneumococcal meningitis (PM). We aimed to assess the long term effect of PCVs implementation on PM in children.

Methods

We conducted a quasi-experimental, population-based interrupted time series analysis based on a nationwide prospective cohort over 16 years in France, recruiting 227 pediatric wards working with 168 microbiology departments from 2001 to 2016. The main outcome was the incidence of pneumococcal meningitis in children for 100,000 inhabitants under 15 years, before and after PCV7 and 13 implementations, analyzed using the segmented regression model with autoregressive error.

Results

During the study period, 1778 PM were enrolled. After PCV13 implementation, a significant PM incidence reduction (-0.8% per month, p=0.02) was observed, followed by an increase during the two last years (+2.3% per month, p=0.0002). The cumulate global effect of PCVs on PM incidence was a 20.8% decrease (95% CI: [-39.2; -3.1]), representing 626 averted PM in children. The recent increase was mainly due to the sharp rise in non-PCV serotype 24F isolates among which we recently found a higher prevalence of penicillin non susceptible strains.
Conclusions

Successive PCVs campaigns led to a significant reduction of PM incidence in children. However, serotype 24F sharply emerged, with a change in penicillin non-susceptibility rate, suggesting competition between distinct clones in this serotype with a very high disease potential.

Figure 1: Impact of PCV implementations on PM in children under 15 years


*: Licensed PCV7, recommended only for patients with underlying conditions.

Figure 2:
Impact of PCVs implementations on pneumococcal meningitis due to serotype 24F and penicillin non-susceptibility rate.

*: Licensed PCV7, recommended only for patients with underlying conditions.
ES18-0549
SCIENCE TRACK

PIDS/ESPID PLENARY SYMPOSIUM 03 - MICROBIOMICS AND IMMUNOLOGY

GUT MICROBIOME AND IMMUNE SYSTEM IN NEONATES AFFECTED BY SEVERE INTESTINAL DAMAGE

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Background

The neonatal intestinal ecosystem is extremely fragile. The immature immune system (IS) plays an essential role in maintaining homeostasis with residential microbial community. This balance is altered in condition of inflammatory and ischemic bowel diseases. The objectives of our study were to define the microbiota profile and intestinal IS anomalies in neonates affected by extended bowel ischemia.

Methods

From September 2016 to July 2017, newborns underwent intestinal resection were enrolled in the study. We determined the mucosal (M), fecal (F) and enteral washing (EW) microbiota profiling through targeted metagenomics followed by α- and β-diversity index assignment of microbial ecology and Kluskal-Wallis analyses of Operational taxonomic units at Phylum and Species levels. Cytofluorimetry was performed on intestinal tissue to phenotype and analyze mucosal T lymphocytes. We considered as control group newborns affected by intestinal focal perforation.

Results

<table>
<thead>
<tr>
<th>Age</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;35 weeks GA</td>
<td>4</td>
</tr>
<tr>
<td>&gt;35 weeks GA</td>
<td>3</td>
</tr>
</tbody>
</table>

In the study period 7 neonates were enrolled (Table) The M, F and EW microbial community was characterized by a predominance of Proteobacteria and Enterobacteriaceae. Specifically, the M microbiota was characterized by higher Shannon index and lower Chao I index, the Phylum level classification showed a significant prevalence of Proteobacteria and reduction of Bacteroidetes and Verrucomicrobia and the Enterobacteriaceae was the most abundant taxonomic family. The cytometric analysis showed a predominance of Th17 associated to high level of Tumor Necrosis Factor-α (TNFα) and Interferon-γ (INFγ).

Conclusions
Our results highlight the relevance of microbiota signatures and immune response in severe neonatal bowel ischemic events. Gut microbiota profile rich of Enterobacteriaceae may be related to a proinflammatory response by the immature IS resulting in homeostasis disruption. Investigating differences in microbial functionality and IS response will provide further evidences in order to transform microbiota signature into microbial ischemia markers.
Enteric fever accounts for the majority of invasive bacterial disease among children in Nepal. Multi-drug resistant S. Typhi is now rare and appears to be replaced by highly fluoroquinolone resistant strains. This study aims to characterize the temporal trends in the evolution of S. Typhi in Nepal.

Methods

Whole genome sequences of 154 S. Typhi strains from Nepali children isolated between 2008-2016 along with 107 other Nepali strains for contextualization were subjected to phylogenomic analysis using BEAST2 to assess population structure and estimate divergence dates. The signal of these Bayesian estimates were then assessed using a date-randomization test. Finally, 5 independent runs were conducted with a chain length of 600,000,000 states, sampling every 300,000 iterations, using LogCombiner. Maximum-clade credibility (MCC) trees were then generated with ‘keep target heights’.

Results

The most recent common ancestor (mrca) for all H58 strains in Nepal existed circa 1993, and both sublineages of H58 (I and II) were present.

Lineage II was significantly more common (40% pre-2010 vs 74%, p=1x10^{-7}) from 2011 onwards and associated with different antimicrobial resistance (AMR) patterns from lineage I (MDR - 59% lineage I vs 0% lineage II, p<1x10^{-15}) and quinolone resistance determining region (QRDR) mutations (50% lineage I vs. 99% lineage II, p<1x10^{-15}).

A distinct monophyletic clade of lineage II isolates harbouring distinct QRDR mutations formed a local monophyletic clade indicative of local clonal expansion in Nepal.

Conclusions
The clonal replacement of the MDR-associated lineage I with the expansion of the quinolone resistance-associated lineage II over time reflect the changing antimicrobial pressure conferred on the S. Typhi population in Nepal. These results underscore the importance of employing vaccination strategies to prevent further development of AMR in S. Typhi.
ESP18-0618
SCIENCE TRACK

ESPID SYMPOSIUM - INFECTIONS IN THE IMMUNOCOMPROMISED CHILD

EFFECTIVE OPSONOPHAGOCYTIC KILLING OF MENINGOCOCCUS SEROGROUP B BY WHOLE BLOOD OF VACCINATED CHILDREN WITH ALTERNATIVE PATHWAY AND TERMINAL PATHWAY COMPLEMENT DEFICIENCIES

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2Radboud University Medical Center, Pediatric Infectious Disease and Immunology- Amalia Children's Hospital, Nijmegen, The Netherlands
3Radboud University Medical Center, Radboud Center for Infectious Diseases, Nijmegen, The Netherlands
4National institute for the Public Health and the Environment, Centre for Immunology of Infectious Diseases and Vaccines, Bilthoven, The Netherlands
5Radboud University Medical Center, Radboudumc Expertise Center for Immunodeficiency and Autoinflammation, Nijmegen, The Netherlands

Background

Children and adults with complement deficiencies have increased risk of serogroup B meningococcal disease and several guidelines recommend meningococcal serogroup B vaccine for inherited complement deficiencies. However, the efficacy of vaccines may be decreased in children/young adults with complement deficiencies because important mechanism for vaccine-induced meningococcal killing may be deficient.

Here, we assessed the efficacy of the MenB-4C vaccine by a serum bactericidal assay (SBA) and opsonophagocytic killing of meningococci in children with alternative pathway or late terminal pathway complement deficiencies.

Methods

We collected pre- and post-vaccination serum from 2 children with alternative pathway deficiency and from 3 children with terminal complement pathway deficiency and performed SBA with both autologous and exogenous human serum on Neisseria meningitidis serogroup B strains H44/76, 5/99 or NZ98/254, which are representative for the vaccine antigens. In addition, an opsonophagocytic killing with whole blood reconstituted with patient serum was performed and antibody titers were determined with a whole cell ELISA.

Results

MenB-4C vaccination induced effective anti-meningococcal antibodies in all complement deficient children and healthy controls. As predicted, children with a terminal complement deficiency failed to show significant vaccination-induced killing in the SBA with autologous complement, whereas children with alternative pathway deficiency and healthy controls showed effective killing. However, vaccination did induce effective opsonophagocytic killing of serogroup B meningococcus in both late terminal and alternative pathway deficient children comparable to healthy controls in a whole blood killing assay.

Conclusions
Children with alternative pathway and late terminal pathway complement deficiencies show effective opsonophagocytic killing after MenB-4C vaccination. Therefore these results underline the recommendation to vaccinate complement deficient children with MenB-4C.

Clinical Trial Registration (Please input N/A if not registered)

N/A
CHARACTERIZING THE EFFECT OF MATERNAL ANTIBIOTIC USE ON THE GUT MICROBIOME OF BREASTFED INFANTS - A LONGITUDINAL COHORT STUDY

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Background

The composition of the developing gut microbiome is thought to have crucial roles in maturation of the immune system and prevention of various diseases. Several factors influence early colonization of the infant’s gut, including exposure to antibiotics. We aimed to assess the changes that take place in the infant gut microbiome and milk glycobiome when breastfeeding mothers consume antibiotics.

Methods

A prospective longitudinal cohort study of 20 mother-infant pairs. Breast milk and infant fecal samples were collected at five different time points before, during and after maternal antibiotic treatment. The glycobiome and gut microbiota were characterized by 16S ribosomal RNA gene sequencing. Antibiotic concentrations in breast milk were determined by liquid chromatography-tandem mass spectrometry.

Results

Among the different antibiotics consumed by participating women, Amoxicillin and penicillin-v were detected in significant levels in the breast milk. Higher concentrations of antibiotics in maternal breast milk appeared to be associated with increased levels of pathogenic bacteria in the infants’ gut, mainly Bacteroidetes, Proteobacteria and Enterobacteriacea. Antimicrobial consumption resulted in rapid reduction in alpha diversity in breast milk, with partial recovery by 30 days post antibiotic treatment. A distinct increase in lactobacillus abundance post antibiotic treatment was also observed in most infants. An overall increase in alpha-diversity was observed in 50\% of infants.

Conclusions

Our preliminary study clearly showed a disruptive effect of maternal antibiotic consumption on the nursing infant's gut microbiome with an impact on the important early colonizers of the infant gut. It is well known that antibiotic consumption influences the gut microbiome, mainly reducing (both alpha and beta) diversity, but larger studies are needed to further define the changes in infant gut microbiome caused by indirect exposure through nursing.

Clinical Trial Registration (Please input N/A if not registered)

N/A
A NOVEL APPROACH FOR THE DIAGNOSIS OF CHRONIC HEPATITIS B VIRUS INFECTION USING NAILS AND HAIR

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2Eastern Yokohama hospital, Department of Pediatric Hepatology and Gastroenterology, Yokohama, Japan

Background

Hepatitis B virus (HBV) has been proven to be integrated into extrahepatic tissues in patients with HBV infection. However, it remains unclear whether nails and hair contain HBV.

Methods

Chronic HBV infection (age: median 18 years, serum HBV DNA level: median >9.0 log copies/mL) were enrolled in this study. HBV DNA in finger nail and hair was measured by real-time PCR. HBsAg of finger nail was measured using enzyme immunoassay. Indirect immunogold labeling electron microscopy and immunochemical staining was performed on nails. Moreover, the infectivity of nails was evaluated using chimeric mice with humanized liver.

Results

Of the 70 nail samples, 65 (93%) were positive for HBV DNA. Of the 60 hair samples, 49 (82%) were positive for HBV DNA. The nail HBV DNA level (median: 5.0 log copies/mL) was significantly higher than hair HBV DNA level (median: 4.3 log copies/mL) (P<0.001). There was a significant correlation in HBV DNA level between nail and hair (r= 0.378, P<0.01). Despite the rapid reduction in serum HBV DNA level due to antiviral treatment, nail and hair HBV DNA level remained the same more than 6 months after the initiation of antiviral treatment. Phylogenetic tree analysis of HBV genome isolated from nails and hair was successful in identifying the source of the infection. Of 64 nail samples, 38 (59%) were positive for HBsAg. Electron microscopy showed numerous small spheres of HBV. HBsAg was detected in nails by Immunochemical staining. Infectivity of nails was not proven in chimeric mice.

Conclusions

Nails and hair are the reservoir of HBV DNA. Moreover, nails could contain HBsAg. However, nails are not an infectious agent. Nails and hair have potential to being useful as diagnostic tools of HBV infection.

Clinical Trial Registration (Please input N/A if not registered)

N/A
Background

We planned this study to know the incidence of scrub typhus in children with acute undifferentiated fever and multisystem involvement and to determine risk factors for mortality.

Methods

Methods:

We prospectively enrolled children (2 months-14 years) with unexplained fever of > 5 days presenting to Pediatric emergency over three years. Demographic profile and treatment history was noted. Detailed fever workup (blood culture, urine culture, malaria rapid diagnostic test, malarial smears, leptospira serology, and WIDAL tests) was performed in all children. Our primary outcome was positive scrub typhus IgM assay by ELISA. Children who were scrub typhus ELISA positive were considered as cases. Remaining hospitalized febrile children who were scrub typhus IgM negative constituted controls and were followed till discharge/death.

Results

Results:
We enrolled 172 febrile children of which 71 (41%) were positive for scrub typhus IgM by ELISA. Remaining 101 (59%) children served as controls and included dengue fever (30%), enteric fever (9%), malaria (8%), viral fever (3.5%), pyrexia of unknown origin (3%), others (6%). There was no age or sex predilection among cases and controls. More children in cases presented with serositis (21% versus 2%) hepatosplenomegaly (74% versus 41%), altered sensorium and seizures (20% versus 3%). On investigations, anemia, hypoproteinemia and hepatitis was more prevalent in

<table>
<thead>
<tr>
<th>S No</th>
<th>Characteristics</th>
<th>Scrub-Typhus (N=71)</th>
<th>Non-Scrumb (N=101)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Age (mth)</td>
<td>85 (40)</td>
<td>87 (40)</td>
<td>0.686</td>
</tr>
<tr>
<td>2.</td>
<td>Weight (g)</td>
<td>20 (14, 30)</td>
<td>20 (15, 25)</td>
<td>0.738</td>
</tr>
<tr>
<td>3.</td>
<td>Male Sex (%)</td>
<td>39 (55)</td>
<td>63 (62)</td>
<td>0.433</td>
</tr>
<tr>
<td>4.</td>
<td>Rash (%)</td>
<td>15 (21)</td>
<td>14 (14)</td>
<td>0.219</td>
</tr>
<tr>
<td>5.</td>
<td>Cough (%)</td>
<td>10 (14)</td>
<td>10 (10)</td>
<td>0.470</td>
</tr>
<tr>
<td>6.</td>
<td>Altered sensorium (%)</td>
<td>16 (23)</td>
<td>2 (2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>7.</td>
<td>Seizures (%)</td>
<td>9 (13)</td>
<td>2 (2)</td>
<td>0.008</td>
</tr>
<tr>
<td>8.</td>
<td>Cyanosis</td>
<td>1 (1)</td>
<td>0</td>
<td>0.410</td>
</tr>
<tr>
<td>9.</td>
<td>Abdominal pain (%)</td>
<td>45 (63)</td>
<td>48 (47)</td>
<td>0.044</td>
</tr>
<tr>
<td>10.</td>
<td>Vomiting (%)</td>
<td>44 (62)</td>
<td>49 (48)</td>
<td>0.088</td>
</tr>
<tr>
<td>11.</td>
<td>Retractions (%)</td>
<td>9 (13)</td>
<td>4 (4)</td>
<td>0.041</td>
</tr>
<tr>
<td>12.</td>
<td>Bleeding tendency (%)</td>
<td>9 (9)</td>
<td>10 (10)</td>
<td>1.000</td>
</tr>
<tr>
<td>13.</td>
<td>Crepts or wheeze (%)</td>
<td>9 (13)</td>
<td>3 (3)</td>
<td>0.029</td>
</tr>
<tr>
<td>14.</td>
<td>Edema (%)</td>
<td>26 (36)</td>
<td>6 (6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>15.</td>
<td>Oliguria (%)</td>
<td>4 (6)</td>
<td>0</td>
<td>0.027</td>
</tr>
<tr>
<td>16.</td>
<td>Hepatosplenomegaly (%)</td>
<td>51 (74)</td>
<td>41 (41)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>17.</td>
<td>Meningitis (%)</td>
<td>6 (9)</td>
<td>1</td>
<td>0.020</td>
</tr>
<tr>
<td>18.</td>
<td>Shock (%)</td>
<td>13 (18)</td>
<td>13 (13)</td>
<td>0.388</td>
</tr>
<tr>
<td>19.</td>
<td>Diarrhea (%)</td>
<td>3 (4)</td>
<td>1</td>
<td>0.307</td>
</tr>
<tr>
<td>20.</td>
<td>Culture positive bacterial Sepsis (%)</td>
<td>1</td>
<td>3</td>
<td>0.645</td>
</tr>
<tr>
<td>21.</td>
<td>Serositis (%)</td>
<td>21 (30)</td>
<td>2 (2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>22.</td>
<td>Total serum Bilirubin (mg/dl)</td>
<td>0.8 (0.4, 3.0)</td>
<td>0.5 (0.3, 0.9)</td>
<td>0.009</td>
</tr>
<tr>
<td>23.</td>
<td>AST (U/L)</td>
<td>180 (101, 378)</td>
<td>74 (42, 148)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>24.</td>
<td>ALT (U/L)</td>
<td>100 (57, 171)</td>
<td>57 (27, 75)</td>
<td>0.001</td>
</tr>
<tr>
<td>25.</td>
<td>Total Protein (g/dL)</td>
<td>5.3 (1.1)</td>
<td>6.2 (1.2)</td>
<td>0.001</td>
</tr>
<tr>
<td>26.</td>
<td>Serum Albumin (g/dL)</td>
<td>2.5 (2.2, 3.2)</td>
<td>3.5 (2.9, 4.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>27.</td>
<td>Prothrombin time (sec)</td>
<td>17 (15, 19)</td>
<td>15 (15, 17)</td>
<td>0.113</td>
</tr>
<tr>
<td>28.</td>
<td>APTT (sec)</td>
<td>34 (31, 38)</td>
<td>32 (30, 36)</td>
<td>0.326</td>
</tr>
<tr>
<td>29.</td>
<td>INR</td>
<td>1.22 (1.09, 1.35)</td>
<td>1.12 (1.09, 1.36)</td>
<td>0.982</td>
</tr>
<tr>
<td>30.</td>
<td>Hemoglobin (g/dL)</td>
<td>10.3 (8.4, 11.6)</td>
<td>11.2 (9.7, 12.6)</td>
<td>0.004</td>
</tr>
</tbody>
</table>
scrub typhus group (Fig. 1). Twelve percent received mechanical ventilation and 20% received ionotrope support versus 2 and 4% in control group. There were two deaths in cases and one in the control group. Cause of death was acute respiratory distress syndrome and meningoencephalitis in the scrub group. Cause of death in controls was meningococcal sepsis.

Conclusions

Pediatric scrub typhus had severe systemic manifestations when compared to other causes of fever.

Funding: Department of Science & Technology, Chandigarh administration, Chandigarh, India
Identifying Unique Markers for Correct Identification of S. Pneumoniae and S. Pseudopneumoniae in the Clinic

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²University of the Balearic Islands, Microbiology- Department of Biology, Palma de Mallorca, Spain

Background

Streptococcus pneumoniae (pneumococcus) is a well-known pathogen and the closely-related S. pseudopneumoniae is implicated in infections, although details of virulence are largely unknown. Differentiation and identification of S. pneumoniae and S. pseudopneumoniae are problematic, due to horizontal gene transfer and homologous recombination, facilitating genotypic ambiguity between these two species. Current identification protocols are unreliable and incite uncertainty for routine use in the diagnostic lab.

Methods

A pan-genome approach was employed to identify unique genes of S. pseudopneumoniae, in 13 genome sequences of S. pseudopneumoniae and 33 closed genome sequences of S. pneumoniae. The detected unique genes were further analyzed by Blast-matching analysis with respect to the whole NCBI Nucleotide database. PCR-amplification primers were designed for these genes and tested with reference strains of S. pseudopneumoniae, S. pneumoniae, as well as strains of other species of the Mitis-group of the Streptococcus genus. Whole-genome sequences were determined for strains producing positive PCRs for the target genes and species identities were confirmed.

Results

Genes were identified from which 887 (16.7%) belonged to the ‘core’ genome of the two species; 94 genes were observed to be unique for S. pseudopneumoniae and 77 for S. pneumoniae. Fourteen genes were selected as unique for S. pseudopneumoniae after Blast-matching analysis. A multiplex PCR was developed, using the best S. pseudopneumoniae biomarker gene target, together with the “Xisco” gene, which has been shown to be a reliable biomarker for identification of S. pneumoniae.

Conclusions

This simple and reliable PCR-based method will facilitate correct identifications of pneumococci for early diagnosis, particularly in regions of the world with limited laboratory facilities.

Clinical Trial Registration (Please input N/A if not registered)

N/A
INEQUALITIES IN NON-INITIATION OF HPV VACCINE: FINDINGS FROM A UK COHORT

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Background

HPV vaccination (HPVv) was introduced in the UK in 2008, with 87-93% of girls receiving at least one dose. Uptake is lower in more deprived areas, however associations with parental and household factors, such as ethnicity and income are less clear. Using data from a UK prospective cohort we tested the hypothesis that HPVv initiation was less likely in girls with parents from black and minority ethnic groups, those not attending school, and those living in households with lower income.

Methods

We estimated the percentage of 5690 14-year-old girls participating in the Millennium Cohort Study and initiating HPVv. We used logistic regression to calculate crude and adjusted odds ratios (OR) and examined associations with parental ethnic group, school type (fee-paying/non-fee-paying/no school) and family income (OECD quintile).

Results

5265 girls (weighted percentage: 92.3w%; 95% CI: 91.3,93.2) received at least one dose of HPVv; 399 (7.2w%; 6.4,8.1) no doses; 26 (0.5w%; 0.3,0.9) not known. Parents from Bangladeshi (86.1w%; 80.3,90.4), Black African (84.9w%; 75.7,91.0) and ‘other’ ethnic groups (81.0w%; 70.4,88.4) were significantly less likely to report initiation of HPVv compared to those of white ethnicity (93.6w%; 92.5,94.5). HPVv initiation was lower in girls not attending school (61.1w%; 32.5,83.7) compared to those attending non-fee-paying (93.0w%; 92.1,93.8) or fee-paying schools (92.0w%; 88.0,94.8). After adjusting for ethnicity, school and income, girls with parents from Black African or ‘other’ ethnic groups, those not attending school, or those living in low income households were less likely to initiate HPVv (Figure).
Conclusions

We found marked inequalities in HPVv initiation by parental ethnicity, attendance at school and household income. Developing interventions to engage parents from these groups is central to reducing inequalities in HPV vaccine uptake.
Influenza is responsible for 3-5 million cases of severe illness each year and annual attack rates are reported from 20% to 30% in children. This study highlights the burden of influenza in young children.

Methods

We examined data from the placebo arm of a randomized clinical efficacy trial of a quadrivalent split-virion inactivated influenza vaccine in healthy children aged 6 to 35 months. Participants were included during the Southern Hemisphere (SH) 2014 season in Africa, SH 2014 and 2015 seasons in Asia, Northern Hemisphere (NH) 2014/2015 in Latin America, and NH 2014/2015 and 2015/2016 seasons in Europe. Influenza like illness (ILI) cases were defined as a fever \( \geq 38^\circ C \) lasting \( \geq 24 \) h concurrently with clinical or respiratory symptoms. In ILI cases, a nasopharyngeal swab was taken for reverse transcription-polymerase chain reaction and viral culture. Participants were considered to have laboratory-confirmed influenza (LCI) if the swab was positive for influenza.

Results

Of the 2,589 participants, most were from Asia (n=1469) and Europe (n=502). Mean age was 19.9 (SD 8.4) months. ILI was reported by 865 (33.4%) participants. 255 participants (29.5%) had a LCI. The overall attack rate was 9.8%. Three children with LCI were hospitalized. For a majority of LCI cases a physician was consulted. Antibiotics (41.4%) were frequently prescribed. Overall, A(H3N2) was most frequently detected (40.7% of positive swabs). Few cases of B/Victoria were reported (8.0%). Distributions varied greatly by region and season.

Conclusions
With more than 2,500 children followed over 4 seasons on 4 continents and an influenza attack rate of 9.8%, this study confirms the significant burden of influenza in children. These results highlight the importance of the WHO recommendation to vaccinate young children annually.

Clinical Trial Registration (Please input N/A if not registered)

N/A
COST-EFFECTIVENESS OF INCREASED INFLUENZA VACCINATION COVERAGE WITH QUADRIVALENT INACTIVATED VACCINE (QIV) IN CHILDREN OLDER THAN 6 MONTHS OF AGE IN GERMANY

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4GSK, Scientific Affairs & Public Health, Wavre, Belgium
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Background

Pediatric influenza vaccination in Germany is only recommended for children at increased health risk. Available evidences suggest that not only children in risk groups have high influenza infection rates and World Health Organization recommends the vaccination of children 6-59 months.

Methods

Using the 4Flu disease transmission model, we compared the total number of influenza infections in Germany at the current vaccination coverage rate versus increased coverage rates of (a) 40% in children 0.5-4 years, (b) 40% in children 0.5-17 years, or (c) 90% in high risk children 0.5-17 years. All scenarios employed QIV only. Births and deaths were simulated based on national demographic predictions. Vaccine efficacy was obtained from NCT01439360 phase III clinical trial for children 6-35 months, and available literature for older age groups. Age-dependent clinical pathways and costs (2017 base-year) were attributed to the simulated influenza cases with inputs collected from national sources and published literature. Productivity loss was calculated by the human capital approach. Discounted results (costs:3%; effects:3%) were evaluated for a population of 100,000 individuals over 20 years.

Results

Increased vaccination resulted in more health gains and lower costs from societal perspective in all scenarios; from payer perspective it was dominant in scenario (b) and (c) while highly cost-effective in scenario (a). Highest health gains and cost savings were generated in scenario (b), averting an average of 39,436 influenza cases and 85 deaths per 100,000 individuals. This equals to 32.6 million
cases and 70,290 deaths in the total German population over 20 years.

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Averted clinical influenza cases, n (%)</th>
<th>Averted influenza deaths, n (%)</th>
<th>QALY gained</th>
<th>Societal perspective</th>
<th>Payer perspective</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) 40% coverage in children 0.5-4 years</td>
<td>7,499 (4.3%)</td>
<td>15 (3.3%)</td>
<td>149.18</td>
<td>- €3,489,261</td>
<td>Dominant</td>
</tr>
<tr>
<td>(b) 40% coverage in children 0.5-17 years</td>
<td>39,436 (22.6%)</td>
<td>85 (19.1%)</td>
<td>830.8</td>
<td>- €18,743,379</td>
<td>Dominant</td>
</tr>
<tr>
<td>(c) 90% coverage in high risk children 0.5-17 years</td>
<td>6,909 (3.9%)</td>
<td>15 (3.4%)</td>
<td>145.15</td>
<td>- €3,296,308</td>
<td>Dominant</td>
</tr>
</tbody>
</table>

QALY: quality adjusted life year; QIV: quadrivalent influenza vaccine; ICER: incremental cost-effectiveness ratio

Conclusions

Increasing the coverage rate in German children and using QIV is predicted to be cost-effective or even cost-saving. Our results could support the expansion of current influenza vaccination recommendation to a broader pediatric population.
EFFECTIVENESS OF A SYSTEMATIC VACCINATION PROGRAMME AGAINST HEPATITIS B IN PREADOLESCENTS IN CATALONIA, 25 YEARS AFTER THEIR IMPLEMENTATION

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Background

At end of the 80’s, hepatitis B virus (HB) infections constituted an important public health problem, with high morbidity (intermediate epidemiological pattern), with predominance of sexual transmission mechanism in adolescence-youth, and lower frequency for parenteral transmission especially among young PDUs.

Vaccination against HB began in the 80s for risk groups with plasma vaccine. By 1991, recombinant vaccine was available in Catalonia and vaccination against HB was implemented in pre-teens 11-12y. At this age risk behaviours has not started.

The objective is to estimate the impact of the Systematic Vaccination against HB in pre-teens by estimating vaccine effectiveness.

Methods

A retrospective cohort study was carried out. The cases of hepatitis B reported between 2000 and 2014 were studied, considering vaccinated and unvaccinated cohorts according to year of birth.

Results

The incidence rate in 1991 was 2.5 per100,000 persons/year, declining to 1.3 in 2015 (48% overall decrease). Being this decline greater in the 20-29y group, by 88.65%. Being vaccine coverage close to 90%, an effectiveness of 99.22% was estimated (95% CI of 97.89%-99.71%).

Conclusions

The high coverage with three doses (90%) and the high effectiveness of the pre-adolescents vaccination program, together with a decrease in the incidence of illness in the youth-adult age groups confirms that it was an optimal strategy in order to control the disease.

However, in recent years reduction of global incidence is stable, probably explained by population, migratory and risky behaviour changes. This indicates that we must continue to work to increase vaccination in those risk groups where there is less health system adherence.
Background

The immunopathogenesis of coronary arteritis in Kawasaki disease (KD) remains poorly understood. The presence of immune complexes in the serum of children with KD was established in numerous studies, leading to the hypothesis that immune complexes contribute to the arteritis, either indirectly through activation of host inflammatory cells or directly through deposition in the vessel wall. Using advanced proteomic technology we studied and characterised, for the first time, the composition of immune complexes in KD and compared these immune complexes with those in children of other febrile illnesses.

Methods

Immune complexes with high molecular weight were precipitated from the serum of 50 KD children, 50 children with other febrile conditions and 10 healthy controls. The immune complexes purification process was monitored by SDS-PAGE protein staining, and Western blotting. The precipitated proteins were trypsin digested and we used liquid chromatography tandem mass spectrometry (LC MS/MS) to identify the recovered peptides in a shotgun manner. Using the bioinformatics program PEAKS, we performed database searches, de novo sequencing and compared protein abundances between the different comparator groups.

Results

KD patients were found to have increased concentrations of immune complexes in their serum as compared to children with other febrile illness. Immune complexes precipitated from KD patients were different in protein composition from complexes isolated from febrile illnesses, with over 20 proteins being significantly different in abundance between KD and febrile groups (P<001).

Conclusions

Immune complexes isolated from children with KD differ from those recovered from other febrile illnesses, both in terms of the quantity, and the nature of proteins within the complex. The pattern of proteins and peptides in the immune complexes provides insight into the nature of the unique inflammatory response in KD.

Clinical Trial Registration (Please input N/A if not registered)
N/A
RECOMBINANT BCG EXPRESSING ESX-1 OF MYCOBACTERIUM MARINUM COMBINES LOW VIRULENCE WITH CYTOSOLIC IMMUNE SIGNALING AND IMPROVED TUBERCULOSIS PROTECTION

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2University Medical Center Groningen, Pulmonary Diseases & Tuberculosis, Groningen, The Netherlands

Background

A feature of the only licensed TB vaccine BCG is the partial deletion of the ESX-1 type VII secretion system, which governs phagosomal rupture and cytosolic pattern recognition, key intracellular phenotypes linked to increased immune signaling. Our objective here was to improve protective efficacy by equipping BCG with the ESX-1 dependent phenotype of cytosolic access.

Methods

BCG was transformed with a vector containing the esx-1 region of Mycobacterium marinum. BCG::ESX1Mmar functionality was assessed by ESX-1 specific T-cell hybridomas. THP-1 wild-type and cGas/STING K.O. cells were used to study phagosomal access and activation of cytosolic nucleotide sensors. BALB/c, C57BL/6 and SCID mice were vaccinated to characterize cellular immunity and virulence. Independent mouse vaccination models at two different institutes were employed to study virulence and vaccine efficacy.

Results

This new ESX-1 proficient BCG can access the host cytosol and activates the cGas/STING/TBK1/IRF-3/type I interferon axis and AIM2-mediated NLRP3 inflammasome activity while maintaining low virulence. This results in both higher proportions of CD8+ T cell effectors against mycobacterial antigens shared with BCG and polyfunctional CD4+ Th1 cells specific to ESX-1 antigens. Importantly, independent mouse vaccination models show BCG::ESX-1Mmar confers superior protection relative to parental BCG against challenges with highly virulent M. tuberculosis.

Conclusions

We describe the virulence-neutral expression of the ESX-1 type VII secretion system of Mycobacterium marinum in BCG. The functioning ESX-1 system enables this novel vaccine candidate to rupture the phagosome and to induce cytosolic pattern recognition and dedicated innate immune signaling in mice, resulting in increased protection against tuberculosis.

Clinical Trial Registration (Please input N/A if not registered)

N/A
THE IMPACT OF VARICELLA VACCINATION ON THE INCIDENCE OF HERPES ZOSTER IN THE UNITED STATES: UPDATED EVIDENCE FROM OBSERVATIONAL DATABASES

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Background

Models including effects of the exogenous boosting hypothesis predict a transient increase in herpes zoster (HZ) incidence among unvaccinated individuals in the decades following the start of universal varicella vaccination (UVV), expected to peak in adults between 15-35 years after UVV begins. The United States (US) introduced single dose UVV in 1996, expanding to a 2nd dose in 2006. Single dose vaccination against HZ in adults was introduced in 2008. The objective of this study was to evaluate age-specific annual incidence of varicella and herpes zoster in the US before and after UVV.

Methods

This was a retrospective study of de-identified administrative claims data covering approximately 1/5th of the US population from the MarketScan® databases between 1991-2016. Annual vaccination rates and the incidence of varicella and HZ per 100,000 person-years by calendar year and age category are reported.

Results

Varicella incidence in all age groups has declined since UVV onset, including in children too young to be vaccinated. HZ incidence increased steadily from 1991 to about 2012 in all age categories ≥18 years, with a subsequent plateau in years 2013-2016 (most evident in the ≥65 age group). A notable decline in the incidence of HZ among children <18 was apparent from 2004 onwards; the rate declined
61.4% from 88/100,000 pre-UVV (1991-1995) to 34/100,000 in 2016.

Conclusions

The annual incidence of HZ in adults increased at approximately the same rate in the years before and after UVV. The hypothesized increase in HZ expected from the modeling of the exogenous boosting hypothesis was not readily apparent, but the impact of varicella vaccination in reducing herpes zoster in the pediatric population and varicella disease in all ages was substantial.
INACTIVATED INFLUENZA VACCINE DOES NOT REDUCE RESPIRATORY ILLNESS IN CHILDREN WITH MEDICAL RISK CONDITIONS

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Background

The effectiveness of inactivated influenza vaccine (IIV) immunization in preventing respiratory illness (RI) episodes in children with medical risk conditions has been unclear and varies from season to season. This study aims to quantify the overall impact of IIV immunization on primary care attended RI episodes in medical risk children, using robust observational data spanning eleven influenza seasons.

Methods

Electronic records of IIV eligible children according to Dutch guidelines were extracted from primary care databases for 2004-2015. Eligibility includes (chronic) respiratory and cardiovascular disease or diabetes. For each year, information on IIV immunization status, primary care attended RI episodes (including influenza like illness, acute respiratory infections and asthma exacerbation) and potential confounders was collected. Generalized estimating equations were used to model the association between IIV status and occurrence of at least one RI episode during the influenza season with “current year immunized” as reference group.

Results

11,797 children (follow-up duration: 38,701 child-years) were eligible for IIV immunization for at least one season. The adjusted odds for primary care attended RI episodes during the influenza season did not significantly differ between current season immunized children and those not immunized (adjusted OR:1.09;95%CI:0.97-1.22).

Conclusions

IIV immunization in children with medical risk conditions does not reduce the occurrence of RI episodes diagnosed during the influenza season in primary care.

Funding: The Netherlands Organization for Health Research and Development (ZonMw)

Clinical Trial Registration (Please input N/A if not registered)

N/A
PROYECT, “EFFECTIVENESS OF PREGNANT PERTUSSIS VACCINATION TO PREVENT WHOOPING COUGH IN CHILDREN UNDER ONE YEAR IN CATALONIA AND NAVARRA, SPAIN”. RESULTS AFTER TWO YEARS

Background

Pregnant Tdap vaccination between 27 and 36 gestational weeks is included in the Adults Vaccination Schedule Catalonia and Navarra since 2015 and high coverage rates have been achieved. We aim to estimate the effectiveness of pregnant Tdap vaccination to prevent whooping cough in children under one year.

Methods

Whooping cough cases were identified through the Notifiable Diseases System in the Epidemiology Units of Catalonia and Navarra.

Case: A child under one year with laboratory-confirmed whooping cough.

Control: Initially two controls per case (same municipality and/or primary health care centre) and same date of birth (+/- 15 days); from May 2017, four controls per case.
We performed an unmatched case-control study to estimate the effectiveness of Tdap pregnant vaccination.

To calculate vaccine effectiveness (VE) we used the formula VE (%) = (1-OR) x 100.

The project had the approval of the Ethics Committee of the Hospital Sant Joan de Deu, Barcelona.

Results

179 cases and 512 controls have been included in the study.

52.5% of cases and 48.6% of controls were females.

Mean age of Cases: 148 days. Mean age of Controls: 144 days

Vaccination status of mothers: 70.8% of cases and 86.5% of controls had their mothers vaccinated during pregnancy.

In 79.2% of cases and 90.0% of controls, mother vaccination recommended by a health care worker.

Crude VE to prevent cases in children <1 year: 67.8% (95%CI: 50.7%, 90.6%).

We did not have enough statistical power to estimate effectiveness in children < 2 months.

Conclusions

Pregnant Tdap vaccination may be effective to reduce the risk of whooping cough in children < 1 year.

Clinical Trial Registration (Please input N/A if not registered)

N/A
Espid Symposium - Tuberculosis

Improving Pediatric Tuberculosis Detection by Using Trained African Giant Pouched Rats: Potential TB Diagnostic Solution for High-Burden Countries

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4 APOPO Rodent Research, Apopo TB, Morogoro, Tanzania

Background

Pediatric tuberculosis (TB) diagnosis is difficult in most resource constraint countries where sensitive diagnostic tools such as GeneXpert is not accessible. Hence up to 94 percent of children with TB are treated empirically especially in TB high burden countries. Sensitive and accurate diagnostic tests are much needed. The African giant pouched rats have been trained to detect pulmonary TB in human sputum. We evaluated the potential of trained rats to detect pediatric TB and the TB yield compared to smear microscopy.

Methods

One month old rats were trained to detect TB in sputum for 6-9 month. Rats are rewarded with food upon correct indication of TB positive sputum sample. Presumptive TB patients seeking TB diagnosis in Tanzania were tested by rats after TB diagnosis in hospitals. Samples suspected to be TB positive were subjected for confirmation using WHO approved concentrated smear-microscopy method. Bacteriologically confirmed pediatric TB yield in ≤5 year old was compared with hospital microscopy.

Results

Sputum samples from 982 children (1–5 year) was tested by rats. Hospitals detected 34 bacteriologically positive children and rats detected additional 23 children yielding 57 bacteriologically TB-positive children. Rats increased pediatric TB detection by 68%. In the age group of 1-14 year old, hospitals detected 331 children with TB while rats detected additional 208 TB positive children who were initially missed by hospitals. Majority of the additional TB patients detected by rats missed by hospitals had scanty TB bacilli.

Conclusions

Trained rats can enhance pediatric TB detection with high TB yield and can recover missed TB positive children. Further evaluation of pediatric TB detection by rats is needed to understand whether they can detect TB through other sample types that can be easily obtained from children.
This point prevalence survey aimed to identify barriers for providing health care and health care needs of refugee children in emergency care.

Methods

An online survey was distributed amongst health care professionals across Europe through research networks, in the period February 2017 – September 2017. Population of interest were children aged <18 years fulfilling international criteria of refugee status. Data on demographics, healthcare needs, perceived barriers in health care provision and available guidelines were collected. Supported by ESPID.

Results

143 respondents from 21 European countries completed the survey, 79% were paediatric specialty consultants, and most worked in academic institutions (81%). Language barriers (60%), unknown medical history (53%), post-traumatic stress disorder (53%) and mental health issues (50%) were important barriers for providing care, whereas funding, type and severity of presenting illness, medication prescribing, and sexual health problems were not. Skin and soft tissue infections as well as safeguarding concerns were seen more frequently amongst refugee children compared to local population. Guidance on immunisations (available for 30% of respondents), safeguarding issues (31%) or screening for infection (32%) or mental health (14%) were not always available. Only 16% reported regular teaching sessions on refugee child health. 71% of respondents indicated a need for guidelines and 80% for structured teaching. Routine point of entry screening was most commonly done by public health services (20%); in 17% respondents stated this did not happen in an organised manner in their catchment area.

Conclusions

We have identified barriers for providing emergency care of refugee children throughout Europe and highlighted specific health issues of this vulnerable group. This study offers important opportunities for improving clinical guidance and education. However, care pathways vary greatly between different countries, making uniform guidance challenging.
Combining Culture and PCR for Assessment of S. Pneumoniae Carriage in Infants in the First Two Years of the Belgian Nasopharyngeal Carriage Study

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²University of Antwerp, Vaxinfectio - Laboratory for Medical Microbiology, Wilrijk, Belgium
³University Hospitals Leuven, Medical Microbiology - Laboratory Medicine, Leuven, Belgium

Background

The Belgian infant pneumococcal conjugate vaccine (PCV) programme (coverage >90%) changed from PCV13 to PCV10 in 2015-2016. In 2016-2017 (Y2), we monitored for the second year (Y2) S. pneumoniae colonization in infants (6-30 months), either healthy in day-care (DCC) or presenting with acute otitis media (AOM) at their physician.

Methods

A single nasopharyngeal swab was taken in November-March (DCC) or November-May (AOM) and transported in STGG-medium. S. pneumoniae was cultured, screened for antibiotic resistance, and serotyped (Quellung). Pneumococcal DNA was quantified using quantitative Taqman real-time PCR targeting LytA and a serotype specific PCR was set-up for serotypes 3, 6A, 19A. Demographic and clinical characteristics and vaccination status were collected via a questionnaire.

Results

In DCC-infants, culture-based pneumococcal carriage prevalence was higher in Y2 (67.7%) than in Y1 (60.8%) (P-value Chi²=0.003), but LytA-based carriage was similar (Y2: 75.7%, Y1: 79.7%, P-value Chi²=0.051). In AOM-infants, pneumococcal carriage prevalence was similar in both years, both culture-based (Y2: 64.8%, Y1:69.2%; P-value Chi²=0.608), and LytA-based (Y2: 77.9%, Y1: 82.1%, P-value Chi²=0.577). LytA-based pneumococcal carriage in DCC-infants of Y2 was related to region, having siblings, AOM-history and antibiotic treatment in the past three months (P-values Chi² <0.020). The culture-based frequency of PCV13-serotypes was low in Y1 and Y2 (Table), but among DCC-infants carrying PCV13-serotypes, PCV13-non-PCV10-serotypes increased from Y1 (16.0%) to Y2 (52.6%) (P-value Fisher’s Exact=0.020). PCR revealed some hidden carriage of PCV13-non-PCV10-serotypes in culture-negative samples: in DCC-infants, five additional PCV13-non-PCV10-serotypes in Y1, four in Y2 and one additional 19A-carrier in AOM-infants in Y2.
Conclusions

One year after the PCV13-to-PCV10 switch in Belgium, culture-based PCV13 and PCV13-non-PCV10 serotype carriage in infants remained rare, although PCR revealed some hidden carriage of the latter.
Sex difference in immune reactions against infectious pathogens poses social implications on infection prevention policies. Sex differences in children are age-specific, whilst there is lack of evidence on age-specific sex difference in most childhood infectious diseases.

Methods

During 2000-2012, 281K children randomly selected from the Taiwanese population contributed 31 million child-months from age 3 months to 18 years. Physician-coded diagnoses of all healthcare visits were recorded in the Taiwan National Health Insurance system. Fifteen diagnoses were identified related to respiratory, gastrointestinal, and urinary tract infections and viral exanthems using the International Classification of Diseases, 9th Revision. Separately for boys and girls, monthly rates of diagnosis-specific healthcare visits were estimated by age, adjusted for year, season, region, and level of urbanisation.

Results

Across 6 diagnoses in respiratory, 2 diagnoses in gastrointestinal, and 3 diagnoses in urinary tract infections, we found consistent male tendency in early childhood, when boys were more likely to have an infection-related diagnosis than girls. As children grow, the male-to-female ratios gradually declined and fell below one in all 9 of the 11 diagnoses applicable for older children. The ratios for infections of the kidney and for cystitis fell below one soon after infancy, and the ratios for the 7 remaining diagnoses fell below one during adolescence. In the 4 diagnoses related to viral exanthems, there was no strong evidence on sex difference except for a widening sex gap in herpes simplex during late adolescence.

Conclusions

Across common diagnoses in respiratory, gastrointestinal, and urinary tract infections, we found consistent male tendency on the burden of diagnosis-specific healthcare visits in early childhood and conversion to female tendency before adulthood. We did not find strong sex differences in viral exanthems during childhood.
ANALYSIS OF 7,438 PERTUSSIS CASES AND 183 CONFIRMED DEATHS REGISTERED IN SÃO PAULO STATE, BRAZIL, 2008 TO 2017

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Title of Case(s)

Analysis of 7,438 pertussis cases and 183 confirmed deaths registered in São Paulo State, Brazil, 2008 to 2017

Background

Pertussis was considered a controlled disease in Brazil, but recently there was an increase in the number of cases and deaths, coinciding with the introduction of RT-PCR. The aim of this study was to describe the pertussis cases and associated deaths in São Paulo State, in the last decade.

Case Presentation Summary

This was a retrospective descriptive study of all pertussis cases reported in São Paulo State from Jan/2008 to Dec/2017, based on the analysis of São Paulo State Health Department (SINAN/SINANNET/SIM/DDTR/VE/CCD/SES-SP) registers.
A total of 7,438 pertussis cases and 183 deaths were confirmed in São Paulo State. A total of 6,377 cases (85.7%) were reported in children < 10 years of age, 327 (4.4%) cases in persons ≥ 10 to 20 years and 734 (9.9%) in adults. In 2014, the overall incidence rate was 5.28 cases/100,000, and the rate in infants <12 months 258/100,000. All deaths were confirmed in infants <12 months of age, with a peak in 2013 and 2014, when 50 and 47 pertussis deaths occurred, respectively. The case fatality rate varied from 2.5% to 5.4% in infants <12 months of age, reaching 9% in infants <2 months of age in 2017.

Learning Points/Discussion

The number of pertussis cases and deaths grew 8-fold from 2008 to 2014. The case fatality rates were very high in infants, leading health authorities to introduce pertussis immunization for pregnant women in 2014. Considering that humans are the only reservoir for Bordetella pertussis, it is essential to improve surveillance in all age groups and reach high coverage rates of pertussis immunization in primary serie and booster doses.
CD4 COUNT IN PAEDIATRIC HIV: IS IT TIME TO REDUCE MONITORING FREQUENCY?
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Background
Paediatric HIV guidelines recommend monitoring CD4 T cell counts every 3-4 months. The clinical utility of this in the context of fully suppressed HIV viral load (VL) has been questioned. VL is the most useful correlate of adherence and combination antiretroviral therapy failure (CART). Transient drops in CD4 count rarely contribute to decision making. We aimed to assess the safety of reduced CD4 count monitoring in children with fully suppressed VL.

Methods

Results
56/75 met inclusion criteria. 53% male. 96% perinatally acquired HIV. 1377 paired CD4 and VL measurements were obtained (402 patient years). No patients had progressive CD4 decline or required co-trimoxazole. Cox proportional hazards regression showed baseline CD4 Z score to be predictive of a low CD4 count (p<0.001). After excluding the first 12 months of data this effect disappeared indicating that CD4 counts remained stable following count recovery. After 12 months 4% of 1125 CD4 counts showed a transient drop (with 100% spontaneous recovery). 25/56 patients
Conclusions

During full VL suppression on CART, no clinically significant fall in CD4 count occurred. Results indicate it would be safe to reduce the frequency of CD4 count monitoring, after a 12 month period of count recovery, to once per year and during times of detectable viraemia. Estimated savings at GOSH were £3864/annum. Although limited by sample size, similar analyses are planned for UK/European cohorts.
ESP18-0125
SCIENCE AND EDUCATIONAL TRACK
ORAL PRESENTATION SESSION 09: VACCINE DEVELOPMENT AND IMMUNOGENICITY

RANDOMIZED, DOUBLE-BLINDED, ACTIVE-CONTROLLED, PHASE I/II CLINICAL TRIAL TO ASSESS THE SAFETY, TOLERABILITY AND IMMUNOGENICITY OF NBP613 IN HEALTHY INFANTS

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2Khon Kaen University- Khon Kaen- Thailand, Department of Pediatrics, Khon Kaen, Thailand
3Chiang Mai University- Chiang Mai- Thailand, Department of Pediatrics, Chiang Mai, Thailand
4SK Chemicals- Seongnam- Republic of Korea, Life Science Research Institute, Seongnam, Republic of Korea

Background

Rotavirus vaccines are considered essential vaccines for infants but, currently, Korea depends on only 2 products developed by global companies. Therefore, the necessity to develop a domestic rotavirus vaccine is being emphasized greatly.

Methods

A randomized, double-blinded, and active-controlled Phase 1/2 study was designed to assess the safety, tolerability, and immunogenicity in healthy infants at the age of 6 to 12 weeks. Subjects were randomized to receive either NBP6131, NBP6132 (Live, Oral, and Pentavalent, SK Chemicals) or RotaTeq®. Solicited adverse events were collected up to 14 days after each dose. Unsolicited and serious adverse events were documented during the entire study period. Blood samples were obtained for serum anti-rotavirus IgA and for serum neutralizing antibodies against human rotavirus serotypes G1, G2, G3, G4, and P1A.

Results

A total of 76 participants completed the study in accordance with the protocol. Most AEs were mild in severity and not related to study drug. There was no SAE related to NBP6131 or NBP6132. All subjects had at least 3-fold increases in serum anti-rotavirus IgA. Most subjects in all groups also achieved at least 3-fold increases in serum neutralizing antibody for G1, G2, G3, and G4. But NBP613 groups had significantly higher proportions of subjects who achieved 3-fold increases in serum neutralizing antibody for P1A compared to RotaTeq®. NBP613 groups showed higher GMT values than RotaTeq® in serum anti-rotavirus IgA titer and serum neutralizing antibody titer. Furthermore, geometric mean fold increase of the serum neutralizing antibody titer for G4 and P1A were generally
higher in NBP613 groups compared to RotaTeq®.

**Adverse Events**

<table>
<thead>
<tr>
<th></th>
<th>RotaTeq® (N=28)</th>
<th>NBP6131 (N=27)</th>
<th>NBP6132 (N=28)</th>
<th>Combined (N=55)</th>
<th>Total (N=83)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solicited Systemic AEs</td>
<td>78.57%</td>
<td>66.67%</td>
<td>82.14%</td>
<td>74.55%</td>
<td>75.00%</td>
</tr>
<tr>
<td>Fever</td>
<td>17.86%</td>
<td>3.70%</td>
<td>14.29%</td>
<td>9.09%</td>
<td>12.05%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>50.00%</td>
<td>40.74%</td>
<td>35.71%</td>
<td>38.18%</td>
<td>42.17%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>46.43%</td>
<td>33.33%</td>
<td>46.43%</td>
<td>40.00%</td>
<td>42.17%</td>
</tr>
<tr>
<td>Irritability</td>
<td>60.71%</td>
<td>48.15%</td>
<td>75.00%</td>
<td>61.82%</td>
<td>61.45%</td>
</tr>
<tr>
<td>Unsolicited AEs</td>
<td>53.57%</td>
<td>66.67%</td>
<td>64.29%</td>
<td>65.45%</td>
<td>61.45%</td>
</tr>
</tbody>
</table>

**Seroconversion Rate in Serum Neutralizing Antibody Titer**

![Seroconversion Rate Graph](image)

**Geometric Mean Fold Increase of the Serum Neutralizing Antibody Titer**

![Geometric Mean Fold Increase Graph](image)

**Conclusions**

NBP613 was generally safe and well-tolerated in infants. It also showed similar or generally higher immunogenicity to RotaTeq®.

**Clinical Trial Registration (Please input N/A if not registered)**

N/A
NO IMPACT OF ROTAVIRUS VACCINATION ON CHILDHOOD SEIZURE HOSPITALIZATIONS IN ENGLAND – AN INTERRUPTED TIME SERIES ANALYSIS.

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Background

Rotavirus infection appears to be an under-recognised cause of childhood seizures. In the US a 20% risk reduction of seizures in the year following rotavirus vaccination (RV) has been reported. England is opportunely placed to explore this with its well-defined RV introduction and high uptake.

Methods

Hospital Episodes Statistics contain centralised records of all acute paediatric admissions in England. Within this dataset, we identified admissions with febrile and afebrile seizures in children <3 years old (ICD-10 codes; G40*, G41*, R56.0*) from 2007-2017, fitting separate regression models by seizure type, age group and peak rotavirus seasonality; offset for English population changes with vaccine use as a covariate.

Results

During our 10-year time series analysis, our examined population encompassed approximately 20 million children. Our first-time seizure admission rate was 1184/100,000 person-years- similar to US studies. Our model did not detect a statistically significant association between RV and admission with febrile (p=0.84), afebrile (p=0.83) or all (p=0.93) seizures, even when limited to admissions in March; the peak of rotavirus season. A decreasing trend in febrile convolution admissions was noted that predated RV rollout.

Conclusions

This is the first ecological study in a country that predominately uses the monovalent vaccine and did not find an association between RV and seizures. It has a large sample size, comparing 6 and 4 years of pre- and post-vaccine use across the English paediatric population. Although a negative finding, it is an important one. We would argue that if a vaccine effect cannot be found on such a population level then it is not clinically nor economically significant. Building on this piece of work we are going to conduct a similar analysis on emergency department presentations with childhood seizures.

Clinical Trial Registration (Please input N/A if not registered)

N/A
Varicella-zoster virus (VZV) causes varicella and zoster (reactivation from latency). Peripheral neurons in dorsal root (DRG), cranial nerves (CNG), sympathetic, and enteric ganglia become infected during varicella. Reactivating infections of DRG and CNG are relatively easy to detect because they infect skin; however, reactivations in the enteric nervous system (ENS) or other ganglia that do not innervate skin are difficult to diagnose. Reactivation of wild-type (WT) or vaccine-type (vOka) VZV in the ENS (enteric zoster) can cause abdominal pain, pseudoobstruction, or bowel perforation. VZV DNA appears in saliva during active VZV infection. We therefore determined whether detection of salivary VZV DNA is helpful in diagnosing VZV infections that lack cutaneous manifestations, such as enteric zoster.

Methods

Nested polymerase chain reaction (PCR) was employed for analysis of salivary VZV DNA. We studied 25 children and adults (6-70 years old) with severe, persistent abdominal pain unexplained after a gastrointestinal (GI) workup. Salivary VZV DNA was detected in 12/25 (48%).

Results

No rash was present in 7/12 (58%). Pain disappeared in 10/10 (100%) after treatment with oral valacyclovir. After disappearance of pain, salivary VZV DNA was no longer detectable in 12/12. GI tissue was available for 3/12; in 1 there were stomach ulcers; in 2 VZV glycoprotein immunoreactivity was demonstrated in colonic nerves and enteroendocrine cells. vOka (in colon and stomach) was identified in 2/3 and WT in 1/3. Underlying immunodeficiency (2 with functional NK cell defects) or autoimmunity (1 with prednisone and cyclosporine- treated Crohn's ) were observed.

Conclusions

Screening saliva for VZV DNA is useful when enteric zoster is suspected; VZV may be an unexpected but important GI pathogen.

Clinical Trial Registration (Please input N/A if not registered)

N/A
THE BURDEN OF CHILDREN HOSPITALIZED WITH PERTUSSIS IN CANADA IN THE ACELLULAR PERTUSSIS VACCINE ERA, 1999-2015

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4Dalhousie University- Izaak Walton Killam Health Centre- and Nova Scotia Health Authority, Canadian Center for Vaccinology- Departments of Pediatrics and Microbiology and Immunology, Halifax, Canada

Background

Previous descriptions of pertussis disease among children have been limited to incidence rates and clinical outcomes in small populations, a specific epidemic or narrow time periods during which both whole-cell and acellular pertussis (aP) vaccines were used. Recent increases in pertussis morbidity and mortality among young infants has led to recommendation of vaccination against pertussis during pregnancy in some countries. The age-specific epidemiology, morbidity and mortality of children hospitalized with pertussis over 17 years across Canada in the aP vaccine era are described.

Methods

Patients ≤16 years admitted with pertussis to 12 pediatric tertiary-care hospitals across Canada during 1999–2015 with confirmed (laboratory–confirmed or epidemiologically–linked) or probable (clinically diagnosed) pertussis were included.

Results

Overall, 1402 patients with pertussis were included. Infants aged <2 months had the highest mean annual pertussis hospitalization and intensive-care unit (ICU) admission incidence, 116·4 (95% CI: 85·3–147·4) and 33·48 (95% CI: 26·3–40·6) per 100,000 population, respectively. The proportion of children requiring ICU admissions was 25·4% and this was highest in infants <2 months of age at 37·9%. There were 21 deaths. Age <16 weeks, presence of any comorbidity, encephalopathy and confirmed pertussis diagnosis were independent risk factors for ICU admission. Age <4 weeks and female sex were independent risk factors for death.

Conclusions
In the aP vaccine era, pertussis still contributes considerably to childhood morbidity and mortality, particularly in infants aged <2 months. Due to the age group most severely affected by pertussis, Vaccination against pertussis during pregnancy has the potential to reduce this disease burden.
MEASLES SURVEILLANCE DATA ANALYSIS IN KEBBI STATE-NIGERIA, 2017
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³Kebbi State Ministry of Health, Epidemiology and Disease Control, Kebbi, Nigeria

Background
Measles is a highly contagious acute viral illness targeted for elimination in most parts of the world especially in developing countries. Globally, it is one of the leading causes of death among young children. It is regarded as a priority disease with epidemic potential in the Integrated Disease Surveillance and Response (IDS R) System in Nigeria. We analyzed surveillance data to describe the epidemiology of measles in Kebbi State, 2017

Methods
We reviewed surveillance data abstracted from Kebbi State IDSR data-base from January to December, 2017. A suspected case of measles was defined as: any person with fever and maculopapular (non-vesicular) generalized rash and cough, coryza or conjunctivitis or any person in whom the clinician suspect measles. A confirmed case was defined as a suspected case with laboratory confirmation (positive IgM antibody) or epidemiological link to confirmed cases in an outbreak. We computed frequencies and proportions

Results
A total of 794 suspected cases of measles were reported during the period under review with an incidence of 16.9/ 100,000 population. The Mean age was 50.2.9±42.5 months. Females constituted 415(52.3%) of the reported cases. Age group 1-4 years were predominant affected (63. 6%). Aliero local government area was the most affected 121(15. 3%). One hundred and twenty-seven (16%) were confirmed positive for measles IgM among which 66.9% had not received measles vaccination. Eighteen of the total patients died during the reporting period given a case fatality rate 2.3%.

Conclusions
Measles vaccination uptake is still poor despite supplemental immunization exercise. We recommended public health enlightenment on measles vaccination and improved surveillance activities in the State.
Background

The Global Burden of Diseases, Injuries, and Risk Factors (GBD) Study 2016 provides an up-to-date analysis of the burden of diarrhoea in 195 countries. This study assesses cases, deaths, and aetiologies spanning the years 1990-2016 and shows how the burden of diarrhoea has changed in people of all ages.

Methods

Diarrhoea has three distinct modeling approaches used in GBD 2016. Mortality was modeled using a Bayesian hierarchical modeling platform that evaluates a wide range of covariates and model types. Incidence was modeled using a compartmental meta-regression tool that enforces a relationship between incidence, prevalence, and remission that predicts morbidity based on scientific literature, population representative surveys, and healthcare data. Diarrhoea deaths and episodes were attributed to thirteen pathogens using a counterfactual population attributable fraction approach. Diarrhoea risk factors are also based on counterfactual estimates of risk exposure and the association between the risk and diarrhoea. Each modeled estimate accounted for uncertainty and was made for each age, both sexes, by year, and by geography.

Results
Diarrhoea was the eighth leading cause of death among all ages (1,655,900 deaths) and the fifth leading cause of death among children under 5 years old (446,000 deaths). Rotavirus was the leading etiology for diarrhoea mortality among children under 5 (128,500 deaths) and among all ages (228,000 deaths). Childhood wasting, unsafe water, and unsafe sanitation were the leading risk factors for diarrhoea.

Conclusions

The Global Burden of Disease study provides a comprehensive, comparable, scientific set of estimates for the burden of diarrhoea, and these estimates provide both a description of the epidemiology of the disease and a potential roadmap for continuing to reduce its burden.

Systematic Review Registration (Please input N/A if not registered)

N/A
Efficacy and Safety of High-Dose Ivermectin on Mosquito Mortality When Co-Administered with Dihydroartemisinin-Piperaquine for Uncomplicated Malaria in Kenya: Randomised, Double-Blind, Placebo-Controlled Trial


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²Kenya Medical Research Institute, Centre for Global Health Research, Kisumu, Kenya
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⁴Kenya Ministry of Health, Kisumu County, Kisumu, Kenya
⁵Radboud University Medical Center, Institute for Health Sciences, Nijmegen, The Netherlands
⁶Imperial College London, Infectious Disease Epidemiology, London, United Kingdom
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Background

Malaria is a leading cause of child death worldwide. Ivermectin is being considered for mass-drug-administration for malaria due to its ability to kill mosquitoes feeding on recently treated individuals. However, standard, single-doses of 150-200 mcg/kg used for onchocerciasis and lymphatic filariasis have a short-lived mosquitocidal-effect (<7 days). Ivermectin is well-tolerated up to 2,000 mcg/kg. Repeated, high doses of ivermectin could generate longer mosquitocidal-effects required for malaria elimination.

Methods

Randomized, double-blind, placebo-controlled trial comparing the safety, tolerability, and efficacy of 3-day ivermectin 0, 300, or 600 mcg/kg/day, co-administered with dihydroartemisinin-piperaquine, in randomly assigned (1:1:1) adults with uncomplicated malaria in Kenya. Patients’ blood taken on post-treatment days 0, 2±4h (Cmax), 7, 10, 14, 21, and 28, was fed to laboratory-reared Anopheles gambiae s.s.; mosquito survival was assessed daily for 28-days post-feeding. Safety outcomes included pupil-diameter, QT-interval, and adverse events. Ivermectin’s effect on malaria transmission was modelled.

Results

Between 20-Jul-2015 and 07-May-2016, 141 patients were randomized. Compared to placebo, ivermectin was associated with higher 14-day-post-feeding mosquito mortality when fed on blood taken 7-days-post-treatment (600 mcg/kg/day: risk ratio [RR] 2.26, 95% confidence interval [1.93-2.65], p<0.0001; hazard ratio [HR] 6.32 [4.61-8.67], p<0.0001; 300 mcg/kg/day: RR=2.18 [1.86-2.57], p<0.0001; HR=4.21 [3.06-5.79], p<0.0001). Mosquito mortality remained significantly increased 28-days-post-treatment. High-dose ivermectin was well tolerated. Modelling predicted that adding 3-day ivermectin 600 or 300 mcg/kg/day to mass drug administration with dihydroartemisinin-piperaquine enhances malaria prevalence reduction by an additional 56%-61% and 44%-54%, respectively.

Conclusions
High-dose ivermectin is well tolerated and reduces mosquito survival for at least 28-days-post-treatment, making it a promising new tool for malaria elimination. Comparable studies are now needed in children.

**Clinical Trial Registration (Please input N/A if not registered)**

ClinicalTrials.gov: NCT02511353. Funding: Malaria Eradication Scientific Alliance (MESA) and U.S. Centers for Disease Control and Prevention (CDC).
ADHESION OF CANDIDA SPECIES TO STAINLESS STEEL SURFACES UNDER VARIOUS GROWTH CONDITIONS

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2Institute of Food Technology, Microbiology, Novi Sad, Serbia
3Biotechnical Faculty, Microbiology, Ljubljana, Slovenia

Background

Invasive fungal infections, such as candidiases, represent a public health problem of major importance. In the past twenty years, Candida species are responsible for around 80% of fungal infections in the hospital environment. The formation of Candida biofilms carries important clinical repercussions because of their increased resistance to antifungal therapy and the ability of cells within biofilms to withstand host immune. Hence, device-related infections are difficult to treat, and affected devices often need to be removed, which can be hazardous for some patients. It is therefore important to focus attention on how to prevent and control biofilm formation in such applications.

The aim of our study is to provide better understanding on adhesion behavior of Candida species to stainless steel surfaces, material typical for medical devices, and effect of various growth conditions.

Methods

We investigated the impact of growth medium (Malt Extract broth and Yeast Peptone Dextrose broth) and different temperatures (7°C, 37°C, 43°C) on adhesion of Candida species to stainless steel (AISI 304) discs with different degrees of surface roughness (Ra = 25.20 – 961.9 nm). The method used to assess adhesion was crystal violet staining.

Results

The results showed that the nutrient content of medium and temperatures significantly influenced the quantity of adhered cells. Adhesion of Candida albicans and Candida glabrata on stainless steel surfaces were significantly higher in MEB, whereas for Candida parapsilosis and Candida krusei it was YPD broth. There was also significant difference in cell adhesion on all types of stainless steel surfaces for all tested yeast.

Conclusions

An understanding of adhesion behavior of Candida spp. under different environmental conditions is key to the development of effective preventive measures against biofilm-associated infection.

Clinical Trial Registration (Please input N/A if not registered)

N/A
CLINICAL FORMS OF MEASLES IN CHILDREN - DURING JANUARY 2016 – NOVEMBER 2017, ROMANIA

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²University of Medicine and Pharmacy “Carol Davila”- Bucharest, Medicine, Bucharest, Romania

Background

Starting January 2016, Romania has been confronted with a significant increase in measles cases, which is a major cause of mortality and morbidity in young children, despite the existence of a safe and effective vaccine. Between January 2016 and November 2017 Romania registered 9946 cases of measles, including 36 deaths – data provided by the National Health Care Institute.

Methods

We performed a retrospective study of all cases of measles in children hospitalized in the Pediatric Departments of the National Institute for Infectious Diseases “Prof. Dr. Matei Bals”, Bucharest, Romania between January 2016 and November 2017. In all cases we have analyzed: age, sex, background, geographic region of the epidemic, vaccination status and complications of the illness. Diagnosis and complications were established on clinical, epidemiological, and paraclinical data.

Results

208 cases of measles were registered in the Pediatric Departments in the studied period. The most affected age group was 0-1 years (27.40%), followed by 1-3 years (31%) with a female ratio of 55.7%. Rural areas were predominant 76.92%. Most of the patients were from regions with outbreaks 84.13%, were unvaccinated 73.07% or were unaware of their vaccination status 18.75%. Most cases presented with respiratory complications 83.17% (pneumonia was the most frequent, acute respiratory failure) followed by digestive 60.09%, hematological 62.50% and ophthalmological complications 42.78%. The most common clinical form was moderate 49.51%, followed by severe 33.65% and mild 16.84%. Three deaths were registered.

Conclusions

Measles is a highly contagious disease, that frequently develops severe complications and can result in death, especially in young children. Because there is no specific treatment, the best measure to control such outbreaks remains routine vaccination along with the additional recommended dose between 9 and 11 months of age.

Clinical Trial Registration (Please input N/A if not registered)
GASTRIC LAVAGE MICROSCOPY FOR DIAGNOSIS OF PULMONARY TUBERCULOSIS: HOW MANY SPECIMENS ARE REQUIRED?

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Background

Most guidelines recommend two gastric lavage (GL) specimens for diagnosing tuberculosis (TB) in young children. Since pediatric TB is paucibacillary and tuberculosis bacilli are shed intermittently, two GL samples may be inadequate. We examined whether additional GL specimens increase diagnostic yield.

Methods

In our institution, children with suspected pulmonary TB (based on clinical and/or radiographic grounds) are routinely offered GL on two consecutive mornings; followed by broncho-alveolar lavage (BAL) if both specimens are smear negative. Over a period of 12 months, we obtained multiple GL specimens, collecting one on each day of hospitalization. Bronchoscopic BAL was reserved only for those children in whom all GL specimens were negative.

Results

Among 94 children with suspected tuberculosis, a median of 5 (range 2-9) GL specimens were obtained. Microscopy confirmed tuberculosis in 27. Only 11 of 27 (40%) children tested positive in the first two specimens; thus 60% cases were diagnosed by obtaining additional GL specimens. The cumulative diagnostic yield increased with each additional specimen (Figure 1A). Among 44 children in whom multiple GL specimens were negative, BAL was confirmatory in 10 (Figure 1B). Obtaining additional GL specimen avoided bronchoscopy in 16 children.
Conclusions

The diagnostic yield more than doubled by obtaining additional GL specimens (beyond the two recommended). There were very small increments after the sixth GL specimen. BAL could be avoided in many children by obtaining additional GL specimens. We suggest that six GL specimen (and not two) are optimal for diagnosing suspected pulmonary TB.
Background

The Non-Polio Enterovirus A71 (EV-A71) is an emerging pathogen associated with large outbreaks especially within the Asian Pacific region but also in south Europe. To date, EV-A71 is classified into three genogroups (A,B,C). Four more have been suggested recently (D, E, F, G). Strains of the genogroups C4 and B5 have been mostly identified in the Asian Pacific region, whereas in Europe strains of the genogroups C2, C1-like and C4 are dominating. Although the clinical course of EV-A71 infection is often mild leading to hand-foot-mouth disease, neurological infections as meningitis and brainstem encephalitis can occur and have devastating outcomes. The route to the CNS of this neurotropic virus is not defined yet.

Methods

In a human in vitro model of the BCSFB consisting of Human Choroid Plexus Papilloma (HIBCPP)- cells, six different genotypes from distinct genogroups were compared concerning their infectivity, effects on barrier integrity and viability of HIBCPP cells following infection. Comparative analyses were performed with Human Brain Microvascular Endothelial Cells (HBMEC) as model for the BBB, and with RD cells, which are commonly used for enterovirus propagation.

Results

The (sub)genotypes showed a different cellular tropism. Whereas C1-like and B5 exhibited the strongest infectivity in HIBCPP-cells, the EV-A71 prototype BrCr has the strongest effects in HBMEC. In RD cells, C2 showed the highest infectivity, whereas it had very weak effects both in HIBCPP-cells and HBMEC.

In contrast to recent findings with E-30, infection with the sub-genotypes C1-like and B5 did not impair barrier integrity over a time course of 72 hrs.

Conclusions

Overall, we could detect cellular tropism of different EV-A71 sub-genotypes, which could affect the clinical course. Future prospective studies on the impact of different genotypes of EV-A71 on the clinical course are warranted.
Clinical Trial Registration (Please input N/A if not registered)
DIFFERENTIAL PROTEOMIC ANALYSIS FOR IDENTIFICATION OF BIOMARKERS TO PREDICT SEVERE DENGUE IN CHILDREN FROM BIKANER, NORTHWESTERN INDIA

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²S.P.Medical college, Medicine, Bikaner, India

Background

The incidence of dengue infection has emerged as a global threat recently. The current study provides a comprehensive understanding of disease severity in dengue fever by proteomic analysis of various proteins differentiation in all stages of dengue illness i.e. dengue with no warning signs (DNWS), dengue with warning signs (DWS) and severe dengue.

Methods

Total 106 children [DNWS (n=38); DWS (n=62), severe dengue (n=6)] were enrolled in the study from January 2016 to December 2017. Diagnosis of dengue illness was made on WHO criteria and ELISA based analysis of IgM and IgG (titre≥1:400) and confirmation was done by RT-PCR. We used 2 multipronged proteomic approaches; one gel-free (iTRAQ) method for comparison of dengue cases and healthy controls; and second gel-based (2D-DIGE) method to study differential expression of proteins from dengue cases at two time points.

Results

In DNWS children, 32 proteins showing over-expression and 4 under-expressed proteins were identified compared to HC. Alpha-1-acid glycoprotein 1 & 2, alpha-1-antitrypsin, apolipoprotein A-II, clusterin and plasma protease C1 inhibitor were up-regulated in DHF patients. In DWS patients, 4 proteins i.e leucine-rich alpha-2 glycoprotein, alpha-2 antiplasmin, haemoglobin subunit beta and alpha-1 antichymotrypsin showed up-regulation and 19 proteins were significantly down-regulated. Angiotensinogen, antithrombin-III, apolipoprotein A-I, apolipoprotein B-100, Ig gamma-1 chain, Ig gamma-4 chain C region, transthyretin showed differential expression and opposite regulation in DNWS and DWS and may facilitate in predicting the progression of DNWS to DWS. The analysis of 2D-DIGE was carried out to identify differentially abundant proteins such as apolipoprotein D, serum amyloid A, haptoglobin and complement 3 in disease progression.

Conclusions

This comprehensive proteomic study provides a robust platform for both understanding the pathogenesis and predicting disease progression from non-severe to severe dengue illness.

Clinical Trial Registration (Please input N/A if not registered)

N/A
**Background**

Dengue is one disease entity with different clinical presentations and often with unpredictable clinical evolution and outcome. The present study describes its clinico-epidemiological profile with expanded dengue syndrome in hospitalized children.

**Methods**

In this prospective hospital based observational study, 1211 children were enrolled from January 2015 to December 2017. Diagnosis of dengue illness was made on WHO criteria and ELISA based analysis of IgM and IgG (titre≥1:400) and confirmation of severe dengue infection was done by RT-PCR. Other possible causes of fever were ruled out thoroughly.

**Results**

Male: female child ratio was 1.46:1. Majority of children were from urban area (60.94%). The distribution of dengue cases was dengue without warning sign 52.52%; dengue with warning signs 38.32% and severe dengue 9.17%. Children in 5-<10 years age group constituted 54% of cases forming the most commonly affected group. Common constitutional symptoms were myalgia (54.58%), headache (54.58%), rash (41.37%), arthralgia (32.70%), vomiting (32.70%), pain abdomen (22.13%), cough (9.08%) and cutaneous hypersensitivity (6.11%). Thrombocytopenia was documented in 92.82% children and bleeding manifestations were observed in 30.24% with petechiae (75.23%) being the most common. Most common atypical manifestation was hepatitis (39.80%) followed by febrile diarrhea (10.16%) myositis (5.70%), renal failure (5.03%), acalculous cholecystitis (2.81%), coagulopathy (2.73%), myocarditis (1.07%), encephalitis (1.07%), isolated seizures (1.07%), ARDS (0.91%), DIC (0.82%), cardiac conduction abnormality (0.58%) and hemophagocytosis syndrome (0.17%). Overall mortality was 1.49% with highest case fatality rate in children aged 5-<10 years (2.14%; OR=3.024 (95% CI=0.925-10.932); p=0.05).

**Conclusions**

Dengue illness had not only the varied typical presentations but multi-systemic atypical manifestations of expended dengue syndrome also in this study. Clinicians should have a high index of suspicion and vigilance as lack of timely detection and management could be fatal.

**Clinical Trial Registration (Please input N/A if not registered)**

N/A
Background

Investigations on the plasmodium induced alterations in human proteome can provide valuable information regarding malaria pathogenesis and host-parasite interactions. This study was conducted to analyze alterations in the human serum proteome as a consequence of infection by malaria parasites (Plasmodium falciparum and Plasmodium vivax) to obtain mechanistic insights about disease pathogenesis, host immune response, and identification of potential protein markers for discrimination between the Plasmodium falciparum and Plasmodium vivax monoinfections with high accuracy.

Methods

This prospective cohort study was conducted on 139 admitted children of malaria. The species diagnosis was made with peripheral smear and rapid diagnostic test and confirmed with polymerase chain reaction analysis. Serum samples from P.falciparum malaria (n=10) and P.vivax malaria (n=14) were analysed by multiple proteomic techniques in comparison to healthy controls (n=15) and dengue illness as febrile control (n=15). The results were validated by employing immunoassay-based approaches.

Results

In isobaric tags for relative and absolute quantitation (iTRAQ)-based quantitative proteomic investigation, 16 and 18 differentially expressed and statistically significant (p<0.05) serum proteins were identified in P.falciparum and P.vivax monoinfection respectively as compared to HC and FC, and almost 66% of them were commonly modulated. Thirteen proteins were found to be differentially expressed in P.falciparum monoinfection in comparison to P.vivax monoinfection. Proteins such as serum amyloid A, apolipoprotein A-I and E and haptoglobin, which successfully discriminated P.falciparum from P.vivax might be prognostic host markers for disease severity also. The prediction of these serum markers with malaria was over 95% accuracy.

Conclusions

In this comprehensive proteomic analysis, multiple differentially expressed serum proteins were identified that can distinguish the malaria patients from the healthy or febrile controls as well as discriminate between the P.falciparum and P.vivax infections with high accuracy.

Clinical Trial Registration (Please input N/A if not registered)
Background

To analyze the incidence of invasive pneumococcal disease (IPD) due to serotypes not included in the 13-valent pneumococcal conjugate vaccine (non-PCV13) and to identify risk factors associated with it.

Methods

Children younger than 15 years of age with IPD were prospectively identified in 27 hospitals in Madrid Region, from May 2007 to April 2016. The 13-valent pneumococcal conjugate vaccine (PCV13) replaced the 7-valent (PCV7) in May 2010. Pneumococcal isolates were serotyped by Quellung reaction, whereas in culture-negative pleural/cerebrospinal fluids, detection of pneumococci and typing were performed with polymerase chain reaction. Clinical and demographic variables were compared between PCV13-type IPD and non-PCV13-type IPD.

Results

There were 912 children ≤15 years with IPD (593 PCV13-type IPD and 319 non-PCV13 type IPD)

Incidence rates of non-PCV13-type IPD for the different age groups remained stable throughout the entire study period.

The 10 most frequent non-PCV13 serotypes in decreasing order were: 15B, 24F, 22F, 23B, 12F, 10A, 8, 25A, 15A, 11A (none of them reached 10% of all non-PCV13 serotypes).

Age 0 to < 24 months (OR 2.5, 95% IC 1.9-3.3) and primary immunodeficiency (PI) (OR: 2.9, 1.4-6.4) were associated with a higher risk for non-PCV13-type, as were primary bacteremia (OR: 3.5, 2.3-5.2) and pneumococcal meningitis (PM) (OR: 5.0, 3.3-7.8). Day care centers attendance, prematurity,
parental smoking and previous hospitalization were no risk factors for non-PCV13-type.

**Table 1: Association between risk condition and non-PCV13-type with the risk of IPD in children <15y in Madrid Region (2007-2016).**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Nº non-PCV13 type IPD / Nº cases of IPD (%)</th>
<th>Nº non-PCV13 type IPD/ Nº cases of IPD (%)</th>
<th>OR (IC 95%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≤ 24 m. vs. &gt; 24 months</td>
<td>≤ 24 month 176/372 (47%)</td>
<td>&gt; 24 months 143/540 (26%)</td>
<td>2.49 (1.89-3.30)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>PI vs healthy children</td>
<td>PI 17/28 (61%)</td>
<td>Healthy children 205/596 (34%)</td>
<td>2.95 (1.36-6.41)</td>
<td>0.0075</td>
</tr>
<tr>
<td>PI (vs. asthma)</td>
<td>PI 17/28 (61%)</td>
<td>Asthma 20/71 (28%)</td>
<td>3.94 (1.57-9.86)</td>
<td>0.0034</td>
</tr>
<tr>
<td>Asthma vs healthy children</td>
<td>Asthma 20/71 (28%)</td>
<td>Healthy children 205/596 (34%)</td>
<td>0.75 (0.43-1.29)</td>
<td>0.35</td>
</tr>
<tr>
<td>Bacteremia vs. pulmonary IPD</td>
<td>Bacteremia 69/131 (52.7%)</td>
<td>Pulmonary IPD 136/561 (24%)</td>
<td>3.48 (2.35-5.16)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Meningitis vs. pulmonary IPD</td>
<td>PM 70/113 (62%)</td>
<td>Pulmonary IPD 136/561 (24%)</td>
<td>5.1 (3.30-7.80)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

PI: primary immunodeficiency  
PM: pneumococcal meningitis  
Pulmonary IPD comprises both bacteremic pneumonia and pleural empyema

**Conclusions**

After 9 years of vaccination with PCV7/PCV13, the incidence of non-PCV13-type IPD has remained stable in Madrid. The higher prevalence of non-PCV13-type in children <24 months of age and in those with PI suggest a lower invasive potential on these serotypes. Non-PCV13 types are significantly more frequent in pneumococcal meningitis and occult bacteremia than in pulmonary forms of IPD.

**Clinical Trial Registration (Please input N/A if not registered)**

N/A
Background

*Neisseria meningitidis* is a globally important cause of meningitis and septicaemia. Capsular group B meningococcus (MenB) accounts for the vast majority of invasive disease in developed countries. The European Medicines Agency licensed a MenB vaccine (4CMenB) in January 2013. However, this vaccine is associated with significant reactogenicity, with fever rates of up to 60%. Here we used RNA-sequencing to describe blood transcriptional signatures following infant immunisations with or without concomitant 4CMenB, and related these to vaccine reactogenicity and immunogenicity.

Methods

One hundred and eighty-seven infants were randomized to receive control immunisations (PCV13 and DTaP-IPV-Hib) or 4CMenB plus control immunisations. Blood samples were taken at 4 months of age (pre-vaccination) then 4 hours, 24 hours, 3 days or 7 days post-vaccination. Gene expression was assessed by Illumina® 100bp paired-end RNA-sequencing. A continuous temperature monitoring device, iButton®, was used to measure temperature for the first 24 hours post-vaccination. Vaccine immunogenicity was measured by serum bactericidal assay titres 28 days after vaccination.

Results

A higher proportion (p <0.0001) of infants receiving concomitant 4CMenB (56.6%) had a fever within 24 hour of their 4-month dose of vaccines, compared with the control group (27.3%). We described transcriptional signatures that differed between the two vaccine groups, both in terms of early-onset genes involved in innate recognition and late-onset adaptive genes encoding antigen-recognition receptors. Moreover, we describe differences in gene expression profiles between infants who experienced fever compared with those who remained afebrile. Finally, we propose models, based on baseline transcriptional data, which are predictive of vaccine-induced immunity.

Conclusions

We demonstrate a novel approach to identifying the molecular mechanisms associated with vaccine-associated fever, which could lead to targeted interventions to reduce reactogenicity or the design of less pyrogenic vaccines.

Clinical Trial Registration (Please input N/A if not registered)

NCT02080559
GENETIC DIVERSIFICATION OF RESPIRATORY SYNCYTIAL VIRUS AMONGST CHILDREN AT THE UNIVERSITY HOSPITAL HEIDELBERG/GERMANY BETWEEN 2014 AND 2017

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\textsuperscript{3}Centre for Child and Adolescent Medicine, University Hospital Heidelberg, Heidelberg, Germany

Background

Respiratory syncytial virus (RSV) is the leading cause of hospitalization in young children with respiratory tract infections (RTI). The aim of this research project is to analyse the spread and diversification of RSV genotypes amongst hospitalized children in Heidelberg/Germany.

Methods

We prospectively analysed nasopharyngeal swabs (NPS) from children (<18 years) who presented with acute RTI at the University Hospital Heidelberg/Germany during winter seasons 2014 to 2017. We performed rtPCR and RSV sequence analysis of the second variable region of the G gene coding for the attachment glycoprotein. Clinical data was obtained using a standardized questionnaire.

Results

RSV was detected in 456/1086 samples (2014/15: n=120/235, 2015/16: n=107/333, 2016/17: n=229/518). Most RSV-positive children were below the age of two years (85.8%) and had lower RTI (78.6%). Phylogenetic analysis of 369 isolates revealed that most RSV-A strains (n=208/210) belonged to the novel ON1 genotype containing a 72-nucleotide duplication. Genotypes NA1 and GA5 were detected only in one case each. Most RSV-B strains could be attributed to the BAIX genotype (n=156/159), two strains to genotype BAX and one to genotype BAIV, all containing a 60-nucleotide duplication. ON1 and BAIX strains could be subdivided into several clusters of new variants (ON1 n=12, BAIX n=9) which might eventually evolve into further (sub)genotypes.

Conclusions

Mapping the spread of novel genotypes using data from different seasons can reveal transmission dynamics and the fitness of the viral strains. Further surveillance of circulating genotypes in combination with corresponding clinical data is needed to understand their full implications.

Clinical Trial Registration (Please input N/A if not registered)

N/A
CROSS-REACTIVE IMMUNOGENICITY OF THE AS04-ADJUVANTED HPV-16/18 VACCINE GIVEN AS A 2-DOSE SCHEDULE IN GIRLS AGED 9-14 YEARS VS 3-DOSE IN WOMEN AGED 15-25 YEARS

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1GSK, Clinical & Epi Development Strep, Wavre, Belgium

Background

These Phase I/II HPV-048 (NCT00541970) and Phase III HPV-070 (NCT01381575) studies investigated up to 5 years after first vaccination the safety and immunogenicity of the AS04-adjuvanted HPV-16/18 (AS04-HPV-16/18) vaccine administered as a 2-dose schedule (0, 6 months [M]) in 9-14 year old girls versus a 3-dose schedule (0, 1, 6 M) in 15-25 years women. Cross-reactive immunogenicity of the AS04-HPV-16/18 vaccine against the HPV types 31 (HPV-31) and 45 (HPV-45) not included in the vaccine was assessed.

Methods

Antibody response to HPV-31 and -45 was measured by enzyme-linked immunosorbent assay (ELISA) in subjects with available samples in study HPV-048 (80 subjects) and in a pre-determined subset of 200 subjects in study HPV-070. Assay cut-off was 59 ELISA units/mL for both.

Results

All subjects except one seroconverted to both HPV-31 and HPV-45 one month after completion of the vaccine schedule (M7; table). Five years after the first dose (M60) in study HPV-048, more than 91% of subjects still had detectable antibodies against HPV-31 and more than 80% against HPV-45 (table). Similar results were obtained in study HPV-070, with at least 83% of subjects seropositive for HPV-31 and HPV-45 three years after first vaccination (table). Geometric Mean Concentrations (GMCs) remained above assay cut-off up to study end in both studies. GMCs were similar with either the 2-dose or the 3-dose schedule (table).
Conclusions

When administered as a 2-dose schedule, the AS04-HPV-16/18 vaccine elicited antibodies against types HPV-31 and HPV-45 not included in the vaccine, up to 5 years after first dose. GMCs were similar in young girls receiving the 2-dose schedule as compared to young women receiving the 3-dose schedule.

Funding: Glaxosmithkline Biologicals SA
Clinical Trial Registration (Please input N/A if not registered)

NCT00541970 and NCT01381575
Background

Brucellosis has not been reported commonly in human because of unawareness about the disease owing to lack of suspicion and lack of diagnostic facilities. This prospective cohort study describes the epidemiology, clinico-laboratory profile and outcome of human brucellosis in children in Bikaner, northwestern India.

Methods

The diagnosis of active brucellosis was confirmed by demonstration of the raised brucella agglutination titre of ≥1:320 in the serum. Detailed history related to the occupation and exposure to the known predisposing factors and presentation of the disease were noted. The possibilities of other disease/infections causing similar illness were investigated thoroughly and stringently.

Results

During last 7 years (2011-2017), 128 children with active brucellosis were admitted in children hospital, S.P. Medical College, Bikaner, India with a wide spectrum of clinical manifestations. The mean age was 8.8±4.3 years (range 2-16 years) and boys were almost twice in number than girls (1.9:1). Fever (82.66%) was the commonest presenting feature (mean duration 17.6±6.6 days). Joint pain was reported in 70.41% children and majority of them were having multiple joint pain. Sacroiliac joint (42.03%) and knee joint (31.88%) were commonly involved. Other modes of presentation were neurobrucellosis (19.38%), manifested as encephalomyelitis polyradiculoneuropathy and myeloradiculopathy; pulmonary involvement (7.14%) presented as pleural effusion; and cardiac involvement presented as infective endocarditis (3.06%). Analysis of risk factors revealed history of raw milk ingestion (91.84%), occupational contact with animals (30.61%) and household contact (16%). All children were treated with standard protocols according to age and respond well.

Conclusions

Brucellosis is an important emerging zoonotic disease presenting with protean manifestations. High degree of suspicion is crucial for diagnosis specifically in vulnerable group of society.

Clinical Trial Registration (Please input N/A if not registered)

N/A
Background

Although there are numerous descriptions of chikungunya fever in literature in adults, various attempts have been made to objectively evaluate the manifestations of chikungunya infection in children in literature. This prospective study described the clinico-laboratory profile of children with chikungunya infection from January 2016 to December 2017.

Methods

The inclusion criteria was fever with any one of the following features; seizure, loose stools, peripheral cyanosis, skin manifestations or pedal edema in children less than one year. Details of disease from onset of illness till admission were noted and a thorough clinical examination was done at the time of admission. Diagnosis of chikungunya was made by specific chikungunya antibody by IgM antibody capture enzyme linked immunosorbent assay (ELISA). Other possible causes were ruled out by scientific and stringent manner.

Results

In this duration, 219 children were diagnosed for chikungunya fever clinically, in which 138 were positive for chikungunya IgM antibody ELISA test. The mean age was 11.2±2.1 years. Male to female ratio was 1.8:1. Children of 8–12 years were most commonly affected (56.65%). The disease manifestations were with the prototypical features of fever, rash and arthralgia. The bleeding manifestations ranged from bleeding gums and epistaxis to hematemesis and melena. Febrile convulsions occurred in 4% children with chikungunya. Eighteen infants were enrolled as chikungunya fever. The most characteristic feature of the infection in infants was acrocyanosis and symmetrical superficial vesicobullous lesions were noted in most infants. Erythematous asymmetrical macules and patches were observed which later progressed to morbiliform rashes.

Conclusions

An entirely different spectrum of disease is seen in infants with chikungunya as compared to older children who need to be carefully observed.

Clinical Trial Registration (Please input N/A if not registered)

N/A
Antifungal drug susceptibility is not well known in neonatal and paediatric candidaemia. Age-dependent differences from adults may exist in young patients with candidaemia. Standardized data throughout Europe focusing on antifungal drug susceptibility of Candida spp. isolated from neonatal and paediatric candidaemia cases was collected and analysed.

Methods

We conducted a retrospective European study over the period 2005-2015. All first positive blood cultures (BC) collected from patients <18yrs of age growing any Candida species were entered into the EUROCANDY REDCap database. Species and antifungal drug susceptibility data were recorded as well. Associated demographic and clinical data were collected.

Results

833 BC with Candida species were reported by 17 hospitals in 8 European countries. Candida albicans grew in 53.2%, Candida parapsilosis in 30.1%, and other species in 16.7% of BC. Overall antifungal susceptibility results showed that 91% (512/562) of all Candida isolates were susceptible to fluconazole and 91.5% (313/342) to caspofungin. Fluconazole resistance was reported in 3.2% (10/314) for C. albicans, 3.1% (6/191) for C. parapsilosis, 11.5% (3/26) for C. tropicalis, 16.7% (4/24) for C. glabrata and all 7 C. krusei isolates were non-susceptible. Caspofungin resistance was reported in 1.0% (2/194) for C. albicans, 3.7% (4/107) for C. parapsilosis, 5.6% (1/18) for C. tropicalis, 0% (0/17) for C. glabrata and 16.7% (1/6) for C. krusei isolates. Between 2005-2010 and 2011-2015, no significant changes in antifungal resistance were observed.

Conclusions

This large-scale data of antifungal resistance among neonatal and paediatric Candida isolates causing bloodstream infections shows a low incidence of fluconazole and echinocandin resistance among C. albicans and C. parapsilosis isolates. These results may help creating evidence-based paediatric guidelines and antifungal stewardship.
Although a proven and effective preventative health measure, childhood immunisation programs remain vulnerable to budgetary pressures. Financing immunisation programs presents a unique challenge in low and middle income economies as numerous vaccines added to the paediatric vaccination schedules come at a higher cost due to newer vaccine technology. Despite this, vaccine-preventable diseases continue to comprise a significant portion of morbidity and mortality. We aimed to review trends in immunization program investments in relation to vaccine coverage, vaccine access, and broader health indicators across emerging economies.

Methods

Immunisation data were obtained from the World Health Organisation (WHO) and expenditure data were obtained from the WHO UNICEF Joint Reporting Form and WHO Vaccine Product, Price and Procurement (VP3) Web Platform from 2006-2016. Using a de-novo weighted average index of vaccine commitment (WAIVC) - calculated based on vaccine coverage, individual vaccine scope, and average vaccine expenditure per income level - correlation analyses were performed between immunisation expenditure per-capita and each WAIVC, infant mortality and life expectancy.

Learning Points Discussion

Correlation analyses and case studies indicate an improvement in immunisation access, vaccination coverage, and scope of available vaccines in countries with sustained increases in vaccination funding (Figure 1). Furthermore, increases in national immunisation expenditure were also correlated with reduced infant mortality and increased life expectancy. Vaccine expenditure comprises a small proportion (less than 2%) of total healthcare spending, yet has not increased in all markets in accordance with the scope of available vaccines.

Our analysis supports the premise that countries with consistent increases in vaccine expenditure have increased vaccine coverage and improved outcomes such as infant mortality and life expectancy, indicating the value of sustained investment in vaccination for improved health outcomes.
Figure 1: The evolution of vaccine commitment in relation to per 1000 capita government expenditures on vaccines in 2006-2016

*Note: Individual correlations between vaccine commitment and per 1000 capita government expenditures on vaccines are shown in square brackets.*
Title of Case(s)
Congenital Zika Syndrome: Beyond microcephaly

Background
To describe other malformations in a group of infants with microcephaly, probably caused by Zika virus in a reference center in Rio de Janeiro, Brazil.

Case Presentation Summary

Methods:
Infants were recruited between December 2015 and March 2017 in a pediatric infectious disease clinic in Rio de Janeiro in this descriptive study. Infants were referred to this study, if they were born with microcephaly in Rio de Janeiro. Exclusion criteria included detection of an alternative cause for the patient's presentation. All children were tested for toxoplasmosis, cytomegalovirus, rubella, dengue, syphilis, and HIV. They had consultation with genetics, ophthalmology, and were submitted to BERA, echocardiogram, and abdominal sonogram, as well as a central nervous system (CNS) radiology exam (sonogram, CT scan, or magnetic resonance).

Results:
22 infants were evaluated. At birth, Zika virus PCR were performed on blood/CSF/urine from 13/22 newborns and they were all negative. Their cephalic perimeter were 22-32 cm, All, but two presented abnormal CNS radiology exams (calcifications and ventriculomegaly). Seven presented ophthalmology alterations (coloboma and macular hypopigmentation), 9 presented cardiac malformations (7 with patent foramen ovale and 2 with persistent arterial duct), 2 with BERA abnormal exam, 2 with congenital clubbing, and 1 with bilateral cryptorchidism.

Learning Points/Discussion
Although CNS malformations were common, the infants with possible congenital Zika syndrome must be investigated for other malformations. These infants need a multidisciplinary follow up.
INTEGRATED PATHOGEN LOAD AND DUAL TRANSCRIPTOME ANALYSIS OF SYSTEMIC HOST-PATHOGEN INTERACTIONS IN SEVERE MALARIA

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Background

The pathogenesis of infectious diseases depends on the interaction of host and pathogen. In *Plasmodium falciparum* malaria, host and parasite processes can be assessed by dual RNA-sequencing of blood. Here we integrate dual transcriptome analyses with estimates of parasite load and clinical information from Gambian children to reveal mechanisms driving the systemic pathophysiology of severe malaria.

Methods

We performed dual-RNA sequencing on whole blood of 46 Gambian children with *P. falciparum* uncomplicated (*n* = 21) and severe malaria (*n* = 25). We accounted for heterogeneity of leukocyte and parasite developmental stage mixtures using gene signature-based deconvolution. We related gene expression to clinical phenotype, parasite load and additional clinical and laboratory markers of malaria severity. We used weighted gene co-expression networks to assess interactions between host and parasite.

Results

We report hundreds of human and parasite genes differentially expressed between severe and uncomplicated malaria, with distinct profiles associated with coma, hyperlactatemia and thrombocytopenia. High expression of neutrophil granule-related genes was consistently associated with all severe malaria phenotypes. We observed previously uncharacterized, severity-associated variation in expression of parasite genes which determine cytoadhesion and rigidity of infected erythrocytes and parasite growth rate. Up to 99% of human differential expression was driven by differences in parasite load, whilst parasite gene expression showed little association with parasite load. Co-expression analyses revealed interactions between species, with prominent co-regulation of translation genes in severe malaria hinting at a molecular arms race between host and parasite.

Conclusions

Our findings highlight the importance of considering both host and pathogen when interpreting the pathogenesis of infectious diseases. We implicate simultaneous contributions of host and parasite genes to human severe malaria pathogenesis, identifying potential new targets for adjunctive therapy.
Clinical Trial Registration (Please input N/A if not registered)

N/A
COMPARISON OF VARIOUS GROUP B STREPTOCOCCAL STRAINS IN AN
OPSONOPHAGOCYTIC ASSAY

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Background

Group B Streptococcus (GBS) remains a major cause of bacterial meningitis and septicemia in infants. Protection against GBS involves antibody-mediated opsonization by phagocytes and the complement system. Therefore, the opsonophagocytic assay (OPA) has been used to evaluate immune responses to GBS vaccines. Of vital importance to OPA outcomes is the choice of target strain used in the assay. Here, we used different GBS strains to investigate their effects on OPA results.

Methods

Twelve GBS strains with four serotypes (Ia, Ib, III, and V), isolated from patients or purchased from the ATCC, were incorporated into the OPA using HL-60 cells (UAB GBS OPA, at http://www.vaccine.uab.edu). Following preparation of target strains (production of assay stock, determination of the dilution factor for each aliquot, and evaluation of viability after freezing), the opsonic indices (OIs) against each strain were determined with a quality control sera panel (MFDS-Ewha GBS QC).

Results

Twelve GBS strains met the suitability criteria as target strains in the OPA. These criteria included: acceptable morphology, sufficient colonies to allow counting using a semi automated counting procedure, and compatibility with baby rabbit complement. The differences of OIs between the lowest and highest values for each serotype ranged from 1 to 9 fold (2 dilutions). However, opsonic index differences were serum dependent. Each strain produced consistent intrastrain OIs with QC sera (2, 3,
Conclusions

These results provide additional evidence of the robustness of UAB GBS OPA using HL-60 cells. This assay will be useful for assessing the immunogenicity of GBS vaccine candidates under development as well as for establishing correlates of protection.

Clinical Trial Registration (Please input N/A if not registered)
ROTAVIRUS SHEDDING DENSITY IN MALAWIAN CHILDREN WITH ACUTE GASTROENTERITIS IS RELATED TO DISEASE SEVERITY

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Background

In low-income countries (LIC) where rotavirus vaccine effectiveness (VE) is reduced, any additional effect of vaccination on rotavirus transmission may contribute to population level impact (herd protection). Rotavirus vaccine provides incremental protection against severe disease, and disease severity is correlated with viral shedding density in some settings. Rotavirus vaccination therefore has potential to reduce virus transmission through reduction in disease severity, but to-date there are no data corroborating this from LIC. We investigated shedding dynamics and predictive factors for rotavirus shedding in Malawian children with rotavirus gastroenteritis (RVGE).

Methods

Children presenting to healthcare facilities in Blantyre, Malawi with RVGE were recruited. All children had two stool samples collected at 3 and 5 days after symptom onset (primary cohort). A subset of 20 children had 10 samples collected over 28 days (nested cohort). Disease severity was estimated using the Vesikari score. Stool samples were analysed for rotavirus load using semi-quantitative real-time RT-PCR. Change in viral load over time was investigated using linear mixed models. Predictive factors for viral shedding density were identified using multivariable linear regression.

Results

374 samples were collected from 196 children for the primary cohort and 178 for the nested cohort. Viral load declined significantly over time (regression coefficient -1.60[95% CI -2.44, 0.74]). A positive association was identified between viral load and Vesikari score, and a negative association between viral load and weight-for-height Z score (regression coefficients 0.17[95% CI 0.04, 0.31] and -0.26[95% CI -0.46, -0.02] respectively.

Conclusions

Viral shedding density is positively associated with disease severity in Malawian children with RVGE. This suggests that reducing disease severity, e.g. through vaccination, could reduce viral shedding density and therefore rotavirus transmission. This may be particularly important in settings where VE is low.

Clinical Trial Registration (Please input N/A if not registered)

N/A
LONG-TERM FATIGUE AND HUMAN PAPILLOMAVIRUS VACCINATION

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Background

After publication of reports of long-lasting fatigue following bivalent HPV (2vHPV) vaccination in 2015, concerns about the safety of 2vHPV was picked up by Dutch national media. This led to more reports concerning adverse events following immunization with 2vHPV, especially of long-lasting fatigue. We studied a possible association between 2vHPV and long-term fatigue.

Methods

Girls born in 1991-2000 with chronic fatigue syndrome (CFS), fatigue ≥6 months and 3-6 months within the years 2007-2008 (pre-vaccination era) and 2009-2014 (post-vaccination era) were selected from a GP-database. Patients with fatigue ≥6 months were asked for consent to link their primary care information with vaccination data. Among vaccinated cases, a self-controlled case series (SCCS) analysis was performed.

Results

Differences between pre- and post-vaccination incidences (CFS: 3.6 (95%CI 0.5-25.7)/10,000py and 0.9 (0.4-2.1)/10,000py; fatigue ≥6m: 7.3 (1.8-29.0) and 19.4 (16.1-23.4); fatigue 3-6m: 0.0 and 16.6 (13.6-20.3), respectively) were not statistically significant. SCCS analyses resulted in a crude relative risk (RR) of 0.51 (95%CI 0.11-2.41) and 0.62 (95%CI 0.07-5.49) after adjustment for age.

Conclusions

Fatigue ≥6m and 3-6m was frequently found in the GP database among adolescent girls with low incidences of diagnosed CFS. No statistically significant increased incidences were found in cohorts eligible for HPV vaccination in the post-vaccination period versus similar age-groups in the pre-vaccination period. SCCS analysis included low number of cases, but revealed no elevated risk on fatigue ≥6m in the high-risk period of 12 months following each dose. Communication of these results to girls and their parents might reduce the effect of negative media attention about the HPV-vaccine.
Pneumococcal conjugate vaccine introduction has resulted in a dramatic reduction in most vaccine serotypes (VTs) as a cause of invasive pneumococcal disease (IPD). However, these decreases have been offset to varying degrees in different countries by an increase in replacement serotypes, primarily non-vaccine serotypes (NVTs). We assessed the trends of serotype replacement IPD in <5-year-olds in countries following the introduction of PCVs.

Methods

IPD datasets for children <5 years old before and after PHiD-CV/PCV13 introduction were identified by literature search and from publicly available surveillance reports in January 2018. Datasets were limited to countries with robust epidemiologic surveillance (n=6). Case numbers before and after PHiD-CV/PCV13 introduction were converted to % change relative to the PHiD-CV/PCV13 introduction year for each country. The average % change over all 6 countries was calculated per year pre/post-introduction.

Learning Points Discussion

Our analysis revealed:

- Sufficient data was available to analyse replacement disease trends for 16 NVTs and 1 VT displayed a lack of vaccine effectiveness.
- After PHiD-CV/PCV13 introduction, 4 of these serotypes (3, 15C, 35F and 38) stabilized, 2 serotypes (10A, 22F) trended downwards, while the remaining 5 serotypes (11A, 15A, 23A, 23B, 33F) continued to trend upwards.
- For the remaining serotypes, a modest reduction in serotype 6C, no change in serotype 8, and trends for increases in disease due to serotypes 9N, 12F and 35B was observed following PHiD-CV/PCV13 introduction.
Substantial variability in serotype replacement is seen in different countries. Ongoing surveillance will be necessary to monitor the future impact of these serotypes.

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FEASIBILITY OF HOME-BASED HIV COUNSELING AND TESTING IN SCALING UP PMTCT AMONG WOMEN DELIVERING AT HOME IN GEITA DISTRICTS COUNCIL, TANZANIA

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Background

Prevention of mother-to-child transmission of HIV reduced pediatric HIV infection. Pregnant woman to be enrolled in the program has to attend Antenatal Clinics, or tested at the health facilities when going for delivery. 49% of women in Tanzania do not deliver at health facilities, this increases chances of Mother to Child HIV Transmission. The study objective was to determine the feasibility of home-based HIV testing (HBHCT) and linking to care for HIV services among women delivering at home (WDH) in Geita district council, Tanzania.

Methods

A longitudinal household survey was conducted in Geita district council in Geita region, Tanzania. We used embedded mixed method to answer study objective. The study involved all mentally-able women who delivered within two years preceding the survey and their children under the age of two.

Results

Most study participants (879; 88.5%) had ever tested for HIV; with the majority (79.7%) having been tested during an ANC visit. Only 12 women (98.8%) did not accept HBHCT. Among the 980 participants who accepted HBCT, 52 (5.3%) [95% CI: 2.1 - 12.8%] tested HIV-positive, half were newly identified during the HBHCT. Among the 52 HIV-positive women, 21 (40.4%) were enrolled in PMTCT services, 26 of whom already knew their positive HIV status before the study. All the thirteen (13) HIV-positive women who delivered at a health facility were enrolled in PMTCT services, contrary to their 13 WDH counterparts where only eight were enrolled in PMTCT services.

Conclusions

HBHCT was acceptable among the women and uptake was high. HBHCT detected new HIV infection as well as seroconversion among women with previously negative HIV tests. HBHCT can be used as an intervention to improve PMTCT services among WDH.
BACKGROUND

Human papillomavirus (HPV) vaccination was introduced to 12-year girls in 2009 with an initial uptake of more than 90%. From 2013, the programme was challenged with case-stories of suspected adverse events reported in the media resulting in public concerns about vaccine safety and a decline in uptake. Reported adverse events peaked in 2015 coinciding with the broadcasting of a television documentary “The vaccinated girls” in March 2015 describing a group of girls reporting disabling symptoms following HPV vaccination.

METHODS

Number of first dose HPV vaccinations reported to The Danish Vaccination Register, per month and calendar-year were calculated. Due to seasonal variation a rolling 6 months average of the particular month and five previous months was calculated.

RESULTS
A large and sustained fall in HPV initiation followed the television documentary, figure. However, in 2017, 30,974 girls initiated the HPV vaccination programme compared with 15,237 girls the previous year. The number in 2017 was only exceeded back in 2012 with 31,794 vaccinated girls. For birth-cohort 2003, which was due for vaccination in 2015, the first dose vaccination coverage has increased from 27% in April 2016 to 68% in February 2018.

Conclusions

The renewed trust in the HPV vaccination programme may be attributed to several factors. First, several recent scientific studies have underpinned the vaccine’s effect and safety. Second, a joint campaign called “Stop HPV” supported by several health authorities and scientific societies was launched in 2017. The campaign engaged doubting parents through the social media and re-focused the attention to the fundamental objective of HPV vaccination: preventing cervical cancer. In order to catch-up with low activity in especially 2015 og 2016 even higher HPV vaccination initiation rates than those presently observed are needed.

Clinical Trial Registration (Please input N/A if not registered)

N/A
TRENDS IN HOSPITALIZATION RATES OF INFANT PERTUSSIS IN DENMARK DURING 2007-2017. IS THERE A NEED FOR INCREASED CONTROL OF INFANT PERTUSSIS?

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Background

Since 1997, the Danish childhood vaccination program has comprised of three doses of an acellular pertussis-containing vaccine (mono-component pertussis toxoid from SSI) recommended at 3, 5 and 12 months of age. In 2004, a 5-year booster was added.

Despite good population control, infant pertussis still poses a challenge since acceptable protection is not achieved until after the first two vaccinations.

Methods

In children below two years, laboratory-confirmed pertussis is notifiable, detailing possible hospital admission.

Hospitalization data was retrieved from the notification registry and stratified by months of age and in the intervals 0-5 months and 6-11 months. Age-specific population data was retrieved from Statistics Denmark. To calculate incidences in infants 0-5 and 6-11 months half the birth cohort was used. To calculate age by month-specific incidences one twelfth of the birth cohort was used.

Results

For 0-5 month-olds, hospitalization rates remained stable in 2007-2011 averaging 142/100,000. In 2012-2017, an increase was observed to an average of 219/100,000 with peak incidences in 2012 (280/100,000) and 2016 (324/100,000).

The highest hospitalization rates were in 2-month-olds averaging 216/100,000 in 2007-2011, increasing to 634/100,000 in 2016 but decreasing again to 158/100,000 in 2017.

In 6-11 month-olds a similar trend was observed, but with much lower hospitalization rates averaging 16/100,000 in 2007-2011, increasing to 48/100,000 in 2016.
Conclusions

Increased hospitalization rates were observed in the latter half of the study period, most markedly for 2-month-olds. The 2016-epidemic saw a doubling of cases in the whole population as well as in infants compared to 2015. This highlights the need for interventions that will decrease the risk of pertussis in infants, e.g. by ensuring timely vaccination, advancing the age of the first vaccination and/or by introducing pertussis vaccination in pregnancy.
Background

A nationwide enterovirus 71 (EV71) epidemic occurred in Taiwan in 1998, which caused 405 severe cases and 78 deaths. Thereafter, nationwide epidemics occurred again in 2000–2001, 2005, 2008, and 2012. To understand current EV71 serostatus, to predict future epidemic and to set up future EV71 vaccine policy, we performed EV71 seroepidemiology in Taiwan in 2017.

Methods

After informed consent was obtained, we enrolled preschool children, 6–15-year-old students as well as women of childbearing age and adult males. They received questionnaire investigation and blood sampling for measuring EV71 neutralization antibody.

Results

Totally, 920 subjects were enrolled with a male-to-female ratio of 1.03. EV71 seropositive rate was 10% (8/82) in infants, 4% (6/153) in 1-year-old children, 8% (7/83) in 2-year-old children, 8% (13/156) in 3–5-year-old children; 31% (38/122) in 6–11-year-old primary school students and 45% (54/121) in 12–15-year-old high school students, 80% (97/122) in 16–49-year-old women of childbearing age and 68% (55/81) adult male in 2017. Risk factors associated with EV71 seropositivity in preschool children were gender, having siblings, classmates with herpangina (HA) or hand-foot-and-mouth disease (HFMD) and contact with HA or HFMD whereas the factor associated with EV71 seropositivity in adults was having children other than age. Compared with the rates in 1997, 1999 and 2007, the rates in children were significantly lower in 2017.

Conclusions

EV71 seropositive rates were very low, 4% to 10%, in preschool children, and not high, 31%, in primary school students. Preschool children will be the first priority to receive EV71 vaccine.

Clinical Trial Registration (Please input N/A if not registered)

N/A
Risk of Herpes Zoster in Children: What Happens When You Are Not Varicella Vaccinated?

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Background

Objectives

To estimate the risk of herpes zoster (HZ) in varicella vaccinated and unvaccinated children and to assess the association between the risk of HZ and the age at the first varicella event.

Methods

Retrospective cohort study using the health databases of the Valencia Region. Statistics: survival analysis to estimate the cumulative risk of HZ between 0 and 7 years of age was developed. Stratification by children with the first varicella event during the first, second and ≥ 2 years of age was considered. To estimate the risk of HZ in vaccinees, a Bayesian model of Poisson regression adjusted by sex, age, year and health department was developed.

Results

187,434 children were susceptible (vaccinated or with a history of varicella) to develop HZ, 36,916 had a varicella event without previous vaccination, 13%, 20% and 67% during the first, second and ≥ 2 years, respectively. The cumulative risk of HZ between 0 and 7 years was 8.6% (95% CI: 7.2-10) in children with previous varicella event during the first, 4.4% (95% CI: 3.2-5) second and 1.2% (95% CI: 3.2-5) ≥ 2 years of age.

Risk of developing HZ was greater in children who had varicella in the first year of life compared to children with varicella event during the second (approximately 2.6 times) and ≥ 2 years (8 times) of life.

Risk of HZ in one dose-vaccinated children was 85% (95% CI: 82-87) lower than unvaccinated children and 92% (95% CI: 89-94) lower in children fully vaccinated against varicella.

Conclusions

Risk of developing HZ in children is associated with the age of the first varicella event. Children vaccinated against varicella have a 92% lower risk of HZ.
Background

Background: Chikungunya is a tropical arthropod borne viral disease. Chikungunya virus can be transmitted vertically from mother to child during perinatal period when the mother is highly viremic. A major outbreak occurred in India in 2016 affecting around 12000 people in the capital city of New Delhi alone. Objective was to study the clinical presentation and biochemical parameters in babies with neonatal Chikungunya.

Case Presentation Summary

Results: A total of 15 cases of Neonatal chikungunya were diagnosed from September to November 2016 of whom vertical transmission were observed in 14 neonates. Mean age at presentation was 92.7 hours with irritability (85.7%), fever (78.5%), encephalopathy (80%), respiratory difficulties, seizures (60%) and circulatory compromise (60%). Eighty five % developed the classical centro-facial hyper pigmentation (Fig) during the second week. Fever and arthralgia in peripartum period was observed in 80% and 60 % mothers respectively. Laboratory parameters showed thrombocytopenia (93%), hypoalbuminemia (80%) and transaminitis (60%). In all 14 neonates and their mothers, serum Ig M was positive. RT PCR from serum sample could be done in only 10 neonates with all showing a positive result. Abnormalities in Ultrasound skull was observed in 4 and in MRI brain in 2 neonates. All were treated symptomatically with requirement of respiratory support in 53%, inotropes in 40% and platelet transfusion 30 %. Mean duration of hospital stay was 12.5 days. One neonate died due to...
multi-organ dysfunction.

Learning Points/Discussion

Conclusion: Chikungunya should be considered in differential diagnosis of neonates who present with fever, rash and unexplained encephalopathy especially in the setting of maternal history of fever and arthralgia in peripartum period. In view of abnormalities seen in neuroimaging these patients will require long term follow up.
HIGH RATE OF PRIMARY RESISTANCE IN ANTIRETROVIRAL NAIVE HIV-1 INFECTED CHILDREN

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Background

Antiretroviral therapy (ARV) has reduced morbidity and mortality of the HIV infection. However, the widespread use of ARV can also increase the rate of transmitted drug resistance (TDR), leading to therapeutic failure. Since 2014, the Brazilian HIV-Aids program offers detection of HIV drug resistance for ARV-naïve children. We aim to describe the cases of TDR in vertically infected children from 2000 to 2017 in our hospital.

Methods

We reviewed the medical records of all children and adolescents living with HIV-Aids treated in a tertiary hospital in São Paulo, Brazil, looking for TDR. We collected demographic data, information related to HIV transmission and diagnosis (maternal use of ARV during pregnancy, perinatal care, breastfeeding, postpartum ARV and symptoms) and description of HIV subtype and mutations related to drug resistance.

Results

We found 56 patients (female n=29, median age at diagnosis 20 months) with vertically transmitted HIV. Eleven had screening for mutations prior to treatment and six had TDR (54.5%). Half of the patients with TDR were exposed to ARV during pregnancy, perinatal and postpartum, while the other three were never exposed to ARV prior to treatment due to late diagnosis. All but one patient presented resistance not related to maternal or neonatal use of the specific ARV class, denoting primary resistance. One child needed to change ARV due to resistance.

Conclusions

We found an impressively high rate of TDR (54.5%) in our hospital, being 83% primary resistance. Other Brazilian study in children showed 13% of TDR from 2000 to 2011 but an increase of resistance in the last three years of the study (50%, 4/8 patients from 2008 to 2011). These results reinforce the need to genotyping all children prior to treatment.
Background

Since 2014, a biennial pattern of rotavirus epidemics has emerged in the Netherlands (NL). A previous study suggested this changing epidemiology cannot be fully explained by a declining birth rate and relatively mild winters. This study investigated whether additional factors can explain the observed pattern, including the type of circulating strains and possible herd effects from the introduction of universal rotavirus vaccination (URV) in neighbouring countries. Similar data from Denmark were used to validate the findings.

Methods

Weekly rotavirus detections were obtained from national sentinel laboratory surveillance for NL (from 2001-2016 week 26) and Denmark (from 2010-2016 week 26), two countries without URV. Circulating genotypes were obtained via EuroRotaNet and were defined as the relative contribution of five common rotavirus strains in each year and country. We used separate time series negative binomial regression models for NL and Denmark to model the association between weekly rotavirus detections and a set of explanatory variables including mean daily temperature, annual population size <2 years and strain prevalence. For both countries, URV introduction in a neighbouring country was included as time-varying binary variable. We corrected for first-order serial autocorrelation, seasonality and natural trends. Models were optimized by allowing time-lags and non-linear associations.

Results

In both models, temperature, population size and strain prevalence were all significantly associated with rotavirus detections. Adding URV introduction in Belgium to the NL model did not improve model fit, whereas URV introduction in Western-Germany had a statistically significant effect (IRR 0.72; 95% CI 0.59-0.86). Similarly, Western-Germany URV introduction had a statistically significant effect on rotavirus detections in Denmark (IRR 0.67; 95% CI 0.60-0.76).

Conclusions

Besides the established driving factors of rotavirus epidemiology, circulating rotavirus genotypes and URV introduction in adjacent geographic regions may influence epidemic patterns.
Background

Two-dose varicella vaccination in Italy became mandatory in 2017 at 12-15 months and 5-6 years of age. Varicella vaccines are available in monovalent and quadrivalent (combined with Measles-Mumps-Rubella) formulations. While quadrivalent forms are hypothesized to lead to higher coverage levels, an elevated risk of febrile seizures when used as the first-dose of measles-containing vaccines has been reported. We estimate long-term costs and benefits of five vaccination strategies in Italy, to facilitate discussions among health policy makers about which vaccine brands and formulations will provide the optimal vaccination strategy.

Methods

A previously published varicella dynamic transmission model was utilized to compare strategies. In addition to assessing a no vaccination (NV) strategy, monovalent (80.8% coverage)-quadrivalent (83% coverage) and quadrivalent (85% coverage)-quadrivalent (83% coverage) vaccination, considering vaccines made by two different manufacturers (MSD and GSK) were analyzed. The model was parameterized with cost and epidemiology data from Italy collected from public health sources, peer-reviewed publications and expert clinical opinion.

Results

Over a 50-year time-horizon, the NV strategy resulted in the greatest burden of illness, with 34.8m cases and 142 deaths. The two-dose quadrivalent-quadrivalent vaccine strategy using MSD vaccines resulted in the lowest burden, 12.0m cases and 99 deaths. This strategy also resulted in the lowest total discounted medical costs over the 50-year time-horizon of €6.8bn, with the highest being €17bn.
Conclusions

Varicella transmission models can be used to support policy decision making when long-term costs and outcomes need to be accounted for. Improved outcomes with the quadrivalent-quadrivalent strategy were driven by the higher vaccine coverage, and the cost benefits by the lower vaccine price. The estimated reduction in hospitalizations across all vaccination strategies was able to offset the additional cost of the vaccines.

Figure: Total and Breakthrough Varicella Incidence 50 years after the start of universal varicella vaccination, by vaccination strategy.
Background

A bivalent HPV vaccine (HPV2; Cervarix, GlaxoSmithKline) was introduced into the Finnish National vaccination programme (NVP) in November 2013 for girls aged 11-13 years and catch-up 14-15 years. We evaluated the association between HPV2 and selected autoimmune diseases/clinical syndromes by conducting a nation-wide retrospective register-based cohort study.

Methods

First diagnoses of the relevant ICD-10 codes in girls aged 11-15 years between Nov-2013 to Dec-2016 were obtained from the hospital discharge register. Population denominators were obtained from the Population Information System and vaccination records from the National Vaccination Register. Registers were linked using unique personal identity codes. Association between HPV2 and 38 selected outcomes were studied using Cox regression, with age as the main time-scale and the first vaccination dose as time-dependent exposure. The hazard ratios (HR) were assessed according to the time since exposure (entire follow-up, 0-180/181-365/>365 days).

Results

Of 240 605 girls eligible for NVP vaccination with HPV2, 134 615 (56%) were vaccinated. After adjustment for hospital district, country of origin (Finnish-born/not) and number of hospital contacts between 9-11 years of age, HRs ranged from 0.34 (95%CI 0.11-1.05) to 8.37 (95%CI 0.85-82.54) for the entire follow-up (Figure 1). The risk was not significantly higher after the vaccination for any
Conclusions

This study found no increased risk for the selected outcomes after the HPV vaccination in girls 11-15 years of age. These results provide valid evidence to counterbalance public scepticism, fears of adverse events and possible opposition to HPV vaccination and consequently can contribute to increase HPV vaccination coverage in Finland as well as elsewhere.

Clinical Trial Registration (Please input N/A if not registered)
N/A
In developing countries neonatal sepsis is responsible for 30-50% of deaths. Most studies on 'risk factor based approach' for treatment of EONS are from developed countries where GBS is the predominant pathogen causing EONS. Very few studies have evaluated perinatal risk factors for EONS in LMIC, where Gram negative organisms predominate with Klebsiella spp. being the commonest.

Methods

Prospective study over 22 months enrolled 1120 preterm infants of 26-34 weeks gestation. At enrolment demographic and clinical data related to 25 putative risk factors for EONS was recorded in first 1020 infants. These were analyzed through univariate followed by multivariate logistic regression and a risk score was developed. Predicted rate of culture proven EONS was compared with the observed rate. The model was applied to subsequent 100 preterm infants with similar baseline characteristics and its predictive accuracy was evaluated.

Results

Out of 23934 infants delivered, 4250 were preterm with 1120 eligible infants. Logistic regression identified 5 risk factors with maximum cumulative score of 9; viz. Birth weight <1500 gm (2), Requirement of respiratory support (1), Lack of Intrapartum antibiotic prophylaxis (1), Per vaginum examination >3 (3) and male sex (2). A cut-off score of 5 or more for starting antibiotic therapy had Sensitivity, specificity, positive and negative predictive values of 85%, 74%, 37%, and 97% respectively. AUC on ROC curve was 0.916. Good concordance was observed between the predicted and observed rate of culture proven EONS.

Conclusions

'Perinatal risk factor based clinical score' thus developed is a simple clinical score without any laboratory parameters which can be utilized for preventing unnecessary initiation of antibiotics in preterm infants with risk factors for EONS, at any level of health facility, with a reasonable level of precision.
How Predictive 2 Negative CRPs (<5) Are of Negative Blood Cultures in Suspected Neonatal Sepsis and Its Potential Role Shortening Hospital Stay for Well Newborns

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Background

In asymptomatic neonates being treated for suspected sepsis, NICE guidelines recommend having blood culture (BC) reports negative at 36-hours before ceasing antibiotics and permitting discharge. Many hospitals rely on 48-hour reports however. Research suggests most pathogenic BCs are positive within 24-hours. Unnecessarily prolonged hospital stays burden resources and families. We assessed the potential use of CRP readings to inform an earlier discharge in symptomatically well, BC-negative patients.

Methods

We identified 445 newborns suspected of neonatal sepsis, each of whom had had a blood culture (BC) sample and a CRP reading taken at birth. A second CRP was also measured 18-hours after the initial. Taking a positive culture as indicative of true sepsis, we then assessed statistically how predictive 2 ‘negative’ (<5) CRPs were of negative BCs, looking at sensitivity, specificity, negative-predictive-value (NPV) and positive-predictive-value (PPV).

Results

From our initial group of 445 patients we notably found the NPV of having 2 negative CRPs to be 0.979.15 cases of the 445 had a positive blood culture. 10 of these had at least 1 positive CRP. Despite the lower than expected resulting sensitivity of 0.666, of the 5 that did not have at least 1 positive CRP, 4 were likely contaminants and 1 clinically irrelevant. Additionally, of the cases with 2 positive CRPs, 9.3% were BC-positive (PPV=0.093). Also notably time to positivity of all positive cultures was below 24-hours.

Conclusions

Given the high NPV, we have shown that a lack of a positive CRP at both 0 and 18 hours is strongly indicative of the absence of true sepsis (NPP). This strengthens the case for its deeper incorporation into the algorithm determining time to discharge in falsely suspected neonatal sepsis.
Procalcitonin, C-Reactive Protein, Resistin, Neutrophil Gelatinase-Associated Lipocalin and APTT Waverform for Diagnosis of Serious Bacterial Infection and Prediction of Outcome in Critically Ill Children.

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Background

The aim of this study was to investigate the utility of biomarkers for the diagnosis of serious bacterial infection (SBI) in children on admission to a Paediatric Intensive Care Unit (PICU) and their use as prognostic indicators.

Methods

A prospective cohort study of consecutive admissions to a PICU was conducted from October 2010 to June 2012. Blood samples were collected daily for measurement of Procalcitonin (PCT), Neutrophil gelatinase-associated lipocalin (NGAL), resistin and Activated Partial Thromboplastin Time (APTT) waveform. The primary outcome was diagnosis of SBI at admission based on clinical and microbiological criteria. Secondary outcome measures included prolonged PICU stay, defined as greater than or equal to the median duration for the cohort.

Results

657 patients were included in the study. 92 patients (14%) fulfilled criteria for SBI. Mortality at 28 days was 2.6% (17/657). PCT and CRP in combination were superior for diagnosis of SBI (AUROC 92.7, 95% CI 88.5-96.9). Using net reclassification improvement, PCT and CRP resulted in a 28% loss in sensitivity (p<0.005) but an 89% improvement in specificity (p=0.03) compared to CRP alone, providing an overall 61% improvement. Median duration of PICU stay was 3.3 days. Using stepwise logistic regression analysis, the following variables were included in the model for prolonged ICU stay: unplanned emergency admission (OR 5.6), unplanned emergency admission (OR 5.6), unplanned surgical admissions (OR 8.3), inotrope score in 1st 12 hours (OR 1.04), age (OR 0.91), long term antibiotics (OR 4.9), PELOD (1.02), platelet count (OR 1), lactate (OR 1.3) and prior antibiotics therapy (OR 0.53).
Conclusions

Combinations of biomarkers, including PCT, improve accurate and timely identification of SBI on admission to PICU and are useful prognostic indicators.

Clinical Trial Registration (Please input N/A if not registered)
HUMAN AND RABBIT ANTIBODIES AGAINST IMMUNODOMINANT B-CELL EPITOPES OF SURFACE PNEUMOCOCCAL PROTEINS REDUCE ADHERENCE TO HUMAN ALVEOLAR EPITHELIAL CELLS (SUPPORTED BY ESPID SMALL GRANT AWARD)

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Background

Streptococcus pneumoniae adherence to human epithelial cells is the first step leading to pneumococcal disease. Recent studies have highlighted a multifunctional role of antibodies against pneumococcal proteins from the opsonophagocytosis to the pathogenic process of adherence. In this study, we aimed to determine the role of human and rabbit antibodies against immunodominant B-cell epitopes within surface pneumococcal proteins in preventing adherence to human alveolar cells.

Methods

Specific antibodies against previously selected immunodominant B-cell epitopes, CbpD-pep[aa291-310], PhtD-pep[aa200-219], PhtE-pep[aa79-98] and ZmpB-pep[aa431-450], purified from sera of children with invasive pneumococcal disease and of preimmunized rabbits, were evaluated for their ability to inhibit pneumococcal adherence to confluent adenocarcinomic human alveolar basal epithelial cells (A549) monolayers (measured as percent reduction in CFU counts compared to those of uninhibited controls). Specific IgG anti-peptide antibodies titers were assessed by ELISA.

Results

Mean % inhibition of serotype 19A adherence to A549 cells was 78.2%(p=0.0035), 84.2%(p=0.0018), 79.8%(p=0.0083) and 74.6%(p=0.109) by human antibodies anti-CbpDs, anti-PhtDs, anti-PhtEs and anti-ZmpBs respectively. Similarly, mean % inhibition of serotype 3 adherence to A549 cells was 89.5%(p<0.0001), 82.9%(p<0.0001), 92.2%(p<0.0001) and 78.9%(p=0.0018) by human anti-CbpDs, anti-PhtDs, anti-PhtEs and anti-ZmpBs respectively. Specific anti-peptide antibodies obtained from preimmunized rabbit sera inhibited bacterial adherence to A549 cells;anti-CbpDs at 80%, anti-PhtDs at 76.7%, anti-PhtEs at 90% and anti-ZmpBs at 96.7%. No significant correlation was found between percent of inhibition and antibody titers assessed by ELISA.

Conclusions

In this study, we demonstrated the inhibitory effect of both human and rabbit anti-peptide antibodies, on pneumococcal adherence to alveolar epithelial cells. Such data support a role of the selected epitopes, other than induction of opsonophagocytosis, on prevention of colonization through blocking pneumococcal adherence to human epithelial cells and enhance their potential as vaccine antigens.
ALTERATIONS IN CELLULAR MICROPARTICLE LEVELS AS A MARKER OF CELLULAR ACTIVATION AND INJURY IN CHILDREN WITH HIV INFECTION

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Background

HIV patients are at an increased risk of cardiovascular disease driven by chronic inflammation. This study was to assess how microparticles, as indices of cellular activation and injury caused by inflammation, differ after treatment with antiretroviral therapy (ART) in children with HIV.

Methods

The plasma samples of 36 children (median age 6.9 years, range 4.5-12.2 years) from the CHAPAS 3 cardiovascular sub-study were analysed. These included; 12 children with HIV on ART, 12 treatment naïve children and 12 sex- and age matched healthy controls. Microparticles, characterised by annexin-V expression, were analysed by flow cytometry. Annexin-V binding with; CD3, CD4 and CD8, indicated T cell activation (TMP). CD14, CD42a and CD144 were quantified to assess monocyte (MMP), platelet (PMP) and endothelial cell (EMP) microparticles respectively.

Results

The overall MP number did not alter between the groups studied. Upon comparison, CD4 TMPs did not alter with HIV or with ART treatment, however, CD8 TMPs and EMPs were elevated in the treatment naïve group compared to the ART treated group and age matched controls. MMP number was elevated in both treatment naïve and ART treated groups compared to controls. However, PMP number was only elevated in treatment naïve groups compared to controls with no difference to ART treatment.

Conclusions

CD8 TMPs are elevated in treatment naïve children relative to ART-treated children and healthy controls. In a similar fashion EMPs, as a marker of vascular injury, are also increased in the treatment naïve cohort. However, MMPs indicating monocyte activity are consistently elevated in the ART treatment and treatment naïve groups compared to controls. Microparticle enumeration may be a useful way of monitoring response to treatment and providing novel avenues for reducing vascular injury.

Clinical Trial Registration (Please input N/A if not registered)

N/A
Dolutegravir-based anti-retroviral therapy is effective and safe in HIV-infected paediatric patients

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Background

Treatment of HIV infection in adolescents is challenging due to long duration of anti-retroviral treatment (ART), and poor adherence. Recently, the integrase strand transfer inhibitor dolutegravir (DTG) has been approved for the use in adolescents with HIV, but evidence in clinical practice is very limited.

Methods

We describe six cases of HIV-infected children/adolescents successfully treated with DTG-based regimen. Data relative to children/adolescents managed at the Referral Center for Pediatric HIV/AIDS of the University of Naples were reviewed. Patients were tested before introduction of DTG, after 1 month and every 3 months in the first 2 years to assess virologic and immunological response, tolerance and development of side effects. Families were asked to report any suspected adverse events.

Results

Six patients (age-range 12-18) were started on DTG-based anti-retroviral regimen due to low adherence to ART, drug resistance mutations, or ART-related side effects. Within 4-8 weeks after DTG treatment onset, a complete viral suppression and an increase of CD4+ cell count was observed. A persistent viral suppression was demonstrated after 2 years of follow-up in 4 patients after 1 year in 2 patients. After one month of treatment a complete normalization of severe dyslipidaemia and hyper-transaminasemia was demonstrated in one patient. During follow-up no adverse events were reported.

Conclusions

DTG-based treatments demonstrated efficacy and good safety profile in adolescents. All patients demonstrated a rapid virologic and immunological response within 4-8 weeks, with good adherence and absence of side effects.
Background: Delhi’s monumental victory over polio was result of improvisation and strategizing to reach each and every child in the state.

Methods

Method: In Delhi, unique polio program structure was shaped using legislative assembly, its population and polling booth as the planning unit for all polio related activity. For first time in country, three tier program management structure was created. Central Pulse Polio Cell overlooked functioning of 10 Zonal Coordinators (second tier) who individually controlled functioning of 5-9 assembly coordinators (third tier). Thus 70 Assembly Coordinators looked after the 70 assemblies. Polling booths were used as polio vaccination booths (currently nearly 7500). This novel structure remains broadly functional even today.

Delhi for first time in country introduced ‘House to House’ (HTH) activity for entire state in addition to booth vaccination strategy with objective of not missing even a single child. Team Movement Points (TMPs) [strategically identified health facilities having cold chain equipment for storing vaccine for booth /HTH activity] were created for first time in the State. TMPs acted as fulcrum for HTH macro-micro planning, manpower sourcing, training, supervision, , local publicity, vaccine /logistics management, reporting /documentation, managing adverse events and ensuring quality. Presently about 9400 teams (2 members each) visit approximately 46 lac household during each round through 352 TMPs. As an innovative measure, to avoid missing out eligible children / re-administration of drops, marking finger tip with 1% gentian violet of children who received polio drops was started by Delhi which was later on replicated at national level as one of the best practices.

Results

Delhi reported last polio case in 2009.

Conclusions

Well-planned macro/micro strategy and constant innovation is vital to public health program.
THE MENINGOCOCCAL SEROGROUP B VACCINE MENB-FHBP (BIVALENT RLP2086) IS SAFE AND IMMUNOGENIC IN HEALTHY TODDLERS AGED ≥12 TO <24 MONTHS


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Background

MenB-FHbp (bivalent rLP2086) is licensed in multiple countries at a 120-μg dose level to prevent serogroup B meningococcal (MenB) disease in adolescents and adults. This ongoing phase 2, observer-blinded, active-controlled, sentinel design study evaluated MenB-FHbp safety and immunogenicity in toddlers aged ≥12 to <24 months.

Methods

Subjects (N=396) were randomized in a 2:1 ratio to receive MenB-FHbp (60 or 120 μg; months 0, 2, 6) or hepatitis A virus (HAV) vaccine (months 0, 6) and saline (month 2). Primary outcomes describe immune responses to vaccination as measured by serum bactericidal assays with human complement (hSBAs) against 4 representative MenB test strains; the lower limits of quantification (LLOQ) thresholds (1:8 for 3 test strains; 1:16 for 1 strain) exceeded the accepted correlate of protection (≥1:4). Safety was also assessed.

Results

Proportions of participants achieving hSBA titers ≥LLOQ at either dose level after dose 3 ranged from 71.6% to 100.0% (Figure). Geometric mean titers rose similarly from 4.0–8.5 (baseline) to 15.1–171.4. Reactogenicity events were more common among MenB-FHbp recipients; 72.7%–79.5%, 62.3%–68.2%, and 38.6%–46.8% experienced injection site tenderness, redness, and swelling, respectively, compared with 31.1%, 21.2%, and 15.2% of controls. Reactogenicity events were mostly mild or moderate in severity and transient (median, 1–3 days). Fever occurred in 36.4%, 37.3%, and 15.2% of 60-μg, 120-μg, and HAV/saline recipients, respectively. Proportions of participants experiencing any adverse events (AEs), immediate AEs, serious AEs, medically-attended AEs, and newly diagnosed chronic medical conditions were similar across groups. Two MenB-FHbp recipients
Conclusions

MenB-FHbp induced robust immune responses and was safe and well tolerated in toddlers following a 0, 2, 6-month schedule at both 60- and 120-μg dose levels.

Clinical Trial Registration (Please input N/A if not registered)

ClinicalTrials.gov, NCT02534935. Funded by Pfizer.
Background

In infants and young children with congenital cytomegalovirus infection (cCMV), kidneys are sanctuary sites of replication and viral particles are secreted into urine in large quantities for years. In spite of this, cCMV does not associate renal disease. We analyzed the prevalence and severity of biochemical manifestations of glomerular and tubular renal dysfunction in patients with cCMV.

Methods

Cross-sectional study within the National Spanish Register of Congenital Cytomegalovirus Infection (REDICCMV; http://www.cmvcongenito.es). First-morning urine samples from patients with confirmed cCMV aged <5 years were analyzed for hematuria, beta-2-microglobulin levels (≤300 µg/mL), protein/creatinine (Pr/Cr; ≤200 mg/mg) and albumin/creatinine ratios (Alb/Cr; ≤30 mg/mg), and viruria (DNA-CMV copies/mL, expressed as log10) where available. Samples obtained under stressful conditions and those with bacteriuria or a positive culture were excluded. Clinical and epidemiological data were collected by means of the Redcap® software.

Results

One hundred and twenty-seven samples from 79 patients were included. Symptom-free elevated Pr/Cr, Alb/Cr and beta-2-microglobulin were observed in 63.0%, 37.8% and 8.3% of samples, respectively; hematuria was observed in 1.6% samples. Median viruria (n=69) was 3.9 log10 DNA-CMV copies/mL. Overall, 14.7%, 24.3%, 10.3% and 44.9% of patients were small for gestational age at birth, developed hypoaucussia, neurodevelopmental delay and received antivirals, respectively. The latter were not associated with proteinuria or albuminuria. Proteinuria positively correlated with albuminuria (r=0.36, p<0.0001) and also with viruria (r=0.16, p=0.049). Persistent proteinuria was observed in 16 out of 22 (72.7%) patients for whom follow-up urine samples were available.
Conclusions

We observed subclinical kidney damage manifesting with proteinuria and albuminuria in 63.0% and 37.8% of the samples, respectively; the former positively correlated with CMV viruria.

Clinical Trial Registration (Please input N/A if not registered)

N/A
THE IMMUNOGENICITY OF THE UK GROUP B MENINGOCOCCAL VACCINE (4CMenB) SCHEDULE AGAINST GROUP B AND NON-B MENINGOCOCCAL STRAINS

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Background

The first two doses of the 2, 4 and 12 month UK schedule of 4CMenB (Bexsero) are approximately 80% effective against group B meningococcal disease. However, the immunogenicity of this schedule is unknown.

Methods

Children enrolled into the ‘Sched 3’ study (randomising 1:1 to receive a 2+1 or 1+1 13-valent pneumococcal vaccine schedule) also received 4CMenB at 2, 4 and 12 months, with blood samples taken at 5 and 13 months. Proportions of participants with human complement Serum Bactericidal Antibody (hSBA) titres ≥4 were determined for MenB reference strains 5/99 (NadA), NZ98/254 (PorA) and 44/76-SL (fHbp), and titres ≥8 with rabbit complement (rSBA) for MenW. Geometric mean titers (GMT) with 95% CIs were also calculated.

Results

213 participants were enrolled. No significant difference in MenB immunogenicity was found between the different PCV13 groups.

The proportion of participants with hSBA ≥4 at 5 months ranged from 88.5% (NZ98/254) to 100% (5/99), and at 13 months from 88.6% to 100% respectively. GMT were not significantly higher post booster dose for NZ98/254 and 44/76-SL (fHbp), and titres ≥8 with rabbit complement (rSBA) for MenW. Geometric mean titers (GMT) with 95% CIs were also calculated.

Conclusions

These results provide the first direct evidence of SBA titres associated with effective protection by 4CMenB against group B meningococcal disease. At 13 months 44/76 hSBA titres were lower than historical data from a 2, 4, 6, and 12-month schedule, with titres post-boost no higher than post-primary immunisation. Understanding the significance of this requires surveillance for vaccine failures due to fHbp-matched strains.
The research was funded by the NIHR-PRP (NVEC, 039/0031). The views expressed are those of the author(s) and not necessarily those of the NHS, NIHR or Department of Health.

Clinical Trial Registration (Please input N/A if not registered)

NCT02482636
Background

Varicella is usually a mild and self-limited illness in children, but serious complications (including CNS involvement, secondary bacterial infections, and death) may arise resulting in significant healthcare resource utilization (HCRU). The objective of this study was to quantify and contrast HCRU associated with varicella in five countries where universal varicella vaccination has not been implemented.

Methods

Five primary data collection studies (Hungary, Poland, Argentina, Mexico, Peru) were conducted between 2014-2017 as part of MARVEL (Multi-country economic and epidemiologicAl buRden of VaricELlia study). Detailed data were obtained on management of primary varicella patients aged 1-14 years between 2009-2016. HCRU evaluated included outpatient visits, allied healthcare contacts, tests performed, prescription and over-the-counter (OTC) medications, and hospital/intensive care unit stays. These results were compared between countries.

Results

A total of 401 outpatients and 386 inpatients were included. Significant differences were observed in the number of skin lesions (a proxy for severity) among outpatients, ranging from 5.3% (Mexico) to 25.3% (Argentina) of patients with ≥250 lesions. Inpatients were more homogenous (37.3% with ≥250 lesions).

The average number of ambulatory medical visits ranged from 1.0 to 1.4. Average duration of hospital stay ranged from 3.7 (Hungary) to 6.8 days (Mexico, Peru). Use of tests/procedures was infrequent in outpatients with the exception of Argentina (13.3%); among inpatients, a test/procedure was ordered for 81.3% of patients, without regional differences. Prescription medications were administered in
44.4% of outpatients, ranging from 9.3% (Hungary) to 80% (Poland and Mexico), and in 86% of inpatients, ranging from 70.4% (Hungary) to 94.9% (Peru). **Conclusions**

This study demonstrates that substantial HCRU is associated with varicella resulting in significant public health burden. Differences observed between countries possibly reflect treatment guidelines, health care resource availabilities and physician practices.
background

Outbreaks of measles have been reported in Italy, due to a low immunization rate of population. We aimed at evaluating measles immunization rate in Italian children during the 2016 season and investigating the determinants of missed vaccination.

methods

An observational cross-sectional study was conducted between November 2016 and March 2017 in two University Hospitals in Naples. A standardized questionnaire was administered face-to-face to all families accessing the department of pediatrics during the study period, asking information on demographic data, presence of chronic conditions/treatments, and immunization records. Reasons for missed vaccination were explored in all families of children with missed or delayed vaccination.

Results

1165 children (median age 84 months) were enrolled: 77.4% adequately vaccinated, 6.6% incompletely vaccinated for age and 16% didn’t receive any vaccine dose. Vaccination rate varied according to age (p=0.0001), with children <24 months showing the lowest rate (65.5%). Reasons for not vaccinating included: fear for side effects (51.3%), underlying chronic conditions (12.1%), skip scheduled appointment (12.1%), refusal of vaccination policies (8.4%), presence of acute illnesses (7.2%), allergy to eggs (4.6%). The presence of any underlying condition was a major risk factor for inadequate immunization (OR 9.0, 95%CI 4.6-17.6, p<0.0001).

Conclusions

We reported inadequate measles immunization rate in children living in Southern Italy: children < 2 years of age and those with chronic conditions presenting the lowest rates. However, only a minority of conditions were true contraindications to vaccine administration, according to international recommendations.
In the era of increasing vaccine hesitancy in various countries, consistent monitoring of beliefs and opinions of the public about the national immunization program is important. Our aim is to develop a system that can recognize tweets with a negative stance towards vaccination.

Methods

We queried a database with Dutch Twitter messages for different key terms related to vaccination, for the period 01-01-2012 until 08-02-2017, collecting 27,534 tweets. Manually 8,259 tweets were annotated, of which 6,540 were annotated twice. The tweets were annotated on relevance, polarity and sentiment (i.e. labels). The agreement on these categories was fair (kappa between 0.23-0.35). We manipulated four aspects of the machine learning setting: the algorithm, the training data, the labels, and the way in which irrelevant tweets were filtered.

Results

The best performance, with a precision of 0.29, a recall of 0.47, an F1-score of 0.36 and an AUC (area under the curve) of 0.66, was yielded by training a Support Vector Machines classifier on strictly and laxly labeled data to distinguish irrelevant tweets and polarity categories. Our system outperformed the rule-based sentiment analyses with a F1-score of 0.20 for Pattern and 0.25 for Coosto and two random baselines with an F1-score of 0.18 and 0.13 (Table 1).
Conclusions

The agreement rates for all categories are low, which reflects the difficulty of this task. However, there is still room for improvement such as including semantic information by means of embedding words, using world knowledge in the form of word lists, add more labeled data or combining rule-based sentiment analysis and machine learning. This social media monitoring will be used into a broader monitoring system of beliefs and opinions about vaccination among the public.

Table 1. Performance of various systems correctly predicting the label of tweets with a negative stance

<table>
<thead>
<tr>
<th>Prediction system</th>
<th>Precision(^1)</th>
<th>Recall(^2)</th>
<th>F1(^3)</th>
<th>AUC(^4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random (0.50(^5))</td>
<td>0.11</td>
<td>0.46</td>
<td>0.18</td>
<td>0.48</td>
</tr>
<tr>
<td>Random (0.15)</td>
<td>0.12</td>
<td>0.15</td>
<td>0.13</td>
<td>0.50</td>
</tr>
<tr>
<td>Pattern</td>
<td>0.14</td>
<td>0.34</td>
<td>0.20</td>
<td>0.53</td>
</tr>
<tr>
<td>Coosto</td>
<td>0.20</td>
<td>0.31</td>
<td>0.25</td>
<td>0.57</td>
</tr>
<tr>
<td>Vaccimoni</td>
<td>0.29</td>
<td>0.47</td>
<td>0.36</td>
<td>0.66</td>
</tr>
</tbody>
</table>

\(^1\) Precision (P) or positive predictive value is defined as the number of true positives (Tp) over the number of true positives plus the number of false positives (Fn) (P = Tp / (Tp + Fn)).

\(^2\) Recall (R) or sensitivity is defined as the number of true positives (Tp) over the number of true positives plus the number of false negatives (Fn) (R = Tp / (Tp + Fn)).

\(^3\) The (F1) score is defined as the harmonic mean of precision and recall (F1 = 2PR / P+R)

\(^4\) AUC = area under the receiver operating characteristic (ROC) curve.

\(^5\) The chance the random system scores a tweet negative
PROJECTED IMPACT OF DIFFERENT VARICELLA VACCINATION STRATEGIES ON VARICELLA MORBIDITY AND MORTALITY IN DENMARK, NORWAY, AND SWEDEN

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Background

Universal childhood varicella vaccination (UVV) has not been implemented in Denmark, Norway, and Sweden. In the absence of UVV, varicella leads to over 240,000 cases (>90% in children <10) and 38 deaths (30% in children <10) per year across these countries. We modeled the potential impact of various options for implementation of UVV, assuming administration at existing vaccination opportunities.

Methods

A dynamic transmission model of varicella infection was calibrated and ‘long’ and ‘short’ interval two-dose administration was considered. Based on the current measles-mumps-rubella (MMR) vaccine schedule [long interval], first dose was assumed at 15 (Denmark, Norway) or 18 (Sweden) months; second dose was at 4 (Denmark), 11 (Norway) or 7 (Sweden) years. Short interval schedules considered were 12m/15m (Denmark, Norway), and 12m/18m (Sweden). Varicella vaccination coverage was assumed the same as for other antigens administered at the same visit.

Results

Reductions in varicella incidence at 25 years post vaccination for the short/long-interval vaccination strategies were 86.2%/88% (Denmark), 87.7%/84.2% (Norway), and 87.7%/89.9% (Sweden) (Figure 1). The relative advantages of long vs short interval strategies persisted at 100 years for Norway and Sweden, but converged for Denmark. Between 61-63 cases of congenital varicella and 738-756 deaths are estimated to be prevented in the first 25 years of UVV.
Conclusions

Varicella vaccination is projected to lead to substantial disease reductions in these Scandinavian countries. Both relative and absolute benefits are projected to be greatest in Sweden. Long-interval coverage strategies are projected to be more effective in Denmark and Sweden despite lower assumed coverage rates with the second dose; the better performance of the short-interval strategy in Norway is attributable to the length of the interval between doses in the long-interval strategy.
During the last years there has been an increase in prevalence and severity of *Clostridium Difficile* (CD) infections. This phenomenon is also occurring among low risk population such as children, considered the reservoir.

**Methods**

We conducted a prospective cohort, approved by our Ethics Committee, among newborn recruited after parents signed written informed consent. We recorded perinatal and neonatal history during recruiting process. We intend to collect three stool samples (1st, 6th and 12th months of age) with an attached questionnaire with the following data: weight, type of feeding, cohabitants at home, history of gastroenteritis, hospital's admissions, antibiotic and antacids intake, day-care centre assistance. Stool samples were processed as show in the diagram. We present the preliminary results of the 1st and 6th month samples.

**Results**

178 patients were recruited, 48,6% males, 88% vaginal deliveries, median gestational age: 39,71 weeks (IC25-75p: 38,71-40,14), maternal GBS (*Group B streptococcus*) colonization: 12,6%, perinatal antibiotics: 15%, hospital's admission: 13,1%. At 1st month, 166 samples were processed, CD prevalence was 7,8 % (3,6 % of toxigenic-strains). At 6th month of age, 150 samples were processed; CD prevalence was 39,4% (24,7% of toxigenic-strains). All of the colonized patients were asymptomatic.

Our preliminary results show association between caesarean and colonization by CD (p=0.01), and also among formula-users for CD and toxigenic-strains (both p<0.001). Breastfeeding may protect against colonization, and caesarean may predispose to toxigenic-strains's colonization but there's no significance yet in these results.
Conclusions

There is a high prevalence of toxigenic CD among healthy infants. Infant formulas and caesarean may predispose to colonization. We need to fulfill this study to confirm these trends. Further studies are necessary to understand the issues and physiopathology of CD isolates.

Clinical Trial Registration (Please input N/A if not registered)

N/A
ESP18-0645
SCIENCE AND EDUCATIONAL TRACK
ORAL PRESENTATION SESSION 12: HIV

T CELL RECEPTOR REPERTOIRE AND THYMIC OUTPUT NORMALIZES AFTER TREATMENT INTERRUPTION IN CHILDREN WITH HIV


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3Great Ormond Street Hospital for Children, Haematology, London, United Kingdom
4Kings College London, Department of Immunology, London, United Kingdom
5Institute of Clinical Medicine, Department of Paediatrics- Aarhus University Hospital, Aarhus, Denmark

Background

The loss of CD4+ T cells in children with HIV can usually recover with antiretroviral therapy (ART). If ART is interrupted, CD4+ cells diminish rapidly but are restored with the reintroduction of ART. How much is through thymic output and/or peripheral cell division is unknown. In this study, we have investigated the impact of ART interruption followed by ART reintroduction on three critical immune parameters: thymic output, T cell receptor (TCR) diversity and peripheral cell division.

Methods

TCR repertoire was estimated by Next Generation Sequencing techniques in purified naive CD4+ T cells and memory CD8+ T cells. Thymic output was measured using a mathematical model, combining naive CD4+ T cell proliferation rates with DNA PCR quantification of TCR excision circles, and IL-8, a chemokine released from naive T cells. Samples from 4 HIV-infected children were available for this study from a randomized controlled trial where one cohort remained on ART and the other had treatment withdrawn for 48 weeks.

Results

IL-8 and thymic output was found to increase rapidly in naive CD4+ T cells when ART was stopped. The increase in thymic output was associated with increased naive CD4+ T cell proliferation, as measured by Ki67. Thymic output and Ki67 returned to pre-interruption levels when the children re-started ART. TCR repertoire diversity and clonotype profiles appeared to be similar before treatment interruption and 3 years after ART re-introduction in both naive CD4+ T cells and memory CD8+ T cells.

Conclusions

Importantly, we found that Thymic output, TCR repertoire and peripheral cell expansion returns to pre-interruption levels, indicating reversibility following treatment interruption. This indicates that the high levels of thymic output in children may be sufficient to reverse the impact of ART cessation.

Clinical Trial Registration (Please input N/A if not registered)
BOOSTING TEENAGERS WITH ACELLULAR PERTUSSIS VACCINES CONTAINING RECOMBINANT OR CHEMICALLY INACTIVATED PERTUSSIS TOXIN: A RANDOMIZED CLINICAL TRIAL.

**Methods**

We performed an investigator-driven phase II observer-blind randomised controlled trial including 62 aP-primed healthy adolescents aged 11-15 years in Geneva, to assess the immunogenicity and reactogenicity of a novel recombinant aP (r-aP) vaccine containing recombinant genetically-inactivated pertussis toxin (rPT or PTgen) and filamentous hemagglutinin (FHA) co-administered with a tetanus-diphtheria (Td) vaccine, compared to a licensed tetanus-diphtheria-acellular pertussis vaccine (Tdap) containing chemically-detoxified PT (cdPT). We also compared the immunogenicity of r-aP to that elicited in 150 whole-cell pertussis (wP)-primed Thai adolescents.

**Results**

Reactogenicity, adverse events and baseline GMCs were similar between both groups. Anti-PT IgG GMCs were two-fold higher 28 days after r-aP+Td (113.74 IU/ml (95%CI, 88.31-146.50) than Tdap (52.43 IU/ml (95%CI 36.41-75.50, p=0.0006)), with Day 28/Day 0 GMC ratios of 18.37 IU/ml (95%CI 13.82-24.42) versus 6.73 IU/ml (95%CI 4.82-9.41, p<0.0001), respectively. PT-neutralizing GMCs were also higher after r-aP+Td (127.68 IU/ml (95%CI, 96.73-168.53)) than Tdap (73.91 IU/ml (95%CI, 49.88-109.52), p=0.0162), with Day 28/Day 0 GMC ratios of 18.18 (95%CI, 13.28-24.87) and 8.82 (95%CI, 5.83-13.36, p=0.0057), respectively. At Day 28, anti-FHA IgG GMCs were similar in both groups. Responses to r-aP remained significantly lower than in Thai wP-primed adolescents (total anti-PT IgG GMCs: 113.74 IU/ml (95%CI, 88.31-146.50) versus 561.87 IU/ml (95%CI, 467.79-674.86, p<0.0001; neutralizing anti-PT GMCs: 127.68 IU/ml (95%CI, 96.73-168.53) versus 275.74 IU/ml (95%CI, 181.63-418.59, p=0.0016).

**Conclusions**

Protection induced by acellular pertussis (aP) vaccines is partial and short lived in teenagers, calling for novel immunization strategies.
Boosting with r-aP induced two-fold higher anti-PT responses than cd/Tdap in aP-primed adolescents, but at markedly lower GMCs than in wP-primed adolescents. Five doses of cdPT-based vaccines may limit the induction of responses to rPT.

Clinical Trial Registration (Please input N/A if not registered)

clinicaltrials.gov NCT NCT02946190.
Background

Surveillance screening for bacterial colonisation is an established practice in most large neonatal units. In our retrospective study we evaluated the correlation between a positive surveillance culture and invasive disease with the same organism. We mapped this to antibiotic usage and outcomes to evaluate the utility of surveillance cultures in changing practice.

Methods

We collected laboratory data between July 2016 and June 2017 in a large neonatal unit in London, then matched it with clinical data for all babies with a positive infection screening swab.

Clinical data included gestational age of the babies, age at first positive swab, whether a septic screen was performed, time between positive swab and positive blood culture, type and length of antibiotic treatment and maternal colonisation.

Results

Of 3981 surveillance swabs 7% was positive in 115 unique patients. 42% of patients had a subsequent blood culture of which 8.6% was positive for the same organism. Of the 66 positive blood culture in our unit 15% (10) had a positive surveillance swab for the same organism. The most common organisms on swabs were E.coli (19%), Enterobacter cloacae (15%) and Group B Streptococcus(13%). 9% of the patients with a positive swab had maternal positivity for the same organism. 30 day mortality rate following positive swabs was 6.9%.

Conclusions

Bacteraemia was preceded by a positive surveillance culture in 15% of neonates, triggering a change in first and second line antibiotics in 3% of cases. Local investigation found regardless how far back a swab was positive in practice it’s often followed by a blood culture that is also positive. A larger prospective study is warranted to further establish if surveillance cultures predict invasive disease and the impact on antimicrobial stewardship in neonatal units.
EFFECT OF MALARIA VECTOR CONTROL AND ENVIRONMENTAL HYGIENE ON ASYMPTOMATIC MALARIA PARASITAEMIA IN NIGERIAN MALARIA ENDEMIC REGION

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⁴Development Africa, Project Director, Lagos, Nigeria
⁵Development Africa, Country Director, Lagos, Nigeria

Background

Malaria is a vector borne diseases with high morbidity and mortality in endemic regions. In view to eliminating the disease, integrated vector and environmental hygiene management have been advocated. There is paucity of studies on effect of intervention malaria vector and environmental management on asymptomatic malaria parasitaemia.

Methods

Longitudinal intervention study carried out in a rural malaria endemic community from October to December 2017. Study participants were 477 individuals living in 100 households selected by snowballing sampling methods. Pre-intervention period, all heads of households were trained on and received vector control and environmental hygiene materials (waste bins, netting of household doors/windows and two long lasting insecticide bed nets). Each household member was screened for malaria using the rapid diagnostic test kits. During the intervention period each household was monitored for a period of 6 – 8 weeks on the vector control and environmental hygiene practices and malaria parasites obtained from them at the end of intervention period.

Results

Of the 100 households selected, 54.0% were from the lower social class, 45.0% middle class and only 1.0% upper class. Mean age [±] of the heads of the households was 37.1 ± 11.0 (16 – 68 years). There were 234 (49.0%) males and 243 (51.0%) female; median age (range 1 – 70 years). During the Pre-intervention period, three-quarter of the heads of the households agreed that malaria is preventable, 51 had nets on their doors/windows and only three had LLIN. Malaria prevalence pre-intervention was 16.8% and 1.3% post-intervention. There was 92.0% reduction in asymptomatic malaria parasitaemia following the intervention.

Conclusions

Vector control and environmental hygiene measures are the most effective methods for malaria elimination endemic region.
Background

Human papillomavirus (HPV) vaccines were originally licensed in a three-dose schedule. However, for adolescents younger than 15 years, two doses of vaccine are now recommended based on immunobridging studies. Limited data are available on effectiveness of less than three dose schedules. We report an interim analysis of HPV prevalence after two-doses of quadrivalent vaccine (HPV6/11/16/18).

Methods

QUadrivalent HPV vaccine Evaluation STudy (QUEST) is a Canadian cohort of girls 9-14 years at enrollment. Based on their provincial immunization program, girls received either two or three doses of vaccine. Comprehensive follow-up includes self-collected vaginal specimens, blood samples and online health surveys. The first available swab of two-dose participants available up to August 20th, 2017 was used to obtain an interim HPV prevalence estimate. Samples were screened for high-risk (hr) HPV using the Roche Cobas HPV Test, and if positive, genotyped by Roche Linear Array HPV Genotyping Test.

Results

For this analysis, swabs from 1133 girls were available. Median time since first dose: 4.4 years (range 3.3-9.3), median interval between the two doses was 198 days (range 63-364), median age of participants at time of swab collection was 15.7 years (range 14.3-22.5) and 14.2% of participants reported to have ever had sexual intercourse. Among sexually active girls a hrHPV prevalence of 9.32% (95%CI 5.31-14.90%) was observed. No cases of infection with HPV vaccine types 16 or 18 were identified (0.00% 95%CI 0.00-2.43%).
Conclusions

In this analysis to estimate HPV prevalence among sexually active recipients of a two-dose quadrivalent HPV vaccination schedules, no HPV16/18 infections were identified, suggesting protection for at least 4 years. Long-term follow-up in the full cohort is awaited.

Clinical Trial Registration (Please input N/A if not registered)
The challenges faced in the management of Invasive Fungal Diseases (IFD) warrant robust antifungal stewardship programmes. A point prevalence study (PPS) was performed to obtain an insight in the paediatric antifungal (AF) prescribing. Demographic, clinical data and diagnosis are presented.

Methods

We performed a modified PPS in 12 centres in England, with weekly prospective data collection on AF use in hospitalized neonates and children over 26 weeks.

Results

In total, 1,210 children and neonates (83% and 17% respectively) were included. 83.7% were admitted to paediatric wards, mainly: haematology-oncology 32.9%, PICU 18.8% and BMT units 13.5%; 16.3% were admitted to neonatal units. Proportion of children on AF/patients admitted was 37.3% (95%CI 35.2%, 39.2%) in haematology-oncology; 21.9% (95%CI 19.4%, 24.4%) in PICU and 63.2% (95% CI 60.4%, 66%) in the BMT wards. 32.5% of the children suffered from a malignancy, 7.1% from a primary immunodeficiency and 16.2% were premature infants. Of the children without a...
specific condition rendering them at higher risk for IFD (44.2%), the following risk factors were more frequently reported: presence of central venous catheter 62.7%, prolonged broad-spectrum antibiotics 44.4%, and immunosuppressive therapy 23.5%. Correlating AF prescription to IFD, 84.7% cases (95% CI 83.6%, 85.8%) had no diagnosis of possible/probable/proven IFD based on EORTC criteria; 8.2% (95% CI 7.4%, 9%) had a possible, 1.1% (95% CI 0.8%, 1.5%) a probable and 6% (95% CI 5.4%, 6.6%) a proven IFD. Indication for AF prescription was prophylaxis in 72.6% (95% CI 71.3%, 73.7%) and treatment in 27.4% (95% CI 26.2%, 28.6%) of them.

Conclusions

The majority of the AF were prescribed to patients without an underlying condition rendering a higher risk for IFD and to those with no evidence of IFD.

Clinical Trial Registration (Please input N/A if not registered)
Background

The overuse of antifungals (AF) and increasing antifungal resistance urge the need for antifungal stewardship programmes. A point prevalence study (PPS) was performed to obtain an insight in the paediatric AF prescribing. AF use and indications are presented.

Methods

We performed a modified PPS in 12 centres in England, with weekly prospective data collection on AF use in hospitalized neonates and children over 26 weeks.

Results

In total, 1,210 children and neonates (83% and 17%, respectively) received AF. Each PPS-week included a mean of 152 (SD 15.5) children (Figure) and each patient was included for a median of 2 PPS weeks (IQR 1-4, range 1-26). In total, 72.6% (95% CI 71.3%, 73.7%) prescriptions were prophylaxis, whereas 27.4% (95% CI 26.2%, 28.6%) were treatment. From those on treatment, empirical treatment accounted for 46.3% prescriptions (95% CI 43.9%, 48.7%), followed by pre-emptive (33%; 95% CI 28.8%, 36.1%) and targeted (20.7%; 95% CI 18.9%, 22.7%) treatment. The
agents prescribed (ratio prophylaxis/treatment) were: 31.2% fluconazole (70/30%); 28.5% liposomal amphotericin-B (60/40%); 25.5% nystatin (65/35%); 11.2% itraconazole (98.5/1.5%); 3.6% voriconazole (66/34%); 3.5% micafungin (55/45%); 2.2% posaconazole (70/30%) and 1.6% caspofungin (25/75%). Initially, 95.4% patients were prescribed one AF while 4.5% received two AFs. Over the study period, 10.6% received two and 0.5% three AFs. 28.6% prescriptions were changed along the consecutive PPS weeks; from those, 65% were de-escalation changes. 47.1% of the patients were discharged on antifungals. From those who were not, the median duration of AF use was 11 days (IQR 7-23, min 1, max 117 days).

Conclusions

AF were mainly prescribed for prophylaxis with nystatin, fluconazole and liposomal amphotericin B being the AF of choice. Only a minority received combination AF therapy.

Clinical Trial Registration (Please input N/A if not registered)
APPLYING MACHINE LEARNING ALGORITHMS TO DEMOGRAPHIC AND CLINICAL DATA CAN SEGREGATE PATIENTS WITH DIFFERENT ETIOLOGIES OF BACTEREMIA

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Background

Applying machine learning techniques to healthcare data is gaining momentum. Early identification of sepsis etiology is a major clinical goal. Our objective for this pilot study was to determine if machine learning techniques could segregate patients with different causes of sepsis utilizing only demographic and clinical data.

Methods

To facilitate manual data extraction from the electronic medical record, 614 patients with either negative or positive blood cultures for *Staph aureus, E. coli*, or *Enterobacter* were selected randomly from a database containing ~25,000 patients less than 18 years-old with any cultures at our institution between years 2008-2016. Demographic and clinical information (earliest vitals and labs within 24 hours of obtaining the culture) were collected retrospectively. Multiple classification machine learning algorithms were used to develop two models to: 1) separate patients with positive and negative cultures; 2) differentiate patients with different organisms isolated.

Results

For the 614 patients (75% for training set), multiple models were built based on 44 variables extracted from the medical records. For differentiating between patients with positive or negative cultures, the Decision Tree model performed best: 95% accuracy, 97% sensitivity. The second model included the 434 patients with *Staph aureus, E. coli*, or *Enterobacter* (distribution 27:28:45%) positive cultures. The Random Forest model performed best differentiating the three groups of patients: 97% accuracy, 97% sensitivity.

Conclusions

Machine learning algorithms applied to enough clinical variables can segregate patients with negative blood cultures from those with different organisms isolated from blood, suggesting this pilot study should be explored with larger, more complex datasets. Machine learning may be an important addition to current diagnostic methodologies for more rapid determination of sepsis etiology and antibiotic optimization even before cultures become positive.

Clinical Trial Registration (Please input N/A if not registered)
IMPACT OF A MATERNAL TETANUS, DIPHTERIA AND ACELLULAR PERTUSSIS VACCINATION PROGRAM ON PREVENTING PERTUSSIS ADMISSIONS, COMPLICATIONS AND MORTALITY IN INFANTS


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2La Imaculada Huercal Overa Hospital, Department of Pediatrics, Almeria, Spain
3Virgen del Rocio Hospital, Pediatric Infectology Unit, Sevilla, Spain
4Juan Ramon Jimenez Hospital, Department of Pediatrics, Huelva, Spain
5Puerta del Mar Hospital, Department of Pediatrics, Cadiz, Spain
6Poniente Hospital, Department of Pediatrics, El Ejido- Almeria, Spain
7Materno-Infantil Hospital, Department of Pediatrics, Malaga, Spain
8Virgen del Rocio Hospital, Department of Pediatrics, Sevilla, Spain
9Torrecardenas Hospital, Department of Pediatrics, Almeria, Spain
10Virgen de las Nieves Hospital, Department of Pediatrics, Granada, Spain
11Virgen Macarena, Pediatrics, Sevilla, Spain

Background

Recently, pertussis has showed the highest rates of morbidity and mortality in infants too young to be protected through routine vaccination. Prenatal vaccination with Tdpa have shown a dramatic impact in some countries like United Kingdom. In our region, this program was started in 2016.

Our main objective was to analyse the impact in hospital admissions and severity of pertussis cases in infants a year after the implementation of maternal Tdpa vaccination during pregnancy.

Methods

Ambispective multicenter study conducted across 14 hospitals of a Spanish Autonomous Region, with a retrospective phase (2012-2015) and a prospective phase (January-December 2016). Related with infants admitted due to confirmed pertussis (positive Bordetella PCR in nasopharyngeal swab), number of cases, severity, complications, risk factors, PICU admission and mortality were analysed.

Results

During the study period, 496 infants were admitted because of pertussis. Final main results are showed in the table. In 2016, a significant decrease in total pertussis admissions was seen compared with the immediate previous year (p<0.05). Eight dead infants were found in the pre-implementation period, while no deaths in 2016.

During 2016, 41 out of 53 cases (77.35%) were infants from unvaccinated mothers.

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<tr>
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<td>93</td>
<td>86</td>
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<td>Risk factors (%)</td>
<td>6 (13%)</td>
<td>14 (15%)</td>
<td>8 (9.3%)</td>
<td>34 (15.6%)</td>
<td>17 (32.1%)</td>
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<td>Complications (%)</td>
<td>21 (45.5%)</td>
<td>27 (29%)</td>
<td>29 (33.7%)</td>
<td>85 (39%)</td>
<td>22 (41.5%)</td>
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Vaccination during pregnancy is an effective way to protect infants during the early months of life. With a continuing resurgence in pertussis, efforts should focus on maximizing Tdap uptake among pregnant women.
Background

Maternal pertussis vaccination attenuates the primary infant antibody response to acellular pertussis vaccine. We aimed to determine the impact of fetal exposure to a maternal dose of aPertussis vaccine on pertussis disease during infants’ first 6-months of life, accounting for receipt of the primary aPertussis series commencing at 6-weeks of age.

Methods

Retrospective cohort study linking administrative datasets (including maternal and infant immunisation, pertussis notification and hospitalisation) through an encrypted personal identifier. The study population was all infants born alive in New Zealand to mothers 28–38 week’s gestation 1 January – 31 December 2013.

Results

A total of 101,460 pregnancies were eligible for nationally-funded Tdap during our study period. 8,298 (12%) infants were born to vaccinated and 61,069 (88%) to unvaccinated mothers. Controlling for sociodemographic, maternity variables, and infant pertussis-containing doses, receipt of <2 first primary dose of pertussis-containing vaccine in infants of vaccinated mothers increased the infant’s risk for pertussis: OR 2.49 (95% CI [1.32, 4.70], p = 0.005). This effect was attenuated (trend only, p-value not significant at 5%) when excluding infants who received their first dose prior to 6-weeks. The finding was supported in subgroup analysis by infants who received 0/1 dose and who received at least 2 doses in first six months of age. There was a small additional protective effect of maternal vaccination among infants who received at least two doses of routine pertussis vaccine (trend reversed, p-value non-significant). Protective effect of infant routine dose on pertussis disease remained significant in all models.

Conclusions

Our findings suggest when the first infant pertussis dose is given at 6-weeks there may be a greater risk for pertussis prior to completion of the primary series.

Clinical Trial Registration (Please input N/A if not registered)
BURDEN OF CARE AND EXPERIENCES OF FAMILIES CARING FOR CHILDREN LIVING WITH HIV IN NORTH INDIA – A MIXED METHODS STUDY
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Background

Family-centered approach of caring for Children living with HIV is common in India. The present study examines the burden of care among caregivers along with their experiences regarding HIV related stigmatization, disclosure and adherence to treatment.

Methods

This mixed-methods study combined quantitative methods, focus group discussions (4), and in-depth interviews (20 Caregiver-child dyads) to triangulate the psychosocial burden of HIV among caregivers. Cases were enrolled from the Immunodeficiency clinic of a tertiary care hospital in Northern India. We quantified the burden of HIV using Family Burden Interview scale (FBIS). Strengths and Difficulties Questionnaire (SDQ) was used to assess the behavioral problems of 20 children aged between 7-18 years. Qualitative analysis was done using thematic coding.

Results

FBIS identified highest burden in the ‘Financial domain’ in spite of free availability of Anti retroviral drugs and many social protection schemes. Mean (SD) FBIS score was 4.1 (±2.71). In addition the ‘Disruption of Family Interaction’ component was affected. Many families opted for treatment away from home, to avoid discrimination. There was underutilization of subsidies, as it was a possible source of disclosure. Total difficulties score (TDS) generated by SDQ was normal for 95% (n=19) of caregiver reported questionnaires. Only 40% of our enrolled children had been disclosed their HIV status. Caregivers deferred disclosure of HIV citing their inability to address the child’s queries and fear of stigma and discrimination

Conclusions

Our study demonstrated significant burden among the families caring for children with HIV. Constructs of stigma, discrimination and non-disclosure emerged as dominant themes lurking beneath the HIV care continuum. The insights gained from our qualitative investigation will be useful in customizing care-giving policies and elaborating various social-safety-net programmes for fast tracking the HIV related 90:90:90 targets.

Clinical Trial Registration (Please input N/A if not registered)

N/A
EPIEMIOLOGY OF CANDIDAEMIA IN A DANISH NATIONWIDE COHORT OF PAEDIATRIC PATIENTS

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Background

Candidaemia is the most frequent fungal infection among paediatric patients. To our knowledge, this is the first nationwide study to provide population-based data on clinical characteristics and outcome of paediatric candidaemia.

Methods

Paediatric patients (<16 years) with candidaemia in Denmark during 2004-2014 were identified through an ongoing national surveillance programme. All unique blood culture isolates were referred to the national reference centre as part of the programme. Clinical data was available for 87.4% (139/159) of the patients and collected from medical records using a detailed abstraction form.

Results

The incidence rate was 10.2/100,000 population for children <1 year and 0.8/100,000 population for children aged 1-15 years. Baseline characteristics varied by age-group (Table). *Candida albicans* (79.4%), sepsis (58.8%), mechanical ventilation (58.8%), total parenteral nutrition (TPN) (58.8%) and treatment with azoles (46.4%) were common among neonates (≤ 28 days). *C. parapsilosis* (20.8%), recent surgery (43.4%), gastrointestinal diseases (37.7%), and treatment with amphotericin B (45.5%) were common in children aged one month-two years. Finally, haematological diseases (40.4%) and prior chemotherapy (45.1%) were common in children 2-15 years. Among children with antifungal treatment, 95.8% received appropriate initial treatment according to susceptibility testing. Overall 30-day mortality was 11.5%: highest among neonates (17.5%).
Conclusions

The incidence rate and mortality for candidaemia among neonates and children aged 1-15 year was low in Denmark compared to international rates. For paediatric candidaemia underlying diseases, species, treatment and outcome differed substantially by age. Mortality for neonates was lower than reported from other studies of neonatal candidaemia. Likewise, the proportion with sepsis and/or TPN was lower than elsewhere reported, though comparative population based data are sparse. Further population based studies are warranted to evaluate risks and management of candidaemia.
HETEROLOGOUS EFFECT OF PCV13 ON ALLERGIC ASTHMA AND TYPE 1 DIABETES MELLITUS


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Background

Allergic asthma (AA) and type-1-diabetes mellitus (DM) share an exacerbated auto-aggression response of the immune system, produced by deregulation of the immune response. Conjugated-13-valent pneumococcal vaccine (Prevenar13®, PCV13, Pfizer) has demonstrated a beneficial immunomodulatory effect in murine models of allergic asthma, achieving the suppression of characteristic clinical symptoms.

We aim to evaluate a heterologous immunoregulatory effect of vaccination with PCV13 in paediatric patients suffering DM and AA.

Methods

A phase IV single-centre randomized clinical trial was carried out to compare results of vaccination with PCV13 in AA (n=20) and DM (n=26) with vaccination in age-matched controls (n=17). Analysis were performed at baseline (T0), at 56±7 days after PCV13 dose1 (T1) and 112±7 days after vaccination (T2). Changes in the proportion of effector immune sub-populations IFN-g/IL-17/IL-4 secretor-CD3+ T cells after PCV13 vaccination were examined. Geometric mean and standard deviation for all groups in each visit are shown.

Results

In DM percentage of IFN-g/IL-17/IL-4 secretor-CD3+ T cell were for: T0:22.36%±7.30%, 8.24%±3.52% and 0.61%±0.49%, respectively; T1:20.12%±6.49%, 9.23%±4.04% and 0.87%±0.67%, respectively; and T2:16.93%±6.22%, 7.95%±2.92% and 0.83%±0.55%, respectively.

In AA group percentages were for: T0: 18.12%±6.69%, 8.14%±3.23% and 0.95%±0.60%, respectively; T1: 16.39%±4.53%, 8.83%±3.40% and 0.26%±0.84%, respectively; and follow-up visit T2: 14.36%±2.48%, 8.08%±3.64% and 1.15%±0.78%, respectively.

In control group percentages were for: T0:13.70%±5.50%, 6.15%±2.84% and 0.84%±0.65%; respectively; T1:12.58%±3.89%, 6.00%±1.43% and 0.81%±0.55% respectively, and T2:14.48%±5.06%, 8.00%±2.96% and 0.89%±0.41%, respectively.
A significant ($p=0.0083$) decline in the percentage of IFN-g secretor CD3+ T cells was found only in DM group. No significant differences were observed in the rest of parameters and/or groups.

**Conclusions**

A moderate immunoregulatory heterologous effect in DM paediatric patients was observed after PCV13 vaccination. Persistence of this effect over time and clinical impact on the pathology should be further explored.

**Clinical Trial Registration (Please input N/A if not registered)**

2014-004799-50
Background

Invasive fungal disease (IFD) remains a significant contributor to morbidity and mortality in children undergoing allogeneic HSCT. Variation in the management of IFD has prompted efforts to understand antifungal consumption in this group.

Methods

Daily data on systemic antifungal administrations were extracted from the electronic prescribing system of a large UK tertiary children’s hospital between 2011 and 2016, and summarised as Days Of Therapy per 100 occupied Bed Days (DOT/100 BD). Descriptive data were obtained from the HSCT clinical database.

Results

407 children underwent allogeneic HSCT during the study period. Median age 45 months (IQR 18-33). Ten children died with IFD (2.5%, 95%CI 1.2 to 4.5%). Total antifungal administration was higher in the pre- (up to day 28 post-HSCT) than post-engraftment period (98.1 v 92.4 DOT/100 BD respectively, p<0.001) during which the most common antifungals administered were liposomal amphotericin B (median 43 DOT/100 BDs, IQR 37-46) and micafungin (median 20 DOT/100 BDs, 15-21). Voriconazole and posaconazole were more commonly administered beyond day 28 (median 13 and 12 DOT/100 BDs respectively, see Figure). Between 2011 and 2016, voriconazole consumption before day 28 increased by 5.3 DOT/100 BDs (95%CI 4.9 to 5.8), and reduced beyond day 28 (by 4.4 DOT/100 BDs, 2.3 to 6.8). Over this period, there was an increase in posaconazole use of 13.0 DOT/100 BDs (95% CI 9.4 to 17.0) and reduction in micafungin use of 3.3 DOT/100 BDs (95%CI 2.0 to 3.7).
Conclusions

IFD contributed significantly to transplant-related mortality. The use of particular antifungals varied according to stage of HSCT and showed significant changes over time. Insights into the rationale for antifungal prescribing are needed to develop antifungal stewardship guidelines in this particular high risk group of children.
Background

Vaccination can protect against life-threatening infectious diseases. This is even more important for children with chronic diseases because of their increased risk of complications upon exposure to vaccine-preventable diseases. We assessed vaccination coverage and seroprotection rate for measles, mumps and rubella (MMR) and diphtheria, tetanus and pertussis (DTP) in children with chronic diseases in a university hospital in Flanders, Belgium.

Methods

Antibody titers were determined by ELISA (MMR) and multiplex assay (DTP) in 106 patients with cystic fibrosis (n=9), diabetes type 1 (n=58), allergy (n=14) and congenital heart disease (n=25), aged 2-16 years. Titers were classified as seropositive if above cut-off value (see table). Vaccination data were retrieved from documents provided by the parents and the general practitioner and verified against the Flemish vaccination register. Patients were considered fully vaccinated if they had been correctly vaccinated for their age according to the recommended Belgian immunisation programme.

Results

Vaccination rates are lower compared to the general population of Flemish children. Moreover, except for tetanus, seroprotection rates for all investigated diseases were lower in children with chronic disease compared to literature data on healthy children. However, complete vaccination compared to incomplete vaccination was still associated with improved protection rates, albeit only statistically significant for measles and rubella (table). No major differences were seen between the different patient groups.
Conclusions

Up to 45% of children with chronic disease remain susceptible to vaccine preventable diseases. This can be explained by the relatively low vaccination coverage (73 to 83%) and possibly by the influence of disease on vaccine immunogenicity. These results highlight the importance of herd immunity and the need for better follow-up of the vaccination status in children with chronic diseases.

Clinical Trial Registration (Please input N/A if not registered)

N/A
IMMUNOGENICITY OF TAKEDA’S BIVALENT VIRUS LIKE PARTICLE (VLP) NOROVIRUS VACCINE (NoV) IN CHILDREN
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Background
Norovirus is a major cause of medically-attended gastroenteritis in children worldwide. We present the initial immunogenicity data of the Takeda bivalent NoV candidate in 1–<9 year-old children.

Methods
As part of a double-blind, randomised, phase 2 dose-finding study conducted in Colombia, Finland and Panama, children in two age cohorts (4–< 9 and 1–< 4 years, n=120 per cohort) received one or two intramuscular doses of NoV formulations with 15/15, 15/50, 50/50 or 50/150 μg GI.1/GII.4c genotype VLPs and 0.5 mg Al(OH)₃ on Days 1 and 29; one dose groups received saline placebo as dose two to maintain blinding. Antibody responses to each VLP were measured on days 1, 29 and 57 as ELISA Pan-lg and as functional histo-blood group binding antigen blocking antibodies (HBGA), expressed as seroresponse rate (≥ 4-fold increase over baseline, SRR), and geometric mean titres (GMT).

Results
All formulations induced high Pan-lg responses after one dose, with SRR against GI.1 of 82–97% and 81–96%, and 79–91% and 80–91% for GII.4c in 1–< 4 and 4–< 9 year-olds, respectively. HBGA SRR after a single dose were 66–83% and 73–96% for GI.1, and 60–86% and 60–100% for GII.4c in 1–< 4 and 4–< 9 year-olds, respectively. Both age cohorts had similar HBGA SRR following two vaccine doses; 92–100% for GI.1 and 85–100% for GII.4c. Post vaccination GMTs varied by genotype, VLP dosage, age cohort, and serostatus at baseline.

Conclusions
In 1–<9 year-old children, high Pan-lg anti-norovirus antibody responses were observed after one dose, and high HBGA responses after two doses of the Takeda NoV candidate formulations

Clinical Trial Registration (Please input N/A if not registered)
NCT: 02153112, EudraCT: 2014-000778-20
TRENDS IN THE INCIDENCE OF INTUSSUSCEPTION BEFORE AND AFTER THE PRIVATE MARKET LICENSURE OF ROTAVIRUS VACCINE IN KOREA: A NATIONWIDE CROSS-SECTIONAL STUDY

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Background

Two globally licensed rotavirus vaccines were introduced in Korea in 2007-2008 and have been available for private market use. A small increased risk of intussusception after rotavirus vaccination, mainly after the first dose, has been identified from the studies conducted in several countries. Korea is one of the countries with the highest incidence of intussusception worldwide. We investigated trends in the incidence of intussusception before (2002–2006) and after (2008–2015) rotavirus vaccine introduction in Korea.

Methods

A cross-sectional study was conducted using the Korean National Health Insurance Data to identify infants aged <12 months who were diagnosed with intussusception (ICD-10 code K56.1) and received non-invasive or invasive reduction (M6781, M6782, G0300, G0310, Q2841, and Q2842) from 2002 to 2015. The annual intussusception incidence, incidence rate ratios (IRRs) and 95 % confidence intervals (CIs) were calculated.

Results

The annual incidence rates in infants <12 months of age have decreased with time since 2002 and up to 2015, ranging from 234.1 to 159.4/100,000. The incidence rate ratio in the postvaccine period (2009-2015) ranged from 0.66 to 0.81 compared to the prevaccine period (2002-2006). Also, the annual incidence rate in infants aged 8-11 weeks has declined from 66.6/100,000 in the prevaccine period to 19.0-50.5/100,000 (IRR range: 0.29-0.76). This declining trend was more pronounced in very young infants (6-14 weeks of age, IRR 0.44 [95% CI, 0.35-0.55]; 15-24 weeks, IRR 0.60 [95% CI, 0.53-0.67]; 25-34 weeks, IRR 0.75 [95% CI, 0.68-0.82]).

Conclusions

The incidence of intussusception in infants aged <12 months have decreased since the introduction of rotavirus vaccine in Korea. If rotavirus vaccines are introduced to the National Immunization Program of Korea in upcoming days, it is needed to monitor the incidence of intussusception in infants constantly.
Enteric fever is a life-threatening infection caused by Salmonella enterica serovars Typhi (typhoid fever) and Paratyphi A, B and C (paratyphoid fever). Around 21 million people are diagnosed with enteric fever annually, of which ~222,000 die. Children are most at risk. Given regulation of protein-coding genes by small RNAs (sRNAs) plays a role in immunity, we performed a pilot-study using a human typhoid challenge model to investigate whether S. Typhi exposure changes the sRNA expression in peripheral blood mononuclear cells (PBMCs).

Methods

sRNA-sequencing was conducted on 8 participants exposed to S. Typhi, using a human typhoid infection model. Sequencing was conducted at baseline (n=8), 1 day after challenge (n=8), at diagnosis in typhoid diagnosed participants (n=4, median day of diagnosis was 7 days post-challenge) and 7 days post-challenge in those not developing typhoid (n=4).

Results

Several sRNAs were differentially expressed in PBMCs 1 day post S. Typhi ingestion (FDR <0.05). We identified an sRNA signature that predicted protection from typhoid at day 1 post challenge. Several sRNAs were differentially expressed in non-diagnosed participants 7 days post-challenge compared with typhoid infected participants at diagnosis (FDR <0.05).

Conclusions

This is the first study on the identity and differential expression of sRNAs in a human infection model. We identified a set of sRNAs that were associated with typhoid infection and a second set that were early predictors of typhoid infection. An extension study is underway to validate these signatures. We are evaluating the role of these sRNAs in the wider regulatory networks to gain biological insights into host responses to S. Typhi.

Clinical Trial Registration (Please input N/A if not registered)

NCT02324751
THE REACTOGENIC MULTICOMPONENT CAPSULAR GROUP B MENINGOCOCCUS (4CMENB) VACCINE ALTERS SMALL RNA EXPRESSION IN PLASMA

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Background

Meningitis is a life-threatening, infectious disease. Capsular group B meningococcus (MenB) accounts for most invasive meningococcal disease in developed countries. The multicomponent MenB vaccine (4CMenB, Bexsero®) was added to the UK infant vaccination schedule in 2015. Small non-coding RNAs (sRNAs) modulate the expression of protein-coding genes. sRNAs are present in plasma where they may act as signalling molecules and thus could participate in immune signalling triggered by vaccination. We investigated the effect of 4CMenB vaccination on plasma sRNA expression.

Methods

4-month-old infants (n=21) were randomised to receive routine vaccinations with or without 4CMenB. sRNA sequencing was conducted on plasma RNA pre and 24-hours post vaccination.

Results

Several sRNAs were differentially expressed post vaccination in both groups. Interestingly sRNA expression was more perturbed post vaccination in the group receiving 4CMenB. Four differentially expressed microRNAs in the 4CMenB group,( hsa-miR-375, hsa-miR-140-3p, hsa-miR-181a and hsa-let-7d are predicted to target genes involved in immune responses including IL1A, NFKBI, CD4, IRF-8 and several MAP kinases.

Conclusions

This is the first study to use sRNA sequencing to establish the identity and extent of differential expression of plasma sRNAs after vaccination. Further analyses are underway to identify potential sRNA biomarkers of vaccine immunogenicity. We are integrating differentially expressed sRNAs into their corresponding regulatory interactions, which may provide biological insights into the reactogenicity of 4CMenB.

Clinical Trial Registration (Please input N/A if not registered)

EudraCT Number: 2014-000126-38
Post-varicella arterial ischemic stroke in children in Denmark 2010-2016

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Background

Varicella, most often a benign disease of childhood, is associated with an increased risk of arterial ischaemic stroke (AIS) in children. The aim of the present retrospective register study was to estimate the incidence of post varicella AIS in the Danish child population and describe clinical characteristics of children admitted with post varicella AIS.

Methods

In the Danish National Patient Register, we identified inpatients 28 days-16 years of age with a discharge diagnosis of stroke and/or cerebrovascular disease from 2010-2016. Medical files were reviewed and children with arterial ischaemic stroke and varicella infection < 12 months before onset of symptoms included in the study. Cases of AIS with varicella infection < 12 months before were considered confirmed cases of post-varicella AIS if an analysis of cerebrospinal fluid (CSF) was positive for varicella zoster virus (VZV) DNA and/or VZV-specific immunoglobulin G (IgG).

Results

We identified 15 children with AIS and varicella < 12 months before onset of symptoms. In nine children, the diagnosis was confirmed by detection of VZV DNA or VZV-specific IgG in CSF. All children were previously healthy, the mean age was 4 years and 67% were male. The median time from varicella rash to AIS was 4.6 months. The most common location of AIS was the basal ganglia and affected vessels were most often in the anterior circulation. Fifty-three percent experienced neurologic sequelae of varying degree.

Conclusions

In Denmark, where varicella vaccination is not part of the childhood vaccination program, the estimated risk of post-varicella AIS was one case (including possible cases) per 26,000 children with varicella.

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URINARY TRACT INFECTION AFFECTS ULTRASONOGRAPHIC PICTURE OF THE KIDNEYS – PRELIMINARY REPORT

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Background

Ultrasonography (USG) is the first line imaging modality in children with urinary tract infection (UTI). However, USG performed in acute phase of infection may reveal misleading results due to active inflammation. Guidelines on UTI management in children differ with respect to recommended USG timing.

The purpose of our study is to investigate how UTI affects USG results in children.

Methods

Prospective, single-center, observational study. We included children < 3 years of age with the first episode of UTI. Children underwent 3 USG examinations: on the first day of treatment, two weeks later and four weeks later.

Results

The study involved 39 children (F: 23) aged 10.7 ± 8.9 months.

There was significant increase in both the left kidney (LK) and the right kidney (RK) length on the first USG comparing to the second and the third. No difference in the kidneys length was observed between the second and the third USG. Initial CRP concentration correlated positively with the RK length and tended to correlate with the LK length. Reduced perfusion in Power Doppler (PD) examination was found in 9 kidneys on initial USG, but only in 2 kidneys on the third USG. Twenty-one children presented with dilatation of the urinary tract elements on the first USG (29 kidneys in total). This number decreased to 15 children (19 kidneys) on the second USG and 16 children (19 kidneys) on the third one.

Conclusions

USG examination to detect a congenital anomaly of the kidneys and the urinary tract should be performed in small children with UTI at least 2 weeks after treatment initiation since a picture of the kidneys and the urinary tract is abnormal in the acute phase of UTI.

Clinical Trial Registration (Please input N/A if not registered)

NCT03270540
Background

This epidemiological survey estimates the burden of whooping cough in children up to 14 years old in Spain during a nineteen-year period (1997-2015).

Methods

Retrospective survey by reviewing data of the National Surveillance System for Hospital Data including more than 98% of Spanish hospitals. All hospitalizations due to whooping cough for children under 14 years old, reported during 1997-2015 period, were analysed. Codes were selected by using the 9th Clinical Modification of the International Classification of Diseases codes: ICD-9-CM 033.0-033.9. In order to explore the latest international outbreak, analyses were stratified comparing 1997-2010 and 2011-2015 periods.

Results

A total of 12,964 hospital discharges for whooping cough in children under 14 years old were reported. 7,413 in the period 1997-2010 and 5,551 in the period 2011-2015. The annual hospitalization rate prior to 2011 was 8.52 cases per 100,000 children; in 2011-2015, it was significantly higher (21.40 cases per 100,000 children). Most of the cases (n= 12,122) occurred in children under 12 months of age, reaching a hospitalization rate of 106.98 and 310.21 per 100,000 children up to 12 months in the periods 1997-2010 and 2011-2015, respectively.

Thirty-four deaths occurred in the period 1997-2010 and 36 in the period 2011-2015. All of them occurred in infants under 1 year old. Mortality rate was significantly higher in 2011-2015. Case fatality rate did not vary significantly among the studied periods.

Conclusions

Whooping cough infections concentrate in children up to 12 months in Spain. Public health measures such as vaccination of pregnant women, care takers, health care professionals and relatives, especially young parents, could reduce the hospitalization burden during the current outbreak.
VACCINATION DELIVERY SYSTEM AND CULTURAL FACTORS EXPLAIN VACCINATION COVERAGE DIFFERENCES ACROSS CANTONS FOR ADOLESCENT VACCINATIONS IN SWITZERLAND: A QUALITATIVE STUDY

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Background

Vaccination recommendations in Switzerland are national, but vaccination coverage varies greatly from one canton to another, particularly for vaccinations recommended in adolescence. To explain these differences, we studied vaccination practices and socio-cultural views from the vantage points of policy makers, of healthcare providers and of community members in 4 cantons with low (LVC) and 4 cantons with high (HVC) vaccination coverage with a focus on Hepatitis B (HBV) and Human Papillomavirus (HPV) vaccines.

Methods

In-depth semi-structures interviews were administered to a policy maker, a private practitioner and 4 to 7 community members (adolescents aged 16 to 19 and parents of adolescents) from each of the eight cantons.

Results

LVCs were notable for less involvement of state in vaccination issues, more autonomy of municipalities for school health, lower density of pediatricians, less information about these vaccines, greater emphasis on individual rather than government responsibility for vaccinations and anticipated hesitancy. Doctors in HVC more actively advocated for vaccines. Community views in HVCs indicated more collectivistic priorities and more reliance on schools as a source of information. In LVCs there was more tendency to consider that an individual weakness of the immune system explains illness and that too many vaccinations may decrease the ability to fight diseases. In both groups, concerns about usefulness and hesitancy were greater for HPV than for HBV vaccine.

Conclusions

Findings suggest more systematic involvement of health and school authorities are likely to be appreciated by adolescents and their parents and to improve vaccination coverage. Interventions should not only target the population but also policy makers and doctors.

Clinical Trial Registration (Please input N/A if not registered)

N/A
COMPARISON OF 2-DOSE AND 3-DOSE REGIMENS OF 9-VALENT HPV VACCINE: RESULTS FROM A 3-YEAR RANDOMIZED IMMUNOGENICITY TRIAL

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Background

HPV-antibody responses to the 9-valent HPV (9vHPV) vaccine among girls and boys receiving 2-dose regimens (at 0,6 or 0,12 months) were non-inferior to a 3-dose regimen in adolescent girls and young women 4 weeks after the last dose. We report antibody persistence through Month 36.

Methods

In this international, randomized immunogenicity trial (NCT01984697), girls (age 9-14 years) received 2 doses of 9vHPV vaccine (Months 0,6 [n=301] or 0,12 [n=151]) or 3 doses (Months 0,2,6 [n=301]); boys (age 9-14 years) received 2 doses (Months 0,6 [n=301] or 0,12 [n=150]); and women (age 16-26 years) received 3 doses (Months 0,2,6 [n=314]). Anti-HPV geometric mean titers (GMTs) and seropositivity rates were assessed by competitive Luminex immunoassay through Month 36.

Results

Anti-HPV GMTs were highest 1 month after completing the 2-dose or 3-dose series, decreased sharply during the subsequent 6 to 12 months, then decreased more slowly through Month 36. At Months 24 and 36, GMTs in girls and boys given 2-dose regimens were generally similar to or greater than those in young women given 3 doses. Month 36 seropositivity rates were ≥83.6% and 81.4% in girls and boys, respectively, vaccinated at Months 0,6, 87.9% among girls and boys vaccinated at Months 0,12, and 91.2% and 77.8% in girls and women, respectively, who received 3 doses.

Conclusions

HPV antibody responses persisted through 3 years in girls and boys who received 2 doses of 9vHPV vaccine, with GMTs similar to or greater than those observed in young women receiving 3 doses. Antibody responses generated by 2 doses of the 9vHPV vaccine in girls and boys may be sufficient to induce high-level protective efficacy through 36 months post-vaccination onset.

Clinical Trial Registration (Please input N/A if not registered)

NCT01984697
Background

In 2012, the UK introduced a temporary programme of pertussis vaccination in pregnancy as a response to an outbreak, which disproportionately affected infants < 3 months of age. Two pertussis-containing vaccines have been used in the UK programme – Repevax (2012-2014) and Boostrix (2014 onwards).

We aimed to compare vaccine responses in infants born to mothers vaccinated with either Repevax or Boostrix-IPV.

Methods

Women were recruited from a tertiary hospital and two primary care sites in England. Women were randomised antenatally to receive Repevax (containing 5 pertussis antigens) or Boostrix-IPV (containing 3 pertussis antigens) at 28-32 gestational weeks. Blood samples were collected from infants at birth, 2 and 5 months. Infant vaccinations were given according to the UK national schedule at 2,3 and 4 months.

Results

Antenatal vaccination with Boostrix-IPV (n=77) was associated with higher concentrations of anti-pertussis toxin (PT) and anti-filamentous haemagglutinin (FHA) immunoglobulin G (IgG) in infants at birth and prior to infant vaccination at 2 months of age, compared to infants born to Repevax vaccinated mothers (n=77). However, there were no differences in concentration of anti-PT and anti-FHA IgG post primary immunisation at 5 months of age. Infants born to women vaccinated with Repevax in pregnancy, had higher anti-fimbriae (FIM) 2 and 3 IgG at birth, 2 months and 5 months of age.
## Conclusions

Despite higher concentrations of anti-PT and anti-FHA IgG pre-vaccination, there were no differences in concentrations post vaccination, between infants born to women receiving Boostrix or Repevax.

The research was funded by the NIHR PRP (NVEC, 039/0031). The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

Jones, Calvert, Southern, Matheson contributed equally

**Clinical Trial Registration (Please input N/A if not registered)**

NCT02145624
Placental transfer of vaccine specific antibody in participants of a randomised controlled trial of two pertussis-containing vaccines in pregnancy

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Background

Antenatal pertussis vaccination aims to boost vaccine specific antibody in the mother and increase transplacental transfer of specific-immunoglobulin G (IgG) to the infant. The efficiency of placental transfer increases through pregnancy.

We aimed to compare transplacental IgG transfer from mothers vaccinated with either Repevax or Boostrix-IPV to their infants. Methods

Women were recruited from one tertiary hospital and two primary care sites, in England. Pregnant women were randomised to receive either Repevax or Boostrix-IPV at 28-32 weeks gestation. Blood samples were collected from mothers at delivery and either cord blood or a peripheral venous infant blood sample. The placental transfer ratio (PTR) is defined as geometric mean concentration (GMC) in the infant sample over GMC in the maternal sample.

Results

Blood samples were available from 57 infants born to women vaccinated with Boostrix-IPV and 53 infants born to Repevax-vaccinated mothers.

Correlation between maternal and infant IgG GMCs at birth was high and PTR was > 1 for all antigens. There was no difference in PTR between groups. PTR was significantly influenced by time from maternal vaccination to birth (6-11% increase for every week increase in time) and time from birth to infant sample (around 2% drop per day for each antigen). Conclusions

Placental transfer for vaccine specific antibody against pertussis, diphtheria and tetanus is high (>100%) and was not influenced pertussis-vaccine used. Infant GMCs were higher with increasing duration from vaccination to delivery, likely reflecting the increasing time available for placental transfer to occur.

The research was funded by the NIHR PRP (NVEC, 039/0031). The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.
Calvert, Jones, Southern and Matheson contributed equally

Clinical Trial Registration (Please input N/A if not registered)

NCT02145624
MATERNAL CHARACTERISTICS AND ZIKA VIRUS INFECTION IN A HIGH-RISK POPULATION: PRELIMINARY RESULTS OF A BRAZILIAN PROSPECTIVE STUDY

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Background

The susceptibility to ZIKV infection and progression to disease are complex traits modulated by environmental and genetic factors. The complexity of providing care to those who are at risk for infection or are already infected with Zika in this evidence-scarce environment cannot be understated. There is little known about why some people become ill from Zika whereas most people do not. The objective of this study was to analyse some maternal characteristics that could be related to ZIKV infection during pregnancy, Jundiaí, São Paulo, Brazil.
**Methods**

This was a prospective cohort study including 457 pregnant women during prenatal care at the same institution through clinical, obstetric, and laboratory evaluation. The maternal diagnosis of Zika virus infection was performed in urine (RT-PCR).

**Results**

Among the 457 pregnant women, it was observed that 10.9% (50) presented RT-PCR positive for Zika virus in the urine and was compared with some maternal characteristics as Rh negative blood type 38.9% vs 9.8% (p<0.001); Obesity 27.3% vs 10.5% (p=0.079); Gestational diabetes 18.9% vs 9.1% (0.034); Chronic hypertension 7.4% vs 11.4% (p=0.376); Urinary infection 17.9% vs 10.5% (p=0.226); Cervical intraepithelial neoplasia (CIN III) 100.0% vs 10.4% (p<0.01); HPV infection 50.0% vs 10.8% (p=0.076).

**Conclusions**

This indicates the urgent need for more studies regarding the factors of risk, pathophysiology of viral infection and the natural protection against the virus. Also, a clear understanding of the existing knowledge and behaviors in a population is essential to successfully implementing good health care strategies. We believe that the rate of ZIKV infection could be explained by a combination of these factors that probably was influenced by the hormonal and metabolic factors of these pregnant women.
THE ROLE OF T CELLS IN THE MURINE IMMUNE RESPONSES TO SYNTHETIC PhtD_pep19 AND PhtE_pep40 PEPTIDES OF PNEUMOCOCCAL HISTIDINE TRIAD PROTEINS D(PhTD) AND E (PhTE)

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Background

We proved the efficacy of selected B-cell epitopes, PhtD_pep19[aa200-219] and PhtE_pep40[aa79-98] derived from PhtD and PhtE proteins respectively, to elongate the survival in a mouse model of lethal sepsis by pneumococcal serotype 3. The kinetics of anti-peptide antibody avidity following repeated immunizations in mice with these epitopes, revealed avidity maturation, suggesting a T-cell dependent response. Moreover, these peptides were predicted by SYFPEITHI algorithm to be good binders to MHCII of BALB/c mice. In this study we further evaluated the role of T-cells to murine immune responses.

Methods

Balb/c mice(n=6/group) were immunized sc with each one of the selected peptides, emulsified either in complete Freund'sAdjuvant (for priming )or in Incomplete Freund's Adjuvant(for boosters). Mice(n=6/group) that received adjuvant alone , were used as controls. Spleens were removed 14 days after the last booster. Splenocytes from all mice were incubated in the presence of both peptides. SpleenCells cultured with ConcavalinA were used as positive, whereas cells cultured with complete RPMI-1640 were used as negative. All cells were then pulsed with 2mCi/mL of 3H-thymidine. Results are expressed as stimulation index(SI). SI>2 were considered positive.

Results

PhtD peptide induced a significant proliferation of murine spleen cells primed with its relevant peptide(SI=7,1),whereas PhtE peptide failed to elicit a significant proliferative response(SI<2), to spleen cells taken by all groups. Spleen cells from mice immunized with Freund's adjuvant showed no proliferative response in presence of either PhtD and PhtE peptides indicating that these peptides don't activate mouse T-cells polyclonally.

Conclusions

The role of T cells in the murine immune response to PhtD peptide is more prominent compared to PhtE, suggesting that PhtD peptide could be a B and T-cell epitope.(This study was supported by ESPID-Small-Grant-Award-2018)

Clinical Trial Registration (Please input N/A if not registered)
CHARACTERIZATION OF NASOPHARYNGEAL COLONIZATION OF STREPTOCOCCUS PNEUMONIAE IN EARLY INFANCY
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Background

Streptococcus pneumoniae is a major cause of infectious diseases including pneumonia and sepsis. Pneumococcal colonization is thought to be the first step in the development of invasive diseases. Besides, the widespread use of antimicrobial agents has led to the high prevalence of resistant pneumococci, resulting in the difficulty of treatment. Therefore, vaccines have been developed to prevent pneumococcal infections.

Methods

A longitudinal birth cohort study was conducted and infants were prospectively examined for nasopharyngeal colonized bacteria at birth, 1st, 6th, 12th, 18th, 24th, 36th, 48th and 60th months of age, especially focusing on the serotype distribution and antimicrobial susceptibilities. Factors associated with pneumococcal colonization and their influences on the clinical outcomes were also assessed. Infants with congenital abnormalities, birth weight <2500 g, or who required mechanical ventilation at any time since birth were excluded.

Results

From 2012 to 2017, nasopharyngeal samples were collected at each planned visit in our series during their first 3 years of life and the prevalence of pneumococcal colonization increased in this period, ranging from 0.3% (2/813) at the age of 1 month to 4.6% (11/241) at 36 months of age. The investigation of serotype disclosed that nearly 80% belonged to non-PCV13 serotypes, including 23A, 15A, 15C and 15B. Besides, the significant increase of non-PCV13 occurred during 2014-2015, the time of which the routine PCV13 was initiated in Taiwan. Higher resistance rate of β-lactam drugs among the pneumococcal isolates was noted in our series and the penicillin nonsusceptibility rate was about 98%.

Conclusions

Under the conditional PCV13 vaccination, the pneumococcal isolates primarily belonged to non-PCV13 serotypes. These replacement serotypes had higher β-lactam resistance, suggesting that we may prescribe antibiotics judiciously to reduce selection pressure in the clinical practice.

Clinical Trial Registration (Please input N/A if not registered)

N/A
Meningitis is one of the significant cause of mortality and morbidity in neonates and children. Interpretation of cerebrospinal fluid (CSF) results using routine tests in neonate is not only difficult but also challenging. This has led to quest for various other markers for rapid diagnosis of meningitis. CSF CRP in adults has been shown to be sensitive enough for the diagnosis of bacterial meningitis and there are no good comparative studies in neonate.

Methods

Study type: Prospective Observational study.

Methods: Neonates with sepsis who qualified for lumbar puncture were included in the study. A detailed history, clinical examination and relevant laboratory investigations including routine CSF analysis along with CSF CRP was done. The neonates were further classified as having meningitis and no meningitis based on the unit protocol.

Results

A total of 100 neonates were included in the study with 50 neonates with meningitis and 50 neonates without meningitis. The median CSF CRP in meningitis and no meningitis group was 5.9(4.7-6.8) and 4.3(2.9-5.6) respectively (p<0.001). At a cut off value of 3.8 mg/l, CSF CRP had a sensitivity of 0.96, specificity of 0.44, with positive and negative predictive values of 0.63 and 0.91 respectively. The area under curve (AUC) for different CSF parameters were 0.76 (0.67-0.85) for CRP, 0.98 (0.96-1) for cells, 0.84(0.76-0.92) for neutrophils, 0.843 (0.76-0.92) for protein and 0.68(0.58 -0.79) for glucose.

Conclusions

CSF CRP has very high sensitivity and moderate specificity for the diagnosis of neonatal meningitis, similar to other CSF parameters and might be useful in situations where delayed analysis of CSF alters the usual clinical picture. The presence of negative CSF CRP in case of ambiguous results of other parameters, can be used to rule out meningitis.

Clinical Trial Registration (Please input N/A if not registered)

N/A
ESP18-0992
SCIENCE AND EDUCATIONAL TRACK
ORAL PRESENTATION SESSION 02: NEONATAL INFECTION

NEONATES TREATED FOR MENINGITIS IN A NEONATAL INFECTION SURVEILLANCE NETWORK ON BEHALF OF THE NEONATAL INFECTION SURVEILLANCE NETWORK (NEONIN)
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Background

Bacterial meningitis is a serious condition in neonates, associated with high mortality and long-term significant sequelae which has not improved in decades, despite the advent of improved antimicrobial-therapy. Clinical presentation of neonatal meningitis is non-specific and affected babies cannot be easily distinguished from those with other septic foci or even unwell babies without infections. Timely and appropriate antibiotic-therapy may promote more favorable outcomes. The study aims to describe the neonates treated for meningitis in an infection-surveillance network and the pathogens involved.

Methods

neonIN is an international web-based surveillance database for culture-proven neonatal infections. Cases of neonates treated for meningitis were extracted and analysed. Repeated growth of the same organism was considered the same episode if occurring within 7 days, or 10 days for Coagulase-negative staphylococci (CONS) and fungi.

Results

492/6227 episodes of sepsis were treated for meningitis. Median birth-weight and gestational-age was of 1180gr(IQR:770-2570) and 29 weeks(IQR:25-36) respectively. Pathogen was identified in CSF in 22.2% of the cases and in blood in 87%. Overall CoNS(115,23.3%) appeared to be the most common isolate in cases that clinicians treated as meningitis. When CoNS was excluded E.coli (81,16.4%) was the most common pathogen followed by GBS (77,15.6%) and Klebsiella sp (41,8.3%).

Table-1 shows stratification for UK and Greece. Infants treated in the UK were of lower birth-weight, earlier gestational-age and had the majority of GBS cases.
Conclusions

Meningitis is a life-threatening disease, with a higher incidence in preterm-infants. A positive-culture from CSF is the traditional standard for diagnosis but in this study appears to be less frequent, reflecting the challenges associated with the diagnosis of meningitis in this population. The potential for under-ascertainment along with the interpretation of CoNS as a cause of meningitis, require further exploration.
MOLECULAR CHARACTERISATION AND CLINICAL IMPACT OF HUMAN BOCAVIRUS AT A TERTIARY UNIVERSITY HOSPITAL IN BARCELONA (CATALONIA, SPAIN)

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Background

Human bocavirus (HBoV) is a causative pathogen of respiratory tract infection (RTI) within the paediatric population. Belonging to the family *Parvoviridae*, it is divided into two species: *Primate bocaparvovirus 1* (includes HBoV1 and HBoV3) and 2 (HBoV2 and HBoV4).

Methods

From October/2014 to May/2017, respiratory specimens from paediatric patients attending a tertiary university hospital in Barcelona (Spain) were collected for respiratory viruses’ laboratory-confirmation. Phylogenetic analyses from partial *VP1-3* sequences were performed from all HBoV laboratory-confirmed specimens. Clinical features were retrospectively studied from medical records.

Results

A total of 206 (2%) cases were HBoV laboratory-confirmed from 10,260 specimens collected. The median age of patients affected was 1.55 years old (IQR 0.98-2.48). Co-detection with other respiratory viruses was highly reported (150; 73%). Phylogenetic analyses of 202 (98%) sequences revealed that all viruses belonged into HBoV1 genotype (99.5%), but one (0.5%) into HBoV2. Non-reported amino acid substitutions were observed. The remaining 4 (2%) viruses could not be characterised.

Up to 53% (109/206) patients had Lower RTI (LRTI), of whom 78 had co-infections (72%) and 76 had comorbidities (70%). LRTI was the cause of hospitalisation in 86/109 (79%). Upper RTI was diagnosed in 69/206 (33%). In hospitalised LRTI cases, the median admission-length was 4 days (IQR 2-6); 73 (85%) required oxygen (median 3 days, IQR 1-4.5); 7 (8%), mechanical ventilation; and 7 (8%), ICU (median 4 days, IQR 4-12). No association was found between co-infections and disease severity.

Conclusions

Recent data on prevalence and genetic diversity of HBoV is here reported. Close monitoring of predominant HBoV1 showed more genetic diversity than previously described, which might suggest
the revision of HBoV1 subclassification. The presence of viral co-detections and patient comorbidities may explain the high prevalence of LRTI.
Background

Respiratory syncytial virus (RSV) is a leading cause of severe lower respiratory tract disease in infants globally. Novavax’ RSV-F Vaccine, a recombinant, near-full-length RSV fusion (F) glycoprotein, is being evaluated in a Phase 3 maternal immunization trial. Transplacental transfer of maternally-derived anti-F neutralizing antibodies elicited by RSV-F vaccination of pregnant mothers is expected to afford protection in infants during the most vulnerable months after birth.

Methods

A Phase 3, randomized, observer-blind, placebo-controlled trial is being conducted in 11 countries to determine safety and efficacy of Novavax’ RSV-F Vaccine given to pregnant women for prevention of RSV lower respiratory tract disease in infants. Healthy, third-trimester, pregnant women are vaccinated with a single dose of aluminum-adjuvanted RSV-F Vaccine. Immunizations are timed so newborns are exposed to the local RSV transmission season in the first 6 months of life; during which they undergo active and passive surveillance for RSV infection identified by RT-PCR. The primary objective is to determine efficacy of maternal immunization against RSV lower respiratory tract infection associated with hypoxemia or tachypnea through the infant’s first 90 days of life; with additional analyses performed up to 180 days. Safety is monitored by an unblinded, independent DSMB.

Results

Over 3,500 women have been vaccinated. The DSMB has made no advisements regarding safety to date, and has recommended trial continuation after 2 futility analyses. Recently, the DSMB conducted an informational analysis and determined vaccine efficacy of 0% could be excluded with at least 90% confidence, implying, with the planned randomization, a point estimate of ≥45%.

Conclusions

Novavax has successfully recruited volunteers into the first, large-scale, Phase 3 maternal immunization trial using an investigational product, allowing for a planned interim efficacy analysis within 12 months.

Clinical Trial Registration (Please input N/A if not registered)
IMPACT OF MODERATE ROTAVIRUS VACCINATION RATES ON THE HOSPITALIZATIONS BY SEIZURES: HETEROLOGOUS OR UNFORESEEN DIRECT VACCINE EFFECTS?

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Background

Recent studies have suggested an association between the vaccination against rotavirus (RV) and a decrease of hospitalization rates caused by any kind of seizures (AKS). Here we analyze the impact of moderate vaccination during 9 years on the AKS hospitalization rates.

Methods

Data of children younger than 5 years old hospitalized by AKS (ICD-9-CM codes 780.3*+779.0*+333.2*+345*) were collected. A study period from 2003-2015 and patients from the Galicia region (NW Spain) were considered. Hospitalization rates were compared before and after the introduction of the RV vaccine (year 2007). Furthermore, hospitalization rates by acute gastroenteritis caused by RV (RV-AGE, ICD-9 code 008.61) were considered in order to analyze possible correlation with AKS rates. Data from year 2007 were excluded from the analysis.

Results

7,105 patients younger than 5 years old were admitted by AKS, and 3,514 by RV-AGE during the studied period. There is a positive and significant correlation between monthly hospitalization rate by AKS and RV-AGE (\(p=0.271\), \(P\text{-value}=0.001\)), with a decrease in the hospitalization rates ranging from 21.6% (95%-IC: 14.0–28.5%) in 2008, to 51.7% (95%-CI: 46.3–56.5%) in 2015, compared to pre-vaccination period rates (from 2003 to 2006) (Figure A). Similar results were observed for patients admitted by convulsions (ICD-9-CM code 780.3*), showing a positive significant correlation with RV-AGE hospitalization rates (\(p=0.322\), \(P\text{-value}=8\times10^{-5}\)). Decrease of hospitalization rates ranged from 36.8% (95%-CI: 29.1–43.6%) in 2008, to 60.8% (95%-CI: 55.2–65.7%) in 2014 (Figure B).
Conclusions

Our results suggest again a protective effect of RV vaccination against seizure-related pathologies. If this is a true heterologous effect of the vaccine or an unpredicted direct effect, needs further investigation. This positive effect should be considered when evaluating the efficiency of vaccination against RV.

Clinical Trial Registration (Please input N/A if not registered)

N/A
HIV FREE SURVIVAL AMONG INFANTS IN A PREVENTION OF MOTHER TO CHILD TRANSMISSION PROGRAM IN RURAL KENYA

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Background

The overall goal of Prevention of Mother to Child Transmission Programs is to have a HIV free living infant. In Kenya, there has been little emphasis on HIV free survival and outcomes of HIV exposed infants at 18 months as measures of effectiveness of PMTCT programs.

Methods

Retrospective cohort study targeting mother-infant pairs seeking HIV care at the Naivasha District Hospital Comprehensive Care Clinic. Consenting mothers completed a questionnaire that assessed socio-demographic characteristics and uptake of PMTCT interventions. Infant HIV status was obtained from records and HIV antibody testing at 18 months for previously untested infants. HIV transmission rates and mortality rates among HIV exposed infants were estimated. Kaplan Meier analysis was used to determine HIV free survival pattern.

Results

One hundred and thirteen mother-infant pairs were enrolled, 99 (87.7%) mothers and 85 (92%) infants received antiretrovirals. Most 100 (88.5%) infants had HIV deoxyribonucleic acid polymerase chain reaction testing at 6 weeks, 84 (80.8%) had follow up HIV antibody testing at 18 months. Infant HIV infection was 2.7% at 6 weeks and 4.4% between 6 weeks and 18 months giving an overall MTCT rate of 7.1%. Infant mortality rate was 0.9% at 6 weeks and 7.1% between 7 weeks and 18 months giving an overall mortality rate of 8%, and an 18 month HIV-free survival rate of 83.9%.

Conclusions

The PMTCT programme was effective in reducing HIV infection and mortality in 83.96% of infants whose mothers were enrolled into it. MTCT rates increase substantially after 6 weeks indicating the urgent need for interventions to reduce breast milk transmission.
Valganciclovir - Resistant Congenital CMV - A Case Report

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Title of Case(s)

Valganciclovir- resistant congenital CMV (cCMV) – a case presentation

Background

Valganciclovir (VGCV) treatment of symptomatic cCMV infections for 6 months improves hearing and developmental outcome at 24 months modestly. 4 case reports on the emergence of CMV drug resistance in cCMV are available. We present a 5th case.

Case Presentation Summary

A mature infant with cCMV was diagnosed on his first day of life due to blueberry muffin signs, severe hepatosplenoomegaly, anemia, thrombopenia, chorioretinitis-scars bilaterally; cerebral ultrasound showed periventricular calcifications. cCMV infection was confirmed by PCR from urine. IV ganciclovir was started from day 2. Due to a GFR around 25ml/kg/min dose adjustments were necessary, drug trough levels were too high several times. CMV UL97 genotyping from plasma, urine and throat swabs was initiated in week 7 p.p. due to elevated viral load (VL).

UL97 mutation C603W was detected from blood at week 7.

A switch to UL97 M460V and M460I mutations was observed in blood and urine two weeks later. In throat swabs, all three canonical UL97 mutations appeared and antiviral therapy was stopped. During antiviral therapy, levels of VGCV were always in the correct range. His further clinical course resulted in the need for bilateral cochlear implants due to deafness; several transfusions due to profound anemia, substitution of fat- soluble vitamins and UDC due to hepatic involvement. He has significant delay of motor functions so far at 14 months of age. Viral load was no longer present in throat swabs at 14 months of age.

Learning Points/Discussion

This case demonstrates the failure of VGCV therapy despite correct levels of VGCV. There is an urgent need for further therapeutic options in cCMV as well as for a good definition, which infants really profit from antiviral therapy.
ANALYSIS OF 7,438 PERTUSSIS CASES AND 183 CONFIRMED DEATHS REGISTERED IN SÃO PAULO STATE, BRAZIL, 2008 TO 2017

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Title of Case(s)

Analysis of 7,438 pertussis cases and 183 confirmed deaths registered in São Paulo State, Brazil, 2008 to 2017

Background

Pertussis was considered a controlled disease in Brazil, but recently there was an increase in the number of cases and deaths, coinciding with the introduction of RT-PCR. The aim of this study was to describe the pertussis cases and associated deaths in São Paulo State, in the last decade.

Case Presentation Summary

This was a retrospective descriptive study of all pertussis cases reported in São Paulo State from Jan/2008 to Dec/2017, based on the analysis of São Paulo State Health Department (SINAN/SINANNET/SIM/DDTR/VE/CCD/SES-SP) registers.

A total of 7,438 pertussis cases and 183 deaths were confirmed in São Paulo State. A total of 6,377 cases (85.7%) were reported in children < 10 years of age, 327 (4.4%) cases in persons ≥ 10 to 20 years and 734 (9.9%) in adults. In 2014, the overall incidence rate was 5.28 cases/100,000, and the rate in infants <12 months 258/100,000. All deaths were confirmed in infants <12 months of age, with a peak in 2013 and 2014, when 50 and 47 pertussis deaths occurred, respectively. The case fatality rate varied from 2.5% to 5.4% in infants <12 months of age, reaching 9% in infants <2 months of age in 2017.

Learning Points/Discussion

The number of pertussis cases and deaths grew 8-fold from 2008 to 2014. The case fatality rates were very high in infants, leading health authorities to introduce pertussis immunization for pregnant women in 2014. Considering that humans are the only reservoir for Bordetella pertussis, it is essential to improve surveillance in all age groups and reach high coverage rates of pertussis immunization in primary series and booster doses.
Liver failure in the course of tuberculosis in a boy treated with isoniazid

Background

Tuberculosis is a worldwide public health problem, caused by Mycobacterium tuberculosis. Current drugs such as isoniazid, pyrazinamide and rifampicin used in the treatment of tuberculosis are potentially hepatotoxic and can lead to drug-induced hepatitis.

Case Presentation Summary

We present the case of a 5-year-old boy treated for tuberculosis. The family history revealed that the boy had contacted with his ill grandfather. On the basis of the radiological imaging and the results of laboratory tests, the diagnosis of lymph node tuberculosis was made. Anti-mycobacterial therapy with a 3-drug regimen (isoniazid, rifampicin, pyrazinamide in standard doses) was started. On the 6th day of treatment, vomiting and yellowing of the skin and the whites of eyes occurred. Laboratory tests revealed increased aminotransferase activity and elevated bilirubin levels. Due to increasing parameters of hepatic insufficiency (increased INR and elevated bilirubin levels), the boy was admitted to the Gastroenterology Unit of the Department of Pediatrics. Laboratory tests demonstrated: ALT 1888 U/L, AST 5517 U/L, total bilirubin 54.1 umol/L, INR 2.12. Tuberculosis treatment was discontinued. N-acetyl-cysteine, ursodeoxycholic acid, acyclovir and parenteral hydration were implemented. The patient was additionally diagnosed with Clostridium difficile infection, which was treated in a standard way. During the hospitalization, general improvement and gradual normalization of laboratory tests were observed. Currently, the boy has regular follow-up appointments in the outpatient setting; test results of liver cell functioning and damage parameters are normal.

Summary. In our paper we would like to draw attention to hepatotoxic effects of drugs used for the treatment of tuberculosis, also in the pediatric population.

Learning Points/Discussion

We would like to draw attention to hepatotoxic effects of drugs used for the treatment of tuberculosis, also in the pediatric population.
CASE OF AUTOIMMUNE HEMOLYTIC ANEMIA IN A CHILD WITH NECROTIZING PNEUMONIA

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A CASE OF AUTOIMMUNE HEMOLYTIC ANEMIA IN A CHILD WITH NECROTIZING PNEUMONIA

Background

Even though AIHA with Mycoplasma and Viral infections are common in children, AIHA associated with pneumococcal pneumonia is a rare presentation.

Case Presentation Summary

A 2½ years old child presented with cough and fever-2 weeks with fast breathing. On evaluation, he was pale, tachypnoic and in respiratory distress with bronchial breathing on right side. Admitted in PICU and started on HFNC initially and later shifted to BIPAP in view of worsening distress. He was started on IV antibiotics, Meropenem and Vancomycin. Chest X-ray showed right upper and middle lobe consolidation. A complete blood counts showed leucocytosis with anemia (Hb-7.9g/dl on admission and 5.9g/dl on next day). CRP was 338mg/dl. Peripheral smear showed normocytic hypochromic erythrocytes with few macrocytes, target cells and polychromatic cells. Coombs test was positive with anti IgG/C3d. Auto antibodies are present at 37 deg C as well as 4 deg C (both warm and cold antibodies). He was treated with IV Immunoglobulin (1g/kg) and later 1 unit of PRBC transfused. CT chest was done due to continuous fever spikes and persistently elevated inflammatory markers and it showed right necrotizing pneumonia with moderated empyema. Blood culture was negative, but PCR was positive for Streptococcus pneumoniae. Right thoracotomy and decortication with evacuation of empyema with lung debridement was done. IV antibiotics continued for 14 days and later changed to oral therapy.

Repeat Chest X-ray showed significant improvement.

Learning Points/Discussion

1. AIHA, though common with mycoplasma pneumonia can be seen with streptococcus pneumonia.
2. A short course of IVIG or Corticosteroids are beneficial for severe hemolytic anemia in acute phase.
3. Treatment of pneumonia itself reduces the hemolysis in due course.
MYCOBACTERIUM BOVIS BCG OSTEOMYELITIS OF THE RIB: A RARE COMPLICATION PRESENTING YEARS AFTER IMMUNISATION

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Background

Bacillus Calmette-Guérin (BCG) is one of the most commonly administered vaccines globally. BCG is used to prevent tuberculosis (TB) and contains live attenuated strains of Mycobacterium bovis. In rare cases a distant complication such as osteomyelitis develops years after the immunisation. In countries where most children are non-BCG-vaccinated, diagnosis of these complications can be challenging. We present a case with BCG rib osteomyelitis.

Case Presentation Summary

A three-year-old Indian-born boy presented with a tender enlarging mass of the right lowest rib. Ultrasound imaging revealed an intramuscular tumour with central necrosis and led to a suspicion of sarcoma. A contrast-enhanced MRI showed a 3.7x2.4x2.8 cm mass in the rectus abdominis muscle. Abdominal MRI and thorax CT did not show signs of metastasis. Biopsy uncovered purulent material that was sent for further testing. PCR was positive for Mycobacterium tuberculosis complex and histopathological examinations showed granulomatous inflammation. The boy had received BCG immunisation in India at infancy. The QuantiFERON-TB Gold Plus test was negative for TB and modified T-SPOT.TB test was highly reactive only to purified protein derivate stimulation. Hence, a BCG osteomyelitis was suspected and treatment with rifampin and isoniazid initiated. Further molecular methods identified the pathogen as Mycobacterium bovis BCG with resistance to pyrazinamide confirming the diagnosis. In follow-up, the biopsy wound over the infected rib developed into a scrofuloderma that started healing well.

Learning Points/Discussion

BCG complications can develop years later and should be kept in mind when young immigrant children present with osteomyelitis. BCG strains have varying susceptibility to antituberculous drugs and reliable information on the worldwide use of different strains is important for choosing the correct regimen.
MEET THE PROFESSOR 16 - TUBERCULOSIS MANAGEMENT CONUNDRUMS

THIS CAN’T JUST BE RESPIRATORY SYNCYTIAL VIRUS! A MILIARY TUBERCULOSIS CASE

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Title of Case(s)

This can’t just be RSV! A miliary tuberculosis case

Background

Miliary tuberculosis is rare in industrialized countries and in vaccinated populations. It results from a massive lymphohematogenous dissemination of Mycobacterium tuberculosis and it can have variable and nonspecific clinical manifestations.

In 2016 Portugal fulfilled the WHO/UNICEF criteria to be considered a low-risk country for tuberculosis and switched from a BCG universal vaccination to a risk group strategy. Case Presentation Summary

GMMF, a 3 month-old boy of gypsy ethnicity, was hospitalized with a hypoxemic RSV acute bronchiolitis. His clinical condition deteriorated and he was sent to an intensive care unit (PICU) for mechanical invasive ventilation. On day seven he returned to the ward. Two days later, his clinical condition worsened and he was transferred to our PICU. The chest radiograph showed bi-apical opacities. Despite ventilatory support, he maintained hypoxemia, weight loss, diarrhea, neurologic abnormalities (poor visual behavior, irritability), and hyponatremia.

A Chest CT revealed apical lobes consolidation, several nodular and cystic formations and enlarged mediastinal lymph nodes. Mycobacterium tuberculosis complex was isolated (PCR and culture) in a bronchial sample; meningeal involvement was confirmed (CSF low glucose, high protein and pleocytosis). Anti-TB therapy was immediately started (INH+RIF+ETB+PZN) and Prednisone with a favorable evolution. The family was screened. His grandmother has a longstanding cough, being the probable source; she refuses screening, as there are prejudices against TB in her community.
Miliary TB is fatal if untreated and early initiation of specific anti-TB treatment can be lifesaving. Since vaccination strategy changed in 2017 in Portugal, it is essential that risk groups are correctly identified and vaccinated shortly after birth, as it should have happened with this infant. Screening of contacts must be done thoroughly, despite existing prejudices against this disease.
Congenital Zika Syndrome: Beyond microcephaly

Background

To describe other malformations in a group of infants with microcephaly, probably caused by Zika virus in a reference center in Rio de Janeiro, Brazil.

Case Presentation Summary

Methods:

Infants were recruited between December 2015 and March 2017 in a pediatric infectious disease clinic in Rio de Janeiro in this descriptive study. Infants were referred to this study, if they were born with microcephaly in Rio de Janeiro. Exclusion criteria included detection of an alternative cause for the patient's presentation. All children were tested for toxoplasmosis, cytomegalovirus, rubella, dengue, syphilis, and HIV. They had consultation with genetics, ophthalmology, and were submitted to BERA, echocardiogram, and abdominal sonogram, as well as a central nervous system (CNS) radiology exam (sonogram, CT scan, or magnetic resonance).

Results:

22 infants were evaluated. At birth, Zika virus PCR were performed on blood/CSF/urine from 13/22 newborns and they were all negative. Their cephalic perimeter were 22-32 cm, All, but two presented abnormal CNS radiology exams (calcifications and ventriculomegaly). Seven presented ophthalmology alterations (coloboma and macular hypopigmentation), 9 presented cardiac malformations (7 with patent foramen ovale and 2 with persistent arterial duct), 2 with BERA abnormal exam, 2 with congenital clubbing, and 1 with bilateral cryptorchidism.

Learning Points/Discussion

Although CNS malformations were common, the infants with possible congenital Zika syndrome must be investigated for other malformations. These infants need a multidisciplinary follow up.
RITUXIMAB AS A SECOND LINE TREATMENT IN TWO CASES OF AUTOIMMUNE ANTI-NMDAR POST-HERPES SIMPLEX ENCEPHALITIS

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Title of Case(s)

Rituximab as a second line treatment in two cases of autoimmune anti-NMDAr Post-Herpes Simplex Encephalitis

Background

Incidence of encephalitis in childhood is 5-10/100000. Herpes Simplex Virus (HSV) is the first cause of severe encephalitis in children. Anti-NMDAr Encephalitis is a rare complication of this condition.

Case Presentation Summary

We present 2 boys, 12 (patient-1) and 3 months old (patient-2) respectively, that presented to A&E with fever, decreased consciousness and complex partial seizures. In both cases MRI (figure1) showed temporal lobe injuries compatible with herpetic meningoencephalitis and HSV-1 PCR in CSF was positive. They had an initial satisfactory evolution on acyclovir and antiepileptic drugs.

After 14 days of treatment, in patient-2 and 25 days in patient-1, both presented sudden deterioration, with new seizures, loss of developmental milestones and appearance of choreoathetosic movements. Repeat MRI showed progression of previous injuries with necrohaemorrhagic encephalitis (figure1). Autoimmune encephalitis was suspected, and then confirmed by presence of antibodies against brain glutamate NMDA receptor in CSF and blood serum.

Both patients received methylprednisolone (30mg/kg/day) during 5 days, 2 doses of Immunoglobulins (1gr/kg/day), and 5 cycles of plasmapheresis. No clinical improvement was observed, so Rituximab was started with 4 weekly doses, showing neurological improvement and decrease in chorea after the second dose. 7 months after treatment, patient-1 showed increasing aggressiveness and sleep disturbances as IgG anti-NMDAr rose in blood serum. Suspecting a relapse, a new cycle of Rituximab was administered with subsequent improvement and negativity of antibodies.

Learning Points/Discussion
Autoimmune encephalitis should be suspected if clinical worsening is observed during evolution of herpetic encephalitis and anti-NMDAr antibodies in CSF and blood serum performed. Treatment with Rituximab may improve significantly the course of the disease and should be considered early as second line treatment.
WHEN BILATERAL SPASTIC PARALYSIS IS THE PRESENTING FEATURE OF HIV INFECTION

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Title of Case(s)

WHEN BILATERAL SPASTIC PARALYSIS IS THE PRESENTING FEATURE OF HIV INFECTION

Background

HIV encephalopathy is the most common neurologic manifestation of HIV infection in children and can be its presenting feature, namely as spastic tetraplegia. Neurodevelopmental impairment in HIV-infected children is still common, especially in non-treated children.

Case Presentation Summary

A previously healthy 8-year-old boy was referred to our institution with a 2-year history of motor and cognitive regression. He first presented dysarthria and subsequently a gait disturbance and bladder and bowel incontinence. He had weight loss and numerous molluscum contagiosum lesions. Neurologic examination was remarkable for dysarthria, muscular atrophy and spastic paraparesis with brisk and spreading stretch reflexes, especially on the right side, bilateral extension plantar responses and extinguishable clonus. MRI revealed cortico-subcortical, cerebellar and brainstem atrophy, with prominent ventricles and sulci, and multifocal white matter lesions which, together with the clinical picture, were suggestive of HIV infection, which was confirmed by serologic testing, viral load was 174456 copies/mL with 148 CD4/mL, CSF viral load was 193258 copies/mL. Antiretroviral therapy (ART) was started and eighteen months later, with an undetectable viral load and 836 CD4/mL, the patient had a better school performance and recovered some motor skills. MRI was repeated at this time and showed a notorious improvement.

Learning Points/Discussion

This presentation of both spastic paraparesis and pseudobulbar palsy was common in the pre-highly active ART era, and is probably associated with the late diagnosis in this child. ART seems to have a good impact on this disease. Contrary to what happens in adults with HIV encephalopathy, ART seems to have a good impact on the disease with radiological regression and good prognosis.
SEQUELAE AFTER MEASLES VACCINATION IN PEDIATRIC PATIENTS WITH SIGNIFICANT NEUROLOGIC DISEASE

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Title of Case(s)

SEQUELAE AFTER MEASLES VACCINATION IN PEDIATRIC PATIENTS WITH SIGNIFICANT NEUROLOGIC DISEASE

Background

Measles outbreaks constitute considerable healthcare burden in the pediatric population and pose significant risk for unvaccinated children due to underlying medical conditions. Measles vaccination is recommended for outbreak control. Our aim is to present a small case series of previously unvaccinated children with severe neurologic disease who were vaccinated during the measles outbreak in Greece (2017-2018) and describe their vaccination side effects.

Case Presentation Summary

Recommendation for trivalent measles-mumps-rubella (MMR) vaccine administration was made to 3 distinct groups of neurologic patients, whose severe underlying condition had prohibited measles vaccination. Vaccination side effects (seizures, fever, neurodevelopmental regression) were retrieved 30 days following vaccination, for both dosages. Overall, 22 children were included (14 with intractable epilepsy, 7 with neurometabolic disease, 1 with severe pervasive developmental disorder). Three children denied vaccination. Side effects included afebrile seizures (3/19), fever (3/19) and seizures with fever (2/19). No child exhibited developmental regression. Afebrile seizures appeared 5-10 days post vaccination and had benign characteristics. No child needed adjustment of its antiepileptic treatment. A patient with Dravet syndrome, received both MMR doses with no sequelae. Fever appeared one week post vaccination, lasted 1-2 days, and was mild. In two children, seizures were in conjunction with fever, resembled typical febrile seizures, with no encephalopathy. Of note, these children received the quadrivalent (MMRV) vaccine.

Learning Points/Discussion

The main side effects of measles vaccination were vaccine-associated seizures, on the grounds of known epilepsy. No aggravation of epilepsy was observed. The seizures had a benign course. MMRV administration was related to increased likelihood for febrile convulsions. No long-term neurologic or neurodevelopmental sequelae were observed.
THE HHV-6 AND HHV-7 IN NEWBORNS IN ST. PETERSBURG, RUSSIA

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²Pavlov First State Medical University, Infectious diseases, Saint-Petersburg, Russia

Title of Case(s)

THE HHV-6 AND HHV-7 IN NEWBORNS

Background

The exanthem subitum (ES) is the common childhood illness for the children of 6-18 months of life. Approximately 90% cases of ES are caused by the HHV-6 and 10% - by HHV-7, which typically occurs later than HHV-6. After birth children have protective maternal antibodies to HHV-6 and HHV-7, which decreased to 6 months of age, but titer of maternal anti-HHV-7 can decrease later. However rare cases of HHV-6 in newborns were observed. Nevertheless, we didn’t find any published references about the cases of HHV-7 infection in newborn.

Case Presentation Summary

Objective. We aimed to find the cases of HHV-6 and HHV-7 ES in newborn children in St. Petersburg, Russia.

Methods. Forty-three newborn infants with fever and/or rash were included at St.Petersburg Filatov's Children Hospital (Russia) from 2015 to 2016. The DNA of HHV-6 and HHV-7 in blood plasma samples were detected by qualitative PCR and quantitative real-time PCR. HHV-6A- and HHV-6B genotypes in blood serum were detected with newly developed real-time PCR kit.

Results. Totally 11 patients (25%) were positive for HHV-6 viral DNA. All of them were infected with HHV-6 of genotype B. There were 6 boys (54%) and 5 girls (46%). The age of patients varied from 14 days to 28 days. HHV-7 was found in 2 patients of 27 and 33 days of life. The most frequent diagnosis was ES. Four patients had rash without fever.

Learning Points/Discussion

It is considered that ES is a rare disease in newborn infants. However in our small sample 25% of infants with fever and/or rash were infected with HHV-6. The clinical manifestations in these patients were milder than classic ES after six months of age.
MACROLIDE RESISTANT PERTUSSIS IN AN INFANT WHOSE MOTHER WAS NOT VACCINATED AGAINST PERTUSSIS

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²Skåne University Hospital, Department of Paediatric Anaesthesia and Intensive Care, Lund, Sweden
³Skåne University Hospital, Department of Paediatric Hematology and Oncology, Lund, Sweden

Title of Case(s)

Macrolide resistant pertussis in an infant whose mother was not vaccinated against pertussis

Background

Pertussis infection has been recognized as a global cause of morbidity and mortality, especially amongst infants in the first months of life. The most severe course of infection is seen in unvaccinated infants, who can develop life-threatening complications.

Case Presentation Summary

A 6 week-old boy was admitted to PICU from a local hospital due to respiratory collapse. The diagnosis of pertussis was made 1 week after initial symptoms including coughing, and he started a 10-day course of erythromycin, 4 days after which he was admitted to our PICU. Despite treatment with azithromycin and cefotaxime, he deteriorated clinically, developing pronounced leukocytosis. While in extremis he obtained two blood exchange transfusions and intravenous immunoglobulin with good clinical effect. The pertussis strain identified showed resistance to erythromycin, clarithromycin and azithromycin. The bacteria had good sensitivity to trimethoprim-sulfamethoxazole and he was therefore given this treatment for 19 days. The total length of antibiotic treatment was 23 days. The patient required invasive mechanical ventilation and high-flow nasal therapy (Optiflow®) for 16 days and 11 days respectively. On day 25 he could be transferred to the standard paediatric department. His mother had not been vaccinated in childhood, and developed similar symptoms few weeks before him.

Learning Points/Discussion

The vaccination of pregnant women, which is well described, can significantly decrease the severe courses of pertussis infection in neonates and infants. Usual treatment of pertussis with antibiotics can fail due to bacterial resistance. Blood exchange transfusion is an important therapy to consider in severe cases of pertussis infection with significant leukocytosis.
Background

For bile duct non-surgical manipulation, our local protocol indicates peri-operative antibiotic prophylaxis (PAP) with 24 hours of endovenous piperacillin-tazobactam. Our purpose is to describe the incidence and characteristics of its infectious complications, to evaluate their association with specific risk factors (common bile duct absence, liver transplantation) and the adherence to the PAP protocol; as a part of our Paediatric Antibiotic Stewardship Program.

Case Presentation Summary

Epidemiological, clinical and microbiological data were collected from all consecutive episodes of bile duct non-surgical manipulation in paediatric patients (≤ 18 years) performed in our center in a 9-years period (from 2009 to 2017). We analyzed 74 episodes in 23 patients.

Median age was 4 years (ICR 1,3-7), 56% female. Biliary atresia was the commonest disease (36.5%). Regarding to risk factors, 53 episodes (61%) occurred in liver-transplanted patients and 54 (73%) in common bile duct absence. There were 19 infectious complications (25.6%), mainly in the first 24 hours: 4 fever without source, 8 sepsis and 7 cholangitis. Blood cultures were positive in 6/18 and bile cultures in 12/13 (mainly Gram-negative bacilli). Thirty episodes were performed under antibiotic treatment due to a previous infection. PAP was correct in 21/44 episodes (48%).

Learning Points/Discussion

Adherence to PAP protocol needs to be optimized in order to evaluate its usefulness in non-surgical manipulation of bile duct, since there is a significant number of infectious complications after these procedures, mainly in the first 24 hours. Neither prophylaxis nor previous antibiotic treatment seem to be effective in preventing them, so bile duct manipulation should be limited to accurate indications. Liver transplantation and common bile duct absence seem to increase this risk.
Prenatal Ultrasound and MRI Brain Prediction of Congenital CMV Infection: A Case Series

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2St George’s- University of London, Fetal Medicine Unit, London, United Kingdom
3St George’s University of London, Paediatric Infectious Diseases Research Group PIDRG, London, United Kingdom
4University of Southampton, Paediatric Infectious Diseases, Southampton, United Kingdom

Title of Case(s)

Prenatal Ultrasound and MRI Brain Prediction of Congenital CMV Infection: A Case Series

Background

Cytomegalovirus (CMV) is the most common cause of congenital infection and the leading cause of neurological disability and sensorineural hearing loss, yet it is under recognised due to the challenges in its diagnosis both postnatally and prenatally, whereby the prenatal pathognomonic features of congenital CMV infection are not well established.

Case Presentation Summary

We report all confirmed cases of congenital CMV infection referred to a tertiary-level fetal medicine unit in London over a 15-year period. 32 cases were identified.

Ultrasound abnormalities were reported in 23/32 (72%) cases. The most common extra-cranial abnormality was intrauterine growth retardation (10/18, 56%), followed by echogenic bowel (9/18, 50%). The most common cranial abnormality was ventriculomegaly (10/15, 67%), followed by microcephaly (8/15, 53%).

10/15 (67%) cases with cranial ultrasound abnormalities had foetal MRI brain evaluation. MRI confirmed the ultrasound cranial findings in all cases and adds additional information to 9/10 (90%) cases. Temporal lobe abnormalities (4/10, 40%) were the most common additional information not detected via ultrasound, whereby 1 case on a background of normal cranial ultrasound that had a brain MRI performed also reported a temporal lobe
abnormality.

<table>
<thead>
<tr>
<th>Case</th>
<th>Ultrasound Extra-cranial Abnormalities</th>
<th>Ultrasound Cranial Abnormalities</th>
<th>Brain MRI findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>None</td>
<td>None</td>
<td>Not performed</td>
</tr>
<tr>
<td>2</td>
<td>Echogenic bowel, liver calcifications, small VSD</td>
<td>None</td>
<td>Not performed</td>
</tr>
<tr>
<td>3</td>
<td>None</td>
<td>None</td>
<td>Not performed</td>
</tr>
<tr>
<td>4</td>
<td>IUGR, pericardial effusion</td>
<td>Microcephaly</td>
<td>Microcephaly, high signal in the white matter (temporal lobes)</td>
</tr>
<tr>
<td>5</td>
<td>IUGR, echogenic bowel</td>
<td>None</td>
<td>Not performed</td>
</tr>
<tr>
<td>6</td>
<td>None</td>
<td>None</td>
<td>Not performed</td>
</tr>
<tr>
<td>7</td>
<td>None</td>
<td>None</td>
<td>Not performed</td>
</tr>
<tr>
<td>8</td>
<td>None</td>
<td>None</td>
<td>Not performed</td>
</tr>
<tr>
<td>9</td>
<td>None</td>
<td>Microcephaly, ventriculomegaly</td>
<td>Borderline ventriculomegaly, polymicrogyria</td>
</tr>
<tr>
<td>10</td>
<td>Foetal hydrops, pericardial effusion, IUGR, cardiomegaly</td>
<td>Hypoplasic cerebellum</td>
<td>Not performed</td>
</tr>
<tr>
<td>11</td>
<td>IUGR</td>
<td>Ventricleomegaly/microphathy</td>
<td>Ventricleomegaly, microcephaly, asymmetry of the anterior cerebral hemispheres, shallow sulci and suspicious of a neural migration disorder.</td>
</tr>
<tr>
<td>12</td>
<td>None</td>
<td>Ventricleomegaly microcephaly</td>
<td>Ventricleomegaly, microcephaly and diffused brain calcifications</td>
</tr>
<tr>
<td>13</td>
<td>Echogenic bowel, ascites</td>
<td>Choroid plexus cysts</td>
<td>Not performed</td>
</tr>
<tr>
<td>14</td>
<td>None</td>
<td>Ventricleomegaly microcephaly</td>
<td>Abnormal gyration, ventriculomegaly, hypoplasic cerebellum</td>
</tr>
<tr>
<td>15</td>
<td>None</td>
<td>Ventricleomegaly microcephaly</td>
<td>Ventricleomegaly, microcephaly, hypoplasic cerebellum, global delayed development of the cerebral hemispheres</td>
</tr>
<tr>
<td>16</td>
<td>Echogenic bowel</td>
<td>Ventricleomegaly/microphathy</td>
<td>Ventricleomegaly, microcephaly, hypoplasic cerebellum, global delayed development of the cerebral hemispheres</td>
</tr>
<tr>
<td>17</td>
<td>None</td>
<td>Ventricleomegaly</td>
<td>Ventricleomegaly and hyper signal in the white matter (temporal lobes)</td>
</tr>
<tr>
<td>18</td>
<td>IUGR</td>
<td>Ventricleomegaly microcephaly</td>
<td>Hyper signal in the white matter (temporal and occipital lobes)</td>
</tr>
<tr>
<td>19</td>
<td>Cardiomegaly</td>
<td>None</td>
<td>Not performed</td>
</tr>
<tr>
<td>20</td>
<td>Echogenic bowel</td>
<td>Ventricleomegaly</td>
<td>Not performed</td>
</tr>
<tr>
<td>21</td>
<td>Pericardial effusion, cardiomegaly, foetal hydrops</td>
<td>None</td>
<td>Not performed</td>
</tr>
<tr>
<td>22</td>
<td>None</td>
<td>None</td>
<td>Not performed</td>
</tr>
<tr>
<td>23</td>
<td>None</td>
<td>Microcephaly, ventriculomegaly, dysgenesis of the corpus callosum, hypoplasic cerebellum</td>
<td>Microcephaly, bilateral ventriculomegaly, dysgenesis of the corpus callosum, cerebellar hypolasia, abnormal echogenicity in the posterior horn and smooth cortex</td>
</tr>
<tr>
<td>24</td>
<td>Echocenic bowel, IUGR, placental calcifications</td>
<td>Ventricleomegaly/microphathy</td>
<td>Ventricleomegaly, intraventricular adhesions, periventricular echogenicity</td>
</tr>
<tr>
<td>25</td>
<td>Echogenic bowel, cardiomegaly, placenomegaly</td>
<td>None</td>
<td>Not performed</td>
</tr>
<tr>
<td>26</td>
<td>None</td>
<td>None</td>
<td>Not performed</td>
</tr>
<tr>
<td>27</td>
<td>None</td>
<td>Ventricleomegaly</td>
<td>Ventricleomegaly, prolongation of the temporal horns</td>
</tr>
<tr>
<td>28</td>
<td>Foetal hydrops, IUGR</td>
<td>None</td>
<td>Not performed</td>
</tr>
<tr>
<td>29</td>
<td>Foetal hydrops, IUGR, oligohydramnios, placenomegaly, cardiomegaly</td>
<td>Microcephaly</td>
<td>Not performed</td>
</tr>
<tr>
<td>30</td>
<td>Pericardial effusion, IUGR</td>
<td>None</td>
<td>Not performed</td>
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<tr>
<td>31</td>
<td>Echogenic bowel</td>
<td>None</td>
<td>Normal</td>
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<tr>
<td>32</td>
<td>Echogenic bowel, IUGR, oligohydramnios, cardiomegaly, hepatomegaly, placenomegaly</td>
<td>Hypoplasic cerebellum, periventricular echogenicity, tectocelestial vasculopathy</td>
<td>Not performed</td>
</tr>
</tbody>
</table>

**Learning Points/Discussion**

Our ultrasound findings on the commonest cranial and extra-cranial abnormalities in congenital CMV infection are consistent with the literature. While these findings are suggestive of a congenital
infection, they are not pathognomonic for congenital CMV infection.

Foetal MRI brain is likely to increase the positive predictive value for the diagnosis of brain abnormalities in congenital CMV infection. The findings of temporal lobe abnormalities could be pathognomonic for congenital CMV infection, supported by the literature which also found temporal lobe abnormalities to be predictive of symptomatic congenital CMV infection.
MEET THE PROFESSOR 07 - HIV MANAGEMENT DECISIONS

WE SEE MORE OFTEN NOW. A HIV INFECTED ADOLESCENT WITH SECONDARY SYPHILIS

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²Istanbul University Istanbul Medical Faculty, Department of Medical Microbiology-Virology, Istanbul, Turkey

Title of Case(s)

HIV infected adolescent with syphilis coinfection

Background

Human Immune deficiency Virus (HIV) infection incidence among adolescents has been rising, both globally and in our country. Sexually transmitted diseases like syphilis can also be encountered in these patients. Here in we present a 16 year old male with HIV-syphilis coinfection.

Case Presentation Summary

On admission; he was conscious, well in appearance, with height and weight percentiles appropriate for age. There were no aphthous lesions in his mouth. He had bilateral cervical multiple lymphadenopathies with maximum diameter of 1.5 cm plus right axillary 1 cm mobile lymphadenopathy. No hepatosplenomegaly was palpated. He had widespread maculopapular rash, which was more intense on extremities. Genital examination was compatible with pubertal male development; it revealed neither lesion nor inguinal lymphadenopathy. Laboratory examination revealed white blood cell count as 1800/mm³ (absolute neutrophil counts: 800/mm³, absolute lymphocyte counts: 900/mm³). Liver transaminases and renal function tests were within normal range. C-reactive protein was slightly elevated, 25 mg/L (<5 mg/L). Urinary analysis was normal. Epstein - Barr virus and Cytomegalovirus polymerase chain reaction tests, rubeola IgM, rubella IgM and parvovirus IgM were negative. Viral respiratory panel [ResPlex II Panel v2.0 (Qiagen, Hilden, Germany)] was negative. The Rapid Plasma Reagin (RPR, Spinreact, Girona, Spain) titer for syphilis was reported as positive with a titer of 1/128. He was successfully treated with intramuscular benzatin penicillin G.

Learning Points/Discussion

Considering HIV infected adolescent patients are under increased risk of sexually transmitted diseases like syphilis, they should serologically be tested during their follow-up.
MEET THE PROFESSOR 13 - SEVERE PNEUMONIA IN CHILDREN

NECROTIZING PNEUMONIA: THE CHALLENGE OF MAKING THE DIAGNOSIS

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²Hospital de Braga, Paediatric Pulmonologist, Braga, Portugal
³Hospital de Braga, High Dependency Unit Care, Braga, Portugal

Title of Case(s)

Necrotizing pneumonia: The challenge of making the diagnosis

Background

Necrotizing pneumonia (NP) is an emerging and severe complication of community acquired pneumonia in children. Despite being uncommon, its incidence is rising. The most common pathogens associated with NP in children are Streptococcus pneumoniae and Staphylococcus aureus.

Case Presentation Summary

A two-year-old female with personal history of epilepsy, due to a probable tuberous sclerosis, medicated with levetiracetam and vigabatrin, presented to the emergency room with a four-days history of fever, anorexia and lethargy. Physical examination revealed prostration and dehydration signs. A complete blood count showed haemoglobin 8.9 g/dL, leukocytes 6,200/mm³ (neutrophils 4200/mm³, lymphocytes 1200/mm³), C reactive protein (CRP) 326 mg/L. Chest radiography revealed a hypotransparency in the upper two-thirds of the right hemithorax. She was empirically treated with ampicillin and azithromycin and transferred to High Dependency Unit Care. At day-three, due to clinical deterioration with persistent fever and prostration, it was decided to change antibiotics to amoxicillin/clavulanate and clindamycin. At day-six, with persistence of the fever and elevation of CRP, antibiotherapy was switched to meropenem and vancomycin. A chest CT, performed at day-eight, showed necrosis of the right upper lobe and a small pleural effusion on the right, which thoracic echography confirmed “a maximum thickness of 2mm”. There was favourable clinical outcome:remained afebrile from day-thirteen, general condition improved and only required intermittent oxygen therapy during sleep, maximum 1L/min. She was discharged after 21-days of ev antibiotics with amoxicillin/clavulanate for ten days. The etiological agent remains unknown:tuberculosis was excluded, blood cultures/serologies were negative.

Learning Points/Discussion

The hallmark of this case is a striking dissociation between the radiological findings and the respiratory symptoms. NP diagnosis should be considered when, despite appropriate antibiotics, the child remains febrile and unwell.
A case of young infant HPeV1 infection with intraventricular hemorrhage

Background

Human parechoviruses (HPeVs) are RNA viruses that are classified in the family Picornaviridae and 16 genotypes are confirmed. HPeVs usually cause mild respiratory or gastrointestinal symptoms, but HPeV1 and HPeV3 are known that they can provoke sepsis and meningoencephalitis leading to neurological sequelae in neonates and young infants.

Case Presentation Summary

We report a case of HPeV1 infection with Intraventricular hemorrhage. The patient was 2 months' male infants who have no abnormality in perinatal history. He was hospitalized with complaint of looked pale and was presented irritability and neck stiffness. Empirical antimicrobial treatment was started immediately as a serious infectious disease and was combined anticoagulant therapy. His general condition improved on day 5, but intraventricular hemorrhage was detected by Computed Tomography scan. HPeV1 was detected by blood and fecal PCR and it was thought that a series of symptoms were caused by viremia of HPeV1. There is no abnormal neurological finding on examination at discharge, it is necessary careful follow-up observation.

Learning Points/Discussion

HPeVs infection in neonatal and young infants, especially HPeV3 can be severer and cause cerebral hemorrhage as a neurological complication. Compared with HPeV3, HPeV1 symptoms are relatively mild and there are few central nervous symptoms. There is no report of HPeV1 that caused cerebral hemorrhage so far. This case is important that it can merge intraventricular hemorrhage even with HPeV1 infection.
Severe acute cytomegalovirus hepatitis in an immunocompetent child - Case report

Background

The clinical course of the infection is usually mild, although a small percentage of patients suffer from protracted and severe fever. CMV infection in immunocompetent hosts may rarely be able to lead to severe organ specific complications. Most cases of CMV induced hepatitis occur in adults with severe immune deficiency. Only a few cases involving immunocompetent patients have been reported. Severe hepatitis is an uncommon presentation.

Case Presentation Summary

We present the case of a 6-year-old child presented with a 1-week history of recurrent fever and nonspecific maculo-papular rash. Her initial evaluation physical revealed fever, angina and moderate hepatosplenomegaly. Laboratory tests showed newly increased transaminase activity (x 300N) and serum bilirubin and prothrombin time were also severely impaired. She was admitted for evaluation of acute hepatitis in the 9th Paediatric Departamen at the National Institute for Infectious Diseases „Prof. Dr. Matei Bals” – Bucharest, Romania.

Learning Points/Discussion

Serology for hepatitis A, B, C, E and HIV were negative. Abdominal imaging indicated moderate hepatosplenomegaly. Cultures were sterile. Additional tests for uncommon viral hepatitis included herpes simplex virus, cytomegalovirus and Epstein-Barr virus. Subsequently, cytomegalovirus serology showed an initial IgM positive and negative IgG titre and repeated titres of cytomegalovirus serology showed seroconversion. Cytomegalovirus DNA qualitative PCR was negative in the day 10 after the onset of the simptome. No antiviral medication was given, but she required fresh plasma suport for the coagulation impairment. She continued to have intermittent daily fever but reported no associated symptoms. She was discharged 10 days after admission in good condition, her serum hepatic profile returned to normal and she reported no more episodes of fever or rash.
Anaphylaxis after immunization

Background

Control, record and analysis of side effects after immunization play a vital role in ensuring the safety of vaccination. For the period 2012-2017 in Belarus 5 cases of anaphylaxis were recorded after immunization.

Case Presentation Summary

In the first 31-year-old male the reaction in the form of an isolated critical blood pressure drop was caused by the planned RV adsorbed diphtheria tetanus caprinized anatoxin (ADSM) in the first minute (prevalence is not calculated). In the second 42-year-old male anaphylaxis developed due to emergency tetanus prophylaxis for 1 hour after the administration of anti-tetanus anatoxin and antitetanus serum (prevalence is not calculated). In a third 58-year-old male anaphylaxis in the form of cardiovascular and respiratory manifestations developed 10 minutes after the administration of anti-botulinum serum type A (prevalence was 1 to 28 doses administered).

In a 17-year-old girl anaphylaxis developed on RV ADSM 15 minutes after the administration of the vaccine in the form of gastrointestinal and cardiovascular symptoms.

In a 7-year-old girl severe refractory anaphylaxis manifested on RV MMR in the first minute after subcutaneous administration of the vaccine. The clinical picture developed fast, the symptoms included weakness, pallor, a single vomiting, rapid loss of consciousness with a lack of pulse and respiration. Resuscitation during 1 hour was unsuccessful, a fatal outcome has been reported. The girl did not have a background pathology, including allergic.

Emergency care was provided to patients in accordance with the national protocols for managing patients with anaphylaxis.

Learning Points/Discussion

As can be seen from the above in Belarus, the prevalence of anaphylaxis after immunization in children is 4.34 cases per 1,000,000 doses of MMR administered and 0.67 cases per 1,000,000 administered doses of ADSM.
ES18-1018
EDUCATIONAL TRACK

MEET THE PROFESSOR 07 - HIV MANAGEMENT DECISIONS

MYCOBACTERIUM AVIUM COMPLEX (MAC) IMMUNE RECONSTITUTION INFLAMMATORY SYNDROME (IRIS) IN HIV-POSITIVE ADOLESCENT

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Title of Case(s)

Mycobacterium avium complex (MAC) immune reconstitution inflammatory syndrome (IRIS) in HIV-positive adolescent

Background

Mycobacterium avium complex (MAC) are developing in HIV-patients with CD4 cells less than 50. IRIS could occur within 3-12 months of initiating HAART.

Case Presentation Summary

First HIV-diagnosed 13 year old boy was hospitalized in our center with complains: weight loss, fatigue.

Blood test: Hb - 95 g/l, platelets – 143 x10^9/l, WBC- 10.7x10^9/l, ERS – 74 mm/h; ALT- 130 U/l, AST - 181 U/l; CD4 – 0.9%-2 cell. viral load - 54667 RNA copy /ml

X-ray: signs of pneumonia.

Antibiotic treatment and ART (TDF/FTC/EFV) were prescribed.

2 weeks later: fever, liver and spleen enlargement appeared. Blood test: Hb- 81 g/l, platelets – 51 x10^9/l, WBC- 18x10^9/l; ferritin -2337 µg/l. CD4 – 2%-8 cell, PCR DNA CMV was positive. Thorax and abdominal CT scans: mesenteric and thorax lymph nodes enlargement, hepatosplenomegaly.

HLH and TB /MAC –infections were suspected.

Ethambutol, rifampicin, amikacin, linezolide, levofloxacin, azithromycin, prednisolone, ganciclovir were prescribed. Clinical, laboratorial, radiological improvement were achieved.

On the 9 months of ART treatment: weight loss, abdominal pain and vomiting, mesenteric lymph nodes enlargement appeared. Laboratory data: Hb- 89 g/l, platelets – 136 x10^9/l, WBC - 6x10^9/l, ESR-50 mm/h, CRP-92 mkg/l, ferritin -967 µg/l, CD4 – 10%-57 cell, viral load - 60 RNA copy /ml,

CT and US image: hepatosplenomegaly, mesenteric lymph nodes enlargement. The biopsy of mesenteric lymph node was made.
Mycobacterium avium complex was diagnosed, worsening of patients condition on 9 months of ART was estimated as a immune reconstitution syndrome (IRIS).

**Learning Points/Discussion**

In our patient the next risk factors for IRIS developing were presented:

- Low CD4 count at initiation of ART;
- High pre-ART HIV viral load;
- Shorter duration of OI treatment prior to starting ART;
- Rapid suppression of HIV viral load.
RISK FACTORS FOR DEATH AMONG UNDER FIVE CHILDREN WITH DIARRHEA AND BACTERAEMIA IN BANGLADESH

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Background

Mortality in diarrhoeal children specifically having bacteraemia had gained less attention in spite of its enormous impact in under five mortality. So we aimed to evaluate risk factors for death among under-five children having both diarrhea and bacteraemia.

Methods

For this retrospective analysis we used hospital patients’ electronic database of Dhaka Hospital of ‘icddr,b’, Bangladesh, and enrolled those were admitted to hospital’s in-patient wards and had bacterial growth in their cultured blood samples on admission, between June 2014 and May 2017. Those who died during hospital stay constituted cases, and those were recovered and discharged considered as controls. Demographic, clinical and laboratory parameters were compared between the groups.

Results

Among a total of 401 diarrheal children with bacteraemia, 45(11%) were the cases and 356 were the controls. Salmonella typhi (34%) was the most predominant isolate followed by Staphylococcus species (16%), Pseudomonas species (9%), Escherichia coli (7%) and Klebsiella species (6%). The cases more often presented with E. coli (22% vs. 5%, p=<0.001) and Klebsiella (18% vs. 4%, p=0.001) bacteraemia compared to controls. Overall resistances against commonly used antibiotics were also found higher among cases. In logistic regression analysis after adjusting for potential confounders, clinical sepsis (p=0.007) and hypoxaemia (p=0.018) were independently associated with cases.
Conclusions

Case fatality rate was considerably high among the children having both diarrhea and bacteremia. E. coli and Klebsiella could be main culprits. Traditional or empirical antibiotics may not be safe in this clinical scenario. Clinical sepsis and hypoxaemia were found to be independent predictors for death in these children. Thus, case management with vigilant examination for the signs of clinical sepsis and hypoxaemia and adequate treatment with proper antibiotics are necessary in this group especially in resource limited settings.
Detection of Pathogenic Viruses in the Ambient Air in Seoul, Korea

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³Sanggye Piaik Hospital- Inje University College of Medicine, Pediatrics, Seoul, Republic of Korea

Background

Asian dust is a meteorological phenomenon in which sand and particulate matter originating from the southeast of Mongolia and northwest of China are transported by the wind to Korea, Taiwan, and Japan. The possible transport of pathogenic microorganisms during Asian dust events could be an important concern for health workers; however, this is still uncertain owing to a lack of supporting evidence. The present study aimed to investigate the presence of pathogenic microorganisms in air samples collected during the Asian and non-Asian dust periods.

Methods

Between March and September 2016, air samples were collected at three weather observation stations in Seoul using a high-volume air sampler. Multiplex PCR was performed using the Allplex™ respiratory and gastrointestinal panel assay kits to detect 46 microorganisms. RT-PCR was performed for klassevirus, Aichivirus, and human parechovirus (HPeV) detection. Semi-nested PCR was performed to confirm the genotypes of human rhinovirus (HRV), norovirus (NoV) GII, and HPeV using primers based on the VP4/VP2, capsid, and VP1 genes.

Results

In total, 71 air samples were collected during the Asian (8 samples) and non-Asian (63 samples) dust events. During an Asian dust event, only one HRV-positive air sample was collected on April 23. During the non-Asian dust period, HRV, HPeV, NoV, enteroaggregative Escherichia coli, enterotoxigenic E. coli, and Blastocystis hominis were detected in four, two, one, one, one, and one air samples, respectively.

Conclusions

This study was the first to confirm the presence of pathogenic viruses, including HRV, NoV, and HPeV in ambient air in Korea. Most of these pathogenic viruses were detected in
ambient air samples during the non-Asian dust period, which suggests that Asian dust might not play a major role in epidemics caused by viral pathogens.
CORRELATION BETWEEN EPIDEMIOLOGY OF RESPIRATORY VIRUSES IN HOSPITALIZED CHILDREN AND CLIMATIC VARIABLES

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Background

Seasonal epidemics of respiratory viruses are common in temperate climate countries, but studies regarding the relationship between incidence of emerging respiratory viruses including human metapneumovirus, coronavirus NL63, and bocavirus are rare. We aimed to investigate the incidence of respiratory viral infections and the influence of climatic factors on seasonal activity of viruses in Seoul, South Korea.

Methods

Between February 2013 and December 2016, a total of 4731 nasopharyngeal specimens from children hospitalized with acute respiratory tract infections were tested to detect 16 common respiratory viruses using multiplex PCR. Meteorological data in Seoul during the study period were collected from the national monitoring system, and the correlation between monthly incidence of respiratory viral infections and climatic factors was analyzed.

Results

Respiratory syncytial virus A (RSV-A), RSV-B, and coronavirus OC43 significantly reached the peak in winter, whereas influenza B, human metapneumovirus (HMPV), parainfluenza virus-3 (PIV-3), and bocavirus significantly peaked in spring, and enterovirus significantly peaked in summer. Mean temperature was negatively correlated with influenza A, RSV-A/B, and coronavirus and positively correlated with PIV-3/4 and enterovirus. Relative humidity was positively correlated with PIV-1 and negatively correlated with influenza B. Wind speed was negatively correlated with adenovirus, coronavirus NL63, but positively correlated with HMPV.

Conclusions

In this study, each respiratory virus showed a specific trend of seasonal incidence depending on climatic variables. There have been several trials to investigate the seasonality of respiratory viruses and how their incidences are correlated with climatic factors including temperature and RH, yet the results are contradictory. Herein temperature has more...
influence on epidemiology of respiratory viruses than other climatic variables. RH and wind speed have been suggested as possible influential factors for epidemics of some respiratory viruses.
EBV AND STREPTOCOCCUS PNEUMONIAE COINFECTION IN CHILDREN WITH INFECTIOUS MONONUCLEOSIS

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Background

Nasopharyngeal pneumococcal colonization varies according to region and community. In Ukraine the rate of S. pneumoniae carriage in healthy children under 5 years of age is approximately 35%-54% (Chernyshova L, 2015). The aim of this study was to analyze the association between acute Epstein-Barr virus (EBV) infection, upper respiratory tract viral infections (URI) and nasopharyngeal (NP) colonization with S. pneumoniae.

Methods

We observed 191 patients 0-5 y.o. - 64 children with EBV primary infection and 127 children with URI. We tested for the presence of 10 common respiratory viruses by real-time PCR; S. pneumoniae was isolated by culture methods. Serotyping was performed using the multiplex PCR. We tested anti-VCA IgM & IgG as markers for acute EBV.

Results

The occurrence of S. pneumoniae NP colonisation in children with primary EBV was significantly higher (70.3%) than in the children with URI (21.3%). Most prevalent S. pneumoniae serotypes in children with acute EBV were 14 (50%) followed by 23F (12.5%) and 6 (9.4%), in children with URI – 19F (27.6%), 6A/B (15.7%), 23F (7.8%). A 6.25% children with EBV have been shown to carry more than one serotype S. pneumoniae.

Conclusions

Our study suggests that there is a high incidence of S. pneumoniae coinfections in children admitted with EBV primary infection. Streptococcus may be a secondary pathogen or have a synergistic effect in the inflamed or damaged tonsillar and pharyngeal tissue.

Clinical Trial Registration (Please input N/A if not registered)

N/A
SEVERITY ADJUSTED RISK OF LONG-TERM ADVERSE SEQUELAE AMONG CHILDREN WITH OSTEOMYELITIS

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2Stanford University, Orthopaedic Surgery, Palo Alto, USA
3Children’s Health System of Texas, Pediatric Orthopaedic Surgery, Dallas, USA

Background

The purpose of this investigation is to assess the prognostic impact of the initial severity of illness on long-term outcomes of children with osteomyelitis.

Methods

Children with osteomyelitis were prospectively enrolled from 2012-2014. Care was accomplished by a multidisciplinary team according to clinical practice guidelines. Data was collected to define severity of illness during the initial hospitalization and assess outcomes. Clinical examination, radiographic imaging, and outcome survey administration were performed at a minimum of 2 year follow-up. A comparison cohort analysis was performed according to initial severity of illness score (SIS) of Mild (0-2), Moderate (3-6), and Severe (7-10).

Results

Of 195 children enrolled, 139 (71.3%) returned for follow-up at an average of 2.4 years. Children with severe illness were less likely to have normal radiographs (Severe – 4.0%; Moderate – 38.2%; Mild – 53.2%, p<0.0001), and more likely to have osteonecrosis, chondrolysis, or deformity (Severe – 32.0%; Moderate – 5.9%; Mild – 1.3%, p<0.0001). Functional outcome scores of PODCI (Severe – 91.8; Moderate – 96.7; Mild – 96.6) and Peds QL (Severe – 86.6; Moderate – 92.4; Mild – 94.4) did not significantly differ between cohorts.

By regression analysis SIS plus age under 3 years and MRSA predicted severe sequelae with an area under the curve of 0.8617 and an increasing odds ratio of 1.34 per point of increase in severity score.

Conclusions

Long term severe sequelae among children with osteomyelitis occurred in 11 of 139 (7.9%) children and were predicted by initial severity of illness. Other risks that diminish the likelihood of complete resolution or increase the risk of severe sequelae included MRSA and young age.
The majority of children with osteomyelitis do not require long term follow-up beyond resolution of infection.
SAFETY OF RE-IMMUNIZATION OF PEDIATRIC PATIENTS WITH A PAST HISTORY OF IMMUNE THROMBOCYTOPENIC PURPURA

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¹St. Marianna University School of Medicine, Pediatrics, Kawasaki, Japan

Background

Immune thrombocytopenic purpura (ITP) is known to be associated with receipt of some vaccines, particularly the measles-mumps-rubella (MMR) vaccine. However, the safety of re-immunization of pediatric patients with a past history of ITP is unclear. In this survey, we assessed the risk of ITP recurrence among pediatric patients with a past history of ITP upon re-immunization.

Methods

We conducted a retrospective chart review and telephone interviews with parents of children younger than 15 years of age who were diagnosed with ITP in our hospital between 2010 and 2015 regardless of precedent vaccination history. Vaccine-associated ITP was defined as a clinical condition in which platelet counts were less than 100x10⁹/L within 28 days of immunization.

Results

During the observation period, 47 children were diagnosed with ITP. Parents of 36 patients of them (76.6%) agreed to the interview and were, therefore, included in the analysis. Fourteen (38.9%) cases were classified as vaccine-associated, and 22 (61.1%) cases, as non-vaccine associated ITP. Following the diagnosis of ITP, 134 vaccine doses were administered to the 14 vaccine-associated ITP patients (100%), and 110 doses were administered to 16 of the 22 non-vaccine associated ITP patients (72.7%). Most frequently, additional vaccine doses were to protect against influenza (101 doses). Only 25 doses of measles containing vaccines were used. Although, 2 cases of ITP recurred (14.3%) among members of the vaccine-associated ITP group, both improved without pharmacologic management. Meanwhile, no ITP recurred among members of the non-vaccine associated ITP group.

Conclusions

Our study suggests that re-immunization of pediatric patients with a past history of immune thrombocytopenic purpura is typically safe.
The incidence of early onset neonatal sepsis is 0.9/1000 live births.

Introduction of National institute of Health and Clinical Excellent (NICE) guidelines in UK (2012) led to increase in babies being commenced on antibiotics, for longer duration and more undergoing lumbar punctures (LP).

Meningitis is very uncommon in asymptomatic babies with only perinatal risk factors for sepsis. Our unit uses first CRP≥20mg/l or second CRP≥50mg/l as guide for LP.

Methods

Data was collected January-March 2017 for all neonates who were started on antibiotics having met our local criteria for screening.

Results

There were 169 such episodes, 46% female and 54% male neonates. Gestation varied between 25+6-40+weeks and 76% were term.

Major Indication for septic screen were for maternal temperature and antibiotics in 39% and 22% were for symptomatic neonates. Other risk factors contributed to the remaining.

Only 1 positive blood culture (Streptococcus Agalactiae) was seen in a symptomatic term neonate with normal CRP’s normal.

13.6% of neonates met our criteria for LP, however none of them were treated for suspected early onset neonatal meningitis.

64% had antibiotics for 2-3 days, 30% for 4-7 days and rest >7 days. None of the neonates treated for suspected early onset sepsis re-presented to paediatrics with suspected partially treated meningitis/sepsis in the first 10 days after being discharged from hospital.
Conclusions

Although the criteria for performing an LP differs from that of NICE, we have shown that there were no cases of early onset neonatal meningitis in this study. We therefore propose that an arbitrary cut off value for CRP should not strongly influence the decision to perform an LP and instead we should rely on a combination of factors particularly the presence of symptoms.
Antibiotic Resistance Patterns of Bacteria Isolated from Neonatal Intensive Care Units (NICU) in Pediatric Hospital in Hamadan, West of Iran

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²Hamadan University of Medical Sciences, Microbiology, Hamadan, Iran

Background

One of the major causes of increasing of bacterial contamination in hospitals is misusing of disinfectants and increasing of antibiotics resistance of bacteria. The aims of this study was the evaluation of bacterial contamination of intensive care units (NICU) and determination of antibiotics resistance patterns in isolated bacteria, west of Iran.

Methods

This was a cross-sectional study that 100 samples were randomly collected from environments and apparatus of neonatal intensive care units including washing sink, floor of wards, beds of patients, phototherapy, oxygen mask, incubator, infant scale, suction and staff fingers. The samples were inoculated into EMB and Blood agar by sterile wet swabs and transferred to medical laboratory for identification. Strains were tested for antibiogram by NCCLS protocol. The antibiotics disks were consisted of: ampicillin, imipenem, ceftriaxone, ceftizoxime, erythromycin, vancomycin, gentamicin, cepahlexine, cefepime and ciprofloxacin. Data was gathered through a questionnaire and analyzed using SPSS 13 software.

Results

The average rate of bacterial contamination of NICU of was 73%. The most contaminated places were washing sink (98%), suction (74%) and the lowest was phototherapy (35%) and oxygen mask (44%), respectively. The most bacteria isolated were as follow: Staphylococcus epidermidis (17%), Bacillus subtilis (12.5%), Acinetobacter baumannii (11.3%) and E. coli (8.2%). Most of isolates (60%-90%) were sensitive against imipenem, ceftriaxone, vancomycin, cefepime and ciprofloxacin, whereas most of them were resistant to ampicillin, gentamicin, erythromycin and cepahlexine.

Conclusions

Our results showed the considerable bacterial contamination (73%) of NICU in particular with Acinetobacter baumannii and the high drug resistance in strains isolated from hospital, it seems that sterilization and disinfection methods in hospitals were not performed correctly.
So, we recommended that health workers should be trained regularly to control the incidence of nosocomial bacteria.
MYCOPLASMA PNEUMONIAE IN PAEDIATRIC PATIENTS: DO MACROLIDE RESISTANCE AND/OR DELAYED TREATMENT MATTER?
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Background
Mycoplasma pneumoniae (MP) is a common pathogen for pneumonia in children especially in the post-pneumococcal conjugate vaccination era. Though self-limited disease was found in the majority of the patients, severe diseases occurred occasionally. The pathogenesis was related to both direct invasion and immune over-reaction. The emergence of macrolide resistance was reported worldwide. It is important to delineate whether macrolide resistance or delayed treatment affects outcome.

Methods
We retrospectively collected pediatric patients with Mycoplasma pneumoniae infection with clinical suspicion and confirmed by positive PCR from respiratory tract specimen subsequently in a tertiary medical center in Taiwan from 2010 to 2017. Patients’ medical history, demographics, clinical manifestations, laboratory parameters, radiographic findings, Mycoplasma pneumoniae bacterial load, co-infection pathogens and treatment course were reviewed from medical charts and performed statistical analysis.

Results
Among 471 children with positive Mycoplasma pneumoniae PCR, 95% were diagnosed with pneumonia. Seventeen percent of patients had extrapulmonary complications, 16% had pleural effusion and 1.5% had respiratory failure. Delayed treatment was associated with prolonged fever after treatment, fulminant disease, and extrapulmonary manifestations (table 1). The mean rate of macrolide resistance was 24% and macrolide resistance was related to longer febrile duration, longer hospital stay, lung consolidation and impaired liver function tests (P<0.05).
Conclusions

Macrolide resistance was fairly common in Taiwan and might lead to delayed appropriate antibiotic treatment. Delayed treatment, no matter macrolide resistance or not, was associated with more severe and/or prolonged diseases among pediatric patients with Mycoplasma pneumoniae infection. Early diagnosis of Mycoplasma pneumoniae as well as the awareness of macrolide resistance makes early effective antibiotic treatment possible and may improve clinical outcomes.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>No delayed treatment (N=186)</th>
<th>Delayed treatment (N=168)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever over 7 days after appropriate antibiotics</td>
<td>5/165 (3%)</td>
<td>11/127 (9%)</td>
<td>0.04</td>
</tr>
<tr>
<td>Fulminant disease</td>
<td>1/185 (1%)</td>
<td>6/169 (4%)</td>
<td>0.04</td>
</tr>
<tr>
<td>Macrolide resistance</td>
<td>7/186 (4%)</td>
<td>37/169 (22%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Extrapulmonary manifestations</td>
<td>23/186 (12%)</td>
<td>43/169 (25%)</td>
<td>0.002</td>
</tr>
<tr>
<td>Impaired LFT</td>
<td>9/134 (7%)</td>
<td>26/129 (20%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Pulmonary consolidation</td>
<td>99/174 (571%)</td>
<td>105/160 (66%)</td>
<td>0.24</td>
</tr>
<tr>
<td>WBC count (/uL)</td>
<td>8576 ± 3559</td>
<td>8965 ± 3864</td>
<td>0.35</td>
</tr>
<tr>
<td>Eosinophil (%)</td>
<td>1.5 ± 1.9</td>
<td>2 ± 2.6</td>
<td>0.03</td>
</tr>
<tr>
<td>CRP (mg/dL)</td>
<td>3.7 ± 3.4</td>
<td>5.2 ± 5.6</td>
<td>0.006</td>
</tr>
</tbody>
</table>

Delayed treatment was defined as the initiation of appropriate antimicrobial agent longer than the mean duration of 5.6 days. Fulminant disease was defined as respiratory failure or Stevens-Johnson syndrome. Data are shown as positive number/testedumber (percentage). Impaired LFT (liver function test) is defined as over the upper limit of normal level. WBS denotes white cell count, CRP C-reactive protein, and LFT liver function test.

Conclusions

Macrolide resistance was fairly common in Taiwan and might lead to delayed appropriate antibiotic treatment. Delayed treatment, no matter macrolide resistance or not, was associated with more severe and/or prolonged diseases among pediatric patients with Mycoplasma pneumoniae infection. Early diagnosis of Mycoplasma pneumoniae as well as the awareness of macrolide resistance makes early effective antibiotic treatment possible and may improve clinical outcomes.
PREVALENCE AND RISK FACTORS ASSOCIATED WITH NEISSERIA MENINGITIDIS CARRIAGE IN SOUTH AMERICAN COUNTRIES

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Background and Objective

The aim of this study is to identify the prevalence of carriage of N. meningitidis, the most frequent serogroups and risk factors associated with oropharyngeal colonization by meningococci in Latin American countries.

Methods

We review the articles published in PUBMED and SCIELO from Jan/2010 to Dec/2017, using the words Neisseria meningitidis, carriage and risk factors and analyzed those from Latin American countries.

Learning Points Discussion

We found 10 studies from Brazil (7), Chile (2) and Colombia (1) in this period. The prevalence of N. meningitidis carriage varied from 4% to 69.5%; the most prevalent strains were non groupable, except in one study. In Brazil, the most common serogroup identified among groupable strains was C in São Paulo State, and B in Bahia State, where conjugated vaccine against Men C was introduced for adolescents in 2010. Serogroups W and Y were more commonly identified in Chile and Colombia, respectively. The risk factors associated with N. meningitidis colonization were: age (>14 years), overcrowding and deprived social condition (low education level, work at oil refineries, frequent attendance to crowded social venues, share a room, number of household members), habits (active or passive smoke, kiss people).

The prevalence of N. meningitidis carrier and risk factors in South American countries were similar to those described in Europe. The low identification of serogroup C in Salvador could reflect the effect of previous campaign of immunization. The colonization by hypervirulent strains and the possibility of capsular switch between different serogroups make clear the necessity to offer vaccines with broader spectrum protection to protect adolescents and young adults.
EARLY BAYESIAN DOSE ADJUSTMENT OF VANCOMYCIN IN CHILDREN: A RANDOMIZED CONTROLLED TRIAL

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³Necker-Enfants Malades hospital - Assistance Publique-Hôpitaux de Paris, Department of Pediatric Immunology - Hematology and Rheumatology, Paris, France
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Background

Methicillin-resistant staphylococcal infections are still a global burden. Area under the curve (AUC) of the serum concentrations versus time to minimum inhibitory concentration (MIC) ratio is the PK parameter that best predicts vancomycin efficacy. Vancomycin pharmacological target is narrow and difficult to achieve because of a wide interindividual variability, especially in children. The aim of this study was to assess if an early Bayesian dose adjustment of vancomycin would increase the rate of target attainment, at the 24th hour of treatment (H24).

Methods

In this prospective randomized controlled trial, the routine care were compared with an early vancomycin plasma concentration monitoring (3h after treatment initiation) followed by an early Bayesian dose adjustment. The Bayesian estimation was made using a published population PK model that included age, body weight and serum creatinine as covariates. The primary study endpoint, analyzed with a Fisher’s exact test, was the proportion of patients achieving the pharmacological target of vancomycin $AUC_{0-24}/MIC \geq 400$ and $\leq 800$ h at H24.

Results

Among the 99 patients aged 3 months to 17 years randomized in ICU, gastroenterology and immunohematology departments, 82 had analyzable data. All of them received continuous infusion of vancomycin. The proportion of patients who achieved the target at H24 was 85%
in the Bayesian group versus 57% in the control group (p=0.007). In the Bayesian group, vancomycin dose was increased in 79% of patients, decreased in 8% and was not modified in 5 patients. There was no difference between the groups regarding iatrogenic events.

**Conclusions**

This study is the first to prospectively assess the contribution of early Bayesian dose adjustment of vancomycin. It increased the proportion of children achieving vancomycin pharmacological target at the 24th hour of treatment.

**Clinical Trial Registration (Please input N/A if not registered)**

NCT02694458
Background

Few studies have focused on bone and joint infections (BJI) in infants younger than 3 months. We describe the clinical and paraclinical features and the outcomes of infants aged under 3 months hospitalized with BJI.

Methods

Children under 3 months of age hospitalized with BJIs from January 2004 to January 2015 in 3 pediatric teaching hospitals were retrospectively included.

Results

Of the 4971 children hospitalized for BJI during the study period, 71 (1.4%) were under 3 months of age. The median age was 25 days [Interquartile range (IQR): 17-43]. The most common sites of infection were hip (32%, n= 23) and knee (32%, n= 23). Symptoms included pain (94%, n= 67), mobility limitation (87%, n= 62) and/or fever (52%, n= 37). Eleven (15%) cases were classified as nosocomial BJI. A pathogen was identified in 51 children (72%). Main pathogens were *Streptococcus agalactiae* (45% of documented cases, n= 23), *Staphylococcus aureus* (22%, n= 11) and *Escherichia coli* (18%, n= 9). The initial median CRP rate was 31 mg/L (IQR 17-68). Of the 34 children followed for more than 1 year, 4 developed severe orthopedic conditions (epiphysiodesis, limb length discrepancy, and/or impaired limb function).

Conclusions
*Streptococcus agalactiae* is the most common causative agent of BJI in infants under 3 months of age. Orthopedic sequelae are rare but severe and require long term follow up of all children.
POPULATION IMPACT OF A CAPSULAR GROUP B MENINGOCOCCAL VACCINE: DIRECT AND INDIRECT PROTECTION – INSIGHTS FROM THE NEW ZEALAND OUTBREAK

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³Royal Children’s Hospital Melbourne, Royal Children’s Hospital Melbourne, Melbourne, Australia

Background

New Zealand (NZ) experienced an outbreak of capsular group B meningococcal disease leading to the implementation of a vaccination programme that targeted the outbreak strain from 2004. The impact of the programme since the campaign ceased is unknown.

Methods

A descriptive analysis of the meningococcal disease incidence rates in NZ from 2001-2013 was performed. A Poisson regression model, was used to estimate the impact of the programme five years after its end.

Results

During the campaign, a sustained decline in rates of total meningococcal disease (16.75/100000 to 1.53/100000) and capsular group B disease (to 10.41/100000-0.68/100000), occurred in all age groups. In the 5-19 year age group, vaccine impact was demonstrated by a statistically significant reduction in the incidence rate ratio in 2013 when compared with the expected reductions if there had been no intervention (IRR=0.06; 95% CI: 0.01 to 0.43, p=0.005). Similar results were found for the capsular group B meningococci non-epidemic strains, implying cross-protection. However, in 2013 the rate of disease in the <1 year and 1-4 year age groups was not significantly different from the rate expected if there had been no intervention.

Conclusions

Evidence of persisting direct protection against the outbreak strain and cross-protection against other endemic strains was identified 5 years after cessation of the MeNZB vaccination campaign. However, the lack of control of disease in subsequent unvaccinated birth cohorts indicates that herd immunity from this programme is negligible 5 years after
implementation.
These findings have important implications for countries introducing new generation MenB vaccine programmes and close monitoring of population impact following introduction of these vaccines is needed.
Influenza represents a significant cause of childhood morbidity and mortality, contributing up to 13% of acute lower respiratory tract infections worldwide. As a result, between 28,000–111,500 children aged <5 years die annually. Current diagnostic approaches to pediatric influenza have not been studied. In addition, post-pandemic anti-viral prescribing rates in hospitalized children have remained low throughout Europe, including in critical care settings. We therefore aimed to determine the different diagnostic and treatment algorithms utilized for pediatric influenza.

Methods

A qualitative survey was developed to explore the diagnostic and anti-infective management practices of pediatric influenza. This survey encompassed 10 questions incorporating 3 clinical patient vignettes and was distributed to ESPID members between October-November 2017.

Results

The survey was completed by 175/1490 (12%) respondents from 50 countries. The majority 113 (72%) were at university teaching hospitals. 93 (53%) had an antigen test, 82 (46%) had a molecular test and 38 (22%) reported having both available. 51 (29%) reported testing availability at all times of day and night. 97 (63%) used a guideline to direct testing and management. Clinical suspicion was considered the most important factor when sending a rapid influenza diagnostic test (RIDT), followed by an immunocompromised state and presence of co-morbidities. Regarding anti-infective management, only 39 (22%) reported treating an otherwise healthy hospitalized child with oseltamivir. If the complication of bacterial pneumonia was present, 59 (33%) respondents recommended oseltamivir in addition to an antibiotic. In a critically ill child without evidence of bacterial co-infection, only 38 (22%) would recommend discontinuation of...
antibiotics.
Graph 1. Resource utilization in a healthy child presenting with influenza-like illness.

Graph 2. Antibiotic use in a critically ill child with influenza without evidence of bacterial infection.
Conclusions

Our survey suggests an increase in the availability of RIDT and low utilization of antivirals in hospitalized children with and without complications of influenza. It also suggests a preference to continue antibiotics in a critically ill child, despite the absence of co-existing bacterial infection.
Background

Dengue infection is caused by dengue virus, incidence of which is increasing in India. In dengue endemic setting early diagnosis and monitoring for complications are important especially in children.

Objectives: 1. To correlate clinical profile and outcome with detection of NS1 antigen, Ig G and IgM and laboratory parameters. 2. To evaluate clinical parameters and blood component utilization

Methods

During one year (1 November 2016 to October 31, 2017) all children who presented to hospital and diagnosed with dengue infection were included. NS1, IgG and Ig M were done (immunochromotography method) for diagnosis. The hemogram and biochemistry parameters were done using automated analyzers. Degree of association between clinical parameters and disease severity was expressed as odds ratio. The blood component utilization was evaluated against platelet count and hemoglobin levels.

Results

213 children (6 months to 15 years) were diagnosed and treated among which 126 were treated as inpatients. NS1 positivity was observed in 72.3% patients. The inpatients were classified as severe (8) and non-severe (205) based on evidence of fluid leakage/platelet levels/presence of bleeding manifestations/any evidence of organ damage. The clinical outcome was assessed (Odds ratio: 2.3 p<.05) Two patients in severe group required platelet transfusions. One death was reported in severe group.

Conclusions

The present series is one of the largest exclusively in children from south India. The triad of testing (NS1, Ig M and Ig G) was useful, as in 27.7% (NS 1 negative - 59) patients, based on IgG and/or Ig M, children were admitted and monitored. Correlation of platelet count and NS1 positivity by non-parametric test (Z score: 3.8 p<.05) indicated NS1 positivity is
associated with higher risk of thrombocytopenia. Efficient fluid management had reduced need for platelet transfusion.
PARECHOVIRUSES - CAUSING MORE SEVERE DISEASE THAN ENTEROVIRUSES

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²University of Leicester, Cardiovascular Biomedical Research Unit, Leicester, United Kingdom
³University Hospitals of Leicester NHS Trust, Virology, Leicester, United Kingdom

Background

Enteroviruses (EV) and human parechoviruses (HPeV) are common causes of neonatal and infant sepsis worldwide and have been described as clinically indistinguishable. Whilst most episodes of EV and HPeV neonatal and infant sepsis and meningo-encephalitis are self-limiting, more severe illness can occur with significant morbidity. There are current concerns about longer-term sequelae following these infections, particularly in HPeV infections.

Methods

We examined and compared the demographics, laboratory results and clinical notes of 163 paediatric patients in Leicester who were admitted with either EV or HPeV found in the cerebrospinal fluid (CSF) during a 3.5 year period (Feb 2014 to Aug 2017).

Results

A greater number of abnormal parameters were found with HPeV than for EV, with a greater likelihood of admission to high dependency unit (HDU) / intensive care unit (ICU) \( (p=0.004) \) and a higher rate of persistent symptoms (i.e. fever, irritability, and feeding problems, \( p<0.05 \)).

Children infected with HPeV were 5 times more likely to have lymphopenia \( (p=0.008) \) than children infected with EV (Table). On the other hand, EV cases were more likely to have higher white cell counts in the CSF \( (p<0.038) \). Although a few babies exhibited developmental delay and other problems at one-year follow-up, it was difficult to assign
these problems to these viral infections, specifically.

**RR – EV compared with PeV**

<table>
<thead>
<tr>
<th>WCC</th>
<th>RR</th>
<th>CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal WCC</td>
<td>1.45</td>
<td>0.80</td>
<td>2.64</td>
</tr>
<tr>
<td>Abnormal Lymph</td>
<td>5.11</td>
<td>1.53</td>
<td>17.05</td>
</tr>
<tr>
<td>Abnormal CSF WCC</td>
<td>0.22</td>
<td>0.05</td>
<td>0.92</td>
</tr>
</tbody>
</table>

**Conclusions**

At present clinical guidelines do not differentiate between treatments or investigations for children presenting with HPeV and EV. This study demonstrates that differences can exist between the HPeV and EV-infected paediatric populations, justifying further investigation both into the clinical progression and outcomes of HPeV and future, potential therapy options.
ESP18-0130
SCIENCE AND EDUCATIONAL TRACK

E-PröPOSTER DISCUSSION SESSION 06: COMMUNITY ACQUIRED INFECTIONS: RESPIRATORY TRACT INFECTIONS

EFFICACY AND SAFETY OF INTRAPLEURAL STREPTOKINASE IN CHILDREN WITH MULTI-LOCULATED EMPYEMA PRESENTING LATE IN THE COURSE OF ILLNESS.
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²Medanta- The Medicity, Department of Pediatrics-, Gurugram, India
³Postgraduate Institute of Medical Education and Research, Department of Medical Microbiology, Chandigarh, India
⁴Postgraduate Institute of Medical Education and Research, Department of Radiodiagnosis and Imaging, Chandigarh, India

Background

Intrapleural fibrinolytic therapy is efficacious in the early stages of multi-loculated empyema. We evaluated the efficacy of streptokinase administered late in the course of disease, and also the effect of 3 versus >3 doses.

Methods

Over 48 consecutive months, the medical management of multi-loculated empyema comprised antibiotics, pleural drainage and intrapleural streptokinase administered as follows. Epoch 1 (18 months): 3 doses only to those presenting within <14 days of illness, Epoch 2 (18 months): 3 doses irrespective of illness duration, and Epoch 3 (12 months): 4-6 doses irrespective of illness duration. Treatment failure (i.e. need for surgical decortication), and hospitalization duration were compared between children receiving Streptokinase within 14 days of illness (Conventional administration) versus >14 days (Late administration). Outcomes were also compared between those receiving 3 doses versus 4-6 doses.

Results

There were 195 children with multi-loculated empyema over 48 months. Comparing, Conventional vs Late administration groups there was no difference in treatment failure rate (14/133 vs 7/46, p>0.05) and duration of hospitalization (median 15 vs 14 days, p>0.05) respectively, confirming that Late administration of streptokinase is as efficacious as Conventional administration. The treatment failure rate with 4-6 doses (5/42) was similar to that with 3 doses vs 18/137). However, the duration of hospitalization was significantly reduced in children receiving 4-6 doses within 14 days of illness, compared to 3 doses within that period (median 11 vs 16 days, p<0.01). There were no adverse events observed.
Figure 1. Comparison of disease severity (at presentation) and outcomes in children with loculated empyema receiving Conventional, Late and No Streptokinase

<table>
<thead>
<tr>
<th>Indicators of Disease severity at presentation</th>
<th>Conventional Streptokinase (Epochs 1 + 2 + 3) (n=133)</th>
<th>Late Streptokinase (Epochs 2 + 3) (n=46)</th>
<th>No streptokinase (Epoch 1) (n=16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presentation with respiratory failure</td>
<td>21 (16%)</td>
<td>6 (13%)</td>
<td>3 (19%)</td>
</tr>
<tr>
<td>Radiographic involvement &gt;50% of unilateral hemithorax or bilateral involvement</td>
<td>30 (23%)</td>
<td>8 (17%)</td>
<td>3 (19%)</td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment failure i.e. need for surgical decortication</td>
<td>14 (10.5%)**</td>
<td>7 (15.2%)*</td>
<td>12 (75%)</td>
</tr>
<tr>
<td>Duration of hospitalization (d)*</td>
<td>15 (10, 21)*</td>
<td>14 (9, 23)*</td>
<td>24 (17, 28)*</td>
</tr>
<tr>
<td>Time to defervescence of fever (d)*</td>
<td>7 (4, 13)</td>
<td>7 (5, 10)</td>
<td>7 (5, 11)</td>
</tr>
<tr>
<td>Time for normalization of respiratory rate (d)*</td>
<td>10 (5, 15)</td>
<td>11 (8, 14)</td>
<td>15 (10, 18)</td>
</tr>
<tr>
<td>Duration of hospitalization among those undergoing surgery (d)*</td>
<td>30 (26, 32)</td>
<td>30 (27, 41)</td>
<td>26 (24, 30)</td>
</tr>
<tr>
<td>Duration of hospitalization among those not undergoing surgery (d)*</td>
<td>14 (10, 20)</td>
<td>12 (8, 17)</td>
<td>14 (12, 16)</td>
</tr>
<tr>
<td>Duration of ICTD (d)*</td>
<td>14 (10, 19)</td>
<td>17 (13, 25)**</td>
<td>14 (10, 20)</td>
</tr>
<tr>
<td>Duration of ICTD among those undergoing surgery (d)*</td>
<td>23 (16, 26)*</td>
<td>20 (17, 30)</td>
<td>18 (11, 21)</td>
</tr>
<tr>
<td>Duration of ICTD among those not undergoing surgery (d)*</td>
<td>13 (10, 16)</td>
<td>16 (13, 24)**</td>
<td>10 (8, 12)</td>
</tr>
<tr>
<td>Mortality</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*Duration presented as median [IQR] in days rounded to the nearest whole number; *p<0.01 for comparison against No Streptokinase; **p<0.05 for comparison against Early Streptokinase

**Conclusions**

Intrapleural streptokinase is safe and efficacious in multi-loculated empyema even when administered late in the course of illness. 4-6 doses administered within 14 days of illness onset is superior to 3 doses.
Hand, foot and mouth disease (HFMD) is a global health concern. *Family Picornaviridae* members, particularly enterovirus 71 (EVA71) and CoxsackievirusA16 (CVA16), are the primary etiological agents of HFMD; however, non-EVA71/CVA16 species, both CVA6 and CVA10 have been recently associated with HFMD outbreaks. Study of the pathogenesis of CVA6 or CVA10 infection and development of antivirals and vaccines is hindered due to the lack of appropriate animal models.

**Methods**

We have developed and characterized two murine models of CVA6 and CVA10 infection which were employed to evaluate the antiviral activities of different drugs and the protective efficacies of inactivated vaccines.

**Results**

Neonatal mice were susceptible to virus infection via intramuscular inoculation and the susceptibility of mice to virus infection was age- and dose-dependent. Five day-old mice infected with lethal doses of the CVA6 or CVA10 strain consistently exhibited clinical signs, including reduced mobility, lower weight gain and quadriplegia with significant pathology in the brain, hindlimb skeletal muscles and lungs of the infected mice in the moribund state. Immunohistochemistry and qRT-PCR analyses showed high viral loads in skeletal muscle and elevated levels of IL-6 was associated with severe viral pneumonia and encephalitis. Ribavirin and IFN-γ administered prophylactically alleviated CVA6/CVA10-associated pathology *in vivo*; however, treatment with IL-6 accelerated the death of neonatal mice. Both specific antiviral serum and maternal antibody played an important role in controlling CVA6 or CVA10 infection and viral replication.

**Conclusions**

These findings indicate that these neonatal murine models are suitable for future studies to develop CVA6/CVA10-specific antivirals and vaccines.

**Clinical Trial Registration (Please input N/A if not registered)**
N/A
THE RISE AND FALL OF MRSA: CENTRAL GREECE, 2003-2017
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²University of Thessaly- School of Medicine- Larissa- Greece, Microbiology, Larissa, Greece

Background

One of the highest rates of community-associated methicillin-resistant Staphylococcus aureus (CA-MRSA) infections in Europe has been reported in Central Greece during 2003-2009, when 58.3% of community-associated staphylococcal infections among children were caused by a methicillin-resistant S. aureus (MRSA) isolate. The present study investigated the recent trends in the prevalence of infections caused by a CA-MRSA isolate.

Methods

From January 2003 to December 2017, we recorded the children examined in the outpatient clinics or admitted to the pediatric wards of the University General Hospital of Larissa, Central Greece, with community-associated staphylococcal infections. The first part of the study (2003-2009) was a retrospective one, whereas the second (2010-2017) was prospective. S. aureus isolates were tested by PCR in order to detect Panton-Valentine leukocidin (PVL) encoding genes.

Results

Of 670 children aged 5 days to 14.6 years, 56 (8.4%) had invasive infections and 614 (91.6%) skin and soft tissue infections (SSTIs). The proportion of staphylococcal infections caused by a CA-MRSA isolate was 59.2% during the first decade (2003-2012) and then declined to 36.6% during the period 2013-2015 and 16.5% in 2016-2017 (P<0.001) (Figure).
PVL-positive were 154 (93.9%) of the 164 MRSA isolates tested and 11 (14.9%) of the 74 methicillin-susceptible S. aureus. The rate of clindamycin-resistant S. aureus isolates was 19.8% in 2003-2012, 22.3% in 2013-2015 and 21.1% in 2016-2017 (P=0.66), whereas the rate of MDR isolates (resistance to ≥3 classes of antimicrobial agents) was 48.6% in 2003-2012, 33% in 2013-2015 and 17.4% in 2016-2017 (P<0.001).

Conclusions

1. In Central Greece during the recent 5-year period (2013-2017), there was a significant decline in the prevalence of invasive infections and SSTIs due to CA-MRSA.
2. MDR S. aureus isolates were significantly reduced.
3. Clindamycin-resistant S. aureus isolates remain common.
DAPTOMYCIN INCREASED DOSING IN CHILDREN: AN 11-YEAR EXPERIENCE

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¹University of Thessaly- School of Medicine- Larissa- Greece, Pediatrics, Larissa, Greece

Background

High rates of methicillin and clindamycin resistance among community-acquired Staphylococcus aureus isolates have been observed in Greece. Therefore, we sought to identify other antistaphylococcal treatment options with effective broad Gram-positive coverage such as daptomycin. Since 2009, as we gained experience and more information became available on increased daptomycin dosing from adult studies, we started using higher daily doses of this antimicrobial agent in all age-groups, including children ≥7 years of age; we report on the clinical outcome and the duration of daptomycin treatment in children managed with such increased dosing.

Methods

We studied retrospectively all pediatric infections treated with daptomycin at the University General Hospital of Larissa, Greece from January 1, 2007 to December 31, 2017.

Results

Of a total of 154 patients (median age 3 years, range 8 days to 14.5 years, 76% <7 years) treated with daptomycin, 52 (33.8%) suffered invasive infection, most frequently musculoskeletal, and 102 (66.2%) non-invasive infection, i.e. skin and soft tissue infection. S. aureus was the most commonly recovered pathogen (n=75) (58.7% methicillin-resistant isolates, 21.3% clindamycin-resistant). In 2009 we started using an increased daily dose of daptomycin. This increased dosage became standard practice during 2010 and in the subsequent years (Table).
Open or closed drainage was performed in 31 (67.2%) of the 48 patients in 2007-2009, 38 (77.6%) of 49 in 2010-2013 and 30 (52.6%) of 57 patients in 2014-2017 ($P=0.166$).

Daptomycin was well tolerated.

**Conclusions**

As experience was accumulated, daptomycin was more frequently used in a high dosage. Such higher daptomycin dose contributed to better clinical outcome and shorter duration of therapy and to decreased frequency of rifampin use as additional treatment against Gram-positive organisms.

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**Table. Dosage and duration of daptomycin treatment throughout the study period**

<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Invasive infection</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daily dose, mg/kg qd</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>8.0 ± 1.8</td>
<td>12 ± 1.2</td>
<td>11.2 ± 1.3</td>
<td>$&lt;0.001^5$</td>
</tr>
<tr>
<td>Number of patients on ≥10 mg/kg qd</td>
<td>11 (22.9)</td>
<td>49 (100)</td>
<td>55 (96.5)</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>Monotherapy</td>
<td>26 (54.2)</td>
<td>18 (36.7)</td>
<td>35 (61.4)</td>
<td>0.391</td>
</tr>
<tr>
<td>Combination therapy</td>
<td>22 (45.8)</td>
<td>31 (63.3)</td>
<td>22 (38.6)</td>
<td></td>
</tr>
<tr>
<td>+ rifampin</td>
<td>10 (20.8)</td>
<td>11 (22.5)</td>
<td>4 (7)</td>
<td>0.048</td>
</tr>
<tr>
<td>+ rifampin + other agent</td>
<td>1 (2.1)</td>
<td>12 (24.5)</td>
<td>4 (7)</td>
<td>0.531</td>
</tr>
<tr>
<td>+ other than rifampin agent</td>
<td>11 (22.9)</td>
<td>8 (16.3)</td>
<td>14 (24.6)</td>
<td>0.798</td>
</tr>
<tr>
<td>Total duration, days</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>12.4 ± 5.9</td>
<td>13.1 ± 8.8</td>
<td>10.3 ± 6.9</td>
<td>0.015$^t$</td>
</tr>
<tr>
<td>Clinical success</td>
<td>47 (97.9)</td>
<td>46 (93.9)</td>
<td>56 (98.2)</td>
<td></td>
</tr>
<tr>
<td>Cure</td>
<td>41 (85.4)</td>
<td>44 (89.8)</td>
<td>55 (96.5)</td>
<td>0.048</td>
</tr>
<tr>
<td>Improvement, any other agent added</td>
<td>6 (12.5)</td>
<td>2 (4.1)</td>
<td>1 (1.7)</td>
<td>0.021</td>
</tr>
<tr>
<td>Failure</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Non-evaluable</td>
<td>1 (2.1)</td>
<td>3 (6.1)</td>
<td>1 (1.7)</td>
<td>0.872</td>
</tr>
</tbody>
</table>

*number in parentheses is percent; qd: once daily; SD: standard deviation; IQR: interquartile range

$^5$2007-2009 vs. 2014-2017 $p<0.001$, 2007-2009 vs 2010-2013 $p<0.001$

$^t$2007-2009 vs. 2014-2017 $p=0.006$, 2010-2013 vs 2014-2017 $p=0.033$
PARAPNEUMONIC PLEURAL EFFUSION/EMPYEMA DUE TO STREPTOCOCCUS PNEUMONIAE IN CHILDREN WITH PNEUMOCOCCAL VACCINATION

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Background

After introduction of general pneumococcal vaccination with conjugate vaccines (PCVs), decreases of the incidence of pneumonia have been observed, but some studies showed increases in parapneumonic pleural effusion/empyema (PPE/PE). We investigated PPE/PE in children immunized with pneumococcal vaccines.

Methods

From October 2010 to June 2017, children <18 years of age hospitalized with PPE/PE necessitating pleural drainage or persisting for >7 days in all German pediatric hospitals were identified. Clinical characteristics of children with PPE/PE due to Streptococcus pneumoniae (SP) with documented vaccination status and serotype were analyzed. Children vaccinated with at least two doses of PCV in their first year of life followed by a booster dose were considered fully immunized.

Results

Of 1,447 children with PPE/PE, 219 (15.1%) had SP-PPE/PE. In 167 (76.3%) SP-PPE/PEs, the vaccination status was available, and in 53 (31.4%) the serotype was identified. According to the serotype-specific vaccine coverage they were classified as breakthrough cases (BCs) or non-BCs. In 26 BCs of 53 SP-PPE/PE (49.1%), the serotypes were: serotype 1 (1x), 3 (19x), 9V (1x), 18C (1x), 19A (2x), 19F (1x), 23F (1x). Nineteen BCs (73% of 26) were fully immunized with PCV-7 (2), PCV-13 (16), or pneumococcal polysaccharide vaccine (PPSV)-23 (1). In 27 non-BCs of 53 SP-PPE/PE (50.9%) the serotypes were: serotype 1 (8x), 3 (8x), 1+3 (1x), 7F (3x), 8 (2x), 19A (3x), 22F (1x), 35F (1x). BCs were younger (median 37.5 months, IQR 21-54 vs. 56 months, IQR 45-72; p<0.01) and longer hospitalized (median 24 days, IQR 18.5-29 vs. 19 days, IQR 14-24; p=0.049) than non-BCs.

Conclusions

Breakthrough cases in children with SP-PPE/PE were mainly due to serotype 3 (73%). They were associated with younger age and prolonged hospital stay.
Clinical Trial Registration (Please input N/A if not registered)

N / A
CENTRAL NERVOUS SYSTEM INFECTION COMPLICATIONS IN CHILDHOOD


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2Università La Sapienza, Sperimental Medicine Department, Roma, Italy

Title of Case(s)

Central nervous system infection complications in childhood

Background

Introduction: Central nervous system (CNS) infections in childhood may complicate even if an appropriate therapy is promptly prescribed.

Case Presentation Summary

Aim of the study: to estimate the incidence of long term sequelae in patients affected by CNS infections

Material and methods: We retrospectively examined the medical records of patients admitted to the Bambino Gesù Children’s Hospital, Rome, Italy, for a CNS infection over a 13-year period (from January 2001 to January 2016).

Results: In our case series, 485 children have been enrolled. The mean age was of 4.2 years (range 42 days to 17.7 years). Out of them, 20% was affected by cerebellitis, 10% by encephalitis, 55% by meningitis and 15% by meningoencephalitis. Eight patients died in the acute phase. Among survivors, 120 patients (25%) had at least one complication during the acute phase. Patients were younger than those without sequelae (3.7 years vs 4.5 years).

In details, 8 patients (8.2%) with cerebellitis, 12 (25.5%) with encephalitis, 58 (22%) with meningitis and 35 (50.7%) with meningoencephalitis developed at least one sequelae.

Neurological sequelae were identified in 17% of survivors. Out of them, 29 children were diagnosed with meningoencephalitis (42%), 11 with encephalitis (23%), 35 with meningitis (13.2%) and 6 with cerebellitis.

Hearing complications were identified in 41 children (8.6%), of which 10 affected by meningoencephalitis (14.4%) and 31 by meningitis (11.7%).
Vision sequelae were detached in 4 patients affected by meningoencephalitis (5.8%), in 15 by meningitis (5.7%) and in 3 by cerebellitis (3%).

**Learning Points/Discussion**

Conclusion: Even if adequate treated, CNS infections cause mortality and morbility in industrialized countries. An adequate screening before hospital dismissal is required to promptly identify sequelae and to avoid long term disability.
Background

Neisseria meningitidis (Nm) pharyngeal carriage is a necessary condition for invasive meningococcal disease. In 2017 tetravalent meningococcal conjugated vaccine (MenACYW) was introduced to the National Immunization Program in Argentina for children and adolescents, with a schedule 3, 5, 15 moa and 11 yoa. We present the first carriage study in children in the prevaccine era. Aims: 1) to assess the rate of Nm carriage in healthy children and adolescents attending a public hospital in Buenos Aires city; 2) to determine serogroup distribution and carriage risk factors by age.

Methods

Between March-December 2017, a cross-sectional study was performed among 1751 children and adolescents 1-17 yoa attending Ricardo Gutiérrez Children Hospital. Oro-pharyngeal swabs were plated and meningococci identified by conventional microbiology methods. Serogroups were determined by PCR.

Results

Group 1 (1-9 yoa): 38 Nm were isolated from 943 samples collected: overall carriage 4.0%. Serogroups distribution: B 26.3%, W 5.3%, Z 5.3%, Y 2.6%, non-groupable 7.9% and non-capsulated 52.6%. Attendance at social venues was the only independent predictor of Nm carriage (adjusted OR:2.02, CI95%=1.01-4.03;p=0.04). Group 2 (10-17 yoa): 76 Nm were isolated from 808 samples: overall carriage 9.4%. Serogroups distribution: B 19.7%, Y 9.2%, W 7.9%, C 5.3%, Z 5.3%, non-groupable 7.9% and non-capsulated 44.7%. Independent predictor of Nm carriage: attendance at night clubs (adjusted OR: 3.38, CI95%=1.28-8.93;p=0.013); passive smoking at home (adjusted OR:0.55, CI95%=0.32-0.93;p=0.025).

Conclusions

Overall carriage was higher in group 2 (10-17 yoa). The non-encapsulated Nm was prevalent in both groups and serogroup B was the most frequent among the encapsulated. Attendance
at social venues in group 1 (1-9 yoa) and night clubs in group 2 (10-17 yoa) was associated with Nm carriage.

Clinical Trial Registration (Please input N/A if not registered)

N/A
MIGRANT, WHAT ASSESSMENT AND HOW? AN EXAMPLE OF ORGANIZATION ON A POPULATION OF UNACCOMPANIED MINORS

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Background

There are currently around 25,000 Unaccompanied Minors (UM) in France. This population is not well knowned. They are under the responsibility of the social security service. In the department of Maine-et-Loire a specialized unit exists which offers a unique and coordinated protocol of medical taking care to each UM. This health's assessment is realised during the first three months after their arrival.

Methods

This epidemiologic, prospective, observational and monocentric study has collected 124 files of UM arrived from the first of January to the 31 of December 2016. The primary research criterion was the presence of an infectious disease. Secondary criterion were the presence of a non-infectious disease, the initiating of a treatment (infectious or non-infectious) and the number of specialized consultations.

Results

Were included 124 UM, 74,2% were presenting one or more infectious disease(s), 79% were presenting one or more non-infectious disease(s). The main infectious disease observed were schistosomiasis 32,3%, other intestinal parasite 41,1%, latent tuberculosis infection 19,4%, active Hepatitis B 6,4%. 76,6% of the UM received a treatment, 62,9% received at least one infectious treatment. The main ones were: treatment against parasites 53,2%, treatment against tuberculosis 18,9%. 55,6% of the UM have benefited from specialized consultations. The mains other diseases were hemoglobine’s abnormalities 40,3%, dental problems 31,4%, psychiactric pathology 11,3%.

Conclusions

These results show that a majority of the UM is affected by one or several diseases, emphasizing the importance of a precocious and thorough physical health checkup for this population to allow a better integration. This vulnerable population needs to be sensibilised to therapeutice education, health's promotion and prevention. This coordinated screening and public health pathway, which is locally efficient, would tend to be nationally evaluated.
THE GLOBAL BURDEN OF SHIGELLA AND ENTEROTOXIGENIC E. COLI: A CALL FOR THE NEED OF ACCELERATING VACCINE DEVELOPMENT EFFORTS

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Background

*Shigella* and Enterotoxigenic *Eschericia coli* (ETEC) are bacterial pathogens frequently associated with diarrhoea, and are a significant cause of mortality and morbidity world-wide. The Global Burden of Disease, Injuries, and Risk Factors study (GBD) is a systematic, scientific effort to quantify the morbidity and mortality due to over 300 causes of death and disability. This study analyzes the global burden of *Shigella* and ETEC diarrhoea for each age, sex, geography, and year from 1990-2016.

Methods

*Shigella* and ETEC mortality was modeled using a Bayesian hierarchical modeling platform that evaluates a wide range of covariates and model types based on vital registration and verbal autopsy data. Incidence for *Shigella* and ETEC was modeled using a compartmental meta-regression tool that enforces a relationship between incidence, prevalence, and remission based on scientific literature, population representative surveys, and healthcare data.

Results

*Shigella* was the second leading cause of diarrhoea mortality among all ages, responsible for 213,800 deaths (129,800–333,100), corresponding to roughly 13.2% of all diarrhoea deaths. *Shigella* was frequently associated with diarrhoea across adult age groups, increasing in the elderly with broad geographic distribution. ETEC was the eighth leading cause of diarrhoea mortality in 2016 among all ages, responsible for 51,200 deaths, roughly 3.2% of diarrhoea
deaths. ETEC was responsible for nearly 4.2% of both under-5 diarrhoea deaths and all ages.

Conclusions

The health burden of bacterial diarrhoeal etiologies are challenging to estimate, and, despite prevention and treatment options, they still represent a major cause of morbidity and mortality globally. Additional emphasis on averting disease due to *Shigella* and ETEC through targeted interventions are urgently needed.

Systematic Review Registration (Please input N/A if not registered)
Impact of Co-Infections on Clinico-Demographic Profile of Hospitalised Children with Chikungunya Infection.

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Background

Arboviral diseases are emerging as a major threat all over the world. More than 12,250 cases of chikungunya were reported across India with national capital reporting 2600 cases in 2016. We conducted a retrospective analysis among a cohort of Chikungunya positive hospitalised children to elicit the clinico-demographic profile of Chikungunya and to understand the impact of co-infections.

Methods

All children (1 month to 14 years) with IgM positive Chikungunya serology by MAC ELISA kit and admitted in pediatric department were enrolled from 1st July 2016 to 30th November 2016. Predesigned case record forms were used to enter baseline data, details of examination, laboratory parameters, details of any coinfection, treatment, and mortality. All children were categorized into either group A (Isolated chikungunya infection) or group B (co-infection). Group A and Group B were compared to see any statistically significant difference in the clinical and lab parameters.

Results

Out of 102 children, 45 (44.1%) were isolated chikungunya and 57 (55.9%) were chikungunya with other coinfections. In the co-infection group, 37 (36.3%) were dengue, 7 (6.8%) enteric, 6 (5.9%) malaria, 5 (4.9%) Pyomeningitis and 2 (2%) viral hepatitis A. Both groups were comparable except vomiting and spleenomegaly (p value < 0.05) which were significantly more in co-infection group. The classic triad of fever, rash and joint pains was present in only 3 cases of isolated chikungunya. Complications were higher in co-infection group. There was one mortality in the co-infection group.

Conclusions

High index of suspicion for chikungunya during monsoon and post monsoon season is warranted as children lack classical triad of fever, rash and joint pains. Coinfections are very common in Chikungunya. Presence of spleenomegaly and vomitings can help us suspect co-infections.
Background

Respiratory syncytial virus (RSV) infection is associated with subsequent wheeze and asthma. We previously reported on the causal relationship between prevention of RSV infection during infancy and subsequent wheeze using a double-blind, randomised, placebo-controlled trial (MAKI). We continued follow-up and analysed the effect of RSV prevention during infancy on asthma and lung function at age 6 years.

Methods

We studied 429 infants born at 33–35 weeks of gestation between 2008–2010 who had randomly received palivizumab for RSV immunoprophylaxis or placebo during their first RSV season. After the first year of follow-up, single, assessor-blind follow-up of children continued until they were aged 6 years. Primary outcomes were parent-reported current asthma and forced expiratory volume in 0.5 seconds (FEV0.5).

Results

395 (92%) children completed this 6-year follow-up study. Parent-reported current asthma was reported in 28/199 (14.1%) children in the RSV prevention group and 47/196 (24.0%) children in the placebo group (absolute risk reduction [ARR] 9.9%, 95% CI 2.2 to 17.6). The difference in current asthma was due to a difference in infrequent wheeze (1-3 episodes in the past year; 12/199 [6.0%] vs 26/194 [13.4%], ARR 7.4%, 95% CI 1.5 to 13.2).

FEV0.5 percentage predicted was similar between the RSV prevention group (89.1% [SD 10.6]) and placebo group (90.1% [11.1]), with a mean difference of 1.0 (95% CI −1.3 to 3.3). The proportion of children with current physician-diagnosed asthma was similar between the
RSV prevention group (19/185 [10·3%]) and placebo group (18/182 [9·9%]), with an ARR of –0·4 (95% CI –6·5 to 5·8).

Conclusions

In otherwise healthy preterm infants, this single-blind, randomised, placebo-controlled trial showed that RSV prevention did not have a major effect on current asthma or lung function at age 6 years.

Clinical Trial Registration (Please input N/A if not registered)

ISRCTN73641710
Title of Case(s)

Global respiratory syncytial virus-associated mortality in young children (RSV GOLD): a retrospective case series

Background

Respiratory syncytial virus (RSV) infection is an important cause of pneumonia mortality in young children. However, clinical data for fatal RSV infection are scarce. We aimed to identify clinical and socioeconomic characteristics of children aged younger than 5 years with RSV-related mortality using individual patient data.

Case Presentation Summary

In this retrospective case series, we obtained individual patient data for clinical and socioeconomic characteristics of children aged younger than 5 years who died with community-acquired RSV infection between Jan 1, 1995, and Oct 31, 2015, through leading research groups for child pneumonia identified through a comprehensive literature search and existing research networks.

We studied 358 children with RSV-related in-hospital death from 23 countries across the world, with data contributed from 31 research groups. 117 (33%) children were from low-income or lower middle-income countries, 77 (22%) were from upper middle-income countries, and 164 (46%) were from high-income countries. 190 (53%) were male. Available data showed that comorbidities were present in at least 33 (28%) children from low-income or lower middle-income countries, 36 (47%) from upper middle-income countries, and 114 (70%) from high-income countries. Median age for RSV-related deaths was 5·0 months (IQR 2·3–11·0) in low-income or lower middle-income countries, 4·0 months (2·0–10·0) in upper middle-income countries, and 7·0 months (3·6–16·8) in high-income countries.

Learning Points/Discussion
This study is the first large case series of children who died with community-acquired RSV infection. A substantial proportion of children with RSV-related death had comorbidities. Our results show that perinatal immunisation strategies for children aged younger than 6 months could have a substantial impact on RSV-related child mortality in low-income and middle-income countries.
HIGH RATE OF CEFTAROLINE-RESISTANCE IN STAPHYLOCOCCUS HAEMOLYTICUS CAUSING LATE-ONSET SEPSIS AND COLONIZING PRETERM NEONATES AND THEIR MOTHERS

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Background

Ceftaroline is a new cephalosporin active against MRSA, but susceptibility of oxacillin-resistant S.epidermidis and S.haemolyticus causing late-onset sepsis (LOS) in preterm neonates warrants characterization before potential use of ceftaroline in treatment of LOS. We aimed to determine susceptibility to ceftaroline in mecA-positive S.epidermidis and S.haemolyticus causing LOS and colonizing potential reservoirs of invasive strains (gut/skin of preterm neonates, their mothers’ breast milk (BM)).

Methods

In 97 previously characterized mecA-positive S.epidermidis and S.haemolyticus strains of diverse multilocus sequence types causing LOS (5 S.epidermidis, 12 S.haemolyticus), colonizing gut/skin of preterm neonates (14 S.epidermidis, 27 S.haemolyticus) or their mothers’ BM (31 S.epidermidis, 8 S.haemolyticus) collected in 2007-2008 (13 S.epidermidis, 4 S.haemolyticus) or 2014-2015 (37 S.epidermidis, 43 S.haemolyticus) oxacillin and ceftaroline MICs were determined by MIC Test Strips (Liofilchem). Isolates with ceftaroline MIC ≤1/1<…≤2/>2mg/L were considered susceptible/intermediate/resistant, respectively, and with oxacillin MIC >0.25mg/L resistant according to EUCAST 2018 breakpoints for S.aureus and S.epidermidis/S.haemolyticus, respectively.

Results

All isolates except two S.epidermidis from BM were resistant to oxacillin with MIC50/90 in S.epidermidis 2/16mg/L and S.haemolyticus ≥256/≥256mg/L. S.epidermidis compared with S.haemolyticus had lower ceftaroline MICs (MIC50/90 0.25/0.5 vs 3/4mg/L; p<0.001) and lower resistance-rate to ceftaroline (susceptible/intermediate/resistant 97.5/0/2.5% vs 6.4/23.4/70.2%; p<0.001). S.epidermidis from BM had lower ceftaroline MICs compared with S.epidermidis colonizing gut/skin of neonates or causing LOS (MIC50/90 0.25/0.5 vs 0.38/0.5mg/L for both; p=0.012 and p=0.02, respectively), but colonizing and LOS-causing
*S. haemolyticus* had similar MICs (Figure). Ceftaroline-resistant *S. haemolyticus* isolates belonged to various sequence types (ST1, 3, 25, 42) and were detected in both time periods.

**Figure.** Distribution of MICs of ceftaroline in *S. epidermidis* and *S. haemolyticus* causing late-onset sepsis or colonizing gut or skin of preterm neonates or breast milk of their mothers.

**Conclusions**

*S. epidermidis* colonizing gut/skin and BM or causing LOS in preterm neonates is mostly susceptible to ceftaroline. However, widespread ceftaroline-resistance in *S. haemolyticus* may limit its potential use in treatment of LOS in preterm neonates.

**Clinical Trial Registration (Please input N/A if not registered)**

N/A
Background

Lyme borreliosis (LB) is a common cause of acute facial palsy in children living in Borrelia burgdorferi endemic areas. LB can be detected by specific antibodies in serum and cerebrospinal fluid (CSF). Need for lumbar puncture in diagnostics of LB in children with facial palsy has been questioned.

Methods

We examined the utility of diagnostic lumbar puncture and sensitivity and specificity of CSF pleocytosis in LB diagnostics among children with acute facial palsy. We collected medical record and laboratory data of patients under 17 years of age (n = 94) treated for facial palsy in the Department of Paediatrics and Adolescent Medicine, Turku University Hospital, in years 2002-2016. Positive IgM or IgG antibodies against flagellar antigen, positive C6 index, positive B. burgdorferi PCR in CSF, or positive intrathecal antibody index were considered as signs of definite LB diagnosis.

Results

Lumbar puncture was performed to 84/94 patients. Forty-two patients (50%) had CSF pleocytosis (>5 x 10E6 cells /L). Diagnostic criteria of LB were fulfilled by 30 facial palsy patients with pleocytosis and by 4 without pleocytosis. The sensitivity and specificity of pleocytosis to predict LB was 88% and 60%, respectively. Positive and negative predictive values were 71% and 90%. LB was detected only by serology in 13 (38%), only by CSF testing in 10 (29%), and by both serum and CSF analysis in 11 (32%) of 34 LB patients.

Conclusions

Lumbar puncture is necessary in diagnostics of LB in children with facial palsy, because serology can be negative in the early phase of illness. CSF pleocytosis predicts LB. In endemic areas antimicrobial treatment against LB can be started based on pleocytosis even before antibody results are available.
PREVALENCE OF SEQUELAE FROM OTITIS MEDIA IN RELATION WITH PNEUMOCOCCAL VACCINE USE IN THE INUIT POPULATION OF NUNAVIK, PROVINCE OF QUEBEC, CANADA.

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Background

Otitis media (OM) constitutes an important public health problem in the Inuit population of Nunavik, Northern Quebec. One of the objectives of the childhood pneumococcal vaccination program is to reduce OM burden. The program was implemented in 2002, and 7-, 10-, and 13-valent conjugate vaccines were used sequentially, 3+1 doses being recommended (offered respectively at 2, 4, 6, and 12-15 months). The study objective was to assess the prevalence of tympanic abnormalities/audiology deficiencies at age 5 years in relation with exposure to different pneumococcal conjugate vaccines.

Methods

Methods: Immunization cards and audiology screening tests at age 5 years of children born in 1994-2010 were reviewed. Children were classified according to the vaccine schedule recommended for their birth cohort or to the vaccines they received. Log-linked binomial regression models were used to assess the relative sequelae risk according to different vaccination schedules.

Results

Among 3,517 children with complete documentation, the overall prevalence of severe and mild audiology sequelae was 18% and 29%, respectively (any sequelae = 47%). The prevalence of minor sequelae was higher in children not vaccinated (34%) than in children vaccinated with PCV7 (22%), PCV7+PCV10 (17%), PCV10 (15%) or PCV10+PCV13 (18%). No substantial differences among vaccine schedules were observed for major sequelae. In multivariate analysis, sequelae risk was lowest in children who received a PCV10+PCV13 schedule.

Conclusions
Pneumococcal conjugate vaccination was associated with a decreased frequency of minor audiology sequelae at age 5 years although no effect was seen for major sequelae which may be trigger by OM with early onset.
ETIOLOGY OF COMMUNITY ACQUIRED PNEUMONIA IN INDIAN CHILDREN BASED ON MULTIPLE BIOLOGICAL SPECIMENS AND MULTIPLE ANALYTIC MODELS.

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**Background**

Attributing etiology in childhood pneumonia based on microbiological analysis of nasopharyngeal samples has several limitations. We sought to determine etiology using multiple biological specimens and multiple analytic models to assign etiology.

**Methods**

A cohort of 222 children (1 month to 12 years) in Chandigarh, India with severe community-acquired pneumonia (WHO ‘Integrated Management of Childhood Illness’ criteria) underwent chest radiography, blood culture, and nasopharyngeal aspirate culture and viral PCR. Multiple additional respiratory specimens (lung aspirate, broncho-alveolar lavage, pleural fluid, sputum, induced sputum) were processed for culture and PCR where clinically feasible. Serology for atypical organisms was also performed. Etiology was assigned in individual children using a hierarchy- of biological specimens and analytic models based on weighting the potential pathogenicity of individual organisms in biological specimens (Figure 1).

**Results**

Microbial etiology of pneumonia could be assigned in 159 (71.6%) children with the Liberal Model, 140 (63.1%) with the Intermediate Model, and 85 (38.3%) children with the Conservative Model. Irrespective of the model used, Viral etiology dominated among those with a single pathogen. RSV was the predominant single pathogen in all three Models (Figure 1). The relative distribution of other viruses was influenced by the analytic Model used. The distribution of single bacterial species also depended on the Model, but Gram-negative organisms outnumbered Gram-positive bacteria. Streptococcus pneumoniae was the dominant bacterial species only in the Conservative Model, closely followed by S. aureus and H. influenzae. There was limited concordance between the organisms identified in various biological specimens.
Conclusions
The microbial etiology in childhood community-acquired pneumonia is predominantly viral, with RSV being the single most frequently identified pathogen. S. pneumoniae does not appear to be as important as suspected.
ESP18-0264
SCIENCE AND EDUCATIONAL TRACK

E-POSTER DISCUSSION SESSION 06: COMMUNITY ACQUIRED INFECTIONS: RESPIRATORY TRACT INFECTIONS

ROLE OF CLINICAL CHARACTERISTICS, RADIOGRAPHIC FEATURES, AND BIOMARKERS IN DISTINGUISHING BACTERIAL VERUS VIRAL ETIOLOGY IN CHILDHOOD COMMUNITY-ACQUIRED PNEUMONIA.

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⁶Postgraduate Institute of Medical Education and Research, Department of Radiodiagnosis and Imaging, Chandigarh, India

Background

This prospective cohort study was undertaken in Chandigarh, India to identify demographic characteristics, clinical features, radiographic findings and biomarkers (CRP, Procalcitonin, Cytokines) capable of distinguishing bacterial versus viral etiology.

Methods

A cohort of 222 children (<12 years) with severe community-acquired pneumonia (WHO ‘Integrated Management of Childhood Illness’ criteria) was enrolled. Microbial etiology was assigned by culture, viral PCR and serology, in multiple biological specimens using three hierarchical Etiology Assignment Models (Figure 1). Various clinical and laboratory parameters were compared between bacterial versus viral etiology in all three models.

Results

There were no statistically significant differences between bacterial versus viral etiology (irrespective of the Analytic Model) for demographic characteristics (age, sex, residence); clinical features (wheezing as a symptom, crackles on auscultation, auscultatory wheeze), and radiographic features (presence of consolidation, streaky hilar opacities, normal radiograph). Total and Differential counts could not distinguish etiology. CRP and Procalcitonin were higher in bacterial than viral pneumonia with all three Models, however multiple cut-off levels did not suggest a clinically useful discriminatory level. Comparison of six cytokines (IL-2, IL-4, IL-6, IL-8, IFN-γ, CCL-22) showed that cut-off values of IL-6 >5000 pg/ml, >1000 pg/ml, and >500 pg/ml could reliably distinguish Bacterial from Viral etiology,
with best performance >5000 pg/ml. Similarly IL-8 >1000 pg/ml could distinguish Bacterial from Viral etiology. The combination of IL-6 >1000 pg/ml and IL-8 >1000pg/ml showed Likelihood ratio + (LR+) 10.345 [CI 1.937 to 53.725], and Likelihood ratio - (LR-) of 0.721 [CI 0.48 to 1.084] narrowly missing statistical significance.

**Conclusions**

IL-6 >5000 pg/ml, IL-8 >1000 pg/ml and the combination IL-6 >1000 pg/ml + IL-8 >1000pg/ml, could differentiate bacterial from viral pneumonia, whereas none of the clinical, radiographic and laboratory features could.
Clinical Trial Registration (Please input N/A if not registered)

Not a clinical trials
Background

Community acquired alveolar pneumonia (CAAP) is considered a bacterial disease, mainly pneumococcal. CAAP rates were markedly reduced following PCV7/PCV13 introduction worldwide. In contrast, non-CAAP lower respiratory tract infections (LRIs) are generally not considered pneumococcal disease. We assessed overall CRE, CAAP and non-CAAP LRI rates in children visiting the pediatrics emergency room in southern Israel before and after PCV7/PCV13 introduction.

Methods

Our medical center serves a captive population of ~75,000 children <5y, enabling incidence calculation. PCV7/PCV13 were implemented in the national immunization program in July-2009/November-2010, respectively. All CRE were computerized. Yearly incidences were calculated for Jul-2002 through Jun-2017. Incidence-rate ratios (IRRs and 95%CI) comparing PCV13 (2014-2017) and pre-PCV (2004-2008) periods were calculated.

Results

Rates (per 1,000 children <5y) of positive CAAP declined by 48% (IRR=0.522; 95% CI: 0.494-0.552); rates of CAAP-negative CRE declined by 32% (IRR=0.676; 0.661-0.690), resulting in a 35% decline in overall CRE rates (IRR=0.651; 0.639-0.665).

Marked and significant declines in CRE, CAAP and non-CAAP rates were seen in both Jewish and Bedouin children (two ethnically distinct populations), with generally more profound declines among Jewish children and children >12 months old. (Table)
Conclusions

PCV7/PCV13 implementation resulted in a marked and significant decline both in CAAP and overall CRE rates in children <5y, with ~15,000 hospital visits with CRE prevented annually per 100,000 population <5 years old.

These findings suggest that a considerable proportion of LRIs resulting in hospital visits with CRE, often not considered pneumococcal, are in fact preventable by PCVs.
Background

Infants born at 33-36 weeks gestational age (WGA) are hospitalized with bronchiolitis more frequently than those born at >36WGA. However, the extent of community-healthcare resource utilization (CHRU) during the bronchiolitis episode, an important component of cost-benefit analysis of treatment or prevention, is unknown. We compared CHRU during first bronchiolitis episode of infants <12m old born at 33-36WGA and those born at >36WGA, between 7 days before and 21 days after hospitalization.

Methods

The Soroka University Medical Center is the only hospital in southern Israel. All infants <12m requiring hospitalization for bronchiolitis, born at ≥33WGA between 2004-2012 during RSV season (November-April), without chronic heart and lung disease and Down’s syndrome, were included. Incidences for hospitalizations and pediatric intensive care unit (PICU) admissions were calculated for all infants in the region. Data of CHRU were retrospectively obtained from the “Clalit” HMO which provides services to ~70% of all inhabitants in the region. CHRU data included physician visits, laboratory tests and treatment. No infant received RSV prophylaxis.

Results

290 infants 33-36 WGA and 2,176 >36WGA were included in the CHRU analyses. The following variables were significantly more common in 33-36WGA vs. >36WGA: duration of hospitalization, PICU admission, duration of hospitalization in hospital and in PICU, specialist consultation, and laboratory tests. Medical examinations after hospitalization and steroid prescriptions were more frequent in 33-36WGA vs. >36WGA but this did not reach statistical significance. Most differences were observed after the hospitalization date, rather than during the 7 days before hospitalization (Table).
Conclusions

The higher rate of hospitalization observed previously, combined with increased hospitalization duration and higher healthcare resource utilization in 33-36WGA, can guide decision makers to use early prevention of bronchiolitis in this high risk population.
Risk Factors for Bloodstream Infection with Extracorporeal Membrane Oxygenation in Children

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Background

Patients with extracorporeal membrane oxygenation (ECMO) support pose high risks for infectious complications due to usages of multiple medical devices and status of critical illness. Bloodstream infection (BSI) is one of the most serious complications. Few report existed on risk factors for BSI during ECMO in children. Our aim of survey was to assess risks for BSI in pediatric patients undergoing ECMO support.

Methods

Patients with ECMO support in the pediatric intensive care unit were included between March 2010 and September 2017 at Tokyo Metropolitan Children’s Medical Center. BSI was defined with positive blood culture of significant organism. Contamination was excluded. Patient resumed ECMO within 48 hours was counted as same single case. Patients’ demographic data were collected retrospectively. BSI and non-BSI groups were compared for risk factors with multivariate logistic regression analysis.

Results

Number of patients and device-days with ECMO were 99 and 1,427 device-days, respectively. Number and incidence of BSI were 11 and 7.7 /1,000 device-days. Age was median 9 month-old (IQR 2–33 month-old). Boys were 49%. Patients with underlying diseases and cardiovascular diseases were 69 % and 38 %, respectively. Causative bacteria were Pseudomonas aeruginosa (36 %), Staphylococcus aureus (18 %) and Staphylococcus epidermidis (18 %). Chi-squared test detected steroid use was associated with developing BSI (P=0.002), but not with multivariate logistic regression analysis (P=0.997).

Conclusions

Steroid use was a possible associated factor for developing BSI in pediatric ECMO patients, but it was not significant with multivariate analysis. Further research may be needed. BSI incidence in ECMO was equivalent to previous report of 15.7 / 1,000 device-days in adults. Causative bacteria included gram negative bacilli unlike catheter-related BSI. Coverage with gram negative bacilli may be warranted in suspected cases.
The epidemiology and outcomes of ventilator associated pneumonia (VAP) are well described in adults. Although children have different anatomy and physiology, have different underlying illnesses, and undergo different surgical procedures from adults, few data exist for pediatric patients, particularly with respect to risk factors and outcomes. This prospective study was executed to determine the prevalence, the risk factors and outcomes associated with VAP in children admitted in pediatric intensive care unit (PICU) in PBM children hospital.

Methods

This prospective cohort study enrolled all children (≤15 years aged) who were admitted to the PICU from January 2017 to December 2017, except those who died within 24 hours. The primary outcome measured was the development of VAP. Secondary outcomes were death and length of stay in PICU. Multiple logistic regression analysis was performed to determine independent predictors for VAP.

Results

There were 124 episodes of ventilator-associated pneumonia in 334 mechanically ventilated children. The mean VAP rate was 11.6/1000 ventilator days. Children with VAP had been in the PICU for a mean of 8.9 days before the development of VAP. There was a preponderance of Gram-negative organisms, particularly \textit{P. aeruginosa} and \textit{Klebsiella pneumoniae}. By logistic regression analysis, genetic syndrome (odds ratio [OR]: 2.37; 95% confidence interval [CI]: 1.01-5.46), reintubation (OR: 2.71; 95% CI: 1.18-6.21), and transport out of the PICU (OR: 8.90; 95% CI: 3.82-20.74) independently predicted VAP. Total parental nutrition, steroids, and histamine type 2 receptor blockers were common drugs that associated with VAP.

Conclusions

VAP occurs at significant rates among mechanically ventilated PICU children and is associated with processes of care. Additional studies are necessary to develop interventions to prevent VAP.
Clinical Trial Registration (Please input N/A if not registered)

N/A
Background

Anemia is a frequent condition in HIV-infected children, but its pathophysiology and the contribution of common causes of anemia in sub-Saharan Africa like iron deficiency and malaria is poorly understood. In addition, iron supplementation in this population is controversial due to lack of evidence on the contribution of iron deficiency to HIV-related anemia and the fear of harmful effects of iron supplementation. As a consequence almost all HIV-infected children in low-income countries present some degree of anemia.

Methods

In an ancillary study of a case-control study on risk factors of anemia in Mozambican children less than 5 years of age, 390 cases (Hb<11gr/dL) admitted to hospital and 272 controls (Hb≥11gr/dL) recruited in the community with documented HIV status were studied. Anemia pathophysiological mechanisms and the impact of HIV infection on the association of each potential etiological factor with anemia were analyzed.

Results

Of the 99 HIV-infected and 563 HIV-uninfected children included, anemic children with HIV infection had an increased risk of undernutrition, Epstein-Barr virus infection, and bacteremia, a decreased risk of malaria, but the same risk of iron deficiency compared to uninfected children. HIV-infected children were less likely to have anemia associated to
*Plasmodium falciparum* hyperparasitemia compared to HIV-uninfected children (p=0.0444). Levels of bone marrow erythropoiesis, dyserythropoiesis and EPO synthesis in response to anemia were comparable between groups (p=0.8165, p=0.3923, p=0.3236).

**Conclusions**

These findings suggest that the pathophysiology of anemia among HIV-infected malaria-exposed children is not related to specific effects of HIV infection. For unclear reasons malaria infection is less frequent among HIV-infected children than in uninfected children. Frequency of iron deficiency in HIV-infected and uninfected children is comparable, suggesting that iron provision recommendations should not differ between the two groups.

**Clinical Trial Registration (Please input N/A if not registered)**

N/A
May Two Transcripts Be Enough to Discriminate Between Viral and Bacterial Diarrhea?

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Background

In 2016 a biomarker signature consisting of 2-transcript host RNAs was proposed for discriminating bacterial from viral infections in febrile children (Herberg et al. 2016).

Methods

Here, we estimate the accuracy of these 2-transcript test in a Mexican cohort of 174 children suffering infectious diarrhea using RNA-seq.

Results

We initially analyzed the population background of the patients, and we found that most of them have a main Native American genetic ancestry (roughly 77%), with variable amount of European background. Our results confirm that the RNA test can discriminate between viral and bacterial infection (T-test; P-value = 6.94x10^{-11}; AUC = 80%; sensitivity: 68% [95% CI: 55%-79%]; specificity: 84% [95% CI: 78%-90%]), but that the signature accuracy varies noticeably depending on the causal pathogen; being the stronger signal the one yielded by Shigella (P-value = 3.14x10^{-12}; AUC = 89; sensitivity: 70% [95% CI: 57%-83%]; specificity: 100% [95% CI: 100%-100%]). It has to be mentioned that the accuracy of this signature increases significantly when analyzing severe plus moderate cases (P-value = 2.13x10^{-6}; AUC = 85%; sensitivity: 79% [95% CI: 58%-95%]; specificity: 78% [95% CI: 65%-88%]). Our results extend the scope of previous attempts of validation by incorporating patients suffering diarrhea, new pathogens, variable levels of disease severity, and different ancestral background of patients. Overall, our results support the feasibility of the clinical application of this 2-transcript based test.

Conclusions
Conclusions. The results broaden the scope of previous attempts by incorporating new pathogens causing diarrhea, variable levels of disease severity, and different ancestral background of patients, and add confirmatory support to the clinical utility of this 2 transcript-based tests.

Clinical Trial Registration (Please input N/A if not registered)

N/A
Identifying Paediatric Sepsis in 2 London Hospitals’ Emergency Departments: An Audit to Inform a New Paediatric Sepsis Pathway

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Background

Timely screening, detection and management of paediatric sepsis continues to be controversial. NICE guidelines indicate that having one risk factor for sepsis should trigger sepsis screening. However recent literature suggested this would over-treat and cause harm with unnecessary investigations. A retrospective audit using NICE guidelines for sepsis was performed on all children who attended Emergency Departments (ED) of either a secondary or its connected tertiary London hospital over 2 days or required the ED Resuscitation Department over 4 days.

Methods

NICE and Paediatric Early Warning Scores (PEWS) were compared for their sensitivity and specificity in detecting children requiring admission for presumed sepsis across sites. This was defined as those admitted and treated with intravenous antibiotics, in agreement with local protocols.

Results

283 children’s notes were reviewed, of which 74 would have been classified as high-risk for sepsis according to NICE guidelines. Sepsis was not documented clearly within any of the patients’ notes examined. 16 of the 283 children eventually received intravenous antibiotics, only 3 of which were eventually diagnosed as having sepsis and 8 had other presumed infective diagnoses. Of those discharged home, only 1 low-risk child was re-admitted for intravenous antibiotics to the same emergency hospital for washout of a septic joint. This audit is changing the local paediatric sepsis guideline.

Conclusions

In this audit, NICE guidelines’ sensitivity would have led to increased costs, unnecessary invasive procedures and inappropriate treatment in a further 59 children. Initial PEWS lacked some sensitivity for immediate escalation. Sepsis was rarely documented and potential joint infection as a septic source should be emphasised. This audit is informing design of an
appropriate local paediatric sepsis pathway across multiple sites that combines rapid screening, treatment and escalation when required.
ONGOING INCREASE OF INVASIVE SEROGROUP W MENINGOCOCCAL DISEASE IN 2017 IN THE NETHERLANDS

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2Academic Medical Center, Netherlands Reference Laboratory for Bacterial Meningitis, Amsterdam, The Netherlands

**Background**

In the Netherlands, the incidence rate (IR) increased from 0.02/100,000 to 0.05/100,000 and 0.29/100,000 in 2010-2014 (average n=4), 2015 (n=9) and 2016 (n=50), respectively. We describe the incidence rate and characteristics of MenW in 2017 in the Netherlands.

**Methods**

All microbiological laboratories in the Netherlands submit *Neisseria meningitidis* isolates from blood, cerebrospinal fluid or other normally sterile material (i.e. invasive meningococcal infections) to the Netherlands Reference Laboratory for Bacterial Meningitis for typing. We compared the IR of MenW in 2017 with the IR in 2015 and 2016. We described age, mortality, clinical manifestation and finetype of the MenW cases in 2017.

**Results**

In 2017, the IR increased significantly to 0.47/100,000 (n=80; IRR \textsubscript{2017 vs 2016} = 1.6 [95%CI: 1.1-2.3]). Of all Men cases in 2017, 40% were MenW (80/198). In 2017, MenW IR was highest in children <5 years (1.0/100,000; n=8) and 15-24 year olds (0.83/100,000; n=16). The case fatality rate was 14% (11/78) and was highest in 15-24 year olds (4/16; 25%). Of 73 patients with known clinical manifestation, 49 (53%) had septicaemia, 11 (15%) had meningitis, 6 (8%) had both septicaemia and meningitis, 9 (12%) had pneumonia, and 8 (11%) had other manifestations. Almost all strains had finetype P1.5,2:F1-1 (70/74; 95%).

**Conclusions**

In the Netherlands, the incidence of MenW disease continues to increase. While the increase started primarily in older adults, the disease now mainly affects children <5 years, adolescents and young adults, and shows a high case fatality rate. In 2018, MenC vaccination will be replaced by MenACWY vaccination in infants and MenACWY vaccination will be introduced in 13-14 year olds. Continuous surveillance is performed to evaluate whether vaccination should be extended to other age cohorts.
IMPACT AND EFFECTIVENESS OF PNEUMOCOCCAL CONJUGATE VACCINATION AGAINST INVASIVE PNEUMOCOCCAL DISEASE IN THE NETHERLANDS IN CHILDREN <5 YEARS

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2Academic Medical Center, Netherlands Reference Laboratory for Bacterial Meningitis, Amsterdam, The Netherlands

Background

The 7-valent pneumococcal conjugate vaccine (PCV7) was introduced in the Dutch National Immunization Program in 2006 and replaced by PCV10 in 2011. We present impact and effectiveness of PCV7/10 on invasive pneumococcal disease (IPD) in children <5 years of age.

Methods

For impact analyses, we used isolates from cerebrospinal fluid or blood that were positive for *Streptococcus pneumoniae* that were submitted to the Netherlands Reference Laboratory for Bacterial Meningitis for serotyping by nine sentinel laboratories, covering 25% of the Dutch population. Nationwide IPD data, available since 2008 for children <5 years, were used to estimate vaccine effectiveness. Vaccination status was obtained by linkage to the national vaccination register. We compared IPD incidence between the pre-PCV7 period (June 2004-May 2006), pre-PCV10 period (June 2009-May 2011) and post-PCV10 period (June 2015-May 2017). Effectiveness of PCV10 was estimated using the indirect cohort design.

Results

IPD incidence decreased significantly from 19.8/100,000 pre-PCV7 to 9.1/100,000 pre-PCV10 to 5.9/100,000 post-PCV10. IPD incidence caused by PCV10-specific serotypes decreased significantly from 2.6/100,000 pre-PCV10 to 0.2/100,000 post-PCV10. Non-PCV10-type IPD incidence did not increase significantly (4.0/100,000 pre-PCV7 and 5.0/100,000 post-PCV10). IPD incidence caused by PCV13-specific serotypes remained constant during the study period and was ~2.0/100,000. The analysis on vaccine effectiveness included 177 IPD cases aged 2-60 months of which 12 vaccine-type cases (1x14, 1x19F, 3x23F, 2x1, 5x7F). Effectiveness of ≥2 doses of PCV10 on vaccine-type IPD was 85% (95% confidence interval: 41 to 96).

Conclusions
Introduction of PCV7 and PCV10 has reduced the burden of IPD considerably in children <5 years of age. Continuous surveillance is warranted to monitor IPD disease burden and to estimate the potential impact of future vaccines.
SEX DIFFERENCES IN ANTIBODY RESPONSE AFTER INFANT AND CHILDHOOD VACCINATIONS

Methods

Lower IgG levels in girls were found at specific time points after vaccination against measles, mumps, rubella, MenC, and polio. The geometric mean concentration/titer ratios ranged between 1.10 for polio type 1 shortly after the first childhood booster to 1.90 for MenC shortly after infant vaccination. There were no significant differences between boys and girls for diphtheria, tetanus, pertussis, and Hib at either time point. Proportion of protected levels were generally high and comparable between boys and girls. Differences were seen at 1-3 years after infant vaccination against mumps (82.5% boys vs. 91.9% girls, p=0.046) and MenC (7.0% boys vs. 18.2% girls, p=0.015).

Conclusions

We found higher IgG levels in girls for measles, mumps, rubella, MenC, and polio at specific time points after vaccination. However, sex-differential IgG levels were generally small and not consistent across or within pathogens. Therefore, we have no indications that these differences cause unequal protection between boys and girls.
IMMUNOGENICITY AND SAFETY OF HEPATITIS B VACCINE IN ADOLESCENTS AGED 14–15 YEARS, PREVIOUSLY VACCINATED WITH 4 DOSES OF HEXAVALENT DTPA-HBV-IPV/HIB VACCINE IN INFANCY


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Background

Hepatitis B is a potentially life-threatening liver infection caused by the hepatitis B virus (HBV). Vaccination commencing in infancy provides long-term protection against acute and chronic HBV infections. Long-term persistence of antibodies against hepatitis B surface antigen (anti-HBs), immunogenicity and safety of a challenge dose of GSK’s monovalent HBV vaccine in adolescents aged 14–15 years, previously vaccinated with GSK’s hexavalent DTPa-HBV-IPV/Hib vaccine according to a 3+1 schedule in their first 2 years of life, were assessed.

Methods

In this phase 4, open-label, non-randomized study, conducted in Germany, enrolled adolescents received 1 challenge dose of monovalent HBV vaccine. Seroprotection status (anti-HBs antibody concentrations ≥10 mIU/mL) and the percentage of adolescents with anti-HBs antibody levels ≥100 mIU/mL were assessed pre- and 1 month post-vaccination. Reactogenicity and safety were also evaluated.

Results

From 302 vaccinated adolescents (mean age: 14.4 years), 268 were included in the according-to-protocol cohort for immunogenicity. At pre-vaccination, 53.7% of participants were seroprotected and 16.8% had anti-HBs antibody concentrations ≥100 mIU/mL (Table). One month post-vaccination, 93.3% and 87.3% of vaccinees reached seroprotection and anti-HBs antibody concentrations ≥100 mIU/mL, respectively (Table).
During the 4-day post-vaccination period, injection site pain (reported by 101 [33.6%] participants) and fatigue (91 [30.2%]) were the most frequently reported solicited local and general adverse events (AEs), respectively. Fifty-five (18.2%) adolescents reported ≥1 unsolicited AE during the 31-day post-vaccination period; 6 (2.0%) of them were considered vaccination-related. Two serious AEs (meniscus injury and eating disorder – not vaccination-related) were reported during the study.

**Conclusions**

One challenge dose of monovalent HBV vaccine elicited robust immune responses and was well tolerated in adolescents aged 14–15 years, previously vaccinated with 4 doses of hexavalent DTPa-HBV-IPV/Hib in infancy.

**Funding:** GlaxoSmithKline Biologicals SA

**Clinical Trial Registration (Please input N/A if not registered)**

ClinicalTrials.gov NCT02798952

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<th></th>
<th>N</th>
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<th>GMC mIU/mL (95% CI)</th>
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<td>(stratified by pre-vaccination status)</td>
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<tr>
<td>Overall</td>
<td>268</td>
<td>93.3 (89.6–96.0)</td>
<td>87.3 (82.7–91.1)</td>
<td>1975.7 (1436.1–2718.1)</td>
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<td>105</td>
<td>82.9 (74.3–89.5)</td>
<td>68.6 (58.8–77.3)</td>
<td>224.7 (143.0–353.1)</td>
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<td>1651.0 (1092.0–2526.4)</td>
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<td>≥10 mIU/mL</td>
<td>144</td>
<td>100 (97.5–100)</td>
<td>99.3 (96.2–100)</td>
<td>9865.7 (7418.8–13119.3)</td>
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Anti-HBs, antibodies against hepatitis B surface antigen; GMC, geometric mean concentration; ATP, according-to-protocol; N, number of adolescents with available results at each timepoint; %, percentage of adolescents with anti-HBs antibody concentration above cut-off; CI, confidence interval; IU, international unit. Note: all participants were vaccinated in the first 2 years of life with 4 doses of GSK’s hexavalent diphtheria-tetanus-acellular pertussis-hepatitis B-inactivated poliomyelitis-Haemophilus influenzae type B (DTPa-HBV-IPV/Hib) vaccine.
VIROLOGIC AND CLINICAL SURVEILLANCE OF RESPIRATORY ENTEROVIRUSES FROM PAEDIATRIC PATIENTS ATTENDED AT A TERTIARY HOSPITAL IN CATALONIA (SPAIN) DURING THREE CONSECUTIVE SEASONS (2014-2017)
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Background

Enterovirus (EV) infections are usually asymptomatic or mild, but symptomatic infections can evolve to severe complications. Outbreaks of EV-A71 and EV-D68 have been recently reported worldwide, sometimes related to severe clinical outcomes. The aim was to describe the EV genetic diversity and the clinical outcomes from paediatric patients attended at a tertiary university hospital in Barcelona from 2014 to 2017.

Methods

Respiratory tract specimens for respiratory viruses' detection were collected from paediatric cases attended at our hospital with suspicion of respiratory tract infection or EV infection. EV laboratory-confirmation was carried out by specific real-time RT-PCR assays. Partial viral VP1 protein-coding sequences were additionally used for genetic characterisation by phylogenetic analyses. Clinical records were retrospectively reviewed.

Results

A total of 381 (7%) from 5,703 cases were EV laboratory-confirmed. Phylogenetic analyses of the partial VP1 (260, 70%) sequences distinguished up to 27 different EV types (Figure 1), which were distributed within EV-A specie (82; 40%), EV-B (90; 42%), EV-C (5; 2%), and EV-D (33; 15%), while the remaining (50, 30%) were belonging to rhinovirus species A (30), B (4) and C (14). EV-A71 was highly related to neurological complications (25/40; 63%), of which 20 (50%) were rhombencephalitis, as well as, most EV-D68 (88%) were associated with low respiratory tract infections (LRTI), but one (3%) with acute flaccid paralysis.
Conclusions

EV-A71 and EV-D68 were the most detected EV types in respiratory specimens. EV-A71 was highly related to neurological disease because of the 2016 rhombencephalitis outbreak in Catalonia. Despite EV-D68 was mostly associated with LRTI, its potential relatedness to neurological diseases makes its monitoring obligatory. The potential neurotropism of EVs reinforces the need for a better virologic and clinical surveillance.
HIGH-DOSE INTRAVENOUS(IV) ACYCLOVIR FOR PAEDIATRIC MENINGOENCEPHALITIS – AN INCREASED RISK OF ACUTE KIDNEY INJURY(AKI)?
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Background

Acyclovir is widely used to treat children with Herpes Simplex Virus(HSV) and Varicella Zoster Virus(VZV) infections. For HSV/VZV meningoencephalitis, US Food Drug Administration recommends IV acyclovir 20mg/kg/dose(high-dose) 8 hourly for children ≥3 months old whereas American Academy of Paediatrics recommends 15mg/kg/dose 8 hourly for children 3 months to 12 years old due to reports of nephrotoxicity, especially in those ≥12 years old with concomitant ceftriaxone.

We sought to determine the incidence of AKI in those receiving high-dose IV acyclovir for meningoencephalitis in our institution, KKH.

Methods

This is a retrospective cohort study of children ≤18 years old admitted to KKH from 1st March 2016 to 31st March 2017 and received at least one dose of high-dose IV acyclovir for meningoencephalitis. We excluded those with pre-existing kidney disease. AKI was defined as an estimated Glomerular Filtration Rate decrease of ≥25% from baseline(paediatric RIFLE criteria).

Results

Of the 214 children on IV acyclovir, 45 had other indications and 30 received low-dose acyclovir for meningoencephalitis; hence, 139 children were included(mean age: 5.28±4.8 years). The median duration of IV acyclovir was 2 days[interquartile range:2-3 days] and all patients were adequately hydrated. Only 18 patients had repeated serum creatinine during treatment and within a week of acyclovir discontinuation. Two patients aged 12 and 15 years old, developed AKI after an average of 3.5 days from initiation, and both had concomitant ceftriaxone.

Conclusions

Our incidence of AKI secondary to high-dose IV acyclovir for paediatric meningoencephalitis was 1.4%, lower than 13.1% reported in two studies, where the median onset of AKI was 1-14 days. High-dose IV acyclovir could be considered for treatment of HSV/VZV
meningoencephalitis in ≤12 years old, but hydration and close monitoring of renal function would be prudent.
CHARACTERIZATION OF CHILDREN WITH TRUE POSITIVE BLOOD CULTURES IN NORTHERN ISRAEL, 2007-2017: A RETROSPECTIVE STUDY

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Background

Vaccination of children with the conjugated pneumococcal vaccine has reduced the burden of invasive pneumococcal disease in countries where there is widespread use. We characterized the true positive blood cultures of children aged 3 months to 18 years who presented to a Medical Center in Northern Israel following Prevnar implementation.

Methods

We retrospectively reviewed demographic, clinical and laboratory data of patients with true bacteremia emphasizing age, young group 3-36 months, and older group 3-18 years, and whether there was a focus of infection or bacteremia without focus. Pneumococcal isolates were typed at the National Laboratory for Streptococcus.

Results

Overall, 909 (2.7%) of the 34066 samples were with growth, but 562 (1.6%) were deemed contaminants and 246 (0.7%) excluded as patients did not meet inclusion criteria thereby yielding 101 true positive blood cultures for analysis. Focal infection with concomitant bacteremia was more common than bacteremia alone overall, 73/101 (72%) versus 28/101 (27.7%), p <0.001, in the young group, 34/51 (66%) versus 17/51 (33%) p=0.02, and older group, 39/50 (78%) versus 11/50 (22%), p = 0.001, respectively. Streptococcus pneumoniae was the most common pathogen overall 29/101 (29%), and in the young group 22/51 (43%), but rare in the older group 7/50 (14%). Notably, in the latter, Brucella spp. predominated 13/50 (26%) followed by Staphylococcus aureus 12/50 (24%). In the young group, pneumococcal bacteremia with Prevnar-13 serotypes was not uncommon.

Conclusions

Our findings are consistent with other studies reporting decreased pneumococcal bacteremia, bacteremia primarily accompanying a focal infection, and changing etiological agents among Prevnar- vaccinated children. Ongoing surveillance is warranted to better understand the public health implications of Prevnar including pneumococcal serotype replacement and increasing prominence of other pathogens.
Background

Clinical research on the impact of mixed infection (P. falciparum and P. vivax) on human health is still controversial, either believed to be beneficial or detrimental, attributed to various factors. This prospective study provides detailed clinicolaboratory spectrum and outcomes of children infected with mixed malaria.

Methods

This prospective cohort study was conducted on 616 children of malaria admitted from January 2013 to December 2017. The species diagnosis was made with peripheral smear and rapid diagnostic test and confirmed with polymerase chain reaction analysis. Severe malaria was defined strictly on WHO criteria (2000).

Results

In this cohort study, the proportion of P.falciparum, P.vivax and mixed malaria was 306 (49.6%), 179(29.1%) and 131(21.3%) respectively. Severe malaria was present in 47.02% children, with greatest risk (64.58%) among children of mixed infection in comparison to P.falciparum monoinfection [49.36%, RR=1.308 {95% CI 0.957-1.673}, p=0.065] and P.vivax monoinfection [40.16%, RR=1.608 {95% CI 1.139-2.138}, p=0.006]. Anemia (66.67%) was the commonest pernicious manifestation of mixed infection malaria followed by hepatic dysfunction (54.17%), renal dysfunction (35.42%) and cerebral malaria (22.9%). Although multiorgan dysfunction was present in 57.96% children, the risk was greatest in mixed infection [62.5%] in comparison to P.falciparum monoinfection [24.36%, RR=2.566 {95% CI 1.741-3.571}, p=0.0001] or P.vivax monoinfection [18.85%, RR=3.315 {95% CI 2.109-5.034}, p=0.0001]. The risk of mortality in severe malaria was 3.7% in which mixed infection had greater risk [8.33%] in comparison to P.falciparum monoinfection [3.20%; p=0.219] or P.vivax monoinfection [2.45%; p=0.100].

Conclusions

This study revealed that mixed infection severe malaria children had almost similar clinical and laboratory findings to those of severe P. falciparum and P. vivax monoinfection malaria. Their risk of subsequent clinical progression to severe illness including multiorgan dysfunction and mortality was the highest of the three groups.
Clinical Trial Registration (Please input N/A if not registered)

N/A
Parapneumonic pleural effusions/empyema (PPE/PE) are serious complications of pneumonia in children. In a nationwide hospital surveillance study, we investigated the bacterial etiology of pediatric PPE/PE.

Methods

From October 2010 to June 2017, children <18 years of age hospitalized with PPE/PE necessitating pleural drainage or persisting >7 days were reported to the German Surveillance Unit for Rare Diseases in Childhood (ESPED). Supplementary 16S-rDNA-PCR of pleural fluid and add-on sequencing was offered to all hospitals. Bacteria from blood culture (BC), pleural fluid culture (PC) and/or pleural fluid PCR (PPCR) were analyzed.

Results

In 488 (33.7%) of 1447 children with PPE/PE (median age 4.7 years, IQR 2.9-9.6), a total of 541 bacterial detections were reported. The positivity rate was 10% in 1078 children tested by BC, 34% in 646 children tested by PC, and 53% in 449 children tested by PPCR. Bacteria were found in 60% of a subsample of 190 children, tested simultaneously with all three methods; of those 25% were detected solely by PPCR. Of all 541 detections, 87% (n=469) were aerobic, gram-positive cocci, most frequently *Streptococcus pneumoniae* (n=219; 41%), *Streptococcus pyogenes* (n=105; 19%), *Staphylococcus aureus* (n=35; 7%), and *Staphylococcus epidermidis* (n=28; 5%). Aerobic, gram-negative rods were the second largest group (n=20; 4%), with *Haemophilus influenzae* (n=13; 2%) as the most frequent pathogen. Aerobic gram-negative cocci represented 11 (2%) and aerobic gram-positive rods 8 (1.5%) of all detections; anaerobic bacteria represented 14 (3%).

Conclusions
This is the largest study thus far investigating the etiology of pediatric PPE/PE with laboratory confirmation. Detection rate could be significantly increased by the use of broad-spectrum PCR. Aerobic, gram-positive cocci, especially *S. pneumoniae* and *S. pyogenes*, accounted for the majority of PPE/PE.

Clinical Trial Registration (Please input N/A if not registered)

N/A
ESP18-0361
SCIENCE AND EDUCATIONAL TRACK

E-POSTER DISCUSSION SESSION 02: PUBLIC HEALTH AND EPIDEMIOLOGY

ANTIBIOTICS PRESCRIBED BY HEALTH CARE WORKERS FOR CHILDREN UNDER 5 YEARS WITH RESPIRATORY SYMPTOMS IN RURAL AREAS IN KYRGYZ REPUBLIC. A FRESH AIR STUDY.

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Background

Irrational use of antibiotics is a serious problem in Kyrgyzstan and internationally. The use of antibiotics for the treatment of viral infections, such as influenza promotes the emergence of resistant strains of bacteria. In 2014, the Kyrgyz Ministry of Health issued an order limiting the issuance of prescription antibiotics for pharmacists. However, this decision is not being adhered to. The aim of this study is to show how often antibiotic therapy is administered unjustified for colds and upper respiratory tract infections in rural areas among children under 5 years.

Methods

The study was conducted in health clinics in rural areas of Kyrgyzstan. Children aged 2 to 59 months presenting with coughing and/or difficult breathing were included. The consultations were observed and we recorded the diagnosis given and what treatment was prescribed as well as the information provided to patient families by the attending family medicine physician, paramedic or nurse. After 5 days, the children’s parents were called to ascertain what information they had received: Whether the child is sick still, whether there had been repeated consultation and whether the child was hospitalized.

Results

In total, 494 children were screened. Of these, 232 fulfilled the inclusion criteria and were enrolled. All were diagnosed with ARVI. Of them, 49% were prescribed the following antibiotics: 86.2% amoxicillin, 8.3% ampicillin, 0.9% cephalosporins, 3.7% macrolides, 0.9% aminoglycosides, re-consultation 3.9%, hospitalization 1.3%.
Conclusions

Overall, the study found widespread irrational use of antibiotics and indications. Lack of knowledge regarding resistance to antibiotics has been widespread. Also the study showed that many parents themselves administered uncontrolled antibiotics to their children.

Note: The data analysis is preliminary and results may be subject to change.

Clinical Trial Registration (Please input N/A if not registered)

N/A
LONG TERM IMMUNOGENICITY AND EFFECTIVENESS OF THE 9-VALENT HPV (9VHPV) VACCINE IN PREADOLESCENTS AND ADOLESCENTS

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Background

The pivotal Phase III immunogenicity study of the 9vHPV vaccine in girls and boys (age 9-15 years) was extended to provide long-term immunogenicity and effectiveness through 10 years post-dose 3. We describe the first interim analysis at month 72. Subsequent analyses are planned at months 96 and 126, respectively.

Methods

Overall, 1272 subjects (971 females, 301 males) who received 3 doses of 9vHPV vaccine at day 1 and months 2 and 6 were enrolled in the study extension. Serum was collected at month 66 to assess antibody responses. Starting at age 16 years, genital swabs were collected every 6 months and tested by PCR to detect HPV DNA. Pap tests were collected annually in female subjects starting at age 21 years. External genital and cervical biopsies were performed as indicated in the protocol. Tissue samples were adjudicated by a pathology panel and tested by PCR to detect HPV DNA.

Results

Geometric mean titers peaked around month 7 and gradually decreased through month 66. Seropositivity rates remained >90% through month 66 for each of the 9vHPV vaccine types. No cases of HPV 6/11/16/18/31/33/45/52/58-related disease (cervical/vulvar/vaginal lesions
and genital warts in females, external genital lesions and genital warts in males) were observed in the per-protocol population (maximum follow-up: 6.4 years [median 5.9 years] post-dose 3). Incidence rates of HPV6/11/16/18/31/33/45/52/58-related 6-month persistent infection in females and males were low (20.3 and 24.3 per 10,000 person-years, respectively) and within ranges expected in vaccinated cohorts (based on results from efficacy trials of 4-valent and 9-valent HPV vaccines).

Conclusions

This analysis demonstrates sustained immunogenicity through 5 years post-vaccination and durable effectiveness through 6 years post-vaccination in girls and boys aged 9-15 years.

Clinical Trial Registration (Please input N/A if not registered)

NCT#943722
SEROIMMUNITY OF HEPATITIS B VACCINE IN CHILDREN WITH IBD WHO GOT FULL SERIES OF VACCINATION IN INFANCY IS INADEQUATE AND DOES NOT DEPEND ON THERAPY TYPE.
Clinical Trial Registration (Please input N/A if not registered)
n/a
INTESTINAL CARRIAGE OF ESBL-PRODUCING GRAM-NEGATIVE BACILLI IN HOSPITALISED NEONATES <2000G IN THE GAMBIA: FEASIBILITY STUDY RESULTS

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Background

Extended spectrum β-lactamase producing gram-negative bacilli (ESBL-GNB) are an important cause of hospital acquired infections (HAI) in resource limited neonatal units and are associated with high neonatal mortality. ESBL-GNB intestinal carriage is a pre-cursor for invasive ESBL-GNB disease and understanding carriage patterns and antibiotic sensitivities is key for both clinical care and research of infection prevention interventions.

Methods

A feasibility study for a clinical trial of early kangaroo mother care (KMC) took place at the neonatal referral unit in The Gambia from April – August 2017. A cohort of hospitalised neonates <2000g and <20h old were prospectively observed with peri-anal swabs at day 0 of admission and weekly to 28d. Paired maternal recto-vaginal swabs were obtained on day 0. Samples were cultured at MRC Gambia Clinical Laboratory on MacConkey and Chrome agar. Antibiotic sensitivity testing was by Kirby-Bauer diffusion method with double disc synergy testing for ESBL detection.

Results

35 neonates (mean weight 1300g) provided 130 samples with 57 GNB isolates, of which 44% (25/57) were ESBL-GNB. 5.7% (2/35) of neonates had intestinal ESBL-GNB carriage at admission, increasing to 58% (7/12) at 7d and 100% (4/4 & 2/2) at 21 and 28d. Nearly one-third (32%, 8/25) of ESBL-GNB isolates were resistant to all antibiotics tested, with highest sensitivity (56%) to chloramphenicol and 12% sensitivity to gentamicin. 9% (2/23) of mothers were positive for ESBL-GNB (E Coli) with no recto-vaginal ESBL-Klebsiella carriage identified.
Conclusions

This small feasibility study indicates that over half of Gambian preterm neonates acquire multi-drug resistant ESBL-GNB, particularly ESBL-Klebsiella, during the first week of hospital admission. Further research to explore transmission, factors associated with ESBL-GNB carriage and impact of early KMC on carriage and invasive disease is planned.
COMPARISON OF MEASLES ANTIBODY LEVELS BETWEEN VACCINATED HIV-INFECTED AND HIV UNINFECTED CHILDREN IN NIGERIA

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Background

Sub-Saharan African countries overwhelmingly bears the burden of global HIV infection and measles outbreaks in children. Despite the significant impact of this double burden in Nigeria, the effect of HIV infection on measles antibody levels has not been well evaluated. This study was therefore conducted to compare the antibody levels in HIV infected and uninfected children.

Methods

The study was a descriptive comparative cross-sectional study among 180 HIV infected and uninfected children aged 2-10 year, recruited between August and December 2015 at the University of Ilorin Teaching hospital, Nigeria. Socio-demographic, clinical and anthropometric parameters were obtained. Blood samples were collected for haematologic evaluation (CD4+ cell count, full blood count) and serologic assay of measles antibody using IMMUNOLAB ELISA kit. Data was analyzed using SPSS version 20.

Results

A total of 90 HIV infected subjects and 90 age and sex-matched HIV-negative controls were analyzed. There were 48 males and 42 females aged between 2 to 10 years with a Male: Female ratio of 1.1:1 in both groups. The mean age was 5.4 years. While the seroprevalence of measles antibody was 46.7% among the HIV negative children, only 9% of the HIV infected subjects had positive antibody level. The antibody titre was also significantly lower among HIV infected subjects compared with controls with median measles antibody values of 3.3U/ml and 9.4U/ml respectively (p <0.001). HIV infected subjects with more than one dose of measles vaccine had significantly higher seroprevalence of measles antibody than those with single dose (38.5% vs 5.2%, p <0.003).

Conclusions

There was a low seroprevalence of measles antibody among vaccinated children in Nigeria. There is the need to strengthen immunization practices in Nigeria.
Clinical Trial Registration (Please input N/A if not registered)

N/A
LONG-TERM IMPACT OF TEN-VALENT PNEUMOCOCCAL CONJUGATE VACCINE (PCV10) ON PNEUMONIA AMONG VACCINE-ELIGIBLE CHILDREN IN FINLAND

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Background

PCV10 was introduced into the Finnish National Vaccination Programme (NVP) in September 2010 using a 2+1 schedule. Uptake is estimated at ~93%. We evaluated the long-term impact of PCV10 on pneumonia among vaccine-eligible children during the first six years after the NVP introduction.

Methods

The vaccinated target cohort eligible for NVP born 06/2010-09/2016 was compared with a calendar-time and age-matched (3-78 months) reference cohort before NVP introduction (Figure). Period 01/2009-08/2010 was excluded because of a nation-wide PCV10 trial conducted in Finland. Hospital in- and outpatient discharge notifications with diagnoses compatible with any hospital-diagnosed pneumonia (HDP, ICD-10 codes J10.0/J11.0/J12-J18/J85.1/J86) were collected from national Care Register and used for calculating rates of HDP and hospital-treated primary pneumonia (HTPP, HDP with pneumonia as the first diagnosis after inpatient hospitalization) before and after NVP implementation. No radiological evaluation data were available. Episode duration was 90 days.

Results

The overall rate of HDP episodes was 8.3 in the reference cohort and 7.8/1000 person-years in the vaccinated target cohort. Compared with the reference cohort, the pneumonia rate was 7% (95%CI 4 to 9) or 0.6/1000 person-years lower in the vaccinated cohort. For HTPP the relative and absolute rate reductions were 24% (95%CI 21 to 27) and 1.0/1000 person-years, respectively. Number of lung abscess/empyema diagnoses (ICD-10 J85.1/J86) was
low and remained constant during the follow-up period.

Conclusions

This nation-wide study provides evidence of the long-term effects of the 10-valent PCV against pneumonia in a routine vaccination program setting. The PCV10 introduction has prevented over 4000 pneumonia hospitalizations during 2010-2016 in the vaccinated target cohort.
Indiscriminate antibiotic use is common among community pediatricians. PCVs are expected to reduce respiratory infections, resulting in decline in antibiotic overuse. We speculated that following PCV implementation, the decline in dispensed antibiotic prescription rates (DAPRs) will be greater among high antibiotic-using clinics (HUC) than low-user clinics (LUC).

Methods

Most children in the Southern Israel district belong to Clalit Health Maintenance Organization (Clalit-HMO) where all dispensed antibiotics are computerized. We enrolled all Clalit-HMO pediatric clinics in southern Israel that: 1) had ≥50 insured children <2y old and; 2) were active both before and after PCV implementation. Yearly DAPRs were calculated by antibiotic category. Clinics were classified as HUC (above median DAPRs) and LUC (below median DAPRs). In the years 2005-09 an average of 9,935.5 and 7,116.5 children <2y were insured in HUC and LUC, respectively. PCV7/PCV13 were implemented in July-2009/Nov-2010, respectively and rapidly reached ≥90% coverage.

Results

The proportion of the various drugs dispensed before PCV implementation is shown in the Figure. Overall mean (±SD) DAPRs during pre-PCV implementation was 3,538.7±139.5 and 1,643.7±38.6 per 1000 child-years, in the HUC and LUC, respectively (P<0.001). Before PCV implementation, no significant overall DAPRs trend was observed. Comparing 2014-16 to 2005-09, overall DAPRs declined significantly in the HUC (32%, P<0.001), but not in LUC. Similar trends were found with amoxicillin, the most common dispensed antibiotic. No decline in azithromycin was seen in HUC, and a significant increase was found in LUC. For other antibiotics DAPRs decreased in both groups, but the decline started before PCV implementation.
Conclusions

PCV7/13 implementation was associated with a significant decline in HUC DAPRs but not LUC DAPRs, resulting in partial closing of the gap between HUC and LUC.
PCV13 VACCINATION EFFECT ON THE INCIDENCE OF RESPIRATORY TRACT INFECTIONS IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background

Patients with juvenile idiopathic arthritis (JIA) have an increased risk of infections. Approximately half of all serious infections in children with JIA are associated with the respiratory tract involvement. Objective: to assess the pneumococcal 13-valent conjugate vaccine (PCV13) immunization effect on the frequency of respiratory infections in children with JIA.

Methods

In a prospective cohort study 2 groups of children in JIA remission (group I (n=25) – children on methotrexate therapy; group II (n=25) – on Etanercept) have been compared with the children without JIA (considered as healthy (n=25)) in a 12 month period: 6 months before PCV13 was administered as a single 0.5 ml subcutaneous injection and 6 months after vaccination. End-points of the study were respiratory tract infections incidence (IR), antibiotic administration episodes before and after vaccination, adverse events post-vaccination.

Results

75 children were included in the study. In group I the IR was 0.126, in group II – 0.116, respectively, that was significantly higher than the IR=0.088 in the control group (p=0.001). The IR decreased after vaccination in patients with JIA and in the control group to 0.021 in groups I and II and to 0.016 in the control group, correspondingly. In 6 months after PCV13 vaccination the frequency of immunosuppressive treatment discontinuation due to infection episodes decreased in group I from 52 to 12 cancelations per 600 person-weeks (p=0.001), and from 49 to 10 – in group II (p=0.001). There were no JIA exacerbation episodes recorded in any patients post-PCV13 vaccination.
Conclusions

PCV13 vaccination of children with JIA is well tolerated and highly effective in respiratory infections episodes prevention resulting in significant reduction of antibiotics administration in these patients.
PHARMACOKINETIC AND PHARMACODYNAMIC MODELING FOR THE PREDICTION OF THE MOSQUITOCIDAL EFFECT DURATION OF HIGH-DOSE IVERMECTIN (IVERMAL TRIAL, KENYA)


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Background

Malaria is a leading cause of child death worldwide. High-dose ivermectin, co-administered for 3-days with dihydroartemisinin-piperaquine (DP), was recently shown to kill mosquitoes feeding on individuals for at least 28-days post-treatment, while 7-days was predicted. The current pharmacokinetic-pharmacodynamic (PK-PD) analysis aimed to determine whether a drug interaction or an unidentified metabolite could be contributing to the prolonged mosquitocidal effect of ivermectin. For safety, the effect of ivermectin-dose on piperaquine concentration and piperaquine-induced QTcF-prolongation were also assessed.

Methods

3-days ivermectin 0, 300, or 600 mcg/kg/day plus DP was randomly assigned to 141 adults with uncomplicated malaria in Kenya. During 28-days of follow-up, 1,393 venous and 335 paired capillary plasma samples, 850 mosquito-cluster mortality rates, and 524 QTcF-intervals were collected. Ivermectin and piperaquine concentrations were measured by liquid chromatography-tandem mass spectrometry (LC-MS/MS). Pmetrics™ 1.5.0 was used for population modelling of both PK and PD data.

Results

The population pharmacokinetics of ivermectin were best described by a two-compartment oral absorption model. The PK-PD model was highly predictive of observed data and showed a consistent relationship between ivermectin concentration and predicted mosquitocidal activity throughout the 28-day study duration. The half maximal effective concentration (EC50) for mosquito mortality rate was 15.9 ng/mL (p5-p95: 5.3-36.4). Predicted median
concentrations of both high-dose regimens remained mosquitocidal for at least 28 days. Ivermectin had no effect on piperaquine’s pharmacokinetics or QTcF-prolongation.

Conclusions

The PK/PD model accurately predicted mosquitocidal activity through-out the entire 28-day study duration, without the need to invoke unidentified variables such as an active metabolite or drug-drug interaction. Ivermectin pharmacokinetic studies are now needed in children.

Clinical Trial Registration (Please input N/A if not registered)

ClinicalTrials.gov: NCT02511353. Funding: Malaria Eradication Scientific Alliance (MESA) and U.S. Centers for Disease Control and Prevention (CDC).
Acinetobacter baumannii is emerging is a global threat in hospitalised neonates. Neonates admitted in NICU are particularly prone to multi-drug resistant isolates of A. baumannii. Gastrointestinal colonisation is found to correlate with subsequent bactremia in adults. However its association in neonates is not well studied. We investigated an association between rectal colonization after NICU admission and subsequent development of blood stream infection (BSI) with Acinetobacter baumannii in preterm neonates.

Methods

All consecutive preterm neonates admitted to NICU between August 2015 to January 2016 were enrolled. Rectal swabs were collected once weekly from all eligible neonates. The swabs were inoculated onto blood and MacConkey agar within two hours of collection. Identification of Acinetobacter baumannii was done by matrix assisted laser desorption/ionization- time of flight mass spectrometry. Antibiotic susceptibility was carried out by Kirby Bauer disc diffusion test. The neonates were followed up for development of BSI during their NICU stay.

Results

A total of 135 preterm neonates were enrolled during study period [mean gestational age 30.6 (3.4) weeks, birth weight 1304 (603) gms and postnatal age of 10 (16.09) days]. Rectal swab was positive in 20 (14.8%) neonates (Colonised Group). Median age to first positive rectal swab was 6.5 days of life. Rest 115 neonates were non-colonised (Non-colonised Group). On repeat rectal swabbing, six neonates became negative [mean time to clearance 7.5 (3.8) days]. A significantly higher proportion of neonates in the colonised group [25% (n=5)] developed Acinetobacter baumannii BSI During NICU stay as compared to non-colonized group [8% (n=9); p=0.036; OR=3.92 [95% CI (1.15-13.29)].

Conclusions

Among preterm neonates admitted in NICU, rectal colonization with Acinetobacter baumannii was significantly associated with an increased risk of Acinetobacter blood stream infections.
Clinical Trial Registration (Please input N/A if not registered)

N/A
THE PNEUMOCOCCAL VACCINE EFFECT ON THE EPIDEMIOLOGY OF COMMUNITY ACQUIRED BACTEREMIA (CAB) AMONG CHILDREN IN ISRAEL DURING THE YEARS 2004-2016

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Background

Pneumococcal vaccine PVC-13 was routinely introduced in mid-2010 to the routine Israeli immunization program. As a result, epidemiology of CAB among children in Israel is changing.

Methods

Retrospective study, analyzing data of children aged 0-18 years who were hospitalized in a tertiary medical center serving northern Israel with CAB between the years 2004-2016. S. pneumoniae proportion among bacteremia cases and the rate per 1000 hospitalized children were compared between pre and post pneumococcal vaccination introduction.

Results

During the study period, 275 CAB events were identified: with S. pneumoniae (26.9%), S. aureus (12.4%), Brucella (11.6%) and E. coli (10.9%). In the post-vaccination period, there was a significant reduction in pneumococcal bacteremia caused by strains covered by PCV-13. Pneumococcal bacteremia rate per 1000 hospitalized patients decreased significantly from 1.59 to 0.6 (p<0.001). However, pneumococcus is still a common pathogen mainly due to types not included in the vaccine. Bacteremia caused by other specific bacteria was not significantly changing, except Group A streptococcus, whose incidence increased in the post-vaccination era. The proportion of penicillin resistant pneumococcal isolates decreased dramatically (50.9% to 5.3%), while there were no other significant changes in antibiotic resistance. During the study period, there was a steady decline in the incidence of all bacteremia. In 2015-2016 the number of cases increased mainly due to Brucella outbreak (15 cases in 2015-2016 compared to 3 in 2010-2014).
Conclusions

This study demonstrates that the introduction of PVC13 has a double positive effect: a sharp decrease in cases with a significant decrease in pneumococcal resistance to antibiotic treatment, there was overall decline in CAB, but this trend was reversed in the years 2015-2016, due to a Brucella outbreak.
STAPHYLOCOCCUS AUREUS BACTEREMIA IN CHILDREN: ANTIBIOTIC RESISTANCE AND MORTALITY

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**Background**

*Staphylococcus aureus* (SA) is a major cause of bacteremia in children. Methicillin-resistant SA (MRSA), poses a public health threat, however, prognosis of children suffering MSSA vs. MRSA bacteremia is not well defined.

**Methods**

We collected all SA bacteremia events in children (0-16 years), from 2002 to 2016, in Hadassah medical center. Positive cultures within 48 hours of hospitalization were considered community associated (CA). Those obtained afterwards or from children hospitalized within the previous year, were considered Health-care associated (HA).

**Results**

We recorded 427 events, 284 (66%) were HA, 64 (15%) were MRSA and 9 (2%) were CA-MRSA. There was no increase in MRSA incidence during the study period. Overall 75 (17.5%) children died, during a follow-up of 3475 patient years (54 MSSA and 21 MRSA). In-hospital and 30 days mortality were 3% and 3.5%, respectively (12 and 16 cases). Controlling for age, sex and place of birth, HA-MSSA and HA-MRSA were both associated with increased 1-year mortality: HR (95% CI) - 4.9 (1.7-14) and 10.5 (3.4-33), respectively. Interestingly, among 1-year survivors, long term mortality was still associated with these factors: HR (95%CI) - 5.6 (1.3-25) and 13 (3-66), respectively. However, when controlling for diagnosis of chronic disease and length of hospitalization there was no increased mortality in MRSA bacteremia.

**Conclusions**
The short- and long-term risk for all-cause mortality is significantly high for HA SA-
bacteremia among children with chronic disease, regardless of antibiotic resistance. The
very low rate of CA-MRSA bacteremia justifies the current practice not to include
Glycopeptides in the empiric treatment of CA bacteremia.
HIGH PREVALENCE OF GIARDIA LAMBLIA AND OTHER GASTROINTESTINAL PARASITES IN CHILDREN FROM URBAN BISSAU, GUINEA-BISSAU
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Background

Guinea-Bissau, Western Africa, is one of the poorest countries in the world. Although previous health interventions have improved childhood mortality and morbidity dramatically, gastrointestinal parasitic infections and associated diarrhea remain a major health concern. Current prevalence and impact of these infections is unknown, and previous studies are outdated. In the present cross-sectional field study, we investigate the prevalence of gastrointestinal parasites among children in the capital of Guinea-Bissau, Bissau and identify potential risk factors for infection.

Methods

From August 2015 to April 2017, a total of 1,274 participants aged 2-15 years were included. We collected fecal samples and obtained information on age, household composition, animal husbandry and hygienic standards. Fecal samples were examined by conventional light microscopy. Potential risk factors were identified by logistic regression.

Results

The prevalence of intestinal helminths and protozoa were 11.5% (95% confidence interval (CI): 9.7% - 13.2%) and 44.0% (95% CI: 41.3% - 46.8%), respectively. Helminth infections were dominated by hookworm, which was present in 7.8% of all included (95% CI: 6.3% - 9.2%). The prevalence of pathogenic protozoa Entamoeba histolytica/dispar and Giardia lamblia was 17.3% (95% CI: 15.2% - 19.3%) and 23.9% (95% CI: 21.5% - 26.2%), respectively. Older children were more susceptible to infection with hookworm and Entamoeba histolytica/dispar, whereas younger children were more susceptible to infection with Giardia lamblia (Odds ratio (OR) 3.56 and 0.52, respectively). Poor hygienic standards, including source of drinking water and toilet access were found to be major risk factors for infections with hookworm and Giardia lamblia.

Conclusions

We find a surprisingly high prevalence of pathogenic protozoans among children from urban Bissau. Future improvement of sanitation standards and education of both children and adults should aid to lower the prevalence.
Clinical Trial Registration (Please input N/A if not registered)

N/A
POTENTIAL IMPACT OF A MONOCLONAL ANTIBODY (MEDI8897) ON THE PREVENTION OF RSV BURDEN IN THE UNITED STATES

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Background

Respiratory syncytial virus (RSV) is a leading cause of viral lower respiratory tract infections (LRTIs) worldwide and is associated with significant morbidity, especially among infants. Several prophylactic approaches are currently under development to address RSV burden among this population. To assess the potential health benefit of those different RSV prevention strategies, we have developed a dynamic disease transmission model that integrates US data from national insurance claims databases. The model can be used to evaluate the potential impact of MEDI8897, a monoclonal antibody passive immunization strategy, for the prevention of LRTI caused by RSV in all infants experiencing their first RSV season.

Methods

We have developed an age-structured dynamic deterministic compartmental model to fit RSV seasonal incidence between 2008 and 2015 in the US population. RSV data were extracted from the Truven Health MarketScan® Databases. The model, which reflects RSV natural history, will be used to assess the direct and indirect effects of MEDI8897 prophylaxis on the number of infections, hospitalizations, and medically-attended LRTIs.

Results

The dynamic RSV transmission model is able to capture seasonal patterns and amplitude of outbreaks, in line with the observed epidemiological RSV data in the US (figure).
Based on the mechanism of action of MEDI8897 and assuming universal administration for children experiencing their first RSV season, the model is expected to predict overall and per age-group averted RSV cases, accounting for direct and indirect protection by MEDI8897.

Conclusions

The dynamic transmission model is a robust tool to evaluate how an anti-RSV prophylactic strategy can address disease burden in infants. An optimal product profile will be key to achieve maximum public health impact, as well as successful implementation, targeting all infants.

Clinical Trial Registration (Please input N/A if not registered)

N/A
LONG TERM IMPACT OF PCV13 IMPLEMENTATION ON COMMUNITY ACQUIRED PNEUMONIA IN CHILDREN: A TIME SERIES ANALYSIS OF A 8 YEARS PROSPECTIVE MULTICENTER COHORT


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Background

In 2010, 13 valent pneumococcal conjugate vaccine (PCV13) was implemented in France, 5 years after PCV7 implementation. We aimed to assess the long term effect of PCV13 implementation on community acquired pneumonia (CAP) in children.

Methods

We conducted a quasi-experimental, population-based interrupted time series analysis based on a multicenter prospective cohort in 8 French pediatric emergency departments (PEDs), from June 2009 to May 2017. All patients from 1 month to 15 years of age with chest radiography-confirmed CAP were enrolled. The main outcome was the number of CAP in children over time, analyzed using the segmented regression model with autoregressive error, adjusted on total PEDs visits, and influenza number over time.

Results

During the study period, 12,587 children with confirmed CAP were enrolled. Children <2 years accounted for 4,600 cases (37%). CAP with pleural effusion occurred in 673 cases (5%). PCV13 introduction was followed by the sustained significant decrease in CAP case number (-1.1% per month, p= 0.0009), and reached 41% decrease in May 2014. However, we observed a slight increase from June 2014 to May 2017 (+0.9% per month, p= 0.004). CAP in children <2 years followed the same pattern. CAP with pleural effusion immediately decreased after PCV13 (immediate 49% decrease, p=0.01), and remained stable thereafter.
Conclusions

PCV13 implementation led to a major reduction of CAP in children, but a recent slight increase is observed and has to be followed. The persistence of a low number of CAP with pleural effusion suggests a lesser virulence of non-PCV 13 serotypes involved.
INVESTIGATION OF COAGULASE-NEGATIVE STAPHYLOCOCCI ISOLATED FROM BLOOD CULTURES IN CHILDREN: IMPACT OF IMPLEMENTING MATRIX-ASSISTED LASER DESORPTION IONIZATION–TIME OF FLIGHT MASS SPECTROMETRY

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Background

Coagulase-negative staphylococci (CoNS) are the most frequent causes of nosocomial bloodstream infections. For CoNS identification at the species level, matrix-assisted laser desorption ionization–time of flight mass spectrometry (MALDI-TOF MS) is a superior method than conventional phenotypic methods. Since January 2015, we routinely used MALDI-TOF MS to identify CoNS isolated from blood cultures. Our aim was to investigate the impact of implementing MALDI-TOF MS for CoNS identification in children.

Methods

Patients aged <19 years with positive blood cultures for CoNS at the St. Marianna University School of Medicine Hospital in Japan were enrolled. We investigated patient characteristics and microbiological data from the pre-MALDI-TOF era (2012–2013; period 1) and the post-MALDI-TOF era (2015–2017; period 2).

Results

In a cohort of 100 patients, 36 were from period 1 and 64 from period 2. Staphylococcus epidermidis was the most common species in both periods, where 25 and 48 S. epidermidis were isolated from each period, respectively. Four strains could not be identified at the species level from period 1, whereas all strains could be identified at the species level from period 2. There was a significant increase in the isolation of Staphylococcus warneri from period 2 only (period 1, n = 0; period 2, n = 7). All S. warneri strains were sensitive to methicillin. Sixty-six cases were assessed to be bacteremia, whereas 34 were contaminants; there was no significant difference among the type of species responsible for bacteremia or contamination.

Conclusions
MALDI-TOF MS is a useful method in rapidly identifying CoNS at the species level. In our cohort, the identification rate for *S. warneri* was significantly increased after introduction of MALDI-TOF MS.

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Background

Respiratory syncytial virus (RSV) is recognised as an important respiratory pathogen, particularly in the youngest population. The primary objectives of this hospital-based surveillance network, created in the 2015-2016 season, are to describe the RSV epidemiology and the genetic features of circulating RSV strains in our area.

Methods

The hospital-based surveillance network is currently composed by five large paediatric hospitals in the Barcelona province (Spain). Since the 2015-2016 season, from October to May, the following information is gathered for every laboratory-confirmed RSV case attended in the participating hospitals: age, gender, and, hospital and ICU admissions. The genetic features of all detected RSV (genetic group) and of a representative sampling of strains (genotype) are further reported.

Results

A total of 3,403 (18%) cases were laboratory-confirmed for RSV from 18,739 tested respiratory specimens, of which 2,561 (75%) cases were hospitalised. RSV epidemics started between epidemiological weeks 44 and 48, and ended between weeks 4 and 5 of the upcoming year. The epidemic peaks occurred between epidemiological weeks 49 and 53,
showing positivity rates close to 60%.
Among the hospitalised patients, 88% (2,248/2,561) were <2 years-old (median age: 4.73 months; interquartile range: 1.57-13.40 months), 56% (1,445/2,561) were males, and 17% (434/2,561) required ICU admission.
Viruses belonging to both RSV genetic groups were co-detected. However, the predominant RSV genetic group shifted among the several seasons. RSV-A was predominant during the 2015-2016 (83%), while RSV-B prevailed during the 2016-2017 (56%) and the 2017-2018 (75%) seasons. Most of the characterised viruses belonged to ON1 (RSV-A) and BA9 (RSV-B) genotypes.

Conclusions
The burden of RSV disease in the most susceptible population (<2 years-old children) and its genetic diversity remark the need to maintain a hospital-based network for the clinical and virological surveillance.
Background

Pneumococcal conjugate vaccines (PCVs) implementations dramatically changed serotype (ST) distribution and antibiotic susceptibility of pneumococcal strains. We aimed to assess the long term trend of pneumococcal penicillin susceptibility in nasopharyngeal carriage of children with AOM.

Methods

We conducted a quasi-experimental, population-based interrupted time series analysis based on a multicenter prospective cohort over 16 years in France, recruiting 121 pediatricians who obtained nasopharyngeal swabs in <2 years children with AOM, from 2001 to 2016. The main outcome was the penicillin non susceptible (PNSP) rate among pneumococcal strains, analyzed using the segmented regression model with autoregressive error, adjusted on day care centers attendance, and antibiotics consumption over time.

Results

During the study period, 9,659 children with AOM were enrolled. PCV7 led to a significant immediate decrease of penicillin non susceptibility rate among nasopharyngeal pneumococcal strains (-31%, p=0.001). PCV13 implementation was followed by a significant decreasing trend (-0.4% per month, p=0.03), followed by a slight but significant rebound since January 2015 (+0.9%, p=0.03). Among the main emergent non PCV13 serotype (15B/C, 11A, 23B, 15A, 35B, 21, 23A, 35F), we identified 3 dynamic patterns represented by 1): serotypes already found as PNSP before PCVs (35B, 15A), which remained PNSP after; 2) serotypes found as penicillin susceptible before PCVs (21, 23A, 35F), which remained susceptible after; 3) serotypes found as penicillin susceptible before PCVs which became
Conclusions

PCVs implementations led to a strong reduction of PNSP among nasopharyngeal pneumococcal strains. However, a slight but significant rebound of PNSP was observed since January 2015. Among the non PCV13 replacement serotypes, three distinct dynamic patterns suggest that beside antibiotics selective pressure, other keys are playing in carriage emergence of PNSP.
SEASONAL OUTBREAK OF DENGUE FEVER IN NORTHERN INDIA - A CLINICAL PERSPECTIVE AND PREDICTING LENGTH OF HOSPITAL STAY.

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Background

India reports frequent outbreaks of dengue fever every year. Dengue fever is now endemic with seasonal outbreaks following the monsoons. Scarcity of hospital beds during these outbreaks can be fatal to some. In this study we attempt to look into the clinical and laboratory features of dengue fever in children and predictors of length-of-hospital-stay (LOS).

Methods

This prospective study was conducted in pediatric ward and pediatric intensive care unit of a teaching hospital in Delhi between September 2017 to December 2017 to determine the clinical and laboratory features of all children admitted with dengue fever and find out any predictive factor for LOS. All clinical and laboratory confirmed dengue cases were included in the study. Patients were divided into dengue fever without warning signs (DF), dengue fever with warning signs (DWS) and severe dengue (SD) as per WHO Classification.

Results

Of the 92 cases, 78 had positive IgM ELISA/NS1 Ag, 14 were clinical cases. The M:F is 1.7:1, the mean age is 7+ 4.2 years. The common clinical features were fever (94%), abdominal pain (61%), vomiting (53%) and lethargy (52%). 61% patients were categorized as DWS, 30% DF and 9% SD. The mean duration of hospital stay was 5 + 2.8 days. 43% were hospitalized for > 5 days. The regression model for duration of hospital stay, high grade fever and altered sensorium was significant (R² =0.33, p=<0.05).

Conclusions

A high proportion of patients with DWS required hospitalization. Admission during critical phase of dengue is life-saving. For clinical practice, the doctors working in the front line should be aware of the factors significantly prolonging LOS. This can identify the patients at highest risks and help focus time and resources during seasonal outbreaks.
Background

Because tympanocentesis is not performed routinely in France for first line acute otitis media (AOM) and to follow the bacterial changes induced by PCV13, we set-up two epidemiological studies: the first, follows the otopathogens from nasopharyngeal flora of children with AOM, and the second investigates the otopathogens recovered from children with AOM complicated by otorrhea. We present the results of this second study.

Methods

Children were prospecively enrolled by 44 pediatricians. Standardized history and physical examination were recorded and conventional cultures of otorrhea were performed.

Results

From October 2015 to January 2018, 443 patients were enrolled. Mean age was 29.0 ± 23.2 months. For children less than 3 years old (n=310), no otopathogen was found in 42.6% (n=132), and non typable H. influenzae (NTHi), S. pneumoniae (Sp), group A streptococcus (GAS) and M. catarrhalis (Mc) accounted for 48.3%, 26.4%, 26.4%, and 6.2% of positive cultures, respectively. Two or 3 bacterial species were recovered in 18.3% of samples mainly when NTHi was found (33%). For older children (n=133), negative culture accounted for 64.7%, and among the positive results, GAS was the leading cause. Among Sp, we found 33.9% of penicillin-intermediate isolates, PCV13 serotypes (ST) accounted for 32.7% (in descending order ST3, 19F, 19A) and non PCV13 ST for 67.3% (in descending order ST 23B, 11A, 10A, 15BC,16F, 23A, 24F, 35B). Among NTHi, only 16.2% were β-lactamase-producers.
Conclusions

After PCV13 use, Sp is ranking now at the third position among otopathogen involved in otorrhea after NTHi and GAS. Before age 3 years of age, NTHi is the leading cause of otorrhea whereas after this age, GAS is predominant. Co-infection with 2 otopathogens is frequent, particularly when NTHi is involved.
Background

Diagnosis of tuberculosis (TB) remains problematic in children, especially in the youngest age group, as clinical presentation can be non-specific and existing immunodiagnostic tests tend to be falsely negative, especially in the youngest and most vulnerable children. Therefore, better diagnostic tests are needed.

Methods

We investigated the diagnostic value of a whole blood Mycobacterium Tuberculosis antigen-specific proliferation assay called “Flow cytometric Assay of Specific Cell-mediated Immune response in Activated whole blood” (FASCIA) in a cohort of children exposed to tuberculosis. The exposed children were included prospectively and classified retrospectively, according to strict clinical, biological and radiological parameters, in three groups: exposed but uninfected (negative controls: 66 children), latent tuberculosis infection (LTBI: 24 children) and active disease (aTB: 35 children). Included children were 0-17 years old. Exclusion criteria were immunodepression or immunosuppressive treatment, TB treatment for more than 5 days before inclusion, (treated) TB infection in the past.

Results

FASCIA provided excellent discrimination of infected versus uninfected children, especially in response to PPD (Purified Protein Derivative), HBHA (Heparin-Binding Hemagglutinin) and CFP-10 (10-kDa Culture Filtrate Protein) (p< 0.0001). Two children that initially presented with a negative tuberculosis skin test (TST) in spite of the presence of active
disease, had a positive FASCIA in an early stage of the diagnostic process. Moreover, based on the proliferation of CD8+ T-lymphocytes also in response to PPD, we were able to provide a relative discrimination between children with aTB and LTBI: 71% was classified correctly based on this test.

Conclusions

FASCIA is a whole blood proliferation assay that holds promise for the diagnosis of TB, especially in young children, as high sensitivity for detecting infection is crucial in this age group.

Clinical Trial Registration (Please input N/A if not registered)

P2016/252
HHV-6 INFECTION IN IMMUNOCOMPETENT CHILDREN, IS REALLY BENIGN INFECTIOUS DISEASE? A CASE SERIES AND SYSTEMATIC REVIEW FROM LITERATURE.

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Background

HHV-6 is commonly responsible for a mild childhood infectious disease, known as exantema subitum. Severe clinical manifestations have been reported in immunocompromised patients which in some cases can be fatal. Rarely, the infection can be clinically relevant in immunocompetent children. Different treatment and diagnostic approaches have been used in these cases.

Methods

We performed a systematic review on clinical cases of HHV-6 complicated infection in immunocompetent children from 1945 up to today. We further reported our clinical experience on complicated cases occurring in immunocompetent children followed at Children’s Hospital “Bambino Gesù” in the last 10 years.

Results

We identified in the literature 218 cases of HHV-6 primary infection with complicated clinical manifestations and three cases of ci-HHV-6 complicated infection. Antiviral therapy has been the preferential therapeutic option: 13 (5.8%) cases were treated with intravenous ganciclovir, while 25 (11.26%) and 2 cases (0.9%) have been treated with acyclovir and foscarnet respectively. Alternative treatments were corticosteroids in 7.2% and Ig iv in 3.6% of the cases. The outcome was not specified in 24.3% of the 222 cases, while an equal percentage (37.8%) of patients with favourable and poor outcome was observed. Applying a linear regression, none significant correlation between antiviral treatment and outcome has been found. We identified and described 15 complicated cases admitted to Children’s
Hospital Bambino Gesù of Rome from 2007 up to now. We reported two cases of long term complications.

Conclusions

This review highlights current differences in clinical presentations and treatment and diagnostic approaches during HHV-6 complicated infection cases. Another striking features emerged, is that HHV-6 infection can be fatal and lead with several morbidities. Randomized clinical trials are needed in order to clarify all these aspects.

Systematic Review Registration (Please input N/A if not registered)

N/A
TARGETING THE GUT MICROBIOTA TO IMPROVE VACCINE RESPONSE IN HIV+ CHILDREN


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Background

Immune dysfunction including impaired vaccine response has been described in HIV-infected children despite antiretroviral therapy (ART). We aimed to assess the potential impact on vaccine response of modulating the dysbiosis of the intestinal microbiota by means of a nutritional supplementation.

Methods

Pilot, double blind, randomized placebo-controlled trial including HIV-infected children receiving a symbiotic nutritional supplement. Peripheral blood and stool samples were collected at baseline and after a 4-week intervention, when patients were immunized against influenza. Antibody titers against the three viral components of influenza vaccine were determined by Haemagglutination Inhibition Assay. DNA was extracted from stool samples and 16S rRNA gene amplicons were pyrosequenced. Inflammatory markers and T cell immunophenotypes and subsets were determined.

Results

Twenty-four HIV-infected children were randomized and 18 of them completed the follow up, were immunized against influenza and had available serum samples. Mean age was 11.5±4.1 and 11 (61%) were female. All were on ART and had HIV RNA<50/ml. A short nutritional intervention was able to induce significant changes in diversity and composition in
the gut microbiota (Adonis, p=0.042). Four patients in the placebo (40%) and 5 in the intervention arm (62.5%) showed a fourfold rise in antibody titers after immunization, as shown in Figure 1, according to randomization group. No significant changes in total CD4 counts, CD4/CD8 ratio, T cells subtypes or inflammatory markers were observed after intervention.

Conclusions

In this pilot study, response to influenza immunization was generally poor among HIV-infected children. Despite its effects on modulating gut microbiota, a four-week nutritional supplementation had mild effect in terms of response to influenza vaccine. The potential immune-regulatory effect of targeting the microbiota early in life in HIV disease deserves further investigation.

Clinical Trial Registration (Please input N/A if not registered)

N/A
SAFETY ASPECTS OF VACCINATING PREMATURE INFANTS AGAINST PERTUSSIS AND PNEUMOCOCCI - A LITERATURE REVIEW WITH FOCUS ON RISK FOR APNEA AND DEATH

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Background and Objective

Premature infants are more vulnerable to vaccine-preventable infections with pertussis and pneumococci. Cardiorespiratory instability is a feared adverse event after immunization of these infants and often leads to deferred vaccination. We aimed to review the risk of apnea and death following the first vaccination in premature infants.

Methods

We conducted a literature review of studies published 1986 - 2017. Articles were retrieved from PubMed, Cochrane Library and Scopus. Studies where the outcomes apnea or death were assessed after vaccination with acellular pertussis and/or pneumococcal conjugate vaccines were included. Of 3679 articles retrieved, 26 were included after reviewing full text, and 8 were included after evaluation with GRADE terminology.

Learning Points Discussion

Most studies did not report apnea alone, but in combination with bradycardia and/or desaturation (ABD events). Post-vaccination Apnea/ABD events were described in 0 - 23 % of children born prematurely. There was a tendency of higher incidence of apnea/ABD events with lower gestational age at birth (Figure 1). No correlation was found between the chronologic age of infants at first vaccination and the occurrence of apnea/ABD events. The infants’ cardiorespiratory stability and overall clinical condition at the time of vaccination seemed to be of importance.
Percentage of children with increased events varied between studies, largely due to differences in methodology and definitions of outcomes. In the only randomised controlled study in this review, no difference was seen between the vaccinated group and the controls.

Apnea occurred from 3-66 hours post-vaccination.

Eight fatal cases were reported. No causal relationship between vaccination and death was found.

One small study showed that pneumococcal conjugate vaccine and hexavalent vaccines given concomitantly gave significantly higher incidence of apnea and bradycardia.

There is a need for prospective studies on concomitant vaccination.
ELIZABETHKINGIA MENINGOSEPTICA MENINGITIS OUTBREAK IN A NEONATAL UNIT IN NEW DELHI

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Title of Case(s)
ELIZABETHKINGIA MENINGOSEPTICA MENINGITIS OUTBREAK IN A NEONATAL UNIT IN NEW DELHI

Background

Elizabethkingia meningoseptica (E.M.), a gram negative bacillus is widely distributed in soil and water. It is responsible for outbreaks of neonatal meningitis and septicemia. Outbreaks usually occur as a result of contamination of respiratory circuits, hospital tap water, sink drains and disinfectants. Accurate diagnosis is essential because the organism is resistant to all commonly used antibiotics for gram negative organisms.

Case Presentation Summary

From August to October 2017 in Neonatal Unit of Lady Hardinge Medical College and Associated Kalawati Saran Children Hospital 7 out of 730 newborns admitted had E.M. Meningitis diagnosed. Environmental screening was conducted and samples cultured from respiratory equipments, tap water, sink drains, suction apparatus, radiant warmers, saline bottles, lipid solutions etc did not grow E.M. Strict infection control measures resulted in the termination of the outbreak.

Results

Clinical details of all the newborns are summarized. (Table). Most newborns presented with apnea, feed intolerance, lethargy and seizures. Cerebrospinal fluid examination (CSF) revealed field full of white blood cells and very high protein (280-850 mg/dl). Culture grew E.M. in all. The organism was resistant to piperacillin-tazobactum, gentamicin, amikacin, meropenem, imipenem, colistin, ceftazidine and aztreonam. It was sensitive to cefoperazone-sulbactum, minocycline, vancomycin and levofloxacin. Two of the seven
patients died. Only two of the five surviving neonates had normal neurologic outcome.

**Table: Clinical Details**

<table>
<thead>
<tr>
<th>Case No</th>
<th>Mode of Delivery</th>
<th>Gestation (weeks)</th>
<th>Birth Weight (Grams)</th>
<th>Admitting Diagnosis</th>
<th>Age of Presentation (day of life)</th>
<th>Antibiotic Used</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cesarean</td>
<td>30</td>
<td>1220</td>
<td>Respiratory Distress Syndrome</td>
<td>22</td>
<td>Cefoperazone sulbactam and Vancomycin (Cef+Vanc)</td>
<td>Discharged and well</td>
</tr>
<tr>
<td>2</td>
<td>Vaginal</td>
<td>40</td>
<td>2620</td>
<td>Transient Tachypnea</td>
<td>4</td>
<td>Meropenem and Ciprofloxacín</td>
<td>Discharged and well</td>
</tr>
<tr>
<td>3</td>
<td>Cesarean</td>
<td>33</td>
<td>1250</td>
<td>Small for Gestational Age</td>
<td>6</td>
<td>Cef+Vanc+ Rifampicin</td>
<td>Discharged, VP shunt for Hydrocephalus</td>
</tr>
<tr>
<td>4</td>
<td>Vaginal</td>
<td>27</td>
<td>820</td>
<td>Respiratory Distress Syndrome</td>
<td>19</td>
<td>Cef+Vanc+ Rifampicin</td>
<td>Died</td>
</tr>
<tr>
<td>5</td>
<td>Vaginal</td>
<td>28</td>
<td>760</td>
<td>Respiratory Distress Syndrome</td>
<td>16</td>
<td>Cef+Vanc</td>
<td>Died</td>
</tr>
<tr>
<td>6</td>
<td>Vaginal</td>
<td>31</td>
<td>1860</td>
<td>Transient Tachypnea</td>
<td>7</td>
<td>Cef+Vanc+ Rifampicin</td>
<td>Discharged, VP shunt for Hydrocephalus</td>
</tr>
<tr>
<td>7</td>
<td>Cesarean</td>
<td>34</td>
<td>2270</td>
<td>Transient Tachypnea</td>
<td>5</td>
<td>Vancomycin+ Rifampicin+ Levofloxacín</td>
<td>Discharged, VP shunt for Hydrocephalus</td>
</tr>
</tbody>
</table>

**Learning Points/Discussion**

E.M. infections are emerging in neonatal units, especially among premature newborns. It is essential that laboratories have the facility to identify the organism correctly. A high degree of suspicion, rapid diagnosis, and prompt institution of appropriate therapy are key factors in management of such infections. In addition, intensified environmental cleaning with proper infection control practices can successfully control the spread of infection.
EFFECT OF VACCINATION PROGRAMMES USING 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINE ON THE INCIDENCE OF PNEUMOCOCCAL MENINGITIS IN CHILDREN UNDER FIVE YEARS-OLD: RESULTS OF SPIDNET MULTICENTRE STUDY


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Background

The SpIDnet network conducts population-based surveillance for invasive pneumococcal disease in the European Union. Using surveillance data from eight sites from six countries, we measured the impact of vaccination with 13-valent conjugate vaccine (PCV13) on pneumococcal meningitis in children under five years of age. The childhood vaccination
uptake was 93-97% in five sites with universal PCV13 vaccination versus 50-77% in the three sites without universal vaccination.

**Methods**

We compared meningitis incidence between each PCV13 year (2011-2016) with the average incidence in the PCV7 period. We calculated site-specific incidence rate ratios (IRR) and corresponding confidence intervals (95%CI). We pooled the IRR across sites using random effect meta-analysis, and calculated the impact as (1-IRR)*100.

**Results**

After six years of PCV13 use, the site-specific incidence of all-type pneumococcal meningitis ranged between 1.12 and 3.43/100,000 children. All-type meningitis incidence decreased by 56% in 2014 (IRR=0.44, 95%CI: 0.33-0.58) and by 29% (IRR=0.71, 95%CI: 0.56-0.90) in 2016, compared to PCV7 period. In 2016, the incidence of PCV7 and additional six PCV13 serotype meningitis decreased by 79% (IRR=0.21, 95%CI: 0.10-0.43) and 87% (IRR=0.13, 95%CI:0.06-0.27), respectively. NonPCV13 serotype meningitis incidence increased each year up to 79% (IRR=1.79; 95%CI: 1.23-2.61) in 2016. In sites with universal programmes, the meningitis incidence decreased by 22%, 79% and 88% for all type, PCV7 and additional six PCV13 serotypes and increased by 111% for nonPCV13 serotypes.

**Conclusions**

All-type meningitis incidence in children under five years-old is low after six years of PCV13 use and decreased as compared to PCV7 period due to the decline in the incidence of meningitis caused by PCV7 and additional PCV13 serotypes. The nonPCV13 meningitis incidence increased each year after the vaccine introduction. Surveillance is crucial to monitor pneumococcal meningitis incidence.

**Clinical Trial Registration (Please input N/A if not registered)**

N/A
LOW POST-TREATMENT PROPHYLAXIS AGAINST SUBMICROSCOPIC P. FALCIPARUM RECURRENCES AFTER DIHYDROARTESININ-PIPERAQUINE AND ARTEMETHER-LUMEFANTRINE AMONG PATIENTS WITH FALCIPARUM MALARIA IN WESTERN INDONESIA

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Background

Artemisinin combination therapy (ACT) is the recommended first-line therapy for uncomplicated falciparum malaria, nevertheless reduced sensitivity to artemisinin and its partner drugs have been observed in the Greater Mekong subregion. Western Indonesia used artesunate-amodiaquine between 2004 and 2012 and high treatment failures were documented. Dihydroartemisinin-piperaquine (DP) has been deployed as the first-line treatment since 2012.

Methods

We enrolled 302 adults and children with uncomplicated falciparum malaria in North Sumatera province, Indonesia. Patients were randomised to receive either the standard 3-dose of DP or 6-dose of artemether-lumefantrine (AL). Patients were followed-up for 6 weeks. Primary endpoint was the PCR-corrected efficacy of DP and AL at day-42, and the secondary endpoint was the proportion of patients with submicroscopic Plasmodium falciparum recurrences at day-42.

Results

Genetic characterisations on pfcrt, pfmdr1 genes and pfkelch13 propeller domain on pre-treatment samples showed high frequency of pfcrt-SVMNT haplotype (88.7%, 63/71), pfmdr1 86Y/184 (72.8%, 67/92), and pfkelch13 wild-type allele (96%, 72/75). Only 4% (3/75) of patients had mixed wild-type and mutant T474A in the pfkelch13. The uncorrected-PCR efficacy at day-42 were 84% and 90.4% in DP and AL groups (P=0.09), respectively. While PCR-corrected efficacy were 99.3% and 100% for DP and AL (P=0.31). However, subpatent recurrences at day-42 were significantly higher at 31.5% and 30.4% in DP and AL groups (P=0.741), with both drugs selected parasites carrying pfmdr1 86N/184F (OR 13.3, 95% CI 2.7-81.4, P=0.0001 for DP and OR 28.6, 95% CI 5.1-277.7, P<0.0001 for AL).

Conclusions
Our study showed that DP and AL remain effective for uncomplicated falciparum malaria in western Indonesia, however high proportion of submicroscopic infection may continue to contribute to post-treatment transmission therefore hinders the efforts to eliminate malaria.

**Clinical Trial Registration (Please input N/A if not registered)**

NCT02325180
PREVALENCE OF HUMAN HERPES VIRUSES 6 AND 7 IN CSF FROM UK CHILDREN WITH FEBRILE CONVULSION, MENINGO-ENCEPHALITIS, SEPSIS, EXANTHEM SUBITUM OR OTHER NEUROLOGICAL INVOLVEMENT

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Background

Although primary infections with Human herpes viruses 6 and 7 (HHV6/7) viruses are usually brief, self-limiting and with no adverse sequelae, mortality and morbidity has been recorded in the young and immunocompromised. The association of primary infection with atypical febrile illnesses, convulsion, meningo-encephalitis, sepsis, and other serious neurological complications is recognized but is likely underestimated due to limited use of HHV6/7 diagnostic testing.

Methods

A one-year (January to December 2017) prevalence study was performed to determine the frequency of primary HHV6/7 infection in cerebrospinal fluid (CSF) of children under 5 years presenting to Sheffield Children’s Hospital with febrile illnesses, convulsion, atypical sepsis, meningo-encephalitis, or other CNS involvement. A real time multiplex qPCR was developed and 396 CSF samples tested retrospectively for HHV6A, HHV6B and HHV7.

Results

The results showed a 7.6% (30/396) prevalence of HHV6/7 DNA in the CSF samples tested. 0.5% (2/396) were HHV6A DNA positive, 4.0% (16/396) were HHV6B DNA positive, 3.0% (12/396) were HHV7 DNA positive, 0.3% (1/396) was co-infected with both HHV6B and HHV7. No results could be reported on one sample (0.3%) due to failure of the internal control. The age of the patients in which the samples tested positive ranged from one month to five years (average 12.5 months).

Conclusions

This study describes important UK prevalence data for HHV6 and 7, which have not been previously described. It highlights the need to consider inclusion of these viruses within
routine viral CSF PCR panels. Their inclusion may aid quick effective management of these patients, allow rational antimicrobial prescribing and reduce length of stay.
EFFECTIVENESS OF ONE DOSE OF ACELLULAR PERTUSSIS VACCINE IN INFANTS FROM SIX EU/EEA COUNTRIES: PRELIMINARY RESULTS

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Background

PERTINENT (Pertussis in Infants European Network) established active surveillance of pertussis among infants in 41 hospitals from six EU/EEA countries since October 2015. Acellular pertussis-containing combination vaccines are recommended in participating countries within primary infant vaccination schedules. We measured the effectiveness (VE) of one dose of acellular vaccine among hospitalised infants aged <1 year using a test-negative design.

Methods
From December 2015 to October 2017, participating sites included all infants aged <1 year presenting with pertussis-compatible symptoms. Cases were patients testing positive for *Bordetella pertussis* by PCR or culture; controls were those testing negative to all *Bordetella* spp. Infants were considered vaccinated against pertussis with one dose only if they had received it >14 days before symptom onset and had not received a second dose before inclusion. We restricted the analysis to infants eligible for vaccination to calculate pooled VE as 100*(1-odds ratio of vaccination). We adjusted VE by site, onset date and age group (2-3 and 4-11 months).

**Results**

Among 1,338 infants with pertussis-compatible symptoms, 278 (21%) were laboratory-confirmed. To compute one-dose VE, we enrolled 92 cases and 169 controls, of which 59 cases (64%) and 114 controls (67%) were 2-3 months of age. Thirty-two cases (35%) and 77 controls (46%) had received one vaccine dose. Adjusted pooled pertussis VE of one dose was 48% (95%CI: 1-73).

**Conclusions**

Preliminary PERTINENT results suggest that the first dose of acellular pertussis vaccine may halve the risk of laboratory-confirmed pertussis leading to hospitalisation in vaccinated infants. The estimate is imprecise at a time of low pertussis circulation despite a large study population. Further recruitment will increase the precision and will allow computation of VE by number of doses, study site and narrower age group.

**Clinical Trial Registration (Please input N/A if not registered)**

N/A
ESP18-0562
SCIENCE AND EDUCATIONAL TRACK

E-POSTER DISCUSSION SESSION 14: ANTIMICROBIALS: RESISTANCE AND PHARMACOLOGY

GENOTYPIC IDENTIFICATION OF AmpC β-LACTAMASES PRODUCTION IN DIARRHOEAGENIC E.COLI FROM CHILDREN UNDER FIVE AND MOLECULAR DOCKING OF THEIR PROTEINS
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Background

AmpC beta-lactamases are bacterial enzymes that hydrolyse 3rd generation extended spectrum cephalosporins and cephamycins engendering resistance to these categories of antibiotic. AmpC β-lactamase expression can increase in the nosocomial pathogens, triggered by exposure to antibiotics and β-lactamase inhibitors with the β-lactam function. Therefore, AmpC β-lactamase is an important target for developing novel effective antibacterial therapies. The objective of this study was to evaluate the Real Time PCR as a rapid diagnostic tool for simultaneous detection of AmpC beta-lactamase producing E. coli and in silico determination of docking sites of AmpC proteins.

Methods

During one year period from July 2012 to July 2013, 120 stool samples were collected, including 80 diarrhoeagenic E.coli and 40 controls from children in University College of Medical Sciences and Guru Teg Bahadur Hospital, East Delhi. E.coli was diagnosed for AmpC beta lactamase production using conventional phenotypic tests. DNA extraction was done, and extracted DNA was used as a template for Real Time PCR. Bioinformatics tools were used to molecular docking.

Results

Real time PCR detected target genes of AmpC beta lactamase in 18.75% and 22.5% in cases and controls respectively. Chi square test and Fisher’s exact test were used to determine statistical significance of data.

Conclusions

Real time PCR assay will save time and help investigators to explore the role of multidrug resistant E. coli. Active binding sites will be useful in synthesis of new drugs. Modeling and docking studies may provide useful insights for developing new antibiotic drugs to minimize multidrug resistance.

Clinical Trial Registration (Please input N/A if not registered)
Background

The need for accurate biomarkers for diagnosis and prognosis is becoming a central issue in enterovirus-A71 (EV-A71) brainstem encephalitis. We aim to determine the diagnostic and prognostic value of inflammatory markers in pediatric patients with EV infection of the central nervous system (CNS), during an outbreak of brainstem encephalitis associated with EV-A71.

Methods

Clinical and radiological data were analyzed from patients with EV meningitis, encephalitis, brainstem encephalitis or encephalomyelitis, admitted to a reference pediatric hospital between 1 May 2016 and 30 April 2017, in whom inflammatory markers of interest had been
initially determined (CSF WBC count, CSF protein, CSF neopterin, blood WBC, neutrophil and lymphocyte counts and serum C-reactive protein).

Results

Forty-two patients were included, out of 72 patients with EV infection of the CNS. Median age was 2.3 years (p25-p75 1.6-2.7). EV was genotyped in 35 out of 42 and EV-A71 was identified in 27 out of 35. Thirty-one (73.8%) were diagnosed with brainstem encephalitis, six (14.2%) with encephalitis, three (7.2%) with encephalomyelitis and two (4.8%) with aseptic meningitis. CSF neopterin levels were elevated (> 61 nmol/L) in 38/42 (90.5%), with a median of 327.5 nmol/L (p25-p75 193.3-513.0). Higher CSF levels of neopterin correlated with the presence of ataxia and/or paresis (p=0.002) and with extensive lesions on brain and spine MRI (p=0.041), unlike the other inflammatory markers determined. Higher WBC correlated with the persistence of such symptoms at day 30 (p=0.048). Other inflammatory markers did not show any statistically significant association.

Conclusions

WBC count elevation had the highest prognostic value for disease severity, as previously reported. On the other hand, elevated CSF neopterin levels could be correlated with the most severe clinical and radiological signs of brainstem encephalitis caused by EV.

Clinical Trial Registration (Please input N/A if not registered)

N/A
ESP18-0570
SCIENCE AND EDUCATIONAL TRACK

E-POSTER DISCUSSION SESSION 14: ANTIMICROBIALS: RESISTANCE AND PHARMACOLOGY

POPULATION PHARMACOKINETICS OF TEICOPLANIN IN PRETERM AND TERM NEONATES: IS IT TIME FOR A DIFFERENT DOSING REGIMEN?
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Background

Although glycopeptides are among the most commonly used antimicrobials in neonates with suspected late-onset sepsis, little is known about the pharmacokinetics (PK) of teicoplanin in term and preterm neonates. We aimed to develop a population pharmacokinetic model in order to evaluate currently recommended dosing regimen.

Methods

By using D-Optimal design approach, a sparse PK study was designed and implemented in 60 neonates with post-menstrual age (PMA) of 26-43wks. Dosing regimen: loading dose 16mg/kg, maintenance dose 8mg/kg once daily (i.v. 30min infusion). Four blood samples per neonate were collected. Concentrations were quantified by high-pressure liquid chromatography–mass spectrometry. Population PK analysis was performed using NONMEM software. Final PK model was validated by nonparametric bootstrapping and visual predictive check and Monte-Carlo (MC) simulation were performed.

Results

The covariate model used was CL=0.0234(WT/1765)⁰.⁷⁵ L/h , V1=0.287(/1765) L, Q=0.159(WT/1765)⁰.⁷⁵ L/h,

V2=0.515(WT/1765) L, while CRCL was also found to be a significant covariate on CL, it was removed for the MC simulations. Inter-individual variability on clearance (CL), central volume (V1), peripheral volume (V2) was 40%, 47%, 51.2%. MC simulation demonstrated that with dose of 8 mg/kg: 81.6% of neonates with weight (WT)<1kg versus 89.6%, 95.1% and 97% of neonates with WT: 1-2kg, 2-3kg, ≥4kg, respectively reach the C_{trough(120h)}>15mg/L. Increase in dose at 12mg/kg results in 93.5% of neonates with WT<1kg
achieving $C_{\text{trough(120h)}} > 15\text{mg/L}$. Respective results were found with the use of AUC/MIC>400 as a target.

Conclusions

Teicoplanin population PK is variable in neonates with weight having the most significant impact on pharmacokinetics. Based on MC simulation ELBW and VLBW neonates need higher doses especially for Staphylococcus spp. with MIC≥1.

Clinical Trial Registration (Please input N/A if not registered)

N/A
Antimicrobial Resistance (AMR) in children and neonates is rising globally. In 2017, the World Health Organisation (WHO) revised their Essential Medicines List for Children to release a list of ‘Reserve Group Antibiotics’. These antibiotics include aztreonam, 4th and 5th generation cephalosporins, daptomycin, fosfomycin, polymyxins, oxazolidinones and tigecycline. Monitoring and utilization reporting of these last-resort antibiotics are crucial to preserve efficacy and reduce AMR. The aim of this study was to describe the use of WHO Reserve group antibiotics in hospitalised children and neonates.

Methods

As part of the GARPEC project, 4 one-day point-prevalence surveys (PPS) and one pilot study were conducted between February 2015 to February 2017. Data on demographics, antibiotic use and clinical diagnoses were collected from patients who received at least one antibiotic for treatment, on the day each PPS was carried out.

Results

A total of 14,749 antibiotic prescriptions were identified from 10,318 patients. An overall WHO Reserve antibiotic prescribing rate of 4.0% (n=582; 95% CI: 3.6% - 4.3%) was estimated. The rate is higher in children, at 4.5% (n=510; 95% CI: 4.1% - 4.9%), than in neonates, at 2.1% (n=72; 95% CI: 1.7% - 2.7%). Overall, the top 3 most common WHO Reserve antibiotics were cefepime (2.3%, n=339), colistin (0.7%, n=105) and linezolid (0.6%, n=90). Our results suggest higher variability for dosing in children > 5 years (Figure 1). Country specific prescribing patterns of reserve antibiotics are also reported.
Conclusions

Our findings suggest high variability in dosing for WHO Reserve antibiotics in children, especially for colistin. This is an area of concern as inappropriate prescribing may increase AMR. Further investigation into monitoring and utilization reporting of reserve antibiotics are warranted.
INCREASED RISK OF SEVERE RESPIRATORY SYNCYTIAL VIRUS (RSV) BRONCHIOLITIS IN INFANTS FROM MOTHERS WITH LOWER LEVELS OF ANTIBODY (AB) TO THE PREFUSION F PROTEIN

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Background

Better understanding of the structure of RSV has accelerated the development of novel detection, prevention and treatment strategies. Among the RSV surface glycoproteins, the F protein is conserved among RSV strains and has two forms: prefusion (pre-F) and postfusion (post-F). The pre-F form is the most potent inducer of neutralizing antibodies and has become the major target for developing new vaccines and monoclonal Abs. The aim of this study was to assess if there is a correlation between the levels of maternal antibodies against the pre-F, post-F or G proteins and their child’s risk of developing severe RSV bronchiolitis requiring hospitalization.

Methods

ELISA assays using recombinant RSV proteins were used to measure specific maternal IgG Ab to pre-F, post-F and G proteins in serum samples obtained during weeks 9-12 of pregnancy. Ab titers of mothers of previously healthy term infants <3 months of age hospitalized at Helsinki Children’s Hospital with RSV bronchiolitis between December 2015 and March 2016 (n=94) were compared with serum samples from control mothers (n=130) whose children were not hospitalized.

Results

All maternal samples had detectable pre-F antibodies. Pre-F and post-F Ab titers were >10-times higher than G Ab titers. Maternal pre-F Ab titers were significantly lower in infants hospitalized with RSV bronchiolitis. There were no significant differences in maternal post-F and G Ab titers between hospitalized infants and controls.
Conclusions

Lower maternal pre-F IgG Ab titers measured during the first trimester are associated with severe RSV infection in young infants.

Clinical Trial Registration (Please input N/A if not registered)

N/A
ESP18-0595  
SCIENCE AND EDUCATIONAL TRACK  
E-POSTER DISCUSSION SESSION 12: SEVERE BACTERIAL INFECTIONS  

BLOODSTREAM INFECTIONS IN FEBRILE NON-HOSPITALIZED PEDIATRIC HEMATOLOGY-ONCOLOGY PATIENTS: A 5-YEAR RETROSPECTIVE STUDY  
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Background  
Fever may be the first manifestation of bloodstream infections in pediatric cancer patients and, therefore, involves hospitalization and administration of broad-spectrum parenteral antibiotics. Knowledge of pathogen distribution is paramount for optimal patient management. The aim of this study was to analyze the causes of bloodstream infections in febrile pediatric oncology outpatients.

Methods  
This retrospective study was conducted in a single institution during the 5-year period 2012-2016. All non-hospitalized pediatric oncology patients admitted with fever to the pediatric oncology department were eligible. Blood cultures were obtained and processed using the BacT/Alert3D automated system and the Vitek2 (BioMerieux, France) bacterial identification system. Categorical variables were analyzed using the x² test.

Results  
191 febrile episodes corresponding to 104 pediatric oncology outpatients were found (40 with hematological malignancies and 64 with solid tumors). 96 (50.3%) patients were neutropenic. All patients had implanted central venous catheters. The rate of bacteremia was 19.9% (16.7% in neutropenic and 23.1% in non-neutropenic patients, p=0.3). Gram-positive bacteria prevailed (55.3%) followed by Gram-negative (42.1%). Polymicrobial bacteremia was detected in 3 (7.9%), while Candida albicans was isolated in 1 case. Staphylococcus epidermidis was the predominant Gram-positive species isolated. Among Gram-negative bacteria isolated, 54% were Enterobacteriaceae with Klebsiella spp. predominating and 46% non-fermenters with Acinetobacter and Pseudomonas spp. equally contributing. Half of Gram-negative bacteremias were due to multi-drug resistant nosocomial pathogens commonly encountered in pediatric oncology department.

Conclusions
While *S. epidermidis* is the most common cause, a variety of Gram-negative pathogens induce bloodstream infections as well, implying possible colonization in the oncology department after prolonged and repeated hospitalizations. These results have important implications for the initial antimicrobial therapy of febrile patients upon admission to the pediatric oncology department.
CIPROFLOXACIN USE IN ESCHERICHIA COLI MENINGITIS: A FRENCH PAEDIATRIC COHORT

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Background

Escherichia coli meningitis remains a burden in neonates and infants with high morbidity and mortality rates. Adjunctive ciprofloxacin therapy has been used in France to prevent neurological complications, based on its bactericidal activity on gram-negative microorganisms, its pharmacokinetic-pharmacodynamics advantages and its anti-inflammatory properties. The objective was to compare the outcome of a cohort of infants with or without adjunctive ciprofloxacin therapy.

Methods

All infants < 12 months with a diagnostic of Escherichia coli meningitis between 2001 and 2016 were included and data collected through the French paediatric meningitis surveillance network. Neurological outcome and mortality were recorded and compared between the ciprofloxacin and non-ciprofloxacin groups adjusted on significant covariates.

Results

Among the 381 patients included, 206 (54.1%) patients were co-treated with ciprofloxacin. The median post-natal age and weight were 15 days (range 1-318) and 3.4kg (range 0.6-13.7). There was no significant difference of mortality between the ciprofloxacin and the non-ciprofloxacin group (22 deaths versus 19, p=0.8). On multivariate logistic regression, only initial severity was significantly associated with death (aOR=98, CI95% [13.2–726.8]). Eighty-eight infants presented short-term neurological complications. On multivariate analysis, complications were associated with very late onset disease (aOR=5.4, CI95% [1.9-15.2]), ciprofloxacin treatment (aOR=1.9, CI95% [1.1-3.3]), blood/CSF glucose ratio <0.1 (aOR=2.6, [1.2–5.3]) and initial severity (aOR=7.4, CI95% [4.2–13.3]).

Conclusions

This study on the interest of adjunctive ciprofloxacin on a large cohort of infants with Escherichia coli meningitis does not evidence an improvement of short-term neurological outcome in the ciprofloxacin group. A combination therapy might not be superior to an empiric therapy with a cephalosporin in paediatric Escherichia coli meningitis.
Most febrile children visiting the ED suffer from self-limiting viral infection. Nevertheless, antibiotic use remains high. We aimed to investigate determinants of antibiotic prescription in febrile children in different ED’s in Europe.

Methods
The MOFICHE study (Management and Outcome of Fever in children in Europe) studies febrile children aged 0 – 18 years at 11 European ED’s starting January 2017. This preliminary analysis is restricted to settings with 300 cases or more. Routine data were collected including patient characteristics, hospitalization and antibiotic prescription. Based on clinical data, patients were categorized as (probable) bacterial infection, (probable) viral infection or unknown cause using a validated flowchart that combined symptoms, CRP and culture results. We developed a multivariable logistic regression model for antibiotic prescription, that included known determinants and settings.

Results

In total, 15,114 children with a median age of 2.9 years (IQR 1.4-5.8) were included of whom 9.6% had ill appearance and 6.9% were triaged as highly urgent. Hospitalization rate varied between 6.7%-62.6%. In hospitalized children, antibiotic use ranged between 2.3%-70.9% per setting. Although antibiotic prescription was related to suspected bacterial infection, variability remained substantial in all three groups (bacterial infection 72%–99%, viral infection 1-52% and unknown cause 14%-67%). Ill appearance, age, hospitalization and working diagnosis only partly explained the variability in antibiotic prescription for settings.

Conclusions

Antibiotic prescription rates vary widely between settings for (probable) bacterial infection, (probable) viral infection and unknown cause and is related to hospitalization, ill appearance, age and working diagnosis. We will further explore the effect of case-mix and quality on antibiotic use.

Clinical Trial Registration (Please input N/A if not registered)

N/A
VIRAL PCR ON CEREBROSPINAL FLUID SAMPLES WITHOUT PLEOCYTOSIS: CLINICALLY USEFUL FOR DEFINITIVE DIAGNOSIS IN INFANTS (RATHER THAN NEWBORNS), BUT LEAVING A DILEMMA FOR FOLLOW-UP CARE

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Background

NICE guidelines suggest consideration of lumbar puncture in neonates, or febrile babies under 3 months, with a CRP >10mg/L. There is uncertainty over which CSF samples should undergo viral PCR testing, given viral infections traditionally have raised CSF WCC (pleocytosis).

As these sick children receive resource-intensive management, and definitive viral diagnosis allows treatment rationalisation, we wanted clarity over the utility of PCR testing samples without pleocytosis.

Methods

The CSF results from our hospital, which has both neonatal and paediatrics wards, were retrospectively analysed for the significance of their viral PCR testing. CSF WCC, glucose, protein, and viral PCR and bacterial culture results were recorded, along with blood markers and follow-up arrangements.

Results

There were 996 CSF samples from 939 patients (13/12/2014-31/1/2018): 511 from neonates, and 485 from Paediatrics. Viral PCR was positive on 82 out of the 519 (15%) samples which underwent PCR: 57 enterovirus, 21 parechovirus, 3 HSV. Of the PCR-positive samples, 69% had no pleocytosis compared to age-corrected CSF WCC normal ranges, and 55% had WCC < 3/mm³. No differences were observed based on causative virus. No PCR out of 213 from babies <5 days old was positive. 39/82 PCR-positive children received audiology follow-up, with one (enterovirus at 2 months, CSF WCC 32/mm³) potentially demonstrating neurological hearing loss.
Conclusions

Most of our CSF viral PCR-positive children do not show pleocytosis, regardless of virus, suggesting pleocytosis in young children/infants is not a sensitive tool for choosing viral PCR testing. With universally negative results, there is limited utility in routinely PCR testing neonates under 5 days old, excepting suspicion of vertical viral transmission. Follow-up for viral infections without pleocytosis is unclear: a cohort study is needed to determine likelihood of neurological sequelae.
POINT-OF-CARE ULTRASOUND IS AN USEFUL TOOL FOR RISK STRATIFICATION IN ACUTE BRONCHIOLITIS

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Background

Acute bronchiolitis (AB) is a common cause of hospital admission among infants. Clinical scores have proven to be inaccurate in predicting prognosis. Point-of-care ultrasound has aroused great interest for diagnosis of respiratory diseases. Our aim was to assess the accuracy of a score based on thorax ultrasound (TU) at admission, to stratify patients at risk of need of respiratory support.

Methods

Prospective, multicenter cohort study including infants <6 months of age admitted for AB, October 2016 to January 2018. TU was performed during the first 24h of admission. Main outcome was NIV use [including CPAP, high-flow nasal cannula oxygen (HFNC)] or mechanical ventilation (MV). The score was based on the presence of ≥3 B lines, single-space B line confluence and/or consolidations.

Results

A total of 146 patients were included (median age 1.7 months [IQR: 1.2-2.8], 47.6% female. Mean duration of symptoms prior to admission was 3.1 days (SD 1.8), and 98% were RSV positive. Median Wood-Downes Score at inclusion was 4 points [IQR 4- 6]. Fifty-eight patients (39.7%) required NIV [CPAP 23 (16%), HFNC 35 (24.6%)], 14 (9.7%) were transferred to PICU and 3 needed MV (3/146). A TU score was built according to the findings (Table 1) with an AUC=0.79 (0.7-0.9). A score ≥4 showed a sensitivity of 81% and a specificity of 65% while a score ≥5 displayed a sensitivity of 58% and a specificity of 86%.

Conclusions
According to our findings, scoring ≥4 points in a TU performed during the first 24h of admission was a predictor of NIV/MV in infants <6 months of age admitted with AB. Point-of-care ultrasound is an accurate tool to identify patients at risk of severe disease that may benefit from prompt respiratory support.

Clinical Trial Registration (Please input N/A if not registered)

N/A
SURVEILLANCE REPORT OF THE SEVENTH YEAR OF DIPHTHERIA OUTBREAK IN INDONESIA

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Background

India and Indonesia are two countries with the highest incidence of diphtheria cases for several recent years. There has been an outbreak of diphtheria in Indonesia since 2011. East Java has been the most affected area, contributing more than half of all clinical diphtheria cases in the country. The aim of this study was to report the surveillance data from 2017, the seventh year of this outbreak

Methods

The data came from the East Java Provincial and all 38 Districts Health Offices. The primary sources of reports were the hospitals, community health centers, private medical doctors, or the patients and the family. Official reports were made on daily and weekly basis. All data were then centralized in Surabaya and being analyzed by the Provincial Expert Committee. Microbiological cultures were performed at the referral laboratory in Surabaya.

Results

All 38 districts reported cases. There were 460 clinical cases of diphtheria in 2017. The highest incidence was found in 2012 with 965 clinical cases in a year. Male (51.74%) were slightly outnumbered female. The majority of the cases were below 15 years of age (70%). Age 5-9 year old was the most common group (23.7%). As many as 84% cases were unimmunized or had uncomplete immunization history. Only 38 cases (8%) showed positive culture results with mitis and gravis as the predominant biotype. The positive culture rate was consistent during the outbreak period. Sixteen patients did not survive.

Conclusions

High number of clinical diphtheria continuously found in this province. Limited effort to perform the good standard in immunization program and several socio-political problems were considered as the main cause of this prolonged outbreak. More data are needed to evaluate the patients with complete immunization history.
A population based observational study of childhood encephalitis in children admitted to paediatric intensive care units in England and Wales

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Background

A retrospective study to define the incidence and mortality rates, usage of healthcare resources, and outcome predictors for severe childhood encephalitis in England and Wales (E&W).

Methods

Analysis of anonymised data for children (<18 years) admitted (2003-2013) to 29 Paediatric intensive care units (PICU) in E&W with encephalitis.

Results

There were 1031 patients identified: PICU encephalitis incidence=0.79/100,000 population/year (95%CI 0.74-0.84). In total, 808/1024 (78.9%) received invasive ventilation versus 118492/177654 (66.7%) non-encephalitis cases (unadjusted odds ratio (95%CI): 1.87(1.61-2.17); p=<0.0001). Eighty-seven deaths (8.4%) occurred in encephalitis patients and 7827 deaths (4.4%) in non-encephalitis patients (unadjusted OR (95%CI): 1.99, 1.60-2.49), p=<0.0001, giving a PICU encephalitis mortality rate of 0.07/100,000 population/year (95%CI 0.05-0.08). The mean length of PICU stay was 4.66 days (95%CI 4.1-5.1). A PICU bed-day cost of £1932 gives a PICU encephalitis bed day cost of approximately £839,270/year at a minimum. The odds of dying for children who received vasoactive treatment would be expected to be 0.12 fold lower than the odds for those who did not (OR 0.122; 95%CI 0.045-0.328, p=<0.001). A one day increase in the duration of invasive ventilation would be expected to increase the odds of the child dying by 1.9 times (OR 1.869; 95%CI 1.216-2.874, p=0.004). For each additional day spent on PICU, the odds of dying would be expected to decrease by 0.6 fold (OR=0.563; 95%CI 0.369-0.858, p=0.0076). For each one unit increase in the PIM2 score on admission, the odds of dying would be expected to increase by 1.1 times (OR 1.058; 95%CI 1.033-1.083, p=<0.0001).

Conclusions
The PICU incidence and mortality rates for encephalitis in E&W are defined. Severe encephalitis poses a cost burden to the health system. Outcomes are poor, more work to improve these are needed.
LOW SPECIFICITY OF NICE GUIDELINE IN RECOGNITION OF PAEDIATRIC SEPSIS
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Background

The recognition of sepsis is a significant challenge to paediatricians, with devastating consequences if missed. In 2016 the NICE sepsis guidelines (NG51) were published, stratifying sepsis risk based on observations and examination into low, moderate and high risk and providing management recommendations.

This study aimed to compare actual recognition and management of suspected sepsis to NICE suggested recognition and management.

Methods

A retrospective audit of NICE sepsis guidelines was performed at a busy paediatric unit in England over two weekends in 2017. Data was collected for each attendance using notes and electronic systems covering admission observations, examination, investigations, initial and final diagnosis.

Results

Of 93 attendances; 64 (69%) had an admission diagnosis of infection. As per NICE, 38 (60%) would have stratified as high risk warranting sepsis management. Based on clinician assessment, only 4 were treated as sepsis and of these 2 had a final diagnosis of sepsis. Of the 34 not treated for sepsis, 24 (63%) were diagnosed with viral illness and none developed sepsis. Another 9 with infection had 2 moderate sepsis risk factors as per NICE but none of these were treated for or developed sepsis.

Conclusions

The NICE guideline had a sensitivity of 100%, specificity of 27%, positive predictive value (PPV) of 4% and negative predictive value (NPV) of 100% for recognising sepsis. In comparison, clinician assessment had a sensitivity of 100%, specificity of 97%, PPV of 50% and NPV of 100% for recognising sepsis. If the guideline had been followed a further 43 children would have undergone inappropriate sepsis management.

This study demonstrates that the NICE sepsis guidelines are poorly specific for sepsis and would lead to unnecessary investigations, antibiotics and admission for a large number of patients.
Background

Group A Streptococcal (GAS) disease shows increasing prevalence worldwide. We characterized children admitted with GAS infection to European hospitals and studied risk factors for severity and disability.

Methods

Prospective, multicenter, cohort study (embedded in EUCLIDS) including children, aged 1 month to 18 years, admitted to hospital in 43 hospitals from 6 European countries between
July 2012 and January 2016. Demographic, clinical, microbiological data and outcomes were collected.

Results

209 (61\%) of 342 patients diagnosed with GAS infection had sepsis as compared to a focal infection. The proportion of patients with sepsis was higher in PICU than non-PICU patients (n=122 (79\%) vs n=87 (47\%), p<0.001). 247 (72.2\%) of patients had GAS detected from a normally sterile site. The most common infections included respiratory n=74 (22\%), skin and soft tissue (SSTI) n=80 (23\%), and bone and joint infections n=62 (18\%). LRTI n=59 (38\%) and infection without a focus n=34 (22\%) were more common in patients admitted to PICU. SSTI n=55 (29\%) and bone and joint infections n=54 (29\%) were most common in patients not requiring PICU (p<0.001). Patients admitted to PICU were younger (median 40 (IQR 22-86) vs 52 (IQR 29-86) months, p=0.005). Five patients (2\%) died. Sequelae at discharge were largely limited to patients admitted to PICU (24 vs 2\%, 13\% overall) and included neurodisability, amputation and skin grafts. Age was not associated with outcome.

Conclusions

In an era where we see a marked reduction in vaccine preventable infections, GAS infection remains on the rise, and for those patients requiring hospital admission is associated with significant short and long-term morbidity, with most severe disease in the younger children. Research efforts should aim at prevention, early recognition, and improved treatment of invasive GAS disease.
ESPI8-0632
SCIENCE AND EDUCATIONAL TRACK

E-POSTER DISCUSSION SESSION 11: VACCINE DEVELOPMENT AND IMMUNOGENICITY

ANTIBODY RESPONSES TO 3 DOSES OF MENB-FHBP (BIVALENT RLP2086) VACCINE ARE COMPARABLE ACROSS STUDIES AND PREDICT SIMILAR ANTIBODY PERSISTENCE AND BOOSTER RESPONSE


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Background

MenB-FHbp (bivalent rLP2086), a vaccine to prevent serogroup B meningococcal disease, is approved in Europe and Australia for individuals aged ≥10 years and in Canada and the United States for individuals aged 10–25 years. A phase 2 and two pivotal phase 3 studies evaluated MenB-FHbp safety/immunogenicity; phase 2 study participants subsequently enrolled in an ongoing extension study. In the current analyses, immunogenicity after 3 MenB-FHbp doses was descriptively compared between phase 2 and 3 studies to determine whether phase 2 extension study results (antibody persistence, booster response) are likely to be representative.

Methods

Phase 2 and 3 studies in adolescents/young adults in the United States, Canada, and Europe evaluated MenB-FHbp administered as a 0,-2,-6-month schedule. The phase 2 extension study evaluated antibody persistence through 48 months after primary immunization and 1 month after a MenB-FHbp booster dose. Immunogenicity was determined by serum bactericidal assays using human complement (hSBAs) against 4 MenB test strains. The lower limit of quantitation (LLOQ) was 1:8 for 3 strains and 1:16 for 1 strain, more conservative than the accepted correlate of protection (≥1:4).

Results
Proportions of subjects achieving hSBA titers ≥LLOQ for each test strain 1 month after dose 3 were similar among the 3 studies (Figure). In the phase 2 extension study, proportions with hSBA titers ≥LLOQ declined during the first 12 months after dose 3, then remained stable through 48 months. Booster dose responses were robust (Figure). Similar patterns were observed for hSBA GMTs across studies.

Conclusions

Bactericidal antibody responses to 3 MenB-FHbp doses were similar in adolescents/young adults in 3 studies conducted in several countries, suggesting antibody persistence and anamnestic responses should also be comparable.

Clinical Trial Registration (Please input N/A if not registered)

ClinicalTrials.gov, NCT01830855/NCT01299480/NCT01352845/NCT01543087. Funded by Pfizer.
INSUFFICIENT PROTECTION FOR PREMATURE INFANTS BY NATIONAL IMMUNIZATION PROGRAM?

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Background

The Dutch National Immunization program (NIP) schedule currently includes a primary vaccination series at 2-3-4 months and a booster at 11 months of age. This scheme may however not provide optimal protection to premature infants given their immature immune system. The goal of this study is to measure vaccination responses in premature infants and by gestational age (GA) following the regular NIP-scheme.

Methods

In this prospective observational study we recruited premature newborns stratified according to GA (< 28, 28-32 and 32-36 weeks). Blood samples were collected at 6 weeks (pre-vaccination), at 5 months (post-primary series) and at 12 months (post-booster). Serum antibody levels were measured against all vaccine components with a multiplex immunoassay using Luminex technology. Percentage of protection was determined using internationally standardized correlates of protection. For pertussis, an arbitrary level of 20 IU/ml was used.

Results

We enrolled 296 preterm newborns (GA< 28: N= 88; GA 28-32: N= 120; GA 32-36: N=91). After analysis of the first 157 serum samples post-primary series, 54.1% (85/157) had insufficient protection against Hib (< 0.15 µg/ml) with geometric mean concentrations of 0.16 µg/ml, 0.20 µg/ml, and 0.15 µg/ml for GA groups, < 28, 28-32 and 32-36 weeks, respectively. For pneumococci, the proportion with insufficient protective antibodies at 5 months (< 0.35µg/ml) varied by serotype from 3.8% (serotype 7F) to 55.4% (serotype 6B). Protection levels were sufficient for diphtheria, tetanus and pertussis, 99.4%, 100% and 88%, respectively.

Conclusions

Preliminary findings indicate that premature infants are insufficiently protected for multiple vaccine components following the primary series of the Dutch NIP scheme, in particular for
conjugated vaccines. Awaiting full results, we conclude that adaptations in the NIP-scheme for premature infants appear necessary.

Clinical Trial Registration (Please input N/A if not registered)

N/A
The objective was to review the aetiology, management and outcomes of febrile children with lower respiratory tract infections (LRTIs) presenting to an emergency department (ED).

Methods

A prospective patient record review embedded in MOFICHE (PERFORM H2020) identified 308 children aged 0-17 years with fever (≥ 38.0) and a clinical diagnosis of LRTI at discharge presenting to the Great North Children’s Hospital ED, from April - December 2017.

Results

14,797 children presented to ED, of 2,851 (19.3%) with fever (≥ 38.0) had LRTI. Mean age was 34 months, 72% had no co-morbidity, 47% had sought prior medical attention and 17% already had antibiotics. 94 (30.5%) children were diagnosed with bronchiolitis.

112/308 (36.3%) children had chest X-rays (CXR) and 62 (19.8%) had blood tests. 53 (47.3%) CXR's showed focal consolidation. 215 (69.8%) children were prescribed antibiotics, of which 14 (4.5%) more than one type. 36 (11.6%) required intravenous antibiotics. 85 (27.6%) received bronchodilators and 81 (26.3%) oxygen therapy. 106 (59.6%) children were discharged home immediately. 86 (27.9%) were admitted for > 24 hours and 4 (1.3%) to the intensive care unit. All children triggered a NICE sepsis criteria, of which 178 (57.8%) a red
flag. 20 (6.5%) triggered high Paediatric Early Warning Scores which were significantly related to longer stays (p=0.003).

Conclusions

Children with fever and clinically diagnosed lower respiratory tract infections present a significant burden of care for emergency departments. The majority are prescribed antibiotics despite viral pathogens in general being more common. There is potential to reduce investigations and antibiotic prescribing in this group improving antibiotic stewardship and reducing morbidity for community acquired infection. NICE sepsis scores over-triggered but PEWS scores were a good predictor for severity.
THE IMPACT OF NUMBER AND TYPE OF ORGAN DYSFUNCTIONS IN SEPSIS IN THE SWISS PEDIATRIC SEPSIS STUDY

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Background

Sepsis has been redefined as disregulated immune response to infection leading to organ dysfunction. We aimed to assess the operationalization of sepsis by organ dysfunction in children and to investigate whether each organ dysfunction is of similar effect.

Methods

We did a multicentre, prospective, cohort study at ten paediatric hospitals in Switzerland from 01.09.2011 to 31.12.2015. We included children younger than 17 years with blood culture-proven bacterial infection and systemic inflammatory response syndrome — according to 2005 paediatric consensus definition — at the time of blood culture sampling.
The primary outcome was in-hospital mortality in the first 30 days after sepsis onset. We used recursive partitioning to generate an unbiased decision tree to identify predictors of survival. For this analysis, we excluded prematurely born neonates and neonates less than 3 days old.

Results

In the 4 1/4 year study period we recruited 925 sepsis episodes. In 40 (4%) of 925 sepsis episodes patients died in the first 30 days after blood culture sampling. In 279 (30%) an organ dysfunction was present, and in 160 (17%) multiple organ dysfunction syndrome (MODS). In episodes with MODS, 34 (21%) of 160 died, while in those without MODS, 6 (1%) of 765 died. In episodes with MODS, presence of cerebral dysfunction further selected episodes with higher likelihood of fatal outcome (21 (46%) of 46 vs. 13 (11%) of 114).
Figure 1. Clinical decision tree to predict the likelihood to die in a child with blood culture-proven sepsis. N = number; MODS = multiple organ dysfunction syndrome

Conclusions
With decision tree analyses we detect patterns defining severity of sepsis. In our prospective cohort, presence of MODS was the strongest predictor of case fatality and cerebral dysfunction the most relevant organ dysfunction. These findings may help discriminate paediatric sepsis patients at substantially higher mortality which is needed to inform the revision of paediatric sepsis definitions.

Clinical Trial Registration (Please input N/A if not registered)

N/A
RAPID INFLUENZA TESTS IN INFANTS AND CHILDREN < 6 YEARS IN PRIMARY CARE. IMPACT ON ANTIBIOTIC TREATMENT AND USE OF HEALTH CARE SERVICES

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Background

Influenza is a universal infection that affects specially infants and toddlers. Clinical diagnosis of influenza is difficult in this age group because of nonspecific signs and symptoms. In absence of a microbiological influenza diagnosis many are submitted to laboratory test or x-rays, treated with unnecessary antibiotics and due to persistence of symptoms demand successive consultations. The aim of the survey was to study the impact of a point-of-care test (POCT) on antibiotic treatment and use of primary care health services.

Methods

Longitudinal, descriptive study 2016/2017 influenza season (week 51/2016 to 9/2017) at 4 primary health care centers. Patients < 6 years with flu symptoms < 72 hours were studied. Nasopharyngeal swabs were tested with 2 POCT (Sofia® Influenza A+B, and Cobas Liat®). Confirmed influenza cases were followed up at 10 days (telephone call). Antibiotic consumption and use of health care services were compared with those of patients of the same age clinically diagnosed without POCT at health care centers of the same area.

Results

189 patients were studied: 92 influenza A and 1 influenza B positive cases (49.2% positive rate). 90 influenza A patients followed-up. Mean age 31.3 months (+/- 16.6) females 52% males 48%. 4.4% of influenza A positives were treated with antibiotics, 7.2% of those diagnosed as influenza-like illness and 9.7% of those diagnosed as viral respiratory infection (p=0.098). Successive visits at a primary care center: Influenza A positive 0.19 visits per patient, while influenza-like illness cases, 1.64 extra visits per patient (p<0.001).
Conclusions

This study shows that an influenza POCT with high sensitivity and specificity has a positive impact on use of antibiotics and subsequent visits at the primary care level in children < 6 years of age.
GENOMIC MARKERS ASSOCIATED WITH RESPIRATORY SYNCYTIAL VIRUS (RSV) DISEASE SEVERITY IN CHILDREN: A SYSTEMATIC REVIEW

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Background

Respiratory syncytial virus (RSV) is a leading cause of hospitalisation in children. The clinical manifestations of RSV infection vary from mild, self-limiting respiratory illness to life-threatening disease. Genetic variation may contribute to disease susceptibility and severity. We aimed to systematically identify genomic markers associated with severe RSV disease in children.

Methods

A systematic literature search was performed using MEDLINE, Embase, Global Health, Scopus and Web of Science databases. Additional articles were identified from reference lists of eligible studies. All human studies investigating the association between genomic markers and severity of RSV disease were included. Two researchers screened 10,820 abstracts, independently assessed study quality and extracted data.

Results

Twenty-two case-control and cross-sectional studies met the inclusion criteria, involving over 18,000 participants. There was a relatively low risk of bias across the included studies. We identified 14 single nucleotide polymorphisms (SNPs) and 6 further haplotypes associated with severe RSV disease. Fifteen SNPs were identified which demonstrated no correlation with disease severity. The 1A⁰ allele of the SPA2 gene was protective against severe RSV disease. Conflicting results were reported for SNPs relating to RANTES, TLR4, IL-9 and TNF genes.

Conclusions

This review identified several genomic markers associated with RSV disease severity. This may aid objective definitions of severe disease, the understanding of the mechanisms of disease, and prediction of clinical outcomes. Substantial heterogeneity precluded meta-analysis, limiting the applicability and generalisability of this review. Future large-scale studies should replicate and validate the included studies.

Systematic Review Registration (Please input N/A if not registered)
N/A
VERTICALLY ACQUIRED HEPATITIS B VIRUS INFECTION IN CHILDREN BORN ABROAD

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Background

Thanks to systematic immunization programs, the prevalence of chronic hepatitis B virus (HVB) infection has decreased dramatically in many countries. Although spontaneous loss of HBsAg has been described in vertically-infected children, long term evolution remains unclear.

Methods

Retrospective, descriptive study, including all children diagnosed with HVB infection in a Referral Center for Tropical Pediatric diseases. Clinical and epidemiological data were collected from medical records, at baseline and follow-up, 1999 to Dec-2017.

Results

A total of 27 patients were included, 16 males. 25 were internationally adopted children from India (9), Vietnam (5), China (2), Ethiopia (2), Russia (2), Senegal (2). The diagnosis was already known at arrival in 56%. According to records, 48% were HBV-immunized. Six patients were diagnosed with hepatomegaly. At baseline median GOT was 107.43U/L, GPT 36U/L and GGT 13.5U/L. Coagulation was normal in all.

At diagnosis, 25 had HBsAg+. Ten were defined as chronically replicative (HBeAg+) and five of them had HBeAc+. 17 were characterized as non-replicative (HBeAg- and HBeAc-). Two patients showed isolated HBcAc+ (HBsAc-, HBsAg-). Viral load was undetectable in 2 and >170x 10⁶ pg/ml in 12. No cases of HCV or HDV were found. Genotype were as follows: A (2), B (7), C (3); D (8); E (2); F (1). Fibroscan was performed at least once along the study period; all F0-F1 stage, with no progression during follow-up. None was referred for liver biopsy and/or started on treatment. Spontaneous HBsAg clearance was described in 6 [median age: 12.5y (IQR 6-16)]

Conclusions
Screening of viral hepatitis is mandatory in all children born abroad, immigrant or adopted. Immunotolerance is the most common situation, with normal hepatic function and a high viral load. Spontaneous clearance is not uncommon.
Background

Infants cared for in neonatal intensive care units (NICU) are at risk for under-immunization at time of hospital discharge. Adherence to the routine immunization schedules such as the schedule recommended by the Advisory Committee for Immunization Practices minimizes the risk of contracting vaccine preventable illnesses in this vulnerable population. We performed an audit of infant immunization rates for the Mayo Clinic Rochester NICU to evaluate and improve this measure.

Methods

Immunization rates were obtained via review of the electronic health records of all infants discharged from the Mayo Clinic NICU. We analyzed additional baseline data including provider and nursing surveys using Pareto Chart, 5 Whys, and Fishbone diagram. We identified the following root causes of the quality gap: lack of provider knowledge of the routine immunization schedule, providers not ordering vaccines when they were due, and parental vaccine hesitancy. In the first plan-do-study-act cycle, three improvement measures were initiated including intranet resources for NICU providers on the routine immunization schedule, education on vaccine hesitancy, and an Excel-based checklist to track when immunizations were due.

Results

Baseline data prior to interventions from January 2015 to June 2017 demonstrated that only 56% (419 of 754) of the infants cared for in the Mayo Clinic NICU were fully up-to-date for recommended immunizations at the time of discharge or hospital unit transfer. Over the first four months of the improvement phase, this rate rose to 92% (99 of 108).
Conclusions

Infants cared for in NICUs are at increased risk of under-immunization at the time of hospital discharge. This study demonstrates that immunization rates for this population can be improved with a small number of quality improvement measures including provider education and checklists to track infant immunization status.
INTRODUCTION OF BLOOD CULTURE INCUBATOR WITHIN THE LOCAL NEONATAL UNIT AND HOW IT IMPACTS ON LENGTH OF HOSPITAL STAY

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Background

Early onset neonatal sepsis (EONS) is a significant cause of mortality and morbidity. NICE guidelines recommend early initiation of antibiotics in babies with suspected EONS, but to stop once 36-hour blood cultures (BC) are negative in clinically well babies with reassuring C-reactive protein (CRP). A delay in the availability of BC results has often resulted in unnecessary prolonged antibiotic treatment, increased hospital stay, bed pressures and parental distress.

AIM - To investigate if introduction of a BC incubator within the neonatal unit would impact on length of hospital stay in babies with suspected EONS.

Methods

Data was collected via electronic records from before (January – March 2015) and after (February – April 2017) introduction of BC incubator.

Inclusion criteria: Babies started on antibiotics within 12 hours of birth for suspected sepsis, had 2 low CRP readings, clinically well and awaiting negative BC result before stopping antibiotics and discharge home.

Exclusion criteria: Babies with positive BC, CRP rise above 10, admitted to NICU or are being kept in hospital because they are clinically unwell (e.g. jaundice, poor feeding).

Results

168 babies met the inclusion criteria (pre-85; post-83). Pre-BC incubator introduction, median length of hospital stay was 2.99 days (range 2.25 – 4.89) whilst post introduction, the median length of stay was 2.14 days (range 1.67 – 3.10). Introduction of a BC incubator significantly reduced the median time of hospital stay by 20.4 hours ($p<0.01$)

Conclusions

Introduction of the BC incubator on the neonatal unit has resulted in timely availability of BC results and improved antibiotics stewardship by preventing unnecessary antibiotic treatment.
of babies. It has also demonstrated cost effectiveness by improving hospital bed turnover and improving patient care with timely discharge of these babies.
CLINICAL AND ECONOMIC BURDEN OF INVASIVE MENINGOCOCCAL DISEASE IN GERMANY

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Background

Invasive meningococcal disease (IMD) is a serious and life-threatening disease. The disease burden has not been systematically assessed in Germany. This study aimed to examine short and long-term clinical characteristics of IMD, healthcare resource utilization (HRU) and related costs in Germany.

Methods

Patients with IMD-associated inpatient admissions between 2009 and 2015 and continuous insurance up to 7 years were selected from 7.3 million eligible patients in InGef database. The baseline risk, 30-day and 1-year mortalities, and IMD complications/sequelae were examined. The short- and long-term HRU cost in IMD patients were compared to an age and sex-matched non-IMD group.

Results

164 IMD cases were identified; 38% presented with meningitis, 35% with septicemia, 16% with both and 11% others. About 30% of cases occurred in children aged <=4 years and 32% of cases in adolescents aged 10-24 years. The 30-day and 1-year mortalities were 4.3% and 5.5%, respectively; 13% and 29% had IMD related complications and/or sequelae (Table 1). The most frequent complication and sequelae were adrenal hemorrhage (11.6%) and chronic renal failure (7.5%), respectively. Although the cost during the baseline period was similar, the mean HRU related cost within 1 month of IMD diagnosis was 9,192 € (SD=21,032 €), 180 times more than the non-IMD group (50 €, SD=162 €). Patients with septicemia costed ~2.4 times higher than patients with meningitis. Cumulative cost of IMD group over a 7-year period was 3.75 times more than those of the non-IMD group (p<0.0001).
Conclusions

IMD resulted in severe complications and sequelae and was significantly associated with short- and long-term healthcare related costs. These data underline the importance of preventive measures against IMD such as vaccinations.
A VALIDATION OF MALARIA ATLAS PROJECT MAP IN SOKOTO, NORTHWESTERN NIGERIA

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²Usmanu Danfodiyo University Teaching Hospital, Department of Community Medicine, Sokoto, Nigeria

Background

The Malaria Atlas Project (MAP) was first developed in 2006, to project estimates of malaria prevalence among children two to ten years of age where this data is not available. This data is obtained from malarial studies and surveys conducted globally and this is modelled to provide estimates of malaria prevalence. The maps consider the vector–transmitted nature of malaria and the factors for vector survival. This study was conducted to compare the true estimates in the rainy and dry season with the MAP projections for Northwestern Nigeria.

Methods

The study was a two-point cross-sectional study conducted in Sokoto, Northwestern Nigeria which has a Local Steppe climate and Sudan Savannah vegetation. Blood was taken from children 2 to 10 years of age and thick and thin films were made. Parasitaemia, parasite density and species identification were done and these results were projected on a GIS map and compared with the MAP projection.

Results

Overall, the prevalence was found to be 34.8% which fell within the 30-40% projected prevalence for the study area by MAPs. However, it was much lower than the projection during the dry season (20.2%) and higher than the projected estimate during the rainy season (49.3%). There was monoparasitaemia of Plasmodium falciparum throughout the study area although the study was not designed to identify other species.

Conclusions

The study concluded that seasonal variation needs to be taken account of by the MAP projections which can interactively provide estimates based on seasons rather than the annual estimates which currently exist. However, for planning purposes, the projections may be utilised as is, with more efforts at validation of the MAPs in other locations and terrains.
Clinical Trial Registration (Please input N/A if not registered)

N/A
ESP18-0695
SCIENCE AND EDUCATIONAL TRACK

E-PORDER DISCUSSION SESSION 04: VACCINE IMPLEMENTATION AND SAFETY

POST VACCINATION FEBRILE SEIZURES: CLINICAL SEVERITY AND LONG-TERM DEVELOPMENTAL OUTCOME DATA

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¹⁰Children’s Hospital at Westmead, Children’s Hospital Education Research Institute, Sydney, Australia

Background

Febrile seizures (FS) are a common paediatric condition affecting 1 in 30 children aged <6 years. While there is an increased risk of FS after some vaccinations, little is known as to whether vaccine-proximate (VP-)FS presentations differ clinically or have different long-term developmental outcomes when compared to non-vaccine proximate (NVP-)FS.

Methods

Prospective cohort study of children <6 years presenting with their first FS to one of five Australian paediatric hospitals between May 2013-June 2014. Clinical features, management and outcome data were compared between VP-FS and NVP-FS groups. A subset of VP-FS and NVP-FS patients were assessed using the Bayley Scales of Infant Development, Third Edition (Bayley-III) 12 to 24 months post initial FS event and compared to healthy controls.

Results

Of 1095 first FS cases, 68 (6.2%) were VP-FS. Compared with NVP-FS, there was no increased risk of prolonged (>1 day) admission (OR 1.39, 95%CI 0.74-2.61), ICU admission (OR 0.60, 0.08-4.53), seizure duration >15 minutes (OR 1.39, 0.71-2.72), repeat FS within 24 hours (OR 0.80, 0.34-1.89) or requirements for antiepileptics (for inpatient management: OR 1.75, 0.87-3.54 or on discharge: OR 1.03, 0.31-3.41). Bayley-III assessment was conducted on 62 VP-FS, 70 NVP-FS and 82 control participants (mean follow up time 14.7 months and 16.7 months for VP-FS and NVP-FS respectively). There was no significant
difference in developmental outcomes between the three groups after adjusting for socioeconomic status.

Conclusions

There was no difference in clinical outcomes of VP-FS compared to NVP-FS, with the majority being simple febrile seizures requiring 1 day or less in hospital and no antiepileptic use. Children with VP-FS demonstrated no developmental delay compared to their peers. This is reassuring for clinicians and parents of children who experience FS following vaccination.
Background

Infants aged <1 year are at highest risk for pertussis-related morbidity and mortality. In the recent years, there has been a dramatic emergence of cases of *Bordetella pertussis* infections. The main objective was to analyse the complications in pertussis-related admissions in infants.

Methods

Ambispective multicenter study conducted across 14 hospitals of a Spanish Autonomous Region, with a retrospective phase (2012-2015) and a prospective phase (January-December 2016). Related with infants admitted due to confirmed pertussis (positive *Bordetella* PCR in nasopharyngeal swabs), number and type of complications were analysed.

Results

During the study period, 506 infants were included, of which 187 cases (36.9%) presented complications. Most of them were <4-month-old infants (179, 95.7%) and had at least 2 pertussis vaccine doses (173, 97.9%). No known risk factors were identified in 145 cases with complications (77.5%).
Distribution of different complications are showed in the attached table. Among complicated cases, 105 patients (56.1%) showed respiratory; 79 of them required thoracic X-ray (42.2%), of which 51 (64.5%) had pathological infiltrates.

Respiratory syncytial virus (RSV) infection was investigated in 393 cases. No statistical differences in RSV coinfection were seen between the group of complications (29, 17.6%) and the group of no complications (31, 13.5%). Influenza could not be detected in the 58 cases in which it was studied.

Among those with any complications, 34.2% (64) required PICU admission. Among the total cohort, 8 deaths were registered (1.58%), all of them with malignant pertussis.

<table>
<thead>
<tr>
<th>Complications</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apnoeas</td>
<td>109</td>
<td>58.28</td>
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<tr>
<td>Acute respiratory insufficiency</td>
<td>83</td>
<td>44.39</td>
</tr>
<tr>
<td>Atelectasia</td>
<td>38</td>
<td>20.32</td>
</tr>
<tr>
<td>Sinusal tachycardia</td>
<td>37</td>
<td>19.78</td>
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<tr>
<td>Pneumonia</td>
<td>37</td>
<td>19.78</td>
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<tr>
<td>Neumothorax</td>
<td>21</td>
<td>11.22</td>
</tr>
<tr>
<td>Pulmonary hypertension</td>
<td>13</td>
<td>6.91</td>
</tr>
<tr>
<td>Acute renal insufficiency</td>
<td>12</td>
<td>6.41</td>
</tr>
<tr>
<td>Shock</td>
<td>11</td>
<td>5.88</td>
</tr>
<tr>
<td>Seizures</td>
<td>6</td>
<td>3.20</td>
</tr>
<tr>
<td>Encefalopathy</td>
<td>2</td>
<td>1.06</td>
</tr>
<tr>
<td>Total</td>
<td>187</td>
<td></td>
</tr>
</tbody>
</table>

Conclusions

*Bordetella pertussis* infection showed a widely variety of complications in a third of a cohort of hospitalised infants, and a mortality rate of 1.5%. Complications did not relate with previously known risk factors, RSV or influenza coinfections. Most frequent complications were apnoea and respiratory insufficiency.
A SYSTEMATIC REVIEW OF INTERVENTIONS TO IMPROVE UPTAKE OF PERTUSSIS (TDAP) VACCINATION IN PREGNANCY

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Background

Immunization against pertussis during pregnancy is recommended to protect infants. Limited data exist on rigorously evaluated interventions to improve pertussis immunization uptake among pregnant women. This systematic review aims to identify and evaluate the most effective interventions used to improve pertussis vaccination uptake during pregnancy.

Methods

We searched the databases of PubMed, Medline and CINAHL for English-language studies. Before and after studies and studies with a concurrent control group were considered for inclusion. Standardized effect sizes were described as the ratio of the odds to be vaccinated in the intervention group compared with the standard care group and absolute benefit increase (ABI) with 95% confidence intervals (CI) were calculated.

Results

Seven studies were included in the review, of which four were randomized controlled trials (RCTs). Strategies to improve uptake were focused on health care practitioners, pregnant women, or enhancing access. Health Care Provider interventions included provider reminder, provider education, standing orders and provider feedback. Interventions directed at pregnant women focused solely on education. The interventions in all four RCTs (3 involved education of pregnant women, 1 had multi-component interventions) did not demonstrate a significant improvement in the uptake of Tdap vaccination during pregnancy. Although all the observational studies reported a statistically significant improvement in the vaccination rate of more than 25%, they had methodological limitations.

Conclusions

Based on the existing research, we recommend midwife delivered maternal immunization program at antenatal clinics, use of provider reminder system to target unvaccinated pregnant women, and making pertussis vaccine easily accessible for pregnant women. High-quality RCTs are needed to further evaluate interventions to successfully improve maternal pertussis vaccination rates.
Systematic Review Registration (Please input N/A if not registered)

The protocol for this review is published in PROSPERO International prospective register of systematic reviews - CRD42017058178.
A CLUSTER RANDOMISED CONTROLLED TRIAL IN SENIOR SCHOOL STUDENTS TO ASSESS THE IMPACT OF 4CMENB ON N. MENINGITIDIS CARRIAGE AND DETERMINE RISK FACTORS FOR CARRIAGE


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Background

Understanding risk factors for carriage and determining whether protein-based MenB vaccines impact on carriage acquisition are important considerations for meningococcal immunisation programs. This study aimed to assess risk factors for carriage prevalence in baseline swabs obtained in the MenB vaccine herd immunity study, a cluster RCT to compare carriage prevalence of Neisseria meningitidis in vaccinated (4CMenB) and unvaccinated school students in South Australia.

Methods

All schools were invited to participate and randomised to intervention (4CMenB at baseline) or control (4CMenB at 12 months) school. Posterior pharyngeal swabs were obtained and risk factor questionnaire completed by all participating students. Carriage was detected by porA real time PCR.

Results

Overall, 34,477 students attending 237 (>95%) secondary schools participated, including 17,919 (52%) females. The majority were from metropolitan (74%), followed by rural (23%)
and remote (3%) schools. 1.8% of students were smokers and 21.1% had a current upper respiratory tract infection (URTI).

Overall carriage prevalence was higher in year 12 compared to year 10 students (4.90% versus 1.91%; OR=2.7 [2.1, 3.3]) and in remote compared to metropolitan schools (6.2% versus 3.0%; OR=2.1 [1.3, 3.6]). A current URTI was associated with carriage (4.0% versus 2.9%; OR=1.4 [1.2, 1.6]), whereas no difference was found with current antibiotic use. Cigarette, e-cigarette and water pipe users had increased carriage (OR=5.3 [4.0, 6.9], OR=3.4 [2.3, 5.1], OR=3.7 [2.9, 4.6], respectively). Attending a pub ≥1 and kissing ≥1 person in the last week were also associated with increased carriage (OR=2.4 [2.0, 2.8], OR=2.6 [2.2, 2.9], respectively). In a multivariable model, location and e-cigarette use were no longer predictors of carriage.

Conclusions

Immunisation programs should take into consideration at risk groups for meningococcal carriage including senior students, smokers and waterpipe users.

Clinical Trial Registration (Please input N/A if not registered)

ClinicalTrials.gov NCT03089086
CEREBROSPINAL FLUID CELL COUNTS AND BIOCHEMISTRY IN NEONATAL MENINGITIS: PREMATURE REASSURANCE

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5Murdoch Children’s Research Institute, Group A Streptococcal Research Group, Melbourne- Victoria, Australia
6Barwon Health, Children’s Services, Geelong- Victoria, Australia
7Bendigo Health, Paediatrics, Bendigo- Victoria, Australia
8The Royal Women’s Hospital, Microbiology and Infectious Diseases, Parkville- Victoria, Australia
9The Royal Children’s Hospital, Laboratory Services, Parkville- Victoria, Australia
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Background

Globally, group B streptococcus (GBS), remains the major pathogen in neonatal meningitis. Disease onset can be rapid in nature and cases of confirmed bacterial meningitis with normal initial cerebrospinal fluid (CSF) cell counts have been described. Initial cell counts are commonly used to guide early clinical management. In many clinical contexts, antibiotics may be administered prior to a lumbar puncture being performed, increasing the risk of a “false negative” CSF culture in true meningitis.

Methods

Retrospective data were collected (2007-2017) across four hospital networks, including both tertiary paediatric hospitals, in Victoria, Australia. Cases of late onset GBS disease (LOD) were initially identified using microbiology database extraction and recaptured with International Classification of Diseases (ICD) discharge coding. Comprehensive demographic and clinical data were collected. LOD was classified as disease occurring from day 7 of life onward.

Results
99 LOD episodes occurred during the study period, of which 44 (44.4%) were clinically treated as meningitis. 27 (61.4%) of these clinical episodes were CSF culture positive for GBS; 1 (3.7%) infant was blood culture negative. There was 6 (22.2%) culture positive CSF episodes where the CSF total white cells were less than 10, amidst a range of red cell counts. 4 (66.7%) of these also had normal CSF biochemistry, one was not done, the other was markedly abnormal. The median C-reactive protein (CRP) in these patients (n=6) was 13.5.

Conclusions

There is a relatively high prevalence of 'normal' CSF cell counts and biochemistry in culture positive GBS meningitis. This highlights the importance of obtaining CSF samples prior to commencement of antibiotics and awaiting culture results prior to ceasing meningitis coverage in children where the clinical suspicion of meningitis was high.
ORAL ANTIBIOTICS FOR NEONATAL INFECTIONS: A SYSTEMATIC REVIEW

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²Franciscus Gasthuis & Vlietland, Pediatrics, Rotterdam, The Netherlands

Background

Bacterial infections still affect a substantial number of neonates worldwide. Although adequate treatment is of great importance, hospitalization for prolonged intravenous therapy has negative consequences for both neonates and family. In older children intravenous-to-oral switch therapy has been proven effective and safe and is now standard care. Therefore we evaluated the available evidence on oral antibiotic use and intravenous-to-oral antibiotic switch therapy in neonates.

Methods

We performed a systematic literature search (Medline, Embase, Cochrane, Web of Science, Google Scholar) searching for studies on oral antibiotic use and IV-to-oral antibiotic switch in neonates (0-28 days). We included both prospective and retrospective studies with no restriction on year of publication.

Results

Thirty papers reporting the use of different types of oral antibiotics in neonates were included. Of those papers, 17 assessed absorption of oral antibiotics, the remaining studies assessed efficacy of therapy. Oral antibiotics are absorbed slower and show a lower bioavailability compared to parenteral antibiotics, but adequate levels can be reached. When compared to older patients, Cmax remains higher over time after both parenteral and oral administration in newborn, mainly due to a decreased clearance. Furthermore, in several efficacy studies the clinical outcome in the oral treated group is equally good compared to parenteral treatment with no bacterial re-infections or substantial side-effects reported.

Conclusions

The use of oral antibiotics in neonates is promising in small studies, but firm evidence is lacking. When intravenous-to-oral antibiotic switch therapy in neonatal infections is proven safe and effective it can lead to a great improvement of quality of life of both child and parents. In addition, reduction of hospital stay and safe home-based treatment will have positive effects on rising health costs and extend health accessibility.

Systematic Review Registration (Please input N/A if not registered)
THE BURDEN OF NOROVIRUS DISEASE IN CHILDREN: A MULTI-COUNTRY STUDY IN CHILE, BRAZIL, THAILAND AND THE PHILIPPINES

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⁷Research Institute for Tropical Medicine, Department of Health, Muntinlupa City, Philippines
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Programa de Microbiologia y Micologia- Instituto de Microbiologia e Immunoterapia- Facultad de Medicina, Santiago, Chile

Background

Noroviruses (NoVs) are an important cause of acute gastroenteritis (AGE) in children worldwide. We aimed to estimate the prevalence of NoV related disease among medically attended AGE in children less than 6 years old.

Methods

We conducted prospective surveillance for at least 1 year in 8 predominantly urban sites across 4 countries: Chile, Brazil, Thailand and Philippines, between 2014 and 2017. We recruited children < 6 years old from 4 separate cohorts: outpatient AGE, hospital community-acquired AGE, hospital nosocomial AGE, and asymptomatic. Detailed demographic and clinical information was collected and stool samples were tested for NoV by RT-PCR. Samples positive for NoV were genotyped. Unadjusted proportions and 95% CI were calculated for each cohort, overall, and stratified per country and age group.

Results

1649 children were included in the analysis. NoV was found in 163 of 689 AGE outpatient cases (23.7%: 95% CI 20.6–27.0), 100 of 562 AGE hospitalizations (17.8%: 95% CI 14.9–21.2), 12 of 56 nosocomial AGE cases (21.4%: 95% CI 12.7–33.8) and 33 of 342 of asymptomatic controls (9.6%: 95% CI 7.0–13.2). The predominant genotypes associated with AGE were GII.4 (55%), GII.17B (10%) and GII.2 (6%). GII.4 was more frequent in the hospital cohort (68%) than in the outpatient cohort (49%) and least frequent among controls (23%).
Conclusions

We have confirmed that norovirus is an important cause of medically attended AGE in children. Our estimates are in line with global prevalence estimates in the literature. GII.4 was the most frequent genotype, with higher prevalence among hospitalized cases. Results from this study provide information that supports NoV vaccine development and decision making concerning future vaccine introduction.

Clinical Trial Registration (Please input N/A if not registered)

N/A
VARIATIONS IN MANAGEMENT OF INVASIVE GROUP B STREPTOCOCCAL DISEASE AT A TERTIARY PAEDIATRIC CENTRE

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Background

Group B Streptococcus (GBS) is the commonest cause of neonatal infection. Incomplete treatment may be associated with worse outcomes and disease recurrence. Multiple conflicting guidelines exist resulting in confusion around treatment duration and need for lumbar puncture (LP). We completed a five year retrospective case note review of management and outcomes of invasive GBS presenting to a tertiary paediatric centre. Results were compared to European Society of Paediatric Infectious Diseases guidelines.

Methods

Any infant aged 0-6 months with positive blood or cerebrospinal fluid cultures identified from microbiology databases between 17/04/2012 - 03/05/2017 was included. Infants with positive urine cultures representing contamination were excluded. Data was collected from patient notes and electronic health records. First audit of the cycle.

Results

46 infants identified, 34 bacteraemia, 12 meningitis. 30(65.2%) male. 31(67.4%) term, 15(32.6%) preterm. 29(63.0%) had early-onset disease, 17(37.0%) late-onset disease.

32(69.6%) infants presented with breathing difficulties, 16(34.8%) poor feeding, 13(28.2%) irritable, 9(19.5%) drowsy and 11(23.9%) febrile.

25/34 with bacteraemia had a lumbar puncture (LP), 9 didn’t (5 too sick). 11/12 with meningitis had LP, (1 too sick). 2 infants had second LP.

6(13.0%) suffered long-term disability. 3(6.5%) died and 2(4.3%) had GBS recurrence (1 meningitis, 1 bacteraemia).
Conclusions

Outcomes for invasive GBS disease in our centre were comparable to national figures. Lack of evidence has led to multiple guidelines which reflects our variations of management. Good evidence exists for all infants with GBS to have at least one LP to confirm diagnosis of meningitis or bacteraemia and this is not universally followed. Future research needs to address optimal antibiotic duration and route. Other recommendations include updating and unifying guidelines locally and nationally while increasing awareness of treatment differences with GBS compared to other bacterial meningitis
The Antimicrobial Resistance and Prescribing in European Children (ARPEC) study highlighted that antimicrobial use for surgical prophylaxis is often prolonged. We conducted a national survey of surgical antimicrobial prophylaxis in the UK to establish whether this practice is due to guidelines recommendations.

Methods

We identified 25 UK surgical units undertaking specialist paediatric procedures and collected their antimicrobial stewardship prophylaxis guidelines through hospital website, the MicroGuide app or personal contacts. Procedures were classified into clean; clean-contaminated and contaminated according to the SIGN guidelines.

Results

Guidelines from 11/25 centres were collected and compared. Three centres had no guidelines. All centres with guidelines had separate advice for penicillin allergy and some separated children colonised with resistant microorganisms. The antimicrobial choice was variable: for lower gastrointestinal clean-contaminated procedures, 4/8 centres recommended co-amoxiclav alone or with metronidazole, 2/8 centres recommended cefuroxime and metronidazole, 1/8 centres amoxicillin, metronidazole and gentamicin and
1/8 centres amoxicillin and metronidazole

<table>
<thead>
<tr>
<th>Table 1</th>
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<tbody>
<tr>
<td></td>
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<tr>
<td>General surgery (8 guidelines)</td>
</tr>
<tr>
<td>Clean (splenectomy, gastric procedures)</td>
</tr>
<tr>
<td>Clean-contaminated (e.g., PEG insertion, bowel inunction, interval appendectomy)</td>
</tr>
<tr>
<td>Contaminated appendectomy (not gangrenous)</td>
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<tr>
<td>Urology (8 guidelines)</td>
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<tr>
<td>Clean-contaminated (Hypospadia repair)</td>
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<tr>
<td>Catheter left in situ (e.g., hypospadia repair)</td>
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<tr>
<td>ENT (8 guidelines)</td>
</tr>
<tr>
<td>Tonsillectomy</td>
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<tr>
<td>Grammnet insertion</td>
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<tr>
<td>Orthopaedic surgery (8 guidelines)</td>
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<tr>
<td>Compound fractures or open surgery of closed fractures</td>
</tr>
</tbody>
</table>

Conclusions

We are presenting results on just under half of the national guidelines, as the data collection is still on-going. At present it appears that the majority of paediatric general surgical guidelines suggest single dose at induction for clean-contaminated and contaminated procedures. This would indicate the need for closer involvement of the surgical units in stewardship programmes. It is of note that a number of major paediatric surgical units do not have prophylaxis guidelines.
IS A BLOOD CULTURE POLICY EFFECTIVE IN DECREASING BLOOD CULTURE CONTAMINATION RATES ON A NEONATAL AND PAEDIATRIC INTENSIVE CARE UNIT?

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Background

A significant proportion of patients are admitted to the neonatal and paediatric intensive care unit (NPICU) for investigation of possible sepsis. Interpretation of blood cultures may be complicated by the presence of contaminants. The Mater Dei hospital paediatric blood culture policy was introduced in 2012. The aim of this study is to document the rate of contamination for blood cultures taken in NPICU over a ten year period (2008-2017) and to compare the contamination rates before and after introduction of the paediatric blood culture policy.

Methods

Blood culture results for all NPICU patients between 2008 - 2017 were retrieved from the Infection Control Unit at Mater Dei Hospital, Malta. The organisms were analysed to identify contaminants. Coagulase negative staphylococci were only classified as contaminants in patients without indwelling devices. The 2-sample z-test for sample proportion was used to test for significant differences in the rates of contaminated blood cultures before and after the introduction of the blood culture policy.

Results

A total of 2810 blood cultures were obtained from 2277 patients. Median patient age was 1 day (IQR 0, 5 days); 2121 patients (93.1%) were neonates. There was a statistically significant drop in blood culture contamination rates, from 9.47% (106/1119) during 2008 – 2011 to 3.72% (53/1422) during 2013-2017, following the introduction of the blood culture policy in 2012 (p <0.0001). Coagulase negative staphylococci accounted for 67.4% (120/178) of the contaminants.

Conclusions

It is very encouraging that the rate of false positive blood cultures on NPICU decreased significantly following the introduction of the paediatric blood culture policy in 2012. Ongoing staff training and feedback is essential in order to achieve further reductions to the 3% standard set by the American Society of Microbiology.
**ESP18-0775**
**SCIENCE AND EDUCATIONAL TRACK**

**E-POSTER DISCUSSION SESSION 04: VACCINE IMPLEMENTATION AND SAFETY**

**EFFECT OF SECRETOR/LEWIS PHENOTYPE ON ROTAVIRUS-SPECIFIC IGA RESPONSE, VACCINE VIRUS REPLICATION AND CLINICAL PROTECTION FOLLOWING MONOVALENT ROTAVIRUS VACCINATION IN MALAWIAN INFANTS**

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²Malawi Liverpool Wellcome Trust Research Programme, Vaccines Group, Blantyre, Malawi
³University of Malawi College of Medicine, Department of Paediatrics, Blantyre, Malawi
⁴University College London, Division of Infection and Immunity, London, United Kingdom

**Background**

Histo-blood-group-antigen (HBGA) Lewis/secretor phenotypes are associated with genotype-specific susceptibility to rotavirus infection. We tested the hypothesis that intrinsic resistance of Lewis negative/non-secretors to G1P[8] infection results in reduced IgA response, vaccine virus replication and clinical protection following monovalent P[8]-based rotavirus vaccine in Malawian infants.

**Methods**

Infants received 2 doses of monovalent G1P[8] rotavirus vaccine (RV1) at 6 and 10 weeks of age. Stool was collected on alternate days for 10 days post-vaccine and vaccine virus shedding determined by qRT-PCR. Post-vaccine serum rotavirus-specific IgA was determined by ELISA, with seroconversion defined as fourfold rise in concentration. HBGA phenotype was determined by salivary ELISA. Clinical protection was determined by comparing vaccinated infants <12 months with rotavirus gastroenteritis (RVGE) to age-matched, vaccinated controls. Rotavirus genotype was determined by RT-PCR.

**Results**

In 202 cohort infants, Leb+ secretor phenotype was associated with increased likelihood of vaccine virus replication (RR 1.5 (95%CI 1.1-2.1) p=0.009), but there was no association between any HBGA phenotype and seroconversion. Genotype was available for 113/120 RVGE cases. G1P[8] RVGE (OR 10.6 (95%CI 3.1-35.7) p<0.001) and P[4] infections (OR 4.9 (95%CI 1.9-10.4) p=0.001) were positively associated with Leb+ secretor phenotype. Comparing 119 RVGE cases to 212 controls, non-secretor phenotype was associated with decreased risk of clinical rotavirus vaccine failure (OR 0.40 (95%CI 0.21-0.78), p=0.007).

**Conclusions**

We found evidence that Leb⁻/non-secretor infants have reduced vaccine virus replication, but adequate IgA response to rotavirus vaccination. Contrary to our hypothesis, non-secretor
infants were at decreased risk of clinical vaccine failure. Any reduced vaccine response in non-secretors is offset by protection against common P[8] and P[4] strains. HBGA phenotype is unlikely to contribute to reduced rotavirus vaccine effectiveness in Malawi or other low-income countries with similar rotavirus strain diversity.

Clinical Trial Registration (Please input N/A if not registered)
GROUP A STREPTOCOCCUS DIAGNOSTIC METHODS AND VIRAL CO-INFECTIONS IN PHARYNGITIS
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²Turku University Hospital and University of Turku, Department of Clinical Virology, Turku, Finland
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Background
Co-detection of group A streptococcus (GAS) and viruses in acute pharyngitis has not been well documented. We aimed to study the occurrence of viral co-infection in relation to GAS diagnostic method.

Methods
This was part of a prospective study done in an emergency department (ED) in febrile children 1-16 years of age with pharyngitis. Throat swabs and blood samples were collected and testing for GAS was performed by 2 different rapid antigen detection tests (RADTs; StrepTop and mariPOC) in the ED and by throat culture in laboratory. In addition, frozen throat swabs were tested for GAS by 2 different nucleic acid amplification tests (NAAT; Focus 3M and Illumigene). Virus diagnostics was performed by NAAT and serology, and interferon response to virus infection was estimated by myxovirus resistance protein A (MxA) blood concentration.

Results
In total, 83 children (median age 5.5 years; interquartile range 3.2-12.2) were recruited in the study. Specimens from 78 and 48 patients were available for RADT and NAAT, respectively. In comparison with throat culture results, sensitivities and specificities of GAS diagnostic tests were 72% and 100% for StrepTop, 100% and 72% for mariPOC, 91% and 87% for Focus 3M, and 91% and 96% for Illumigene, respectively. In GAS positive patients, virus detection and elevated blood MxA level (≥175 µg/L) were more frequent when GAS diagnosis was based on mariPOC (54%) than when it was based on throat culture (44%)
Conclusions

In comparison with throat culture, diagnostic performance of different GAS tests varies greatly. In children with febrile pharyngitis, enhanced sensitivity of the GAS assays seems to be associated with increased co-detection of viruses and interferon responses questioning the clinical significance of GAS detection in these patients.

Clinical Trial Registration (Please input N/A if not registered)

N/A
SAFETY AND TOLERABILITY OF TAKEDA’S BIVALENT VIRUS-LIKE PARTICLE (VLP) NOROVIRUS VACCINE (NoV) IN CHILDREN

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²Takeda Vaccines Inc., Clinical Development, Boston, USA

Background

Norovirus is a major cause of medically-attended gastroenteritis in children worldwide. We present the first safety and tolerability data of the Takeda bivalent NoV candidate in 1–<9 year-old children.

Methods

As part of a double-blind, randomized, phase 2 dose-finding study conducted in Colombia, Finland and Panama, children in two age cohorts (4–<9 and 1–<4 years, n=120 per cohort) received one or two intramuscular doses of NoV formulations with 15/15, 15/50, 50/50, or 50/150 μg Gl.1/GII.4c genotype VLPs and 0.5 mg Al(OH)₃ 28 days apart; one dose groups received saline placebo as dose 2 to maintain blinding. Solicited adverse events (AEs) were monitored for 7 days, any unsolicited AEs for 28 days following each injection and serious adverse events (SAEs) for the entire study period.

Results

No vaccine-related SAEs were reported. Generally AEs were mostly mild/moderate in severity, of short duration, with no increase after a second dose in either cohort. Fever ≥ 38°C occurred in 4.2–5.4% of 1–<4 year-olds (6.9% after placebo), and 5.1–6.9% of 4–<9 year-olds (0% after placebo). The most common local reaction was injection site pain in 25.8–25.9% (vs. 16.9% for placebo) of 1–<4 year-olds and 37.9–62.7% (22.4% placebo) of 4–<9 year-olds. Other local reactions were minimal (<4.2%). Most frequent systemic AEs of any severity in 1–<4 year-olds were irritability (20.7–21.7%; placebo 13.6%), loss of appetite (20.8–20.7%; 11.9%), drowsiness (8.6–14.2%; 6.8%) and in 4–<9 year-olds were fatigue (15.5–20.3%; 10.3%), myalgia (10.3–20.3%; 6.9%), and headache (13.8–19.5%; 8.6%).

Conclusions

The Takeda NoV candidate formulations were well tolerated with clinically acceptable reactogenicity profiles in children aged 1–<9 years.

Clinical Trial Registration (Please input N/A if not registered)
NCT: 02153112, EudraCT: 2014-000778-20
EXPOSURE TO CHILDREN AGED <5 YEARS IS A RISK FACTOR FOR RESPIRATORY TRACT INFECTION IN ADULTS ≥60 YEARS
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¹Wilhelmina Children’s Hospital- University Medical Center Utrecht UMCU, Department of Paediatric Infectious Diseases, Utrecht, The Netherlands
²Julius Center for Health Sciences and Primary Care- UMCU, Department of Primary Care, Utrecht, The Netherlands
³University of Antwerp, Department of Primary and Interdisciplinary Care ELIZA, Antwerp, Belgium
⁴University of Oxford, Nuffield Department of Primary Care Health Sciences, Oxford, United Kingdom

Background

Respiratory tract infections (RTI) can cause severe disease in older adults. There is a gap in knowledge on risk factors causing RTI in older adults. Here we studied the relationship between exposure to children aged <5 years and the risk of RTI during winter in adults ≥60 years.

Methods

The REspiratory Syncytial virus Consortium in EUrope (RESCEU) study is an ongoing cohort study conducted in adults ≥60 years. During the winter season 2017-2018 (from October to April) participants are monitored weekly for respiratory symptoms (cough, runny nose, wheeze and/or shortness of breath) to detect RTI in the Netherlands, Belgium and the United Kingdom. Baseline data on risk factors and demographics were obtained before the 1st of October. We defined frequent exposure as contact with children aged <5 years more frequently than once a month. Multivariable regression analysis was used to adjust for cardiorespiratory comorbidity.

Results

The study population consisted of 516 adults with a median age of 70 years of whom 51% were female. 288 (55%) of the participants indicated any exposure to children aged <5 years, of whom 195 (37%) indicated frequent exposure to children. From October to December at least one RTI was reported by 196 (38%) participants. The risk of RTI was significantly increased for adults with frequent exposure compared to those without any exposure (47 vs 28%, OR 2.36; 95% CI 1.58-3.55; p<0.001). The risk was also increased in adults with infrequent exposure compared to adults without exposure to children (44 vs 28%, OR 2.06; 95% CI 1.23-3.43; p<0.01).
Conclusions

This ongoing study shows that exposure to children aged <5 years is a risk factor for RTI in adults ≥60 years.
RISK OF FEBRILE CONVULSION ATTRIBUTABLE TO FIRST DOSE OF MEASLES–MUMPS–RUBELLA–VARICELLA VACCINE DEPENDING ON SUBJECTS’ HISTORY OF FEBRILE CONVULSION: AN EXPLORATORY ANALYSIS

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²Leibniz Institute for Prevention Research and Epidemiology, Clinical Epidemiology, Bremen, Germany

Background

Personal or family history of febrile convolution (FC) are strongly associated with higher risk of developing FC. An increased risk of FC was observed 5–12 days after the first dose of measles–mumps–rubella–varicella (MMRV) vaccination¹. Our exploratory post-hoc analysis built further on preliminary assessments and reused data of a previously published matched cohort study¹. We aimed to investigate whether the exclusion of children with personal or family history of FC would impact the risk of FC 5–12 days after MMRV vaccination.

Methods

From the whole cohort (children who received a first dose of either MMRV, MMR, or MMR+V vaccine¹), we defined scenario 1: children without personal history of FC. For scenario 2 (children without personal or family history of FC) we applied a range (20%–40% of FC cases and 5% of non-FC cases) of conditional probabilities to estimate the prevalence of family history of FC based on literature. We calculated the attributable risk (AR) of FC after MMRV versus MMR and MMR+V vaccination for each scenario and conditional probability.

Results

The FC incidence rates and ARs are listed in the table. Using the whole cohort as reference¹, the AR of FC after MMRV versus MMR decreased by 0.4 and 0.9–1.7 cases/10,000 vaccinated children in scenario 1 and 2, respectively. Compared to MMR+V, AR of FC decreased by 0.0 and 0.5–0.9 cases/10,000 vaccinated children in scenario 1 and 2, respectively.
**Table. Incidence rates and attributable risk of FC for MMRV and comparator vaccines within 5 to 12 days after vaccination, according to scenario**

<table>
<thead>
<tr>
<th></th>
<th>Whole cohort</th>
<th>Scenario 1</th>
<th>Scenario 2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Matched MMR cohort (MMRV versus MMR)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incidence rate/10,000 children (95% CI)</td>
<td>MMRV (n=74,054)</td>
<td>6.0 (4.7–7.2)</td>
<td>5.3 (3.7–7.2) (2.4–8.3)</td>
</tr>
<tr>
<td></td>
<td>MMR (n=74,085)</td>
<td>2.6 (1.9–3.5)</td>
<td>1.9 (1.8–3.1) (1.9–3.6)</td>
</tr>
<tr>
<td>AR (95% CI)</td>
<td></td>
<td>3.5 (2.8–4.1)</td>
<td>3.1 (1.1–5.1) (0.7–4.4)</td>
</tr>
</tbody>
</table>

**Matched MMR+V cohort (MMRV versus MMR+V)**

<table>
<thead>
<tr>
<th></th>
<th>Whole cohort</th>
<th>Scenario 1</th>
<th>Scenario 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence rate/10,000 children (95% CI)</td>
<td>MMRV (n=31,927)</td>
<td>6.5 (4.7–8.3)</td>
<td>6.0 (3.6–9.3) (1.8–6.5)</td>
</tr>
<tr>
<td></td>
<td>MMR+V (n=31,959)</td>
<td>4.4 (3.1–6.1)</td>
<td>3.3 (1.6–6.1) (9.3–4.7)</td>
</tr>
<tr>
<td>AR (95% CI)</td>
<td></td>
<td>2.2 (1.4–4.1)</td>
<td>2.2 (1.2–5.6) (1.7–4.8)</td>
</tr>
</tbody>
</table>

FC, febrile convulsion; AR, attributable risk (= cumulative incidence in the MMRV group - cumulative incidence in the comparison group MMR or MMR+V); CI, confidence interval; MMRV, quadrivalent measles-mumps-rubella-varicella vaccine; MMR, measles-mumps-rubella vaccine; MMR+V, measles-mumps-rubella and varicella vaccine administered separately, on the same day; n, number of children in a given cohort.

**Conclusions**

The history of FC impacts the risk of FC attributable to MMRV vaccine. This risk could be reduced by vaccinating populations without history of FC with MMRV and populations with history of FC with MMR+V.

**Reference:**

**Funding:** GlaxoSmithKline Biologics SA
Background

Over the last decades the incidence of EOS has decreased in many countries due to implementation of group B Streptococcus (GBS) screening and intrapartum antibiotic prophylaxis (IAP). In Estonia pregnant women are not routinely screened for GBS carriage, however IAP is administered to women with identified risk factors. We aimed to describe the causative agents of EOS and evaluate their susceptibility to empiric antibiotic regimens (ampicillin or penicillin combined with gentamicin) in Estonia.

Methods

We conducted a prospective surveillance study using a web-based database (neonIN) in 2 maternity hospitals in Estonia. All neonates admitted with culture-proven EOS, occurring in the first 3 days of life in 2013-2017, were included. Coagulase-negative staphylococcal (CoNS) infections were included only if treated with antibiotics for at least 5 days. Low birth weight (LBW) was determined as birth weight <2500g, normal birth weight (BW) as ≥2500g.

Results

Altogether 72 episodes of EOS fulfilled the criteria. The incidence of EOS (excluding CoNS) was 1.6/1000 live births and the incidence of CoNS-related EOS 3/1000 neonatal admissions. The incidence of GBS-infection was 0.64/1000 live births, in comparison to 1.2/1000 in 2007-2008. In normal BW neonates 88% of infections were caused by Gram-positive bacteria, while in LBW 32% (50% excluding CoNS) by Gram-negatives (Table1). Overall 97% of Gram-positives (excluding CoNS) were susceptible to penicillin, 64% of Gram-negatives were resistant to ampicillin, 21% to gentamicin.
Conclusions

Over the last decade the incidence of EOS has remained stable in Estonia, although the incidence of EOS-GBS is higher than in countries using GBS-screening and IAP. The current empiric antibiotic regimen is adequate for normal BW neonates, but may not be sufficient for LBW neonates. The Estonian programme for prevention and empiric treatment of EOS should be revised.

Table 1. Demographic characteristics, main pathogens and antibiotic resistance patterns.

<table>
<thead>
<tr>
<th></th>
<th>LBW (n=28)</th>
<th>Normal BW (n=44)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gestational age (weeks) (mean,SD)</strong></td>
<td>28 (± 3.9)</td>
<td>39 (± 1.7)</td>
</tr>
<tr>
<td><strong>Birth weight (g) (mean,SD)</strong></td>
<td>1352 (± 598)</td>
<td>3470 (± 389)</td>
</tr>
<tr>
<td><strong>Male (n,%)</strong></td>
<td>15 (53.6)</td>
<td>26 (59)</td>
</tr>
<tr>
<td><strong>GBS (n,%)</strong></td>
<td>1 (3.6)</td>
<td>20 (45.5)</td>
</tr>
<tr>
<td><strong>CoNS (n,%)</strong></td>
<td>13 (46)</td>
<td>8 (18.2)</td>
</tr>
<tr>
<td>Resistant to gentamicin (n/N, %)</td>
<td>10/13 (77)</td>
<td></td>
</tr>
<tr>
<td><strong>E. coli (n,%)</strong></td>
<td>4 (14)</td>
<td>3 (6.8)</td>
</tr>
<tr>
<td>Resistant to ampicillin (n/N, %)</td>
<td>4/7 (57)</td>
<td></td>
</tr>
<tr>
<td>Resistant to gentamicin (n/N, %)</td>
<td>1/7 (14)</td>
<td></td>
</tr>
<tr>
<td><strong>Other Enterobacteriaceae (n,%)</strong></td>
<td>4 (14)</td>
<td>2 (4.6)</td>
</tr>
<tr>
<td>Resistant to gentamicin (n/N, %)</td>
<td>2/6 (33)</td>
<td></td>
</tr>
<tr>
<td><strong>Staphylococcus aureus (n,%)</strong></td>
<td>-</td>
<td>1 (2.3)</td>
</tr>
<tr>
<td><strong>Enterococcus spp. (n,%)</strong></td>
<td>-</td>
<td>4 (9)</td>
</tr>
<tr>
<td>Resistant to ampicillin (n, %)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td><strong>Other Gram-positive bacteria (n,%)</strong></td>
<td>7 (25)</td>
<td>6 (13.6)</td>
</tr>
</tbody>
</table>

n - Number of cases
N - Number of cases studied
Background

In 2013, Italian Ministry of Health recommended to improve the surveillance of Adverse Event Following MMRV tetravalent vaccine, used by some Italian Regions, that implemented universal mass vaccination for measles and varicella. In fact an additional risk of seizure related to the vaccine were reported by the Ministry.

Adverse event following immunization (AEFI) is any untoward medical occurrence which follows immunization and which does not necessarily have a causal relationship with the usage of the vaccine. Post-marketing surveillance of AEFI is strictly recommended by public health authorities and the most frequently adopted surveillance system is the passive system; this model is badly affected by the risk of underreporting.

Methods

Apulia is region in the south-east of Italy (4,000,000 of inhabitants) in which, following Ministry commitment, since May 2017 a post-marketing active surveillance of MMRV AEFIs has been implemented. Immunized children (12-15 months of age) are enrolled on voluntary basis and they are a interviewed 20 days after the immunization to investigate the incidence of AEFI.

Results

At 2017, 31 December, 972 children were enrolled; 789/972 (81.2%) completed post-vaccination follow-up. 419 AEFIs are registered with a reporting rate of 52.6x100 doses. 382/419 (91.2%) AEFIs were not serious while 37/419 (8,8%) were serious: 30 cases of hyperpyrexia, 4 cases of lymphadenopathy, 1 case of ALTE and 2 cases of rash. For 2/37 serious AEFIs hospitalization was needed.

For 37 serious AEFIs the evaluation of causality assessment was performed using algorithm proposed by WHO: for 30 the classification was "consistent causal association to immunization", and for 7 "inconsistent causal association to immunization".

Conclusions
The post-marketing safety profile in our study is consistent with pre-licensure data and no emerging signals were detected.

Clinical Trial Registration (Please input N/A if not registered)

N/A
RISK FACTORS FOR CENTRAL LINE-ASSOCIATED BLOODSTREAM INFECTIONS IN CHILDREN WITH TUNNELED CENTRAL VENOUS CATHETERS – A PROSPECTIVE OBSERVATIONAL STUDY OVER 7 YEARS

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²Department of Biostatistics and Epidemiology, University of Zurich, Zurich, Switzerland

Background

Central venous catheters (CVCs) have become an integral part of medical practice in pediatrics. Central line-associated bloodstream infections (CLABSIs) belong to the most common complications of CVCs accounting for significant morbidity and mortality. This prospective single center study on the use of tunneled CVCs in children aims to identify risk factors for CLABSIs.

Methods

Children having a tunneled CVC inserted at the University Children’s Hospital between January 2009 and December 2015 were enrolled. Data regarding underlying disease, age, CVC dwell time and CLABSI was collected. Hazard ratios (HR) for CLABSIs were calculated using Cox regression models stratified by age and diagnosis. Life tables were generated to examine the influence of CVC dwell time on CLABSI incidence rate.

Results

55 CLABSIs were observed in 193 patients with 284 tunneled CVCs over seven years. The overall CLABSI-incidence rate was 2.13 per 1000 catheter days. Patients with gastrointestinal disorders and patients aged 2-5 years showed the highest incidence rate of 3.14 and 4.33 CLABSIs per 1000 catheter days respectively. The combination of underlying gastrointestinal disease and age 2-5 years was identified as significant risk factor for CLABSIs (HR 9.44, p < 0.001). Life tables showed an increasing CLABSI risk in patients without gastrointestinal disease after 90 days dwell time.

Conclusions

In this pediatric setting every fifth tunneled CVC was removed due to CLABSI. Regular reevaluation should prompt to remove tunneled CVCs if no longer needed possibly before day 90 after insertion. In young children with underlying gastrointestinal disorders the need for tunneled CVCs urges for evaluation of further preventive measures such as antimicrobial
locks or antimicrobial coated CVCs. Prospective studies are needed for benchmark and identification of CLABSI prevention measures in children requiring tunneled CVCs.

Clinical Trial Registration (Please input N/A if not registered)

N/A
THE INCIDENCE OF NEONATAL INFECTIONS (MENINGITS AND SEPSIS) DURING A 42 YEAR PERIOD, FROM 1975-2016 IN WESTERN PART OF SWEDEN

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¹Sahlgrenska Academy- Institute of Clinical Sciences, Pediatrics, Gothenburg, Sweden
²Sahlgrenska University Hospital, Neonatology, Gothenburg, Sweden
³Sahlgrenska University Hospital, Pediatrics, Gothenburg, Sweden

Background
The main neonatal pathogens are Group B Streptococci (GBS), Staphylococcus Aureus (SA) and Escherichia Coli (E.Coli). The main aim of this study is to document the incidence of very early, early and late-onset neonatal invasive infections like sepsis and meningitis in Gothenburg, Sweden and five surrounding municipalities over a 42 year period.

Methods
Information regarding positive culture in blood and cerebral spinal fluid (CSF) among children younger than 28 days was collected from the Clinical Microbiological Laboratory at the Sahlgrenska University Hospital which serves all hospitals in the study area. Patients´ characteristics, risk factors, signs and symptoms of infection and outcome were registered. Cases of infection were classified according to infant´s age at the time of test taken for culture. Very early-onset, VEO (<24 hours of life), Early-onset, EO (1-6 days of life), and Late onset, LO (7-27 days of life).

Results
Total 1007 episodes identified in 990 infants during the study period. The mean incidence was 3.22 /1000 live births. GBS 22%, SA 20% and E.Coli 10%. Median age 3 days, 243 (24%) VEO, 332 (33%) EO and 432 (43%) LO. Male/female ratio, 572/435 (57%/43%). The median gestational age was 29 weeks and median birthweight 1195 g among the 93 patients that died as a consequence of the infection compared to 37 weeks and 2900g among the patients that survived. The mortality among patients with infection decreased from 15% (1975-1984) to 6% (2007-2016).
Conclusions

The trend is showing a decline in VEO and EO, it could be attributable to the start of a risk-based approach for intrapartum antibiotics in 2008. The premature infant is at increased risk for mortality and opportunistic infections with longer hospital stay.
AUDITORY STEADY-STATE RESPONSE PROVES PRACTICAL IN HEARING EVALUATION AMONG SURVIVORS OF BACTERIAL MENINGITIS IN LUANDA, ANGOLA

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\textsuperscript{1}Children’s Hospital, Helsinki University Hospital, Helsinki, Finland
\textsuperscript{2}Faculty of Medicine, University of Helsinki, Helsinki, Finland
\textsuperscript{3}David Bernardino Children’s Hospital, Luanda, Angola
\textsuperscript{4}Faculty of Medicine, University Diego Portales, Santiago, Chile
\textsuperscript{5}Eye and ear Hospital, Helsinki University Hospital, Helsinki, Finland

Background

Survivors of childhood bacterial meningitis (BM) often develop hearing loss. We assessed estimated hearing thresholds among BM survivors using auditory steady-state response (ASSR) providing frequency-specific estimation of hearing.

Methods

Survivors from two prospective BM treatment trials (ISRCTN62824827; NCT01540838) from Luanda Children’s Hospital were called for follow-up visit in January 2017 with a median duration of 26 months after BM. We examined hearing of 46 survivors using ASSR and ABR (Eclipse Interacoustics, CE-Chirp\textsuperscript{®}). The electrodes were placed on cleaned skin on mastoids, vertex and low forehead. Sound stimuli were delivered to both ears using headphones with intensities of 80, 60, 40 and 20 decibels (dB) nHL at a rate of 90 Hz in ASSR. We calculated mean of estimated thresholds with frequencies of 500, 1000, 2000 and 4000 Hz for better and worse ear and compared it with ABR.

Results

The median age of children was 84 months (IQR 90.5). Out of 46 children, 6 (13\%) and of 92 ears, 17 (18\%) were deaf (mean estimated threshold > 80 dB nHL). Of children, 17\% suffered from profound hearing loss (61–80 dB nHL) or deafness while mild hearing loss (31–40 dB nHL) occurred in 4.3\% of children (Figure 1). Any hearing loss (>30 dB nHL) of either ear was measured in 20/46 (44\%) of survivors. The ASSR correlated with ABR measurement in worse and better ear (Spearman rho 0.812 and 0.80 respectively, p<0.0001 for both).

Conclusions
ASSR can be measured reliably also in developing country setting providing wider estimation of hearing. However, results were in line with ABR measurements.

**Clinical Trial Registration (Please input N/A if not registered)**

ISRCTN62824827 and NCT01540838
ESP18-0879
SCIENCE AND EDUCATIONAL TRACK

E-POSTER DISCUSSION SESSION 05: ANTIBIOTIC STEWARDSHIP AND INFECTION CONTROL

PATTERN AND TRENDS OF ANTIMICROBIAL USE IN PEDIATRIC ONCOLOGY DEPARTMENT
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²Hippokration Hospital of Thessaloniki, Pharmacy department, Thessaloniki, Greece
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Background

Monitoring of antimicrobial use is important in guiding antimicrobial stewardship programs especially in the era of multidrug resistance. The literature regarding antimicrobial stewardship programs in hospitalized critically ill children in areas with multidrug-resistant organisms is limited. This study aimed to assess the pattern and time trends of antibiotic consumption (AMC) in a Pediatric Oncology department.

Methods

This was a retrospective study conducted in a Pediatric Oncology department. Data were separated in 3 periods: 2001-2006, 2007-2012 and 2013-2017. Data of antimicrobial consumption were obtained from the hospital pharmacy and expressed as defined daily doses per 100 bed-days (DDD/100BD) as recommended by the World Health Organization for adults. Number of bed-days was obtained from Hospital Office of Statistics.

Results

Median total AMC showed no significant change among 3 study periods: 125.9 DDD/100BD for 2001-2006, 130.6 DDD/100BD for 2007-2012 and 116.5 DDD/100BD for the last period. 3rd and 4th generation cephalosporins were the most commonly used antimicrobial agents (27%) throughout study period. Their consumption ranged between 24.4 to 34DDD/100BD. Consumption of aminoglycosides was high during the first period (ranked second). During the next two periods there was a significant decrease: from a median of 27.1 DDD/100BD during the 1st period to 14.6DDD/100BD in the 3rd period. On the other hand, glycopeptides showed a slight increase between the three periods (from 25.3 to 29.2DDD/100BD). Consumption of both carbapenems and fluoroquinolones increased during the study period: from 6.9 to 12.9 DDD/100BD and from 3.1 to 8.2 DDD/100BD, respectively.

Conclusions
High rates of carbapenem use and glycopeptides are of concern. Longitudinal analysis of antibiotic consumption is essential to guide antimicrobial stewardship in pediatric oncology patients.
TRAIL, IP-10, CRP, AND IMMUNOXPERT™ LEVELS IN CHILDREN WITH ACUTE RESPIRATORY TRACT INFECTIONS – AN INTERIM ANALYSIS FROM THE AUTOPILOT-DX-STUDY

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Background

Respiratory tract infections are the most common diagnosis in children, resulting in high healthcare burden. Differentiating between viral and bacterial etiology is essential in order to enable the adequate use of antibiotics. In recent studies the novel protein-based assay ImmunoXpert™ (integrating TRAIL, IP-10, and CRP) has shown high sensitivity and specificity for distinguishing between viral and bacterial etiology.

Methods

In a large prospective, double-blind, international, multicenter study, the AutoPilot-Dx-Study (www.autopilotdx.org), we aim to recruit 1200 children presenting with either respiratory tract infection or fever without source in Germany and Italy to validate the diagnostic accuracy and potential clinical utility of the ImmunoXpert™ test. Expert panel adjudication is utilized as a reference standard in the study. Of 563 patients recruited so far an interim analysis in 134 patients with respiratory tract infection, and available TRAIL, IP-10, CRP, and ImmunoXpert™ results was performed. Here, we compared bacterial with total viral infections and viral subgroups.

Results

Children with a viral infection including respiratory syncytial virus (RSV), influenza (FLU), rhinovirus (RV), and adenovirus (ADV) had significantly higher TRAIL levels
(150.1±137.5 vs. 67.5±23.4 pg/mL), and lower ImmunoXpert™ scores (23.3±27.4 vs. 58.5±28.2) compared to children with a bacterial infection. TRAIL and IP-10 levels, exhibited no significant differences between the various viral subgroups, whereas CRP levels were higher in ADV infections compared to RSV, FLU and RV infections (66.6±54.4 vs. 15.6±20.6, 8.2±4.4, 25.5±37.4 mg/L, respectively).

Conclusions

Detection of viral infections correlated significantly with elevated TRAIL levels. Despite increased CRP levels in ADV infections ImmunoXpert™ scores were indicative of a viral infection. These virus-specific proteomic fingerprints appear useful for reducing antibiotic misuse and need to be explored in a larger number of patients.

Clinical Trial Registration (Please input N/A if not registered)

NCT03052088
NEURODEVELOPMENTAL AND GROWTH IMPAIRMENT AMONG VERY LOW-BIRTH-WEIGHT INFANTS WITH NEONATAL SEPSIS

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¹Serviço de Neonatologia B, Maternidade Bissaya Barreto- Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal

Background

Neonatal infections are frequent complications and one of the major causes of mortality and morbidity in very low-birth-weight (VLBW) infants receiving intensive care. Aim: To determine if neonatal sepsis in VLBW infants are associated with increased risks of adverse neurodevelopmental and growth sequelae in early childhood.

Methods

Observational, analytical and retrospective case-cohort study of VLBW infants admitted in a Neonatal Intensive Care Unit (NICU) between January/2005 and December/2015. Deaths and major malformations were excluded. Infants with and without sepsis were compared for the main risk factors and complications of prematurity. Sepsis was defined by clinical and analytical criteria, with or without positive blood culture. Outcomes at 24 months included: anthropometric measurements, Griffiths Mental Development Scales and major neurosensory abnormality. Severe neurodevelopmental impairment were defined by: cerebral palsy, neurodevelopmental delay (developmental quotient <2sd), hearing impaired and/or blindness. WHO growth charts were used to determine growth status at follow-up; impairment growth was defined by <-2sd for gender and age.

Results

This study included 504 WBLW infants; 18.3% had at least 1 sepsis during NICU. In univariate analysis, VLBW preterm with sepsis were: mostly outborn (p=0.002); had lower birth weight (p<0.001), increased need for resuscitation (p<0.001), ventilation (p<0.001) and postnatal steroid (p<0.001), had more bronchopulmonary dysplasia (p=0.001), patent ductus arteriosus (PDA) (p=0.001), intraventricular hemorrhage grade 3 or 4 (p=0.005) and cystic periventricular leukomalacia (p<0.001). After adjusting for birth weight, gestational age, twinning, in/outborn, PDA, postnatal steroid and brain injury, VBLW preterm with sepsis had an increased risk for neurodevelopmental impairment (p=0.005; OR: 3.6 IC95%: 1.3-8.1) and impairment head growth (p=0.05, OR: 3.7 IC95%: 1.8-5.9).

Conclusions
This study suggests that neonatal infections among VLBW infants are associated with poor neurodevelopmental and head growth outcomes in childhood.
Background

The clinical significance of virus detection by PCR in febrile children is unclear due to high asymptomatic detection rates and potential co-bacterial infection. Previous studies showed that TNF-related apoptosis induced ligand (TRAIL) can serve as a useful biomarker for distinguishing between bacterial and viral infections when combined with IP-10 and CRP (ImmunoXpert™). Here we evaluate TRAIL levels in children with acute bacterial and viral infections that had a confirmed viral detection.

Methods

The “AutoPilot-Dx” study (www.autopilotdx.org), a multinational multicenter collaboration was designed to validate the diagnostic accuracy of the ImmunoXpert™ test. We analyzed the first 74 febrile children recruited that had both PCR viral detection and etiology determination. Patient etiology (59 viral and 15 bacterial) was assigned by majority adjudication of three experts based on comprehensive clinical and laboratory investigation. Viruses were detected using multiplex-PCR applied to nasopharyngeal swabs (Allplex™, Seegene). Serum TRAIL levels were measured using ELISA (MeMed).

Results

Bacterial diagnoses were assigned to 29%, 21% and 21% of patients with rhinovirus (RV) adenovirus (ADV) and respiratory-syncytial virus (RSV) detection, respectively, highlighting that viral detection does not necessarily indicate underlying etiology. Notably, TRAIL levels were markedly increased in viral patients as compared to bacterial patients (mean±SD
[pg/ml]: viral 171±136; bacterial 68±27; p-value<0.001), irrespective of the detected virus, with RV (viral 136±104; bacterial 71±34), ADV (viral 145±116; bacterial 72±30) and RSV (viral 134±82; bacterial 72±25; Figure 1) being the most frequently detected viruses.

Conclusions

High TRAIL levels are strongly indicative of viral infection. Viral detection using nasopharyngeal PCR does not necessarily reflect the underlying infectious etiology. The unique dynamics of TRAIL in response to bacterial versus viral infections can complement molecular viral detection in the management of febrile children.

Clinical Trial Registration (Please input N/A if not registered)

NCT03052088
ESPO8-0887
SCIENCE AND EDUCATIONAL TRACK

E-POSTER DISCUSSION SESSION 11: VACCINE DEVELOPMENT AND IMMUNOGENICITY

THE MENINGOCOCCAL SEROGROUP B VACCINE MENB-FHBP (BIVALENT RLP2086) IS Safe AND IMMUNOGENIC IN HEALTHY CHILDREN AGED ≥24 MONTHS TO <10 YEARS

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Background

The MenB-FHbp (bivalent rLP2086) vaccine is licensed in Europe and Australia for prevention of serogroup B (MenB) meningococcal disease in those aged ≥10 years and in the United States and Canada for those aged 10–25 years. This phase 2, randomized, double-blind, controlled study evaluated MenB-FHbp safety and immunogenicity in children aged ≥24 months to <10 years.

Methods

Subjects (n=400) were randomized 3:1 to receive either 3 doses of MenB-FHbp (months 0,2,6) or hepatitis A vaccine (months 0,6) and saline (month 2). Immune responses were assessed using serum bactericidal assay using human complement (hSBA) against 4 test strains representing diverse MenB meningococci. Immunogenicity endpoints included proportions of subjects with hSBA titers ≥ the lower limit of quantitation (LLOQ) 1 month after vaccinations 2 and 3. Half the subjects per group were tested for 2 of 4 test strains; remaining subjects were tested for the other two. The LLOQ thresholds (1:8 for 3 test strains; 1:16 for 1 strain) are higher than the accepted correlate of protection (≥1:4). Safety was assessed.

Results

Proportions of MenB-FHbp recipients with hSBA titers ≥LLOQ for each test strain 1 month after dose 3 ranged from 79.1%–100% (Figure). Among MenB-FHbp recipients, 46.6%–84.4% reported local reactions and 14.6%–59.5% reported systemic events (generally mild/moderate in severity). Adverse event percentages during the vaccination phase were
similar between vaccine (62.6%) and control groups (63.2%) and were predominantly unrelated to vaccine (>97.6%). Two MenB-FHbp recipients withdrew due to an AE.

Figure. Proportions of Subjects Achieving hSBA Titers ≥1:16 (PMB80) or ≥1:8 (Other Strains)* Before Vaccination and After Doses 2 and 3

HAV=hepatitis A vaccine; hSBA=serum bactericidal assay using human complement; MenB-FHbp=bivalent rLP2086; LLOQ=lower limit of quantitation.

*Test strains expressing factor H binding protein (FHbp) variants A22, A56, B24, and B44 correspond to strains PMB80, PMB2001, PMB2948, and PMB2707, respectively; hSBA LLOQs are 1:16 for strain PMB80, and ≥1:8 for strains PMB2001, PMB2948, and PMB2707. n=number of subjects with hSBA titer ≥LLOQ.
Conclusions

Three MenB-FHbp doses in children aged ≥24 months to <10 years demonstrated an acceptable safety/tolerability profile and elicited robust bactericidal antibody responses predictive of protection against diverse MenB strains in most subjects.

Clinical Trial Registration (Please input N/A if not registered)

ClinicalTrials.gov, NCT02531698. Funded by Pfizer.
ACUTE GASTROENTERITIS: INCIDENCE AND DISEASE BURDEN AMONG INFANTS WITH MEDICAL RISK CONDITIONS

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1Julius Center for Health Science and Primary Care UMC Utrecht, Epidemiology of Infectious Diseases, Utrecht, The Netherlands
2University Medical Center Utrecht, Medical Microbiology, Utrecht, The Netherlands
3National Institute for Public Health and the Environment, Centre for infectious disease control, Bilthoven, The Netherlands
4Julius Center for Health Science and Primary Care UMCU, Public Health, Utrecht, The Netherlands

Background

Infants with medical risk conditions are vulnerable to common childhood infections including acute gastroenteritis (AGE). To guide targeted prevention programs, we quantified AGE incidence, severity, and virus prevalence among rotavirus unvaccinated medical risk infants.

Methods

This prospective birth-cohort study was part of the Risk-group Infant Vaccination Against Rotavirus (RIVAR) project recruiting newborns with prematurity, low birth weight or severe congenital conditions in 13 Dutch hospitals (NTR5361). Parents of participants were instructed to report each AGE episode (and to collect a stool sample) until the child’s age was 18 months. For each reported episode, AGE severity was assessed by Modified Vesikari Score (MVS). Stool samples were analyzed by realtime PCR for rota-, noro-, adeno(40/41)- and astrovirus. Parents also recorded any AGE symptoms and related health care usage on monthly questionnaires. The AGE incidence rates (IR) was based on the number of reported episodes and additional unreported episodes identified by monthly questionnaires.

Results

Between November 2014 and April 2017, 318 infants participated. The mean AGE IR was 82/100 person-years (py) (95%CI: 73.1-90.8/100py) and increased by age IR: 52/100 vs. 94/100 py for ages 1-5 vs. 6-18 months, respectively. Among 147 AGE samples analyzed, norovirus was identified in 38 (26%) and rotavirus in 28 (19%). Adeno- and astrovirus together accounted for 16% (N=24). Based on the MVS, 52 of 145 (36%) episodes were severe and 40 of 135 (30%) episodes required any healthcare. Severe AGE occurred most
frequently in rotavirus positive 15 (58%) episodes.

Conclusions

The observed AGE incidence, severity and healthcare usage among medical risk infants confirms substantial disease burden. Norovirus and rotavirus are the dominant pathogens and rotavirus is most frequently severe. Their prevention in medical risk infants should be prioritized.

Clinical Trial Registration (Please input N/A if not registered)

NTR5361
PROLONGED SHEDDING OF ROTAVIRUS VACCINE VIRUSES DOES NOT ASSOCIATE WITH LEWIS AND SECRETOR STATUS AND ROTAVIRUS IMMUNOGLOBULIN A RESPONSE

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Background

Positive Lewis (FUT3) and secretor (FUT2) statuses predispose to rotavirus infection by P[8]-type rotaviruses, contained in the rotavirus vaccines (RotaTeq® and Rotarix™). We investigated the Lewis and secretor status and rotavirus IgA seroconversion of children with prolonged RotaTeq® vaccine virus shedding.

Methods

126 infants were given RotaTeq® vaccine according to 2, 3, and 5 months schedule. Excretion of vaccine strains in stools after the 1st dose was seen in all (100%) vaccine recipients by RT-PCR. FUT2 and FUT3 enzyme expression was studied with ELISA from a saliva sample at the age of 1 to 2 years. Serum samples were collected from 7 children who continued to shed vaccine strains for at least 4.5 months, and rotavirus VP6 IgA was measured with ELISA.

Results

Out of the 126 children, 102 (81.0 %) shed the vaccine strains only after the 1st dose and 24 (19.0 %) children continued to shed for at least 2.5 months. The Lewis and secretor status of the children according to duration of shedding is presented in Table 1. There was no statistically significant difference between the groups for prevalence of Lewis and secretor status. Serum IgA was positive in 6 out of 7 (85.7 %) children with long term shedding.

Table 1. Prevalence of Lewis and secretor status in children according to the duration of shedding.
Conclusions

We found no association between Lewis or secretor status and prolonged shedding of RotaTeq® vaccine strains. Most of the children with prolonged shedding seroconverted by rotavirus IgA indicating that lack of antibody response was not the reason for prolonged shedding.

<table>
<thead>
<tr>
<th>Duration of shedding</th>
<th>p-value</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>After 1st dose only (&lt;14 days)</td>
</tr>
<tr>
<td></td>
<td>(n=102)</td>
</tr>
<tr>
<td><strong>Lewis positive, n (%)</strong></td>
<td>65 (63.7 %)</td>
</tr>
<tr>
<td><strong>Lewis negative, n (%)</strong></td>
<td>37 (36.3 %)</td>
</tr>
<tr>
<td><strong>Secretor, n (%)</strong></td>
<td>33 (32.4 %)</td>
</tr>
<tr>
<td><strong>Non-secretor, n (%)</strong></td>
<td>69 (77.6 %)</td>
</tr>
</tbody>
</table>
Trends in Streptococcus pneumoniae Antimicrobial Resistance before and after the Implementation of the 13-valent Pneumococcal Conjugate Vaccine (PCV13), in a Greek Tertiary Children’s Hospital

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Background

In Greece, PCV7 was replaced by PCV13 at the end of 2010, aiming to target the residual burden of pneumococcal disease caused by non-PCV7 serotypes. The goal of this study was to compare antimicrobial susceptibility of pneumococcal strains colonizing nasopharynx or causing pneumococcal disease among young children during the PCV7- and PCV13-eras.

Methods

An 11-year retrospective study (2007-2017) was carried out recording antimicrobial susceptibility of pneumococcal clinical and non-clinical strains, covering 4 years before and 7 years after PCV13-implementation in the National Immunization Program in 2010. Oxacillin susceptibility of each isolate was determined using Sensi-Disc BD. Susceptibility to different antimicrobials was determined with VITEK 2 Card-AST-GP68 (BioMerieux,Inc.). Pneumococcal isolates were classified as susceptible, intermediate and resistant based on current CLSI breakpoints. Statistical analysis was assessed using GraphPad Prism version 6 and Fisher’s exact test (a p<0.05 was considered as significant).

Results

A total of 434 pneumococci were isolated; 171 during the PCV7-era and 263 during the PCV13-era. From PCV7- to PCV13-era, the prevalence of penicillin non-susceptible (intermediate/resistant) strains decreased (28.8% vs. 9.94%, p<0.05) and the percentage of the highest MIC recorded increased from 0.6% to 3.4%. Resistance to erythromycin, tetracycline and cotrimoxazole decreased during the PCV13-era compared to the PCV7-era (32.1% vs 24.37%, 20.26% vs 12.13%, 35.58% vs 26.02% respectively), while resistance to clindamycin increased (6.85% vs 12.86% respectively). Resistance to ceftriaxone appeared to remain almost stable. Pneumococcal isolates carrying multiple antimicrobial resistance (≥3) decreased in the PCV13-era compared to the PCV7-era, from 21.5% to 15.21%.

Conclusions
During PCV-7 era, serotype 19A has emerged as an important cause of invasive disease and was associated with increasing prevalence of antimicrobial resistance. In accordance with previous reports, it appears that PCV13-introduction led to reduction of pneumococcal resistance to first-line antimicrobials.
MENINGOCOCCAL B VACCINE (4CMenB) IMMUNOGENICITY PRE- AND POST-VACCINATION AMONG UNIVERSITY STUDENTS IN THE US

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⁷Public Health England, Vaccine Evaluation Unit, Manchester, United Kingdom

Background

Recently, a multi-component Meningococcal B (MenB) vaccine (4CMenB; Bexsero) was licensed in the US. Prior to licensure, 4CMenB was used to control a MenB outbreak at a US University. Students were offered two doses of vaccine one month apart. We conducted an immunogenicity study to assess responses against multiple MenB strains.

Methods

We collected blood samples to quantify serum bactericidal antibodies using human complement (hSBA) both before vaccination and one month after the second dose of vaccine among both vaccinated and unvaccinated university students aged 18 years or older. We compared the proportion of vaccinated and unvaccinated participants that seroconverted (exhibited ≥4-fold rise in titers) against the outbreak strain-M14 240298 (matched to fHbp in 4CMenB, mismatched to NadA in 4CMenB), the 44/76-SL strain (matched to fHbp in 4CMenB), and the 5/99 strain (matched to NadA in 4CMenB).

Results

We analyzed 92 paired samples (59 from participants vaccinated with 2 doses of 4CMenB; 33 unvaccinated). hSBA responses among vaccinees were highest to the 5/99 strain with 98.3% (95% CI: 90.9-100) seroconverting and somewhat lower to the 44/76-SL strain with 78.0% (95% CI: 65.3-87.7) seroconverting. Only one unvaccinated individual exhibited a ≥4-fold rise in titers to at least one vaccine reference strain. Seroconversion to the outbreak strain was low in vaccinated participants (18.6% [95% CI: 9.7-30.9] and no unvaccinated participants seroconverted (0% [95% CI: 0-10.6]). None of the participants with very low pre-
vaccination hSBA titer against the outbreak strain seroconverted following two doses of 4CMenB.

**Conclusions**

While 4CMenB recipients exhibited a robust response to the well-matched MenB vaccine strains, our results indicate that seroconversion against the outbreak strain was low among vaccinees, especially among naïve individuals.

**Clinical Trial Registration (Please input N/A if not registered)**

N/A Not a clinical trial
Significantly lower rates of antibiotic prescribing for hospital acquired infections in low income settings than high income settings in the GARPEC study

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\textsuperscript{2}PENTA Foundation, n/a, Padua, Italy

Background

There is very limited data on neonatal and paediatric hospital-acquired infection (HAI) rates globally. Future interventional studies of infection prevention and control will require baseline data on hospital structures and prescribing for HAI. This study aims to describe the characteristics of centres participating in the Global Antimicrobial Resistance, Prescribing and Efficacy among Neonates and Children (GARPEC) project, and prescribing patterns for HAI.

Methods

GARPEC recruited a global convenience sample of 90 hospitals treating paediatric and neonatal infections. Hospital data including bed counts, presence of Neonatal Intensive Care Unit (NICU) and Paediatric Intensive Care Unit (PICU) wards and annual admissions were collected (REDCap\textsuperscript{TM}). Antibiotic (ATC code J01) prescription data were collected through four point prevalence surveys (PPS) between February 2016 and February 2017.

Results

68\% (61/90) of centres provided both PPS and hospital data representing 5 WHO regions. Most facilities were paediatric and neonatal units within larger hospitals. PICU/NICU size and annual admissions were comparable between high income countries (HIC) and low/middle income countries (LMIC). HIC reported more NICU admissions per year (Table 1). 34\% (715/2088) of paediatric prescriptions in HIC (n=27) were for HAI versus 20\% (694/3514) in LMIC (n=34). 41\% (196/475) of neonatal treatment indications in HIC were for HAI versus 22\% (257/1186) in LMIC.
Conclusions

In these centres, HAI accounted for a higher percentage of prescriptions in HIC than LMIC. Previous limited data has suggested that rates of HAI are higher in LMIC, suggesting possible under-diagnosis and treatment of HAI in LMIC or more frequent use of combination therapy in HIC in the GARPEC study. Given the sampling bias of the GARPEC facilities, future studies are needed to validate these findings in other settings, perhaps conducting combined HAI and antibiotic PPS.

<table>
<thead>
<tr>
<th>Hospital Type</th>
<th>High Income Countries (n=27)</th>
<th>Low Income Countries (n=34)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stand-alone children's hospital</td>
<td>10 (37%)</td>
<td>13 (38%)</td>
</tr>
<tr>
<td>Specialist children's hospital</td>
<td>0 (0%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Paediatric and neonatal units within a larger adult hospital</td>
<td>16 (59%)</td>
<td>18 (53%)</td>
</tr>
<tr>
<td>Specialist adult hospital with a paediatric ward</td>
<td>1 (4%)</td>
<td>2 (6%)</td>
</tr>
<tr>
<td>Teaching Hospital</td>
<td>24 (89%)</td>
<td>32 (94%)</td>
</tr>
<tr>
<td>Have PICU</td>
<td>22 (82%)</td>
<td>24 (71%)</td>
</tr>
<tr>
<td>Have NICU</td>
<td>21 (78%)</td>
<td>31 (91%)</td>
</tr>
<tr>
<td>Mean PICU beds</td>
<td>14 (range: 4-55)</td>
<td>14 (range: 3-27)</td>
</tr>
<tr>
<td>Mean NICU beds</td>
<td>30 (range: 5-98)</td>
<td>24 (range: 6-88)</td>
</tr>
<tr>
<td>Mean PICU admissions per year</td>
<td>587 (range: 37-2917)</td>
<td>616 (range: 134-1760)</td>
</tr>
<tr>
<td>Mean NICU admissions per year</td>
<td>980 (range: 200-4346)</td>
<td>666 (range: 114-2000)</td>
</tr>
<tr>
<td>Paediatric HAI prescriptions</td>
<td>34% (715/2088)</td>
<td>20% (654/3514)</td>
</tr>
<tr>
<td>Neonatal HAI prescriptions</td>
<td>41% (196/475)</td>
<td>22% (257/1186)</td>
</tr>
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</table>

Table 1. Summary of hospital characteristics and prescribing for hospital-acquired infections for GARPEC facilities participating in 4 PPS between February 2016 and February 2017.
ESPI8-0935

SCIENCE AND EDUCATIONAL TRACK

E-POSTER DISCUSSION SESSION 02: PUBLIC HEALTH AND EPIDEMIOLOGY

PERTUSSIS IN THE AMERICAS REGION: RECENT EPIDEMIOLOGICAL DATA PRESENTED AT THE 2017 GLOBAL PERTUSSIS INITIATIVE (GPI) ROUNDTABLE MEETING; CANCEUN, MEXICO, NOVEMBER 2017


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⁴Dalhousie University. Canadián Center of Vaccinology. Halifax- Nova Scotia Canada, Not applicable, Halifax, Canada
⁵Vanderblit University Medical Center- Nashville- TN USA, Not applicable, Nashville, USA
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Background and Objective

Pertussis remains among the leading vaccine-preventable diseases in many developed and developing countries, including those from the Americas region. The GPI is an expert scientific forum, which publishes consensus recommendations for pertussis monitoring, prevention, and treatment across many regions of the world. Here, we report the proceedings of a regional GPI meeting, held in Mexico in November 2017.

Methods

Information on current pertussis epidemiology, surveillance, vaccine strategies, diagnostic capabilities, disease awareness, and major local obstacles was presented by researchers from Argentina, Brazil, Canada, Colombia, Costa Rica, El Salvador, Mexico, Peru, Puerto Rico, United States, Uruguay and Venezuela.

Learning Points Discussion

Pertussis outbreaks have been detected during the last decade in the majority of participant countries. Currently, for the primary vaccination schedule series: 7 countries use wP vaccine and the other 5 aP vaccine. Improvements in pertussis surveillance have been accomplished after those outbreaks. Molecular-based diagnosis based on polymerase chain reaction is available in most of the countries. Due to improvements in surveillance, pertussis prevalence in the most vulnerable population (infants <1 year) is much better defined. Based on these data and recommendations from organizations such as the GPI, 7/12 countries introduced maternal immunization during pregnancy. Interestingly, countries in which this strategy has been introduced >two years ago have began to detect a reduction in the infant case-fatality rate.

CONCLUSIONS: Surveillance and vaccination strategies are not homogeneous among different regions of the Americas. However, all countries need to maintain and improve pertussis surveillance and to reach primary dose coverage of above 90%. Moreover, countries without maternal immunization programs should strongly consider them.
CLINICORADIOLOGIC EVALUATION OF VENTILATOR ASSOCIATED PNEUMONIA IN PEDIATRIC INTENSIVE CARE UNIT OF A TERTIARY CENTER

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Background

Appropriate empiric antibiotherapy can be life-saving in the early course of ventilator associated pneumonia (VAP), when the etiologic agent has not been determined yet. The clinicoradiologic characteristics and microbiologic agents of VAP in our pediatric intensive care unit (PICU) were evaluated in this study.

Methods

Patients (aged 0-18 years) with the diagnosis of VAP in our PICU between the years of 2011-2016 were included. Data regarding demographic and clinical characteristics was gathered retrospectively from patients’ files and hospital computer system.

Results

In total, 702 (53%) out of 1323 patients admitted to PICU during study period were mechanically ventilated. Seventy-three patients developed VAP. The incidence density was 10.3% per 1000 ventilator days. Median age of the patients was 10 (1-188) months and 24 of them (32.9%) were female. Median length of hospital stay, PICU stay and mechanical ventilation (MV) were 22 days (12-128), 29 days (4-184) and 17 days (4-184), respectively. PICU admission was due to respiratory (n=33, 45.2%), cardiovascular (n=7), neurologic (n=20), metabolic (n=2) and post-operative reasons (n=11). Pseudomonas aeruginosa (n=23, 31.5%) was the most common pathogen. Others were Acinetobacter baumanii (n=21, 28.8%), Stenotrophomonas maltophilia (n=9), meticillin resistant coagulase-negative Staphylococcus (n=7), Klebsiella pneumoniae (n=6) meticillin resistant Staphylococcus aureus (n=3), Corynebacterium spp. (n=1), Escherichia coli (n=1) and Serratia marcescens (n=1). The duration of MV was significantly longer among the gram-negative related-VAP
The presence of consolidation and/or pleural effusion was significantly higher in the VAP patients with gram-positive etiology (p values are 0.009/ 0.01, respectively).

**Conclusions**

The possibility of gram-negative bacteria is correlated with the duration of MV. Besides; the presence of consolidation and/or pleural effusion increases the risk of gram-positive bacteria. These parameters must be considered when choosing empiric antibiotic therapy.
E-POTER DISCUSSION SESSION 10: GLOBAL INFECTIOUS DISEASES

CHILDREN VISITING FRIENDS AND RELATIVES ABROAD: EPIDEMIOLOGICAL CHARACTERISTICS IN A REFERENCE UNIT OF INTERNATIONAL PEDIATRIC TRAVELERS

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Background

Due to migratory movements, children commonly travel to visit their friends and relatives abroad (VFR). They constitute a risk group, due to their integration with the local population and lower perception of risk. The purpose of this work was to analyze the characteristics of these VFR-children.

Methods

Children below 18 years old travelling abroad seen in the Pediatric Travelers Unit of a National Reference Center for Tropical Diseases were included in the study. Epidemiological and clinical data, together with data regarding immunizations and antimalarial prophylaxis were collected retrospectively January to December 2017.

Results

A total of 1433 children attended the consultation: 50% VFR, 28% tourists, 8% changed residency, 7.5% to study abroad, 6.5% others.
53% VFR were women. Median age: 46 months [20-95]. Regarding comorbidities, 7% of VFR had comorbidities, mostly minor: 53% atopic dermatitis and/or asthma. Immunizations were up to date in 96% of VFR.
Median pre-trip consultation time in VFR was 24 days [12-45] and 2.3% consulted only 72 hours before traveling.
Destination: America 74.5% [23.5% Ecuador, 14% Bolivia, 10% Colombia], Africa 18% and Southeast Asia 6.5%.
Median duration of VFR trip: 30 days [23-45].
Vaccination in VFR: 53.5% yellow fever; 40% VHA, 50.5% typhoid fever (36% parenteral), 9.5% meningococcal tetravalent.
Antimalarial chemoprophylaxis in 21%: atovaquone/proguanil 75%, mefloquine 25%.

Conclusions

In our study, half of the travellers served are VFR, they tend to be young (preschoolers) and their trips are long. Most of them are healthy and correctly vaccinated.
Latin America is the most visited destination. Half of travellers received yellow fever and
typhoid vaccine. We restrict VHA vaccination due to stock-outs. We emphasize the importance of the pre-international travel consultation, especially in VFR.
BACKGROUND
Bronchiolitis is a common lower respiratory tract illness caused by viral infection in children 2 years of age and younger. Recent practice guidelines recommend limiting use of bronchodilators, corticosteroids, antibiotics, and diagnostic testing for patients with bronchiolitis. Wheezing episodes induced by various viral infection are diagnosed as bronchiolitis. Although respiratory syncytial virus (RSV) is the major cause of bronchiolitis, other agents cause wheezing episode in young children. We sought to determine whether corticosteroids are efficacious in treating hospitalized children with wheezing according to causative agents of RSV or rhinovirus.

METHODS
This study included children under the 24 months old with acute bronchiolitis or respiratory infection presenting wheezing from June 2016 to Dec 2017. The infectious viruses were analyzed by multiplex real time PCR. 409 children infected by RSV or rhinovirus were analyzed retrospectively. Outcome measures was the length of hospital stay (LOS). LOS was compared by virus and by use of steroid. T-test was applied to compare mean difference among independent groups for the variables length of hospital stay (in days). P < 0.05 was considered significant.

RESULTS
Cases of rhinovirus, RSV-A and RSV-B infection were 151, 142, and 116 respectively. Systemic steroids were used in 39.6% of patients. In rhinoviral infectious cases, LOS in patients with steroid treatment was shorter than steroid free patients (4.04 vs 4.58, p=0.01). In RSV-A and RSV-B, LOSs in patients without use of steroid were shorter than patients with steroid treatment (4.24 vs 5.93, p=0.00, 4.30 vs 6.31 p=0.00 respectively).

CONCLUSIONS
In patient of bronchiolitis showing wheezing in young children, the use of steroid might be considered according to causative viruses, especially rhinovirus.
Background

Late-onset sepsis due to Gram-negative bacteria (GNB) is an important cause of morbidity and mortality in hospitalised neonates. Multi-resistant GNB (MRGNB) infections and outbreaks are of growing concern in neonatal-units (NNUs) across the UK and globally. To develop strategies to prevent and control these infections the NeoHIEC Study was undertaken in NNUs in the South-London (SL) neonatal network.

Methods

The NeoHIEC-Study is a large observational cohort study conducted in SL NNUs and aimed to describe the epidemiology of colonisation with MRGNB in hospitalised neonates. During the first 8 months of the study (October 2013-May 2014) weekly or monthly peri-anal swabs (depending on intensity of NNU) were collected from neonates in 8/10 SL NNUs (2 tertiary, 6 secondary care NNUs), stored and analysed in batches. All identified GNB were subjected to antibiotic susceptibility testing using BSAC methodology and interpretive criteria. MRGNB were defined as isolates resistant to ≥3 antibiotic classes.

Results

1858 samples were collected and 1341 GNB isolated; the majority (1318, 98.3%) were Enterobacteriaceae (Klebsiella sp (39.5%), E. coli (27.6%) and Enterobacter sp (21.0%)). 19.8% were MRGNB and 17.4% ESBL-positive. Median-age at colonisation was 28 days (IQR: 16-66). Overall resistance to antibiotics and specific resistance profiles for isolates is shown in the table. No significant differences in pathogen distribution or resistance profiles was found between the 2 tertiary-units but the proportion of MGRNB in the tertiary-units
(combined) was double that of the secondary-units (combined) (22.2 vs 11.6%, p <0.0001).

<table>
<thead>
<tr>
<th>Overall resistance rates in different antibiotics</th>
<th>Amoxicillin</th>
<th>Ceftazidime</th>
<th>Tobramycin</th>
<th>3rd gen Cephalosporins</th>
<th>Ciprofloxacin</th>
<th>Piperacillin</th>
<th>Gentamicin</th>
<th>Carbapenem</th>
<th>Colistin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resistant n (%)</td>
<td>1129 (84.2)</td>
<td>522 (37.6)</td>
<td>57 (4.2)</td>
<td>150 (11.2)</td>
<td>100 (7.5)</td>
<td>72 (5.4)</td>
<td>29 (2.9)</td>
<td>62 (4.8)</td>
<td>54 (4.0)</td>
</tr>
<tr>
<td>Intermediate n (%)</td>
<td>6 (0.7)</td>
<td>25 (1.8)</td>
<td>8 (0.6)</td>
<td>20 (1.5)</td>
<td>14 (1.0)</td>
<td>12 (0.9)</td>
<td>9 (0.7)</td>
<td>29 (2.2)</td>
<td>50 (3.7)</td>
</tr>
<tr>
<td>Overall resistance rates for the most common Enterobacteriaceae</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Escherichia n = 387 n (%)</td>
<td>226 (61.4)</td>
<td>187 (47.8)</td>
<td>19 (5.2)</td>
<td>81 (21.2)</td>
<td>87 (22.5)</td>
<td>9 (2.3)</td>
<td>27 (6.9)</td>
<td>6 (1.6)</td>
<td>10 (2.7)</td>
</tr>
<tr>
<td>Klebsiella n = 500 n (%)</td>
<td>518 (98)</td>
<td>63 (12.5)</td>
<td>15 (4.7)</td>
<td>55 (11)</td>
<td>25 (5.1)</td>
<td>22 (4.4)</td>
<td>5 (1.0)</td>
<td>8 (1.6)</td>
<td>6 (1.2)</td>
</tr>
<tr>
<td>Enterobacter n = 268 n (%)</td>
<td>252 (98)</td>
<td>288 (82.8)</td>
<td>8 (3.1)</td>
<td>61 (21.6)</td>
<td>8 (3.1)</td>
<td>37 (18.1)</td>
<td>12 (4.5)</td>
<td>82 (11.8)</td>
<td>4 (1.4)</td>
</tr>
</tbody>
</table>

Conclusions

Hospitalised neonates are frequently colonised with *Enterobacteriaceae*; rates of colonization with MRGNB are moderate and may correlate with the NNU level of care.

On behalf of the NeoHIEC Study consortium, South London, UK.

Clinical Trial Registration (Please input N/A if not registered)

N/A
CLINICAL FEATURES AND RISK FACTORS FOR SEVERE CLINICAL OUTCOME OF ITALIAN CHILDREN HOSPITALIZED FOR MEASLES

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²Anna Meyer Children’s University Hospital, Pediatric Infectious Diseases Unit, Florence, Italy
³Ospedale Pediatrico Bambino Gesù, Department of Pediatric infectious diseases, Rome, Italy

Background

Measles is a high communicable disease with potentially severe complications. Outbreaks have been recently reported in developed countries, however risk factors for severe course are poorly investigated in these settings.

The aim of the study was to report the clinical features, complications and outcomes of measles in a national pediatric population and, specifically, to investigate the risk factors for severe course.

Methods

The Italian Society for Pediatric Infectious Diseases conducted a retrospective observational study in children hospitalized during the 2016-2017 epidemic season in 19 Italian hospitals. Presumptive diagnosis at hospital admission was recorded. Logistic regression analysis was used to detect risk factors for severe outcome, defined by the presence of complications at discharge, the need of intensive care or death.

Results

We enrolled 249 children (median age 14.5 months, 85% not immunised). Clinical diagnosis of measles at admission increased from 30% to >70% during the outbreak (p<0.001).

Two-hundred and six children (83%) developed complications and 3 (7.5%) died.

Pancreatitis (OR10.8, p<0.01) and encephalitis (OR9.07, p<0.03) significantly predicted severe outcome. Neutropenia was more commonly related to B3-genotype rather than D8 (29.5vs7.7%, p=0.01). Increased C-reactive protein predicted severe outcome (AUC 0.67, 95%CI 0.52 to 0.82) and value>2 mg/dl had higher risk of complications (OR2.0, p=0.01) or severe outcome (OR4.13, p<0.01).

Conclusions
The risk of severe clinical outcome is independent from age, genotype and underlying conditions, but is related to the development of organ complications (like encephalitis or pancreatitis) and is predictable by C-reactive protein value.
Genetic diversity of Rotavirus strains associated with acute diarrhea among children in a tertiary care hospital based screening study in Odisha (India)

Background

Rotavirus is the commonest cause of childhood diarrhea globally, which causes hospitalizations and also death frequently in developing countries. Present study aimed to estimate the burden of Rotavirus associated diarrhea in children and to do genotyping in order to identify the regional distribution of different strains as detected in a series of cases attending the same hospital in Odisha.

Case Presentation Summary

A total of 321 stool samples (over 16 months period) were obtained from children <5 years of age presenting with acute diarrhea upon admission into the Pediatrics ward of a tertiary care teaching hospital. Initially each sample was screened for rotavirus antigen by enzyme immunoassay (EIA). Subsequently RNA from each EIA positive sample was subjected to reverse-transcription PCR for genotyping. Overall results showed Rotavirus to be associated with diarrhea in nearly one third of the children recruited in this study. Detection rate was highest among children of 2-3 year age group, followed by <1 year age group. Of the EIA positive samples which were subjected to genotyping of the virus 87.62% had single G and P types, while 12.37% were of mixed type (with more than one G and/or P type). G3P[8] was the most frequently detected genotype (39.25%) followed by G1P[8], G2P[P4], G1P[P6] and G3P[P6].

Learning Points/Discussion
Rotavirus associated diarrhea was diagnosed among children of 2-3 years age group more frequently. The majority of the identified strains belonged to the G1, G3 and P[8] genotypes, suggesting high coverage of current rotavirus vaccines. Large-scale studies are needed to document the significance of the increase in genotypes of uncommon and mixed combinations.
CO-ADMINISTRATION OF GSK’S HEXAVALENT DTPa-HBV-IPV/Hib VACCINE AND MULTICOMPONENT MENINGOCOCCAL SEROGROUP B VACCINE (4CMenB): A REVIEW

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²GSK, Vaccines, Siena, Italy

Background and Objective

GSK’s hexavalent DTPa-HBV-IPV/Hib vaccine is included in many national immunization programs. With the increase of vaccines indicated for routine paediatric vaccination, there is more need for co-administration to minimize immunization visits. Co-administration potentially affects the immunogenicity and safety of co-administered vaccines. We aimed to summarize co-administration data of DTPa-HBV-IPV/Hib and 4CMenB vaccines.

Methods

We considered all manufacturer-sponsored trials assessing co-administration of GSK’s DTPa-HBV-IPV/Hib (+PCV7) and 4CMenB vaccines. Immunogenicity, safety/tolerability data from the 3 identified, previously published, randomised studies (Table) are described here.

Learning Points Discussion

1. All DTPa-HBV-IPV/Hib immunological non-inferiority criteria were met in the concomitant-accelerated versus control groups, except for pertactin (not considered clinically relevant). ≥79% of 4CMenB vaccinees had hSBA titers ≥1:5 against vaccine-specific MenB antigens. Fever rates (≥38°C) were higher in the concomitant-accelerated (44–59% participants) versus control group (23–36%) post-each dose.

2. Seroresponse rates for DTPa-HBV-IPV/Hib were non-inferior in the concomitant versus control groups, except for IPV-2 (not considered clinically relevant). ≥84% of 4CMenB vaccinees had hSBA titers ≥1:5 against vaccine-specific MenB antigens. Fever rates (≥38.5°C) were higher in the concomitant (65.3% infants) versus control group (32.2%). Higher rates of tenderness at the injection site, change in eating habits or irritability were associated with 4CMenB co-administration.

3. Paracetamol prophylaxis did not decrease immune responses to 4CMenB and had no clinically relevant effects on immune responses to DTPa-HBV-IPV/Hib. Occurrence of fever (≥38.5°C) was higher in infants receiving 4CMenB (70.3% infants) versus MenC (27.1%) post-primary vaccination, but was significantly decreased by prophylactic paracetamol, as were other solicited local and systemic reactions.
Conclusions: 4CMenB and DTPa-HBV-IPV/Hib co-administration had an acceptable immunogenicity and tolerability profile. Currently, GSK’s DTPa-HBV-IPV/Hib vaccine is the only hexavalent vaccine studied in co-administration with 4CMenB.

Funding: GlaxoSmithKline Biologicals SA

Table. Study design of the 3 co-administration studies with GSK’s DTPa-HBV-IPV/Hib and 4CMenB vaccines

<table>
<thead>
<tr>
<th>Study group</th>
<th>N</th>
<th>Vaccination schedule*</th>
<th>Vaccines</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Study 1 (Gossger N et al. JAMA. 2012;307:573–82)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Concomitant</td>
<td>622</td>
<td>2-4-6 mo</td>
<td>4CMenB + DTPa-HBV-IPV/Hib</td>
</tr>
<tr>
<td>Intercalated</td>
<td>632</td>
<td>2-4-6 mo</td>
<td>4CMenB</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3-5-7 mo</td>
<td>DTPa-HBV-IPV/Hib</td>
</tr>
<tr>
<td>Concomitant-accelerated</td>
<td>317</td>
<td>2-3-4 mo</td>
<td>4CMenB + DTPa-HBV-IPV/Hib</td>
</tr>
<tr>
<td>Control</td>
<td>314</td>
<td>2-3-4 mo</td>
<td>DTPa-HBV-IPV/Hib</td>
</tr>
<tr>
<td>Immunogenicity sub-study</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Concomitant</td>
<td>1958</td>
<td>2-4-6 mo</td>
<td>4CMenB + DTPa-HBV-IPV/Hib</td>
</tr>
<tr>
<td>Control</td>
<td>659</td>
<td>2-4-6 mo</td>
<td>DTPa-HBV-IPV/Hib</td>
</tr>
<tr>
<td>Safety sub-study</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Concomitant</td>
<td>513</td>
<td>2-4-6 mo</td>
<td>4CMenB + DTPa-HBV-IPV/Hib</td>
</tr>
<tr>
<td>MenC</td>
<td>490</td>
<td>2-4-6 mo</td>
<td>MenC + DTPa-HBV-IPV/Hib</td>
</tr>
<tr>
<td><strong>Study 3 (Prymula R et al. HVI. 2014;10:1993–2004)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary vaccination</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4CMenB</td>
<td>188</td>
<td>2-3-4 mo</td>
<td>4CMenB + DTPa-HBV-IPV/Hib</td>
</tr>
<tr>
<td>4CMenB + paracetamol$^5$</td>
<td>184</td>
<td>2-3-4 mo</td>
<td>4CMenB + DTPa-HBV-IPV/Hib</td>
</tr>
<tr>
<td>MenC</td>
<td>185</td>
<td>2-3-4 mo</td>
<td>MenC + DTPa-HBV-IPV/Hib</td>
</tr>
<tr>
<td>Booster vaccination</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4CMenB</td>
<td>155</td>
<td>12 mo</td>
<td>4CMenB + DTPa-HBV-IPV/Hib</td>
</tr>
<tr>
<td>4CMenB + paracetamol$^5$</td>
<td>161</td>
<td>12 mo</td>
<td>4CMenB + DTPa-HBV-IPV/Hib</td>
</tr>
<tr>
<td>MenC</td>
<td>165</td>
<td>12 mo</td>
<td>4CMenB (first of 2 doses) + DTPa-HBV-IPV/Hib</td>
</tr>
</tbody>
</table>

Mo, month; 4CMenB, multicomponent meningococcal serogroup B vaccine; DTPa-HBV-IPV/Hib, hexavalent diphtheria-tetanus-acellular pertussis-hepatitis B-inactivated poliovirus-Haemophilus influenzae type B vaccine; MenC, meningococcal serogroup C conjugate vaccine; MMRV, measles, mumps, rubella and varicella vaccine; N, number of infants randomised. *only results after primary vaccination are discussed in the abstract. $^5$Paracetamol was administered prophylactically just before or at the time of vaccination, followed by 2 further administrations at 4–6 h intervals after vaccination by the parents/guardians. Notes: 7-valent pneumococcal conjugate vaccine (PCV7) was also co-administered with DTPa-HBV-IPV/Hib in all study groups but results are not presented here; in study 1, immune responses to DTPa-HBV-IPV/Hib were only assessed in the Concomitant-accelerated and Control groups; Study 3 included 5 other study groups that are not reported here.
TREATMENT AND OUTCOMES OF CHILDREN WITH URINARY TRACT INFECTIONS DUE TO EXTENDED SPECTRUM BETA-LACTAMASE PRODUCING BACTERIA IN EUROPE: TOO CUTE STUDY


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6Great Ormond Street Hospital, Department of Paediatric Infectious Diseases, London, United Kingdom
7Hospital Pediátrico- Centro Hospitalar e Universitário de Coimbra, Serviço de Urgência e Unidade de Infecciology, Coimbra, Portugal
8Robert Debré University Hospital, Pediatric Infectious Disease Department and Antibiotic Stewardship Mobile Unit, Paris, France
9Vilnius University Faculty of Medicine- Children’s Hospital, Vilnius University Hospital Santaros Clinics, Vilnius, Lithuania
10Bambino Gesù Children’s Hospital, Immunology and Infectious Disease Unit, Rome, Italy
1112 de Octubre hospital, Department of Infectious Diseases, Madrid, Spain
12St Georges University Hospitals NHS Foundation Trust, Department of Microbiology, London, United Kingdom
13Alder Hey Children’s NHS Foundation Trust, Department of Paediatric Infectious Diseases and Immunology, Liverpool, United Kingdom
14Aristotle University and Hippokration Hospital, Third Department of Pediatrics, Thessaloniki, Greece
15University Medical Centre of Ljubljana, Department of Infectious Diseases, Ljubljana, Slovenia
16Regional University Hospital of Malaga, Department of Paediatrics, Malaga, Spain
Background

There is an increase of extended spectrum beta-lactamase (ESBL) producing bacteria in children globally. To date, there is limited evidence on the effectiveness of antibiotic treatment in childhood with ESBL urinary tract infections (UTIs). The “TOO CUTE” study aimed to evaluate the spectrum of antibiotics used in European children with ESBL UTIs and clinical and microbiological outcomes.

Methods

TOO CUTE is a multinational retrospective cohort study which was conducted in 14 hospitals in Europe. Children aged 0 to 18 years with a confirmed ESBL febrile UTI were included in the study. Information was collected on demographics, clinical presentation, antibiotic treatments, clinical and microbiological outcomes.

Results

We included 142 patients; 84 females (59.2%). About 55.6% of patients (79/142) had at least one comorbidity. E. coli (122/142; 85.9%) was the predominant isolated pathogen. ESBL isolates were often resistant to co-amoxiclav (66/119; 55.5%) and ciprofloxacin (60/107; 56.1%) but rarely resistant to mecillinam (2/39; 5.1%) and fosfomycin (5/59; 8.5%). One third of patients (49/142; 34.5%) were initially treated with cephalosporins and 16.2% (23/142) with aminoglycosides. Fifteen patients had clinical (10.6%) and 7 microbiological (4.9%) failure during treatment. A total of 100 patients with an initial empirical antibiotic treatment were switched to another antibiotic, mostly to penicillins with or without a beta-lactamase inhibitor (29/100; 29.0%) or to carbapenems (15/100; 15.0%) or aminoglycosides (15/100; 15.0%). Among 113 patients with complete clinical follow-up, 16 (14.2%) had recurrent signs/symptoms of a UTI, 14.8 days (SD 7.6) after the end of treatment.

Conclusions

There is variation of antibiotic use for ESBL febrile UTIs treatment in European children. New, pragmatic trials are needed to explore the effectiveness of new or older antibiotics against resistant febrile UTIs in children.
THE IMPLICATIONS OF AVAILABLE LIQUID AMoxicillin AND CO-AMOxicillin FORMULATIONS FOR FACILITATING ADHERENCE TO RECOMMENDED ANTIBIOTIC TREATMENT DOSE AND DURATION

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Background and Objective

A large proportion of oral antibiotics in young children is used as liquid formulations, preventing an exact pill count dispensing strategy. We investigated whether available liquid amoxicillin and co-amoxicillin preparations are likely to facilitate adherence given the treatment regimens recommended for young children with respiratory tract infections in Switzerland.

Methods

All liquid formulations for amoxicillin and co-amoxicillin (4:1) available in Switzerland were identified by searching the national formulary compendium.ch. Dosing guidelines were collected by directly contacting all teaching/university paediatric departments. The total amount of antibiotic in mg required to treat children weighing 10kg, 15kg and 20kg under each identified recommendation was calculated.

Learning Points Discussion

- One concentration of amoxicillin (250mg/5ml, 2 brands) and one concentration of co-amoxicillin (400mg amoxicillin/5ml, 4 brands) are available.
- Amoxicillin suspension is dispensed in a standard pack size of 100ml, while co-amoxicillin is available in 35ml 70ml and 140ml bottles.
- Available pack sizes are appropriate only for a small proportion of regimens and weights (Amoxicillin: 25mg/kg BD for 5 days in a child weighing 20kg or 10 days in children weighing 10kg or 20k; Co-amoxicillin: 40mg/kg BD or 26.7mg/kg TDS for 7 days in children weighing 10kg, 15kg or 20kg).
- Some regimens can only be achieved by dispensing multiple packs, increasing the risk that the second bottle will not be administered and/or kept at home for future use.
- Equally considerable left-over volumes are expected for increasingly recommended shorter treatment durations which could be confusing to families.
- Problems could be mitigated by moving from exact weight-based to weight-banded dosing with appropriate pack sizes and by considering the use of dispersible tablets that enable dispensing of an exact pill count.
IMPACT OF RADT ROUTINE USE ON ANTIBIOTIC PRESCRIPTION PATTERNS AND RATES: A LEVEL II HOSPITAL PROSPECTIVE STUDY

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Background

Acute pharyngitis (AF) is one of the most common causes of pediatric emergency room (ER) visits. Bacteria account for 15-40%, with Group A beta-hemolytic streptococcus (GAS) being the most common. Distinction between viral- and GAS-AF minimizes unnecessary use of antibiotics (AB). Rapid antigen-detection tests (RADTs) are indicated in multiple guidelines, whenever epidemiological and clinical determinants warrant. In Portugal RADT is not available for routine use in all ER. The aim of this study was to determine patterns and antibiotic prescription changes, before and after RADT implementation.

Methods

Prospective study performed in the ER of a level II hospital, from Dec2017-Feb2018, by the application of an anonymous questionnaire. Demographic, epidemiological and clinical variables were assessed and a blind question about AB prescription intention was included. Questionnaires were performed before (n=75) and after (n=62) RADT availability. RADTs were performed according to manufacturer guidelines. Adequacy of AB prescription was also evaluated. Descriptive and bivariate statistical analysis using SPSS©v24.0 was applied.

Results

Study included 137 patients, with a median age of 6.3 years [min, max:1-17] and females representing 53.6%. AB prescription was performed in 66.7% (50/75) of the episodes, when considered only clinical variables. Presence of exsudate, palatal petechial or scarlatiniform rash were the clinical signs that most frequently led to AB prescription decision (p<0.05). After RADT availability, it was observed an overall decrease of 23.2% in AB prescription. In the children subgroup with negative RADT, 31.9% clinician would have prescribed AB if the test was not available.

Regarding AB prescriptions, almost 1/3 did not follow completely national guidelines recommendations.
Conclusions

RADT use resulted in an important improvement in AB prescription rates. Health professionals training in appropriate AB choices is a major issue in economics and public health.

Clinical Trial Registration (Please input N/A if not registered)

N/A
Epidemiology of Group A Streptococcal Invasive Infections in Brussels: A Retrospective Multicenter Study From 2005 to 2015

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Background

There is a wide diversity of Group A Streptococcus (GAS) emm-types worldwide which hinders the development of an efficient multivalent vaccine. Continuous monitoring of circulating strains is therefore important in order to identify epidemiological evolution. We have performed a retrospective study on invasive GAS infection (iGAS) in a network of 5 hospitals in Brussels for a period of 10 years (2005-2015).

Methods

Patients were identified by a positive GAS culture on a microbiological sample originating from a sterile anatomical site. Relevant epidemiological and clinical data (age, sex, origin, underlying clinical condition, diagnostic, outcome, risk factors) were reviewed. Antibiotic susceptibility profiles were tested against clindamycin, erythromycin and tetracyclin using Disk Diffusion method. We have analysed these results using CLSI breakpoints for sensitivity and resistance.

Results

159 patients were included. The predominant clinical manifestation were sepsis and severe skin infections with all cases presenting with a positive GAS blood culture. The presence of a chronic disease, a social condition or an immunosuppression were also identified as risk factor for iGAS. Two peaks of incidence were clearly noted (2-5 years old and above 70 years old). The fatality rate was 11,9% (95% CI: 7,8-17,9). In terms of antibiotic resistance, 5% of the strains were resistant to erythromycin, 2,5 % to clindamycin and 1,2% to tetracyclin.

Conclusions
Our study confirms that GAS is associated with significant morbidity and mortality in high-income countries. The rates of resistance towards erythromycin and clindamycin, although still relatively low, must be carefully monitored.
HIGH RATE OF FAECAL COLONIZATION WITH CARBAPENEM-RESISTANT ENTEROBACTERIACEAE IN NEONATES CORRELATED TO HOSPITAL ACQUIRED INFECTIONS AND MORTALITY IN A LARGE VIETNAMESE NEONATAL INTENSIVE CARE UNIT

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Background

WHO has declared carbapenem-resistant Enterobacteriaceae (CRE) as first priority pathogens. High prevalence of CRE-infections has been found among critical ill patients in Vietnamese hospitals. CRE screening at admission and discharge was conducted in an 80 patient-bed Neonatal Intensive Care Unit at Vietnam National Children Hospital in Hanoi during spring 2017.

Methods

Rectal faecal swabs were plated directly on Chrom-ID-Carba agar (BioMérieux), selective for Enterobacteriaceae with KPC, NDM and Oxa-48 carbapenemases. Antibiotic susceptibility testing (AST) was conducted using VITEK-2 system. Clinical data were collected from the patient records.

Results

Of 310 neonates 194 (62.5%) were male, 126 (40.6%) preterm and 140 (45.2%) were delivered by caesarean section, 265 (85.5%) were referred from another hospital. Diagnosis at admission included respiratory distress syndrome 188 (60.6%), pneumonia 63 (20.3%), sepsis 43 (13.9%), congenital heart disease 32 (10.3%) and neonatal jaundice 25 (8%). Hospital-acquired infections (HAIs) at admission were diagnosed in 103 (33.2%), with sepsis in 60/103 (58.2%) and pneumonia 54/103 (52.4%). Colonisation with CRE increased from 101 (32.6%) at admission to 221 (82.5%) of 268 screened at discharge. Carbapenem-resistant Klebsiella pneumoniae and Escherichia coli increased from at admission 62 (20%)
and 31 (10%) to at discharge 187 (60.3%) and 104 (33.5%), respectively. CRE colonization at admission correlated significantly with HAI at admission and crude mortality (p<0.01). CRE colonization at discharge correlated significantly with HAI diagnosis at discharge, crude mortality and NICU treatment more than 7 days (p<0.01). Invasive procedures CVC and intubation as well as carbapenem and colistin use was significantly associated CRE colonization at discharge (p<0.01).

Conclusions

This study shows high CRE colonization and a significant correlation with HAI and crude mortality. Interventions are urgently needed to stop transmission of CRE in Vietnamese hospitals.
HEALTHCARE-ASSOCIATED VIRAL INFECTIONS IN HOSPITALIZED CHILDREN AT THE KAROLINSKA UNIVERSITY HOSPITAL

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Background

Nosocomial infections are associated with significant mortality, prolonged length of hospital stay and increased healthcare costs. Limited data are available on the healthcare-associated viral infections (HA-VIs) in children. The aim of this retrospective pilot study was to assess the epidemiology of HA-VIs in hospitalized children at Karolinska University Hospital (KUH). We collected patients clinical and laboratory data from all the medical and surgical pediatric and neonatal units during December 2016 to December 2017.

Methods

We used the Centers for Disease Control and Prevention (CDC) definition to classify an infection as healthcare-associated. Because of the variable length of incubation period of viruses, we included infections during the incubation time range of each virus. Infection rates were calculated as the number of infections per 1000 patient days.

Results

In total, there were 31 HA-VIs in 26 patients within the study period resulting in an overall rate of 0.9/1,000 patient-days. The highest rate was observed in the long-term intensive care unit (5.9/patient days) followed by the neonatal unit (3.6/patient days). There were 8 (25%) gastrointestinal infections and 23 (74%) respiratory infections. Rhinovirus was the most common respiratory pathogen (82%) and norovirus was the most common gastrointestinal pathogen (50%) detected. HA-VI cases occurred year-round, but most were identified during the autumn (32%) and spring (35%) months.

Conclusions

In this retrospective pilot study, we found lower HA-VI rates at KUH compared to rates reported in the United States and within the European Union. However, our results need to be confirmed with a prospective study set up with the possibility for daily monitoring of symptoms and follow up after discharge from the hospital. Infection control efforts should be developed and focused on units with high HA-VI rates.
ES18-1015
SCIENCE AND EDUCATIONAL TRACK

E-POSTER DISCUSSION SESSION 06: COMMUNITY ACQUIRED INFECTIONS:
RESPIRATORY TRACT INFECTIONS

RESPIRATORY INFECTIONS IN CHILDREN WITH IMMUNOGLOBULIN A DEFICIENCY:
DIAGNOSTIC VALUE OF SERUM IGA VERSUS MUCOSAL IGA VALUES
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Background

Immunoglobulin A (IgA) is found in respiratory and intestinal tract mucosa. Children with IgA deficiency are at risk of recurrent respiratory tract infections. Mucosal secretory IgA (slgA) differs from serum IgA in molecular structure and probably also function. While the protective role of slgA as the first line of defense at the epithelial barrier is well recognized, the function of circulating IgA is not completely understood. However, the latter is used as reference test for IgA deficiency. This study aims to research the significance of slgA as a predictor of symptoms in children with respiratory infections.

Methods

Sixty-two children, <7 years, with recurrent respiratory tract infections were included. Saliva, feces and serum samples were collected and slgA levels were measured using sandwich ELISAs. Disease severity was determined by: 1) prospective number of days with at least one respiratory tract symptom during the winter season, as recorded by a daily mobile phone application and 2) the presence of physician-diagnosed pneumonia. Study participants were stratified according to low (<median) versus high (>median) (s)IgA levels. Results were compared by unpaired T-test.

Results

Pneumonia occurrence rates and symptomatic winter days were higher in children with low salivary and fecal slgA concentrations just before the winter season. For serum IgA concentrations the opposite was observed, i.e. higher serum IgA concentrations were present in children who ultimately got more respiratory infections that winter. On this number
of patients tested, the difference did not reach statistical significance.

Conclusions

These pilot results show a trend towards an inverse relation between mucosal IgA and airway infection frequency. We conclude that mucosal IgA likely has a separate protective role in prevention of respiratory tract infections that is not seen for serum IgA.

Clinical Trial Registration (Please input N/A if not registered)

N/A
IMPACT OF PREVIOUS EXPOSURE TO ANTIMICROBIALS ON TYPE AND RESISTANCE OF UROPATHOGENS

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Background

Prior exposure to antimicrobials has been associated with increasing resistance of uropathogens in adults, but data for children are fewer and have focused mainly on prophylaxis. In this audit we investigated the impact of any antibiotic exposure on the development of unusual and resistant pathogens in children with UTI.

Methods

Differences in types of uropathogens and resistance patterns were investigated in children < 16 years hospitalized for UTI during 2007-2017, divided in 3 groups, i.e., lack of any exposure to antibiotics, exposure to antibiotics in the previous 6 months for any reason but prophylaxis, and ongoing exposure to prophylaxis for previous UTI.

Results

A total of 711 uropathogens were identified, (E. coli 56.4%, Klebsiella spp 10.8%, Enterococcus spp 9.8%, other 23%). As compared to children without any exposure to antibiotics, children on prophylaxis had more commonly non-E. coli (69.8% vs 30.1%, p<0.0001) and ESBL phenotype pathogens (24.1% vs 5.7%, p<0.0001), and similarly children with exposure to antibiotics for any other reason had more commonly non-E. coli (51.2% vs 30.1%, p<0.0001) and ESBL phenotype pathogens (23.7% vs 5.7%, p<0.0001). In a regression model including predisposing factors, namely type of delivery, NICU hospitalisation and abnormalities in urinary tract imaging, prophylaxis remained the strongest predictor for non-E. coli (OR 3.09, 95% CI 1.9-4.9, p<0.0001) and ESBL-phenotype (OR 2.8, 95% CI 1.4-5.7, p=0.0035) pathogens. Recent use of antibiotics was also an important determinant of non-E.coli (OR 1.8, 95% CI 1.2-1.9 p=0.0017) and ESBL-phenotype (OR 2.1, 95% CI 1.2-3.9, p=0.0087) pathogens.

Conclusions

Our findings suggest that exposure to antibiotics for any reason is, similarly to prophylaxis, a significant predictor of changes in type and resistance uropathogens.
PNEUMOCOCCI DETECTED IN SALIVA BY lytA-PCR WHEN PRESENT ARE AT VERY LOW DENSITY AND IN MOST CASES MAY BE NON-PNEUMOCOCCAL STREPTOCOCCI CONTAINING PNEUMOCOCCAL GENE HOMOLOGUES

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Background

The presence of pneumococci (Sp), detected by PCR, in a high proportion of saliva samples from healthy children has previously been reported. Having obtained similar results, we analysed paired nasal swab and saliva samples from children, in which both samples were lytA PCR positive (Ct<35), using molecular serotyping by microarray.

Methods

The products of standard culture on selective agar plates from the 49 sample pairs, obtained from healthy children aged 6 months to 5 years attending pre-school nursery in Coimbra, Portugal, were subjected to molecular serotyping analysis by microarray as previously described.

Results

Among the 49 nasal samples, 45 had evidence of Sp by microarray, 4 only related non-Sp and one no evidence of Sp or related species. In 28 there was evidence of single Sp serotypes and in 9 of multiple serotypes. By contrast only 3/49 saliva samples had evidence of Sp by microarray, in each case matching the Sp detected in the nasal sample from the same child but in all 3 at low abundance within a complex mix of other species.

Conclusions

These results suggest that the common finding of qPCR results suggestive of the presence of Sp in saliva samples in young children may, in reality, reflect the presence of genetically related streptococci from the oral flora, usually in complex mixtures. While our findings do not definitively rule out the presence of small numbers of viable pneumococci whose presence is masked by the rich oral microbial flora, nevertheless, they suggest that transmission of Sp via saliva may be less important than via nasal secretions in this age group.
Work supported by an investigator-led project grant from Pfizer.

Clinical Trial Registration (Please input N/A if not registered)
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Background

Neonatal sepsis is a major cause of neonatal morbidity and mortality especially for the hospitalised neonate. Late preterm (LP) neonates may have a different epidemiology of infections as compared with term neonates, and be at higher risk of infections due to their more immature immune system and the need for NNU-admission after birth. Little data about the risks and epidemiology of infection in LP are published. This study compares the demographics and pathogens responsible for sepsis in the LP infant through the neonIN surveillance network.

Methods

neonIN is an international web-based surveillance database for culture-proven neonatal infections. Cases of neonates with culture-proven sepsis from participating neonatal-units were extracted and analysed. Late-preterm neonates were defined as those with a gestational age of 33+0 to 36+6 weeks. Repeated growth of the same organism was considered the same episode if occurring within 7 days, or 10 days for Coagulase-negative staphylococci(CoNS) and fungi.

Results

507 LP neonates with culture-proven sepsis were identified. Median birth-weight and a median gestational-age was of 2180g(IQR: 1750-2560) and 34 weeks(IQR:34-36) respectively. Median postnatal-age at the time of infection was 11 days(IQR:3-26). Overall CoNS was the most common pathogen accounting for 40.2%(202) of all cases. When CoNS was excluded the most common pathogen was E. coli(55,10.9%) followed by Klebsiella sp(40.8%),GBS(32,6.4%) and Enterococcus sp(38,7.6%). Characteristics of all cases as well as pathogen distribution by country are displayed on the table below.
Conclusions

LP neonates are vulnerable to infection. The closed setting of the neonatal intensive-care and the immunologic immaturity of LP infants make them susceptible to nosocomial infections and they appear to have a distribution of pathogens similar to that of more preterm infants rather than that of term infants.
EMPIRICAL ANTIBIOTIC TREATMENT FOR LOWER RESPIRATORY TRACT INFECTIONS IN A TERTIARY PAEDIATRIC HOSPITAL- THE OUTCOME OF PAEDIATRIC ANTIMICROBIAL STEWARDSHIP

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Background

With increasing antimicrobial resistance worldwide, it is imperative to rationalise the use of existing antimicrobials. Stewardship programmes are useful tools to improve prescribing. A paediatric antimicrobial stewardship (AMS) programme was implemented in Bristol Children’s Hospital in 2016. From this prospective survey we report the changes to the empirical antibiotic use for lower respiratory tract infections.

Methods

Data were collected prospectively weekly from August 2016 to January 2018 on all antimicrobials prescribed in Bristol Children’s hospital on the paediatric medical, surgical and adolescent wards. Two periods of 5.3 months were selected to compare empirical treatment of lower respiratory tract infections (LRTIs) at the beginning of the programme (1.8.16-11.1.17) and 1 year later (1.8.17-11.1.18). Data were collected in REDcap and analysed in Excel and Stata (version 15). The AMS programme includes weekly audit and feedback, education sessions, and update of antimicrobial guidelines (end of period 2).

Results

There were 157 antimicrobial prescriptions for LRTIs across the two periods (73 in 1, 84 in 2). The mean number of antimicrobials for LRTI fell from 1.66 in period 1 to 1.55 in period 2, p 0.4. A similar number of antibiotics were intravenous in each time period (55% in period 1 and 58% in 2).

The patterns of antibiotic prescribing changed. The co-amoxiclav prescriptions fell from 42.5% (31/73) to 22% (19/85), p 0.006. The proportion of patients on a macrolide fell from 24.7% (18/75) to 9.3% (8/86), p 0.009.

Conclusions
Changes in prescribing practice are difficult to establish, but this prospective survey demonstrates that implementation of an AMS programme facilitates changes to enable better antibiotic prescribing.
INTRACRANIAL COMPLICATIONS OF ACUTE SINUSITIS AND MASTOIDITIS: A 14-YEAR REVIEW OF 25 CASES

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Background

Intracranial complications of sinusitis and mastoiditis are rare but can result in severe morbidity and mortality.

Methods

Retrospective study of children admitted with intracranial complications of sinusitis and mastoiditis during 14 years (Fev-04 to Jan-18). Records were reviewed for demographic data, clinical features, intracranial complication, microbiologic data, antimicrobial therapy, surgery and outcome.

Results

A total of 25 records were reviewed.

In the sinusitis group (n=15), 9 were male, median age was 12 years (4-17). Intracranial empyema was present in 11, cerebritis in 6 and meningitis in 6. Isolated microorganisms: S. pyogenes (n=3); S. constellatus (n=2); Peptostreptococcus micros (n=2); and single cases of S. intermedius, S. anginosus, H. influenzae, G. morbillorum and Fusobacterium nucleatum. Fourteen children underwent surgery.

In the mastoiditis group (n=7), 6 were female, median age was 5 years (1-6). Intracranial complications were thrombosis (n=6) and intracranial empyema (n=3). S. pyogenes was isolated in 1. Surgery was performed in 6 patients.

In the group with both infections (n=3), all were male, median age was 1 year. There were 2 cases of intracranial thrombosis and intracranial empyema. S. pyogenes was isolated in 1. All children underwent surgery.
The most common symptoms were fever (n=25), headache (n=17) and vomiting (n=15). All children received intravenous antibiotics. The preferred initial regimen was ceftriaxone, vancomycin and metronidazole.

Persistent sequelae were evident in 1/24 (vision loss).

No deaths occurred.

Conclusions

There were more suppurative complications in sinusitis and thrombosis in otomastoiditis. Bacterial species were isolated in 11 and infections were polymicrobial in 2. *S. pyogenes* was the most common pathogen, isolated in 5 and anaerobic organisms were recovered from 4. All received antibiotic treatment and 23/25 underwent surgery. The prompt medical and surgical management may have contributed to the favorable outcomes observed.
AGE-ADJUSTED SEPSIS-3 CRITERIA LACK PROGNOSTIC ACCURACY IN CHILDREN VISITING THE EMERGENCY DEPARTMENT WITH SUSPECTED BACTERIAL INFECTION

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Background

Recent attempts to translate Sepsis-3 criteria to children have been restricted to PICU patients only and did not target children visiting emergency departments (ED). We compared the prognostic value of Sepsis-3 criteria with SIRS criteria in children visiting the ED with suspected bacterial infection, and studied whether the addition of lactate would increase prognostic accuracy.

Methods

Non-academic, single-center, retrospective study in children admitted with suspected bacterial infection between March 2013 and January 2018, defined as initiation of antibiotic therapy within 24 hours after ED entry. Age-adjusted quick SOFA score (respiratory rate, mental state, systolic blood pressure), quick PELOD-2 score (mental state, blood pressure, heart rate), and both scores including lactate were compared to SIRS criteria. Outcome measure was mortality or PICU transfer.

Results

867 ED visits met inclusion criteria (474 (55%) male; median age 2.5y, IQR 8m-6y), of which 58 (6.7%) visits resulted in death or PICU transfer. Quick SOFA score was the best, yet poor, predictor for adverse outcome (AUC 0.56, 95% CI 0.47-0.64, not significant) compared to quick PELOD-2 score (AUC 0.53, 0.45-0.61) and SIRS (AUC 0.53, 0.45-0.60). The addition of lactate as scoring variable did not improve prognostic accuracy.

Conclusions

The currently proposed risk-stratification tool of Sepsis-3 criteria, the quick SOFA score, lacks prognostic accuracy in our cohort of children visiting the ED for suspected bacterial infection.
infection. Future studies in larger groups should identify bedside variables suitable for risk-stratification. We urge pediatric sepsis task forces to translate Sepsis-3 criteria into criteria applicable to both PICU and ED patients.
Recent measles outbreak in childhood population in Western Attica

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Background

The spread of measles across Europe has recently reached Greece, which is now facing an ongoing epidemic, the first since the outbreak of 2009. With the present study we aim to present the main epidemiological features of the current outbreak among children in our region, since the beginning of the epidemic in June 2017.

Methods

All probable and confirmed cases diagnosed in the Paediatric Department of our hospital serving a large population of Western Attica, were reviewed. Nationality, age, vaccination status, cause of admission, diagnostics and complications were recorded.

Results

As of January 2018 70 cases were recorded. The vast majority were Greek Roma children (89%), while the rest were non-minority Greek children (3%) and Syrian refugees (8%). In terms of age, were infants (7%), children between 1 and 12 years old (86%) and adolescents (7%). 67 out of 70 (96%) were completely unvaccinated while the rest were partially immunized.

Fifty three patients (72%) were hospitalized in our clinic. Main causes were prolonged and unrecessive fever, reduced feeding, respiratory distress and febrile seizures. Among hospitalized children 23 had complications such as ear (49%) and lower respiratory tract infections (44%) and gastrointestinal symptoms (11%), while less commonly hepatitis, myositis and pancreatitis were noted (1% to 2%). Only 12 cases were laboratory confirmed (serology and PCR of pharyngeal swab) at the beginning of the epidemic, while the rest were clinically diagnosed due to typical features and contact history.

Conclusions

Measles, although a vaccine preventable disease, is still a major cause of morbidity in populations with suboptimal vaccination coverage such as Roma communities. Vaccination strategies in this susceptible population are imperative.
Clinical Trial Registration (Please input N/A if not registered)

N/A
SERIOUS COMPLICATIONS TO SINUSITIS IN CHILDREN UNDER FIVE YEARS OLD ARE STILL A CHALLENGE AFTER THE INTRODUCTION OF PNEUMOCOCCAL CONJUGATE VACCINE IN STOCKHOLM

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⁵Public Health Agency of Sweden, Solna, Stockholm, Sweden
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⁷Karolinska University Hospital, Astrid Lindgren Children’s Hospital, Stockholm, Sweden

Background

Previous research has shown a decrease in hospital admissions due to sinusitis in children in Stockholm after the introduction of PCV in 2007. The objective of this survey was to analyse the rate of serious complications - postseptal orbital complications and surgery - to sinusitis in hospitalized children under five years old in Stockholm County after the introduction PCV.

Methods

This was a population-based, descriptive observational survey with retrospectively collected data from 1 July 2008 to 30 June 2016 in Stockholm County. Tertiary care admissions of children with a discharge diagnosis of sinusitis and related complications were reviewed and compared to the four years prior to the introduction of PCV.

Results

217 children were admitted, for a yearly incidence of 22.4 per 100,000 for boys and 14.6 for girls. CT-verified postseptal orbital complications (orbital cellulitis, subperiostal abscess or orbital abscess) occurred in 29 children (13%) and surgery was necessary in nine (4%), five girls and four boys. There were 53 positive bacterial cultures from blood, nose or surgical site in 37 children. *Streptococcus pneumoniae* was found in two blood and 12 nasal cultures, but in none of the children with postseptal complication or surgery, where *Streptococcus pyogenes* (n=4), *Haemophilus influenzae* (n=3) and *Staphylococcus aureus* (n=1) was found.

Conclusions
This study confirmed a decrease of hospital admissions for children with sinusitis by 50% compared to the four years preceding the introduction of PCV in Stockholm County. The number of postseptal complications and surgeries were still low, although increased in relation to number of admissions. Other pathogens than *Streptococcus pneumoniae* caused the most severe cases in the PCV era.
ASSESSING THE ONGOING IMPACT OF ROTAVIRUS VACCINATION IN THE UK

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³Public Health England, South West Regional Laboratory, Bristol, United Kingdom

Background

The United Kingdom added rotavirus vaccine (Rotarix GlaxoSmithKline) to the national immunisation schedule in July 2013. We reported significant reductions in rates of disease after the first year of vaccination with a smaller fall in the second year. We have continued active surveillance to now report the epidemiological trends for four years after vaccine introduction.

Methods

During the 2012-2017 rotavirus seasons, children presenting to our regional paediatric emergency department with gastroenteritis symptoms (>2 loose stools and/or >1 episode of vomiting in the last 24 hours) had stool virology analysis (real-time PCR), severity assessment and clinical outcome recorded.

Results

Adjusting for an overall rise in rates of attendance; the number of gastroenteritis attendances and admissions remained half of that in the pre-vaccine era (Table 1). In 2017 the proportion of rotavirus positive samples plateaued at 10%.

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Total ED attendances</td>
<td>16709</td>
<td>15816</td>
<td>16134</td>
<td>18305</td>
<td>20157</td>
<td>23652</td>
<td></td>
</tr>
<tr>
<td>No. Attendances (%all attend)</td>
<td>1464 (8.8)</td>
<td>1239 (7.8)</td>
<td>706 (4.4)</td>
<td>863 (4.7)</td>
<td>852 (4.2)</td>
<td>1145 (4.8)</td>
<td></td>
</tr>
<tr>
<td>Proportion attendances admitted</td>
<td>20%</td>
<td>23%</td>
<td>19%</td>
<td>24%</td>
<td>20%</td>
<td>19%</td>
<td></td>
</tr>
<tr>
<td>No. Admissions (%all attend)</td>
<td>297 (1.8)</td>
<td>288 (1.8)</td>
<td>137 (0.8)</td>
<td>204 (1.1)</td>
<td>174 (0.9)</td>
<td>216 (0.9)</td>
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<tr>
<td>Percentage attendance samples RV+ve</td>
<td>54</td>
<td>65</td>
<td>36</td>
<td>30</td>
<td>10</td>
<td>11</td>
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</tbody>
</table>

Conclusions
In the fourth year of rotavirus vaccination in the UK, there have been sustained reductions in numbers of hospital attendance and admissions consistent with those seen in the first year after introduction. With high levels of vaccine coverage in the UK we are not seeing evidence of biennial cycling as in the USA.

Clinical Trial Registration (Please input N/A if not registered)
ESPR18-1080
SCIENCE AND EDUCATIONAL TRACK

E-PARTER DISCUSSION SESSION 02: PUBLIC HEALTH AND EPIDEMIOLOGY

CHILD MORBIDITY AND DISEASE BURDEN IN REFUGEE CAMPS OF MAINLAND GREECE
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Greece ¹Infectious Disease Unit, 3rd Department of Pediatrics, Medical Faculty,
Aristotle University School of Health Sciences, Hippokration General Hospital, Thessaloniki,
Greece.

Background

The crisis conflicts in Syria have forced a lot of people to relocate and stand in refugee camps of mainland Greece. Our aim was to assess disease burden in two camps of northern Greece during a six month winter period and to compare this burden between different age groups.

Methods

Refugees of all ages with health problems were examined daily by specialty doctors and cases were classified in two categories, infectious or non-infectious. Furthermore, they were stratified according to the site of the disease, the age group and gender.

Results

A total of 2631 patients were examined. Of these, 9.8% were infants, 12.7% toddlers, 13.4% children and 7.9% adolescents. The rest 1453 (55.2%) were adults. Based on gender, 1269 (48.2%) of the refugees were male and 1362 (51.8%) were female. Most of the visits (58.38%) were due to infectious diseases. The most common site of communicable disease was the respiratory system (37.5%), followed by various skin disorders (12.8%), the urinary tract (3.9%) and gastrointestinal system (3.7%). Non-infectious diseases were mostly due to cardiovascular (8.0%), gastrointestinal (5.3%) obstetrics-gynecological (3.5%) and surgical (2.4%) causes. Infants, toddlers and children suffered more frequently from respiratory infections, while in adolescents and adults non-infectious diseases were more common (p-value<0.001). Toddlers and children were more likely to become ill in comparison to infants, whereas infants were more likely to get sick compared to adolescents and adults.
Conclusions

During a winter period, infectious diseases especially of the respiratory tract are the main reason for care seeking among refugees in Greek camps, with toddlers suffering more than other age groups. Overall mortality and referral percentage were very low indicating that adequate primary care is provided in this newly established refugee hosting model.

Clinical Trial Registration (Please input N/A if not registered)
ESP18-1095
SCIENCE AND EDUCATIONAL TRACK

E-POSTER DISCUSSION SESSION 12: SEVERE BACTERIAL INFECTIONS

SERIOUS INFECTIONS IN ADOLESCENTS IN EUROPE: SYNDROMIC PRESENTATION, CAUSATIVE MICROORGANISMS AND OUTCOMES (“THE EUCLIDS PROJECT”)

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²Health Research Institute of Santiago, Genetics- Vaccine- Infectious Diseases and Paediatrics, Santiago de Compostela, Spain
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⁵Medical University of Graz, Paediatrics, Graz, Austria
⁶Medical Research Council Unit, Medical Research Council Unit, Banjul, The Gambia
⁷University of Liverpool Institute of Infection and Global Health, Clinical Infection Microbiology and Immunology, Liverpool, United Kingdom
⁸Radboud Institute for Molecular Life Sciences, Department of Pediatric Infectious Diseases and Immunology, Radboud, The Netherlands
⁹University Children’s Hospital Bern, Paediatrics, Bern, Switzerland
¹⁰Erasmus MC-Sophia Children’s Hospital University Medical Center, Paediatrics, Rotterdam, The Netherlands
¹¹Great North Children’s Hospital, Paediatrics, Newcastle upon Tyne, United Kingdom
¹²University Medical Centre Nijmegen, Paediatrics, Nijmegen, The Netherlands
¹³Imperial College of London, Paediatrics, London, United Kingdom

Background

There is limited information to define the current burden of infectious diseases in adolescents. We aimed to describe the clinical characteristics and outcomes of a hospital-based cohort of adolescents admitted for a serious focal infection (SFI) and/or sepsis, recruited to a multi-centre study across Europe.

Methods

The clinical data of patients aged 10-18 years old with sepsis or serious focal infection and prospectively recruited to the EU Childhood Life-threatening Infectious Disease Study (EUCLIDS) from July 2012 to December 2016 were analysed for this report.

Results

A total of 531 adolescents with a median age of 159.6 months (13.3 years old) (IQR = 43.8 m) were recruited. A 40.5% of patients (n = 215) had sepsis and a 59.3% (n = 315) had SFI.
The main focal infections were central nervous system infection (n=75, 14.1%), osteomyelitis (n=71, 13.4%), pneumonia (n=70, 13.2%) and skin and soft tissue infection (n=61, 11.5%). A causal microorganism was identified in 48.4% (n=257) of the total cases. The most prevalent bacterial causative agent was *Staphylococcus aureus* (n=107, 20.2%), followed by *Neisseria meningitidis* (n=31, 5.8%), *Streptococcus pneumoniae* (n=21, 4.1%) and Group A Streptococci (n=19, 3.6%). *Neisseria meningitidis* was the most common causative organism of CNS infection (n=21), severe sepsis (n=10) and septic shock (n=9). The overall mortality rate was 2.8% (n =14/494) and 14.7% of patients (n=78) were discharged with sequelae. A moderate to severe disability was reported in 44.2% of those.

**Conclusions**

Despite prompt and adequate treatment, sequelae and moderate to severe disability in survivors remain significant. Increased efforts to decrease the health and social burden of infectious diseases across childhood are urgently needed with particular focus on the prevention of *N. meningitidis* and *S. aureus* infections in adolescence.

**Clinical Trial Registration (Please input N/A if not registered)**

N/A
EVIDENCE OF EARLY IMPACT OF ROUTINE PAEDIATRIC IMMUNIZATION WITH 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINE ON ANTIMICROBIAL RESISTANT PNEUMOCOCCAL DISEASES


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3Pfizer Inc, Pfizer Innovative Health, Collegeville- PA, USA
4Pfizer Inc, Patient & Health Impact, New York, USA

Background

Pneumococcal diseases are an important cause of healthcare resource use, morbidity and mortality and antibiotic use around the world. Following the introduction of the 7-valent pneumococcal conjugate vaccine (PCV7), multiple studies have demonstrated reductions in antimicrobial resistant (AMR) *Streptococcus pneumoniae*. We reviewed the current evidence on the impact of the 13-valent pneumococcal conjugate vaccine (PCV13) on AMR in pneumococcal diseases.

Methods

A systematic literature review was conducted in PubMed (June 2008 to June 2017), searching on AMR associated with invasive pneumococcal disease (IPD), acute otitis media (AOM), empyema and/or nasopharyngeal carriage (NPC) in all age groups in randomized controlled trials or observational studies reporting results before and after PCV13 introduction, where vaccine uptake was at least 70% in the relevant country.

Results

From 2301 publications: 34 met inclusion criteria, 29 studies described the impact of routine PCV13 programs on AMR, 22 studies were from countries with only PCV13 in use, and 19 studies described impact on IPD. A substantial reduction in penicillin, cephalosporin or macrolide resistant IPD was observed in all age groups (Table). For IPD, reductions were primarily driven by reduction of vaccine serotype 19A. Similar findings for pneumococcal OM in children were described in 5 studies in France. Regarding AMR NPC, one randomised clinical study in Israel described significant reductions. Results remained unchanged in France and Norway in post-licensure observational studies with conflicting results in 2 Massachusetts studies. There were no studies reporting on AMR NPC in adults or on empyema.
Conclusions

Most studies found reductions in AMR pneumococcal diseases and NPC associated with PCV13 introduction, indicating that reductions in AMR are important to consideration of the overall public health value of introducing PCV13 into a national immunization program.

Systematic Review Registration (Please input N/A if not registered)

N/A
USE OF HISTAMINE-2 RECEPTOR ANTAGONISTS IS ASSOCIATED WITH INFECTION IN NEWBORNS HOSPITALIZED, BUT NOT NECROTIZING ENTEROCOLITIS AND MORTALITY: A SYSTEMATIC REVIEW AND META-ANALYSIS

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¹Federal University of Sergipe, Postgraduate Program in Health Sciences, Aracaju, Brazil
²Federal University of Sergipe, Medicine Department, Aracaju, Brazil
³Federal University of Sergipe, Department of Medicine, Aracaju, Brazil
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⁵Federal University of Sergipe, Post Graduate Nucleus in Medicine, Aracaju, Brazil

Background

Histamine-2 receptor antagonists (H2RA) have been commonly prescribed “off label” in neonate hospitalized in neonatal intensive care unit (NICU). Some studies showed that the use of H2RA may predispose to infections, necrotizing enterocolitis (NEC) and mortality in this population. This meta-analysis systematically examined the association between H2RA and infections, NEC and mortality in preterm infants.

Methods

A systematic review was made using PubMed, Web of Science and SCOPUS databases up to April 30, 2017. Publications were identified using the search terms “histamine-2 receptor antagonists”, “infection”, “necrotizing enterocolitis”, “mortality” and related terms. Forest plot test was used to graphically present the effect sizes and the 95% confidence interval for the six conditions/terms (infection; pneumonia; sepsis; NEC; urinary tract infection; mortality).

Results

Three case–control and three cohort study were included. Meta-analysis showed a significant association between infection and H2RA (RR of 2.13, 95%CI: 1.20–3.78). Specific analysis found higher incidence of sepsis (RR 2.39; 95%CI: 1.09-5.23; I² = 91%), pneumonia (RR 2.70; 95%CI: 1.41-5.19; I² = 0%) and urinary tract infection (RR 8.32; 95%CI: 2.32-29.91; I² = 91%) in H2RA neonates.

Conclusions

Exposure to H2RA is associated with increased risk of infections in preterm infants.

Systematic Review Registration (Please input N/A if not registered)

CRD42017060887
IMPORTED MALARIA IN MIGRANT CHILDREN NEW TO CANADA – A RETROSPECTIVE REVIEW TO INFORM THE VALUE OF PRE-DEPARTURE EMPIRIC MALARIA TREATMENT

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²University of Ottawa, Department of Family Medicine, Ottawa, Canada
³Children’s Hospital of Eastern Ontario, Division of Infectious Diseases, Ottawa, Canada

Background

Malaria is a common illness in migrants to the West. Hospital care, including intensive care unit stays, can result in significant financial costs. Pre-departure anti-malarial treatment of migrants to Canada from malaria-endemic countries could prevent morbidity and reduce costs to Canada’s universal health care system.

Methods

Health records for children diagnosed with malaria at the Children’s Hospital of Eastern Ontario were retrospectively reviewed from 2010-2017. Patient demographics, details of care, and costs of inpatient/outpatient care of malaria were determined and compared between migrants (immigrants/refugees) versus children who acquired malaria while traveling to visit friends and relatives.

Results

24 migrants and 9 VFRs with malaria were identified. 20/24 (83%) migrants and 9/9 (100%) VFRs had *Plasmodium falciparum* malaria; 18/24 (75%) migrants and 3/9 (33%) VFRs were from East Africa, and 5/24 (21%) and 6/9 (67%) were from West/Central Africa. Migrants were median 12.0 years (IQR 8.8, 14.0) versus VFRs 6.4 years (4.0, 11.0) (p=0.09). Time from arrival to Canada to onset of symptoms was similar between groups (migrants – median 5 days; VFRs – 3 days). Similar proportions of migrants and VFRs were admitted to hospital (80% and 71%) and admitted to intensive care (27% and 29%). Total costs of care for malaria over the study period were $174,485 CAD for migrants, and $61,656 CAD for VFRs.

Conclusions

A significant burden of malaria was found among migrant children shortly after arrival to Canada. Assuming a cost of empiric pre-departure lumefantrine-artesunate treatment for malaria of $3/person, the cost of treating all newcomers from Africa to Canada in the same 8-year period (194,267) would be ~$582,000CAD, just 3-fold higher than the cost of treating children at a single tertiary care center in Canada’s 6th largest city.
Background

The number of notified cases of Tick-Borne Encephalitis (TBE) in Sweden has been increasing the past years. This is despite the increased use of TBE-vaccine, which is not subsidized by the healthcare system. Stockholm County is a high endemic area and an earlier study has shown that low-income households have lower vaccination coverage even when at risk for TBE-exposure. Our study aim was to determine cost-effectiveness of subsidizing TBE vaccine in Stockholm County.

Methods

In three different cohorts with individuals aged 3, 40 or 60 years, long-term costs and health outcomes were modeled through a Markov model with two arms of comparison: current vaccination strategy and subsidized vaccination strategy. The Markov model predicts the costs and effects (in term of Quality-adjusted Life Years (QALYs)) over a 20 years time horizon. The primary results are presented as an incremental cost effectiveness ratio (ICER) which is the cost required to achieve one additional QALY with a subsidized strategy compared with current vaccination practice.

Results

Our results indicate that vaccination has the potential to be cost-effective as the cost per QALY is below conventional thresholds for cost-effectiveness. The younger the cohort is, the more benefit and less cost is predicted; and the lowest ICER is associated with subsidizing vaccination to the cohort of children.

Conclusions

Given the setting of Stockholm County, in terms of TBE-incidence and vaccination coverage, and applicable TBE-related health-costs our analysis indicates a low cost per QALY if offering free vaccinations doses to children 3-18 years old. To ensure an equal access to
information and vaccination in a child-cohort it should be given at the child-health care and in schools.

Clinical Trial Registration (Please input N/A if not registered)

N/A
C-REACTIVE PROTEIN CONCENTRATION CAN HELP TO IDENTIFY BACTEREMIA IN CHILDREN VISITING THE EMERGENCY DEPARTMENT: A SINGLE MEDICAL CENTER EXPERIENCE

J. YAN1, Y.H. Huang1
1Chiayi Chang Gung Memorial Hospital, Department of Pediatrics, Chiayi, Taiwan R.O.C.

Background

For febrile children that are evaluated in a pediatric emergency department (PED), blood culture can be considered the laboratory gold standard to detect bacteremia. However, high rates of negative, false-positive, or contaminated blood cultures in children often result in this testing being non-contributory. This study determined the factors associated with true-positive blood cultures in children.

Methods

This retrospective study was conducted at a tertiary medical center’s pediatric emergency department. The blood culture utilization reports were prepared by an infectious disease specialist and were classified as bacteremia, non-bacteremia, and contamination.

Results

We registered a total of 239,459 PED visits during the eight-year period, and 21,841 blood culture samples were taken. Of the laboratory test studies, higher C-reactive protein (CRP) levels and lower hemoglobin levels were observed in the bacteremia group compared to non-bacteremia plus contaminant groups (all p < 0.001). The cut-off value calculated for each age group was adjusted for better clinical usage and significantly improved the blood culture clinical utility documented in the following age groups: 0 to 1 years old(CRP level of 30(mg/L), odds ratio: 5.4, p<0.001), 1 to 3 years old(CRP level of 45(mg/L), odds ratio: 3.7, p<0.001), and 12 to 18 years old(CRP level of 50(mg/L), odds ratio:6.3, p=0.006).Using the CRP cut-off value established in this study, we could reduce the blood culture samples in the PED by 14,108 (64.6%).

Conclusions

This study provides new evidence that CRP may be a useful indicator for blood culture sampling in certain age groups and may help to improve the efficiency of blood culture in the pediatric emergency department.

Clinical Trial Registration (Please input N/A if not registered)

N/A
THE CLINICAL VALUE OF PLASMA HEPCIDIN LEVELS TO PREDICT BACTERIAL INFECTION IN FEBRILE CHILDREN

J. YAN¹, Y.H. Huang¹
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Background

Febrile children are frequently evaluated for the risk of bacterial infections in the pediatric emergency department (PER). Hepcidin is an acute phase inflammatory protein. This study determined the plasma hepcidin level in febrile children.

Methods

This study was conducted data pediatric emergency department and 123 febrile children was enrolled. Levels of plasma hepcidin were measured by enzyme-linked immunosorbent assay. We also evaluated the clinical characters and routine blood tests with the hepcidin levels.

Results

We have significant higher plasma hepcidin levels in bacterial enteritis (p = 0.026) and combined with urinary tract infection (p = 0.007). In addition, the hepcidin level had a significantly positive correlation with CRP level and length of hospital stay (R = 0.296, p = 0.001 and R = 0.213, p = 0.018).

Conclusions

This study provides evidence that higher plasma hepcidin levels in febrile children with bacterial infection and its level correlated CRP level and length of hospital stays. Thus, hepcidin level can be potentially utilized as a biomarker to identify febrile children with bacterial infection especially bacterial enteritis.

Clinical Trial Registration (Please input N/A if not registered)

N/A
Critical illness polineuropathy is a severe, life-threatening condition that may occur in ICU in patients of all age groups and all kinds of diseases. Our goal was to establish electrophysiological features of critical illness polineuropathy in children with meningococcal infection complicated with sepsis and meningococcemia.

Methods

We evaluated peripheral nervous system involvement in 14 critically ill children, admitted in ICU with meningococcal infection complicated with sepsis and meningococcemia. Age of the group varied from 4 months to 10 years. All patients undergo conduction studies and neurological investigation. Sensory and motor fibers of n. ulnaris et n. medianus, motor fibers of n. Tibialis and sensory fibers of n. Suralis were tested. Lowering of the amplitudes, conduction velocity slowing and asymmetry were accounted for the motor and sensory fibers.

Results

In 10 cases diagnosis of critical illness polyneuropathy (CIP) was established. Lesions mostly involved lower limbs nerves. Typical changes of the compound motor responses are presented on the Fig. 1. According to our data, severe course of CIP was seen in 40% of all cases. Average time of CIP onset in children was 5-7 days from the beginning of mechanical ventilation.

Conclusions

Critical illness polyneuropathy in children with meningococcal infection complicated with sepsis and meningococcemia is a severe condition which may lead to the disability of the patients. Average time of its onset is the 5-7 days from the beginning of the mechanical ventilation. More often sensory and motor fibers of lower limbs nerves are affected. Conduction studies is a valuable tool in diagnostic process in establishing the critical illness polyneuropathy in children with infectious diseases.

Clinical Trial Registration (Please input N/A if not registered)

N/A
ACCURACY OF XPERT MTB/RIF IN DIAGNOSING EXTRAPULMONARY TUBERCULOSIS IN CHILDREN

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2B J Wadia Hospital for Children, Pediatrics, Mumbai, India

Background

Aim: To assess the accuracy of Xpert MTB/RIF assay in diagnosing extrapulmonary tuberculosis (EPTB) in children.

Methods

Methods and Materials: A total of 182 children diagnosed to have EPTB were tested by Xpert MTB/RIF Assay from Dec 2014 to April 2017. The diagnostic accuracy, specificity and sensitivity of the Xpert assay was calculated as compared to TB culture.

Results

Results: 58(32%) had lymph node TB, 37(20%) had neuro TB, 36(20%) had bone TB, 31(17%) had pleural TB, 15(8%) had abdominal TB, 2(1%) had abscess, 2(1%) had congenital TB and 1 (1%) had disseminated TB. The specimens tested were 62(34%) biopsies, 38(41%) CSF samples, 29(16%) pleural fluid, 25(14%) pus, 13(7%) gastric lavage, 6(3%) ascitic fluid, 4(2%) fine needle aspirations, 1(1%) BAL, 1(1%) bone tissue, 1(1%) ET aspiration, and 2(1%) sputum samples. Xpert MTB/RIF was positive in 84(46.2%). Only 168 of the 182 children were tested with TB MGIT culture of which 75(44.6%) grew mycobacterium tuberculosis (MTB). Sensitivity and specificity of the Xpert MTB/RIF assay was 72% [60.9-80.9%] and 72% [62.2-80.2%] respectively when compared to MGIT; a Kappa coefficient of 0.44 [0.29-0.59] shows moderate agreement between the Xpert assay and MGIT (table 1).

Table 1: Sensitivity, specificity, Cohen's Kappa, p value and diagnostic accuracy of the Xpert MTB/RIF assay for types of EPTB

<table>
<thead>
<tr>
<th>Type of TB</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Cohen's Kappa</th>
<th>P value</th>
<th>Diagnostic Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal TB</td>
<td>50[15-85%]</td>
<td>83.33[43.7-97%]</td>
<td>0.35[0.25-0.95]</td>
<td>0.5</td>
<td>70[39.68-89.22%]</td>
</tr>
<tr>
<td>Bone TB</td>
<td>72.73[15.9-86.9%]</td>
<td>69.23[42.4-87.3%]</td>
<td>0.41[0.08-0.74]</td>
<td>0.38</td>
<td>71.43[54.94-83.67%]</td>
</tr>
<tr>
<td>Lymph Node TB</td>
<td>80.77[62.1-91.5%]</td>
<td>55.17[37.6-71.6%]</td>
<td>0.35[0.1-0.74]</td>
<td>0.05</td>
<td>67.27[54.1-78.19%]</td>
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**Neuro TB**

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<tr>
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<tbody>
<tr>
<td>Neuro TB</td>
<td>75(50.5-90%)</td>
<td>85(64-94.8%)</td>
<td>0.6(0.28-0.93)</td>
<td>0.5</td>
<td>80.56(64.97-90.25%)</td>
<td>0.5</td>
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**Pleural TB**

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<tbody>
<tr>
<td>Pleural TB</td>
<td>25(4.6-70%)</td>
<td>82.61(62.9-93%)</td>
<td>0.069(-0.3-0.4)</td>
<td>0.5</td>
<td>74.07(55.32- 86.83%)</td>
<td>0.5</td>
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</tbody>
</table>

**Conclusions**

**Conclusion:** Xpert MTB/RIF assay is a useful contribution to the diagnosis of EPTB. It also shows good concordance with TB MGIT results.
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13A. SCIENCE: PUBLIC HEALTH | EPIDEMIOLOGY

MORBIDITY OF PEDIATRIC REFUGEES IN THE AREA OF PIRAEUS, GREECE
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Title of Case(s)

MORBIDITY OF PEDIATRIC REFUGEES IN THE AREA OF PIRAEUS, GREECE

Background

During the current European refugee crisis starting in 2015, Greece, and particularly the area of Piraeus, hosted a large population of refugees. Children refugees constituted a considerable proportion of this population.

Case Presentation Summary

We prospectively recorded and evaluated the morbidity characteristics of pediatric refugees that presented in the pediatric emergency department (PED), were admitted in the pediatric clinic, or were evaluated in the Pediatric Neurology Department of our hospital during a 1-year period (01/10/2015-01/10/2016), by reviewing the available data from individual patient records.

A total of 93 children (mean age: 5 years, 71.2% male) were evaluated. The majority of them was Syrians (48.2%), living in camps in the port of Piraeus (55.2%) and reached the hospital with a public ambulance (46.1%). Fever was the main reason of presentation at PED (36%), followed by respiratory tract infections (17%) and gastrointestinal infections (16%). Data regarding patient and family history were unknown in most of the evaluated patients. No case of tuberculosis was identified. One relapsing case of malaria from P. vivax due to initial treatment failure was noted. Mean duration of hospitalization was 3.2 days. In a considerable proportion discharge was due to parents’ will. During hospitalization the typical laboratory and imaging tests were performed in the majority of the evaluated patients. Antibiotics for common community-acquired bacteria were administered in 39.7%. Follow up assessment was remarkably uncommon.

Learning Points/Discussion

The evaluated children refugees had common community-acquired infections, received common antibiotic agents and had short length of hospitalization. The morbidity of the evaluated children refugees can be considered as similar to the common pediatric seasonal morbidity. Of note, the majority of the evaluated patients were boys.
IMMUNISATION AGAINST HEPATITIS A IN MIGRANT CHILDREN: THREE VACCINATION STRATEGIES, A RETROSPECTIVE STUDY

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Background

Hepatitis A is endemic in many countries. Swiss guidelines recommend vaccinating patients native from endemic areas who might temporarily return. In Geneva’s Hospital, migrant children are screened and vaccinated if seronegative. Since Hepatitis A prevalence is decreasing worldwide, more children are seronegative at arrival, questioning the benefits of systematic serology. Other Swiss hospitals vaccinate systematically, regardless of serostatus. This study’s aim is to assess migrant children’s immunity according to origin and age, and the cost-effectiveness of different immunization strategies.

Methods

We retrospectively analysed 329 children’s serostatus (aged 1 to 16) between 2012 and 2015, using ELFA (Enzyme-Linked Fluorescent Assay) method. Serology and vaccine costs were based on local prices. Groups were compared with chi-squared test and the age-seropositivity relationship was studied with linear regression.

Results

The predominant regions were the Eastern Mediterranean and European Regions with mostly negative serologies (71% and 83%) and the African Region with mostly positive serologies (79%). Immunity varied depending on birth country. Regardless of regions, seropositivity increased with age (P <0.001). The most cost-effective vaccination strategy was an individualized approach based on age and origin, reducing costs by 2% compared to systematic serology and by 17% compared to systematic vaccination.
Conclusions

Many migrant children older than 5 years old are seronegative and at risk of clinical infection. New guidelines according to age and origin should be defined to reduce immunization costs. We recommend systematic vaccination for patients younger than 5 years old or native from low endemicity areas (≤ 25% of seropositivity). For the others, we propose serology-based vaccination.
Prevention of common sports related infections in children

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Background

Sports activations in children can result of different infectious diseases. Basketball, football, handball or volleyball children players or individual children sports fighters karate or judo, children tennis players or skiing competitors should be encouraged to practice good hygiene, avoid sharing towels or other personal items, and inform coaches about active skin or respiratory and gastroenterology or other infections.

Methods

Information on age, gender and municipality of residence for the participating children was retrieved from the Bosnian National Health Data and Children Sport Registry in Bosnia and Herzegovina. Primary care pediatrician may appear to be peripheral in this athletic milieu of organized sports, leadership from physicians has always been welcome and expected regarding issues of public health and safety. Information on one or more of the included infectious in children outcomes at baseline and follow-up was available in a total of 100 children in the intervention group and 100 children in the control group without active sports activity.

Results

All children athletes have an increased risk of cutaneous infections, respiratory, meningoencephalitis and gastroenterology infections all of them twice or three times. In both team and individual sports the skin is exposed to a range of infectious organisms in the most cases 44%. Respiratory infectious are second with 37%, gastroenterology infectious disease are third with 12%, meningoencephalopathy about 1 % and others 6%.
Conclusions

Infectious pathogens include those spread by skin contact, by contaminated food or water species, by respiratory droplet, by airborne particles or by certain vectors in infectious disease in children. Although this research focuses on organized sports as a risk factor for disease transmission among children, the same concerns apply to adults.

Clinical Trial Registration (Please input N/A if not registered)

N/A
THE EPIDEMIOLOGIC CHARACTERISTICS AND ASSOCIATED METEOROLOGICAL RISK FACTORS OF JAPANESE ENCEPHALITIS IN TAIWAN

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Background

Japanese encephalitis (JE) is one of the severe vector-borne viral encephalitis worldwide. With the establishment of JE surveillance and vaccine use, the persistent transmission of Japanese encephalitis virus (JEV) occurred in Taiwan. The purpose of this study was to assess the epidemiologic characteristics and the associated meteorological factors of JE in Taiwan.

Methods

We analyzed data reported to Taiwan Center for Disease Control (Taiwan CDC). Meteorological data were obtained from the Taiwan Central Weather Bureau. The relationships between weather variability and the incidence of JE in Taiwan were determined via Poisson regression analysis and a case-crossover methodology.

Results

Between 2000 and 2014, a total of 379 confirmed JE were reported to Taiwan CDC. The annual incidence rate of JE cases was from 0.07 per 100,000 in 2000 to 0.18 per 100,000 in 2007 (0.13 on average). The age distribution shifted from mainly children to adults, with 90% of confirmed JE cases older than 20 years. Male to female ratio was 1.5:1. The eastern region had highest incidence rate in Taiwan. The incidence of JE showed significant seasonality, with the majority of cases occurring in summertime (for oscillation, p< 0.001). The number of JE cases started to increase at temperatures of 22°C ($r^2 = 0.88$, p< 0.001). Similarly, the number of JE cases began to increase at a relative humidity of 70-74% ($r^2 = 0.75$, p< 0.005).

Conclusions

The JE remains a prominent public health problem in Taiwan. The number of JE cases was positively associated with mean temperature and relative humidity in the period preceding the infection.
Title of Case(s)
Aseptic meningitis in children with herpes zoster

Background
Neurological complications related with varicella zoster virus (VZV) reactivation is very uncommon, particularly in immunocompetent children. Only a few cases were described in the literature.

Case Presentation Summary
During 2017 at Lviv Infection Diseases Hospital we observed 3 cases aseptic meningitis in children with herpes zoster. Three boys (6 y.o., 12 y.o. and 17 y.o.) were kept under observation. All patients presented with a 1-2 days history fever, headache, photophobia, vomiting, clinical signs of meningeal irritation followed by pain and rash in different regions on trunk. Blistering and painful rash onset a median of 2 days (range 0 to 6 days) after meningeal symptoms occurred. The CBC counts, basic metabolic panels results and serum immunoglobulin’s (IgM, IgA, IgG) levels were normal. CSF analysis revealed a moderate leukocytes cells counts of 366,3±23,6 cells/μL (96,5% lymphocytes, 2% monocytes, 1,5% segmented neutrophils) and a normal total CSF protein levels (0,61±0,21 g/L). CSF were positive for VZV and negative for enterovirus and HSV by real-time PSR. Acyclovir was administered IV at a dose of 10 mg/kg three times a day for 10 days. The therapy was highly effective and the all patient's condition improved.

Learning Points/Discussion
The incidence of neurologic complications in herpes zoster is not well described in the literature. Aseptic meningitis is one of the rare but possible complications of VZV reactivation.
In Nigeria, *Tunga penetrans* infestation is a common cutaneous disease of neglected populations and its impact on their health status and quality of life is severe. Study on prevalence, health impact, and knowledge and attitude towards management practices of infestation was conducted in southwestern Nigeria.

Methods

We performed a community-based cross-sectional study in two local government of Lagos state and participants were examined for the presence of tungiasis and disease-associated morbidity.

Results

Of 340 participants enrolled in the study, 248 (72.9%) were infested with average lesion of 769. Infestation was age-dependent (*p*<0.05). Younger age group (1-10 year) and male participants were heavily infested with average lesion of 206 (16-214) and 453 (12-463) respectively. Finding on sex pattern of disease was slightly comparable (75.0 (67.1 – 81.6) vs 71.4 (64.3 – 77.5); *p*>0.05). Distribution and abundance of infestation vary with locations. Majority of the infested individuals are suffering from pain and itching that result in loss of sleep and productivity. Also, large proportion of infested persons were characterized with oedema (34.7%), desquamations of skin (54.8%), chronic lesion (15.7%) and 15.3% deformation of nail. The knowledge of our study participants about the disease is poor, 15.6% and 65.6% associated *T. penetrans* and sand respectively as the causative agent of the infestation. About 30.3% applied kerosene to relieve the induced pains.

Conclusions

This study underscores the public health implication of sand flea infestation in Nigeria and the need to be categorized as neglected tropical disease is exigent to receive necessary intervention.
Background

Acute respiratory infection (ARI) is the most common reason for admission to paediatric wards in Viet Nam. However, few studies have explored the ARI disease spectrum observed in central Viet Nam or differences between primary (district), secondary (provincial) and tertiary (national) level hospitals. We conducted this study to assess the ARI disease spectrum, duration of hospitalisation and outcome in children hospitalised with an ARI in Viet Nam.

Methods

We conducted a retrospective descriptive study of ARI admissions to primary (Hoa Vang District Hospital), secondary (Da Nang Hospital for Women and Children) and tertiary (National Hospital of Paediatrics in Ha Noi) level hospitals in Viet Nam over a 12-month period (1st September 2015 to 31st August 2016).

Results

ARIs accounted for 27.9% (37,436 / 134,061) of all paediatric admissions; nearly half (47.6%) of all children admitted to Hoa Vang District Hospital. Most (64.6%) children hospitalised with an ARI were <2 years of age. Influenza/pneumonia accounted for 69.4% of admissions; tuberculosis for only 0.3%. Overall 284 (0.8%) children died; most deaths (269/284; 94.7%) occurred at the tertiary referral hospital. The average duration of hospitalization was 7.6 days (median 7 days). The average direct hospitalization cost per ARI admission was 157.5 USD in Da Nang Provincial Hospital. In total, 62.6% of admissions were covered by health insurance.
Conclusions

ARI is a major cause of paediatric hospitalization in Viet Nam, characterized by prolonged hospitalization for relatively mild disease. There is huge potential to reduce unnecessary hospital admission and cost.
ENCOURAGING RATIONAL ANTIBIOTIC USE IN CHILDHOOD PNEUMONIA - FOCUS ON VIET NAM AND THE WESTERN PACIFIC REGION

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Background and Objective

Pneumonia is the biggest killer of children. Optimal management of childhood pneumonia is challenging in settings where clinicians have limited information regarding local pathogen and drug resistance profiles. This frequently results in unnecessary and poorly targeted antibiotic use. Restricting antibiotic use is a global priority. We conducted a comprehensive literature review to explore the antibiotic resistance profile of bacteria associated with pneumonia in the Western Pacific region. We also considered current management practices, diagnostic dilemma factors that increase unnecessary antibiotic use; offering some suggestions to address.

Methods

We searched the PubMed, Google Scholar and Embase databases using the search terms: antibacterial agents OR antibiotics OR drug therapy AND community acquired pneumonia OR acute respiratory tract infection AND child OR children OR childhood. Manuscript titles and abstracts were reviewed to identify original research papers that included children less than 5 years of age with pneumonia; with a geographic focus on Viet Nam and the Western Pacific Region.

Learning Points Discussion

Antibiotic use generates selective pressure that increases the prevalence of drug resistant strains; hence strategies to improve rational antibiotic use are important to protect it as a precious resource. The main factors that promote unnecessary antibiotic use in the Western Pacific Region, using Viet Nam as an exemplar, are listed in table 1

Optimal child pneumonia management presents an opportunity to reduce excessive antibiotic use in the Western Pacific Region. However, encouraging the rational use of antibiotics requires education of health-care professionals, facilitation of cultural change, improved clinical guidance and the establishment of functional microbiology laboratories to monitor disease etiology and drug resistance patterns; together with the removal of inappropriate incentives and effective enforcement of national regulations to restrict antibiotic use in health care and agriculture.
Table 1. Physician related factors that contribute to excessive antibiotic use in the Western Pacific region

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<th>Factor identified</th>
<th>Examples from the Western Pacific Region</th>
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| Professional hierarchy                  | - Junior physicians adopt the prescription habits of senior physicians without rigorous discussion or review of the evidence.  
- In Viet Nam, inappropriate antibiotic use is a particular problem in obstetrics, gynecology and surgery wards where professional hierarchy is most pronounced. |
| No consideration of "societal risk"     | - Doctors and patients often prefer newer and more expensive antibiotics, which are considered more "powerful".  
- Physicians provide antibiotics to help individual patients; potential societal risks are not considered.  
- In the absence of functional microbiology services, physicians have limited information on local drug-resistance profiles and the impact of excessive antibiotic use; |
| Perceived patient/parent expectation    | - Doctors strive for patient satisfaction and if patients request antibiotics it is usually prescribed. In Korea, 73% of doctors prescribe antibiotics for a common cold if requested by parents. In Malaysia, 67% of patients believe that antibiotics help viral infections.  
- Doctors have no time or motivation to explain the rationale for not using antibiotics. |
| Fear of poor patient outcome or litigation | - Fear of poor patient outcomes is often listed as a key motivation for the use of broad-spectrum antibiotics by doctors.  
- Fear of litigation is not yet a major driver in the Western Pacific, but is likely to become a more prominent factor with increased development.  
- Near universal use of empiric broad spectrum antibiotics is common in places with poor microbiology services.  
- In Viet Nam, antibiotic use was reduced in hospitals with functional microbiology laboratories. |
| Inadequate microbiology services        | - Doctors’ prescribing habits is influenced by personal income generated and incentives provided by pharmaceutical companies. In China, as in many other Western Pacific countries, drug prescriptions supplement a doctor’s income.  
- In South Korea, drug dispensing by health care workers was banned in 2000, resulting in major reductions in antibiotic use. |
THE POWER OF SURVEILLANCE DATA TO CHANGE PUBLIC HEALTH POLICY AND PRACTICE IN RARE PAEDIATRIC CONDITIONS ACROSS BORDERS AND CONTINENTS

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Background

National paediatric surveillance units (PSUs) from 11 countries from Europe, Australia and North America form the International Network of Paediatric Surveillance Units INoPSU founded in 1995. This network is an invaluable resource for paediatric public health research and monitoring of rare conditions in children with a focus on infectious diseases. International collaboration among PSUs includes conducting similar studies in several countries by sharing protocols, publishing jointly and thus advancing public health policy development. INoPSU membership is open to all PSUs worldwide.

Methods

Researchers and public health agencies use PSUs to study rare conditions in children, including emerging problems. PSUs collect data through comprehensive national networks of paediatricians and/or paediatric clinics with high return rates. All PSUs use a similar surveillance method that applies active case finding and notification on a monthly or weekly basis. Both, negative and positive reports are collected. Positive reports are followed by an specific questionnaire that asks for detailed demographic, epidemiological as well as diagnostics and clinical data.

Results

Several countries have adopted catch-up vaccinations for pertussis in adolescents and persons with close contact to infants (Australia, Germany, New Zealand, the Netherlands, Switzerland). In response to the emerging Zika epidemic several countries rapidly implemented surveillance of congenital Zika syndrome and microcephaly (Australia, Canada, New Zealand, UK). Several countries revised guidelines for toxoplasmosis screening during pregnancy (Ireland, Switzerland, UK). The study of haemolytic uremic syndrome helped understand the variability in shiga-toxin producing serotypes across nations (Australia, Canada, Germany, New Zealand, Portugal, Switzerland, UK).

Conclusions

Studies performed through PSUs have contributed significantly to the advancement of paediatric public health across the globe. Dozens of papers have been published in peer-reviewed journals and many national and international guidelines and recommendations cite them.
Clinical Trial Registration (Please input N/A if not registered)
Title of Case(s)

Concurrent infection with dengue fever, scrub typhus and viral hepatitis A in a young girl

Background

Acute undifferentiated febrile illness is the most common presenting symptom in children during the monsoon in the endemic areas. Incidence of both vector- and water-borne diseases are highest during these seasons, co-infections of dengue with typhoid, malaria, leptospirosis, scrub typhus and other arboviruses can occur in endemic areas. Co-infections of dengue, scrub typhus and viral hepatitis A has not been reported earlier.

Case Presentation Summary

A 4 year old female child was admitted in with complaints of fever 4 days prior to admission, pain abdomen and vomiting 3 days prior to admission. Respiratory rate was 66 breaths/minute, Pulse rate of 134 beats/minute, Blood pressure 80/60 mmHg, CFT of 4 seconds. Child was having pallor, icterus, periorbital and pedal edema. Per abdomen examination revealed distension and hepatomegaly. In view of shock and respiratory distress, child was started on non invasive ventilatory support. Initial laboratory results revealed low platelet counts with raised hematocrit, markedly deranged liver function tests. At this stage possibility of dengue fever was kept and child managed with intravenous fluids and NIV support. However as child continued to have high grade fever and reduced platelet counts over next 3 days. At this time child’s work up for other causes was done. Reports came out to be positive for scrub typhus (ELISA), for which oral Azithromycin was added. Fever subsided but LFTs didn’t show much improvement. Blood samples were sent for viral markers. Anti HAV came reactive. After 14 days of hospital stay child was discharged.

Learning Points/Discussion

In case of coinfection with dengue and scrub typhus, vigilant monitoring of vitals, platelets transfusion, and timely treatment with doxycycline/azithromycin are necessary. This possibility of concurrent infection should be thought early enough to decrease morbidity and possibly mortality as well.
NAIVE B-CELL OUTPUT IN HEALTHY AND HIV-INFECTED CHILDREN FROM SOUTH AFRICA AND THE UK


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Background

In this study, we aimed to quantify healthy ranges of naïve B-cell output and KREC (kappa-deleting recombination excision circles) levels. Additionally, we sought to determine the dynamics of naïve B-cell output in ART (anti-retroviral therapy)-treated HIV-positive children in South Africa and the UK.

Methods

Naïve B-cell output was quantified using a mathematical model combining KREC levels to reflect B-cell emigration into the circulation, flow cytometry measures of naïve un-switched B-cells and their rates of proliferation using the marker Ki67. Samples were from a Child Wellness Clinic (n=288 HIV-uninfected South African children, 2 weeks – 12 years), the Children with HIV and Early Antiretroviral Therapy (CHER) trial (n=218 HIV-infected South African children, 7 weeks - 8 years) and from GOSH (Great Ormond Street Hospital) (n=16 HIV-uninfected British children, 6 - 18 years).

Results

Naïve B-cell output increases from birth to 1 year, followed by a decline. Comparison to British children revealed higher naïve B-cell outputs in South African children (p=0.013). HIV-infected children on ART had higher naïve B-cell outputs than their uninfected counterparts (p=0.010), and there was a trend toward lower naïve B-cell output with ART-interruption compared to continuous ART.

Conclusions

The results of this study suggest that HIV in the context of ART can influence B-cell output, which differs between UK and African children. Further work is required to fully understand the causes and consequences of HIV on B-cell dynamics in children.

Clinical Trial Registration (Please input N/A if not registered)
TO STUDY THE STATUS OF HIV DISCLOSURE IN CHILDREN AND ADOLESCENTS

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Background

Disclosure to HIV-infected children regarding their diagnosis is important as expanding numbers of HIV-infected children attain adolescence and may become sexually active. HIV disclosure is an important step towards long-term disease management and necessary for the transition from pediatric care into adolescent.

Methods

Cross sectional study carried out on 144 caregivers of Children and adolescents aged between 6 to 16 years of age attending the pediatric ART clinic. The subjects were enrolled consecutively and were interviewed using a structured questionnaire after taking written informed consent. The questionnaire included information on the demographic details, the disclosure status of HIV infection in children and perceptions about disclosure of status to the child.

Results

The mean age of children was 11.40 ± 2.86 years. Although 93.8% of caregivers believed children should know their HIV status, the prevalence of disclosure to the child was only 33.3%. Disclosure had been done primarily by caregivers (72.9%). Caregivers reported that (22.9%) children self-disclosed. Majority of caregivers felt 10-12 years as the appropriate age for disclosing the HIV infection status. Most of children 89.6% acquired HIV through vertical transmission. Majority of care givers 83.3% believed that care givers are most suitable person for disclosure. Furthermore, in our study 66.7% children were unaware of this HIV status and most common reason (92.7%) of non disclosure was inability to understand about illness and fear as child may tell secret to others and rest were too young to understand the disease.

Conclusions

Prevalence of HIV disclosure was 33.3 % there was increase in drug compliance, improvement in behaviour, school performance and attendance. Most common reason for their non disclosure was child does not understand illness and child may tell secret to others.

Clinical Trial Registration (Please input N/A if not registered)

N/A
MUCOCUTANEOUS MANIFESTATION IN HIV POSITIVE PAEDIATRIC PATIENTS

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Background

HIV infection in children is becoming a common occurrence with prevalence of 0.3% and perinatal transmission being the most common mode of acquiring HIV among children.

HIV is a multisystemic disorder and mucocutaneous manifestations can be taken as marker of declining CD4 counts.

Methods

102 HIV positive children between age of 18 months to 18 years attending pediatric HIV clinic of PGIMER and Dr RML Hospital, New Delhi were screened for mucocutaneous manifestations and clinical details were obtained using a performa. Also CD4 count and various biochemical tests were done.

Statistical testing was conducted with statistical package for the social science system version SPSS 21.0. For all statistical test a p-value less than 0.05 were taken to indicate a significant difference.

Results

Mean age of cases were 10.54 +/- 3.58 years with male preponderance. Majority of cases were in stage I (97.6%). 99% of patients were on HAART with 71.9% patients having CD4 count more than 500. Mucocutaneous manifestations were present with infectious dermatoses (76%) being more commoner than non-infectious.

Conclusions

This study designed to evaluate various mucocutaneous manifestations and its correlation with CD4 count, found low prevalence of mucocutaneous manifestations among the study group.

Clinical Trial Registration (Please input N/A if not registered)

N/A
AN AUDIT OF MICROBIOLOGICAL ANALYSIS AND ANTIMICROBIAL RESISTANCE OF GHARO WATER SAMPLES (KARACHI-PAKISTAN) IN WINTER SEASON 2015-2016

K. FATIMA

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Background

The people often complain and greatly suffer with non-availability of civic facilities including drainage system, potable water, sanitation etc. scarcity of water supply harboring predominantly with water borne diseases as well as gastro and diarrhoea

Methods

collected around 60 drinking water samples (1 Litre) from various spots of Gharo transported to IIDRL-KU analyzed by Membrane Filtration Technique (MFT) conventional and rapid (QTS 10) methods. Kirby Bauer disc diffusion method and Minimum Inhibitory Concentration (MIC) Micro dilution method.

Results

: all the samples testedwere found positive for potential gram-negative Escherichia. Coli (60%), Enterobacter aerogenes (40%), Proteus vulgaris (10%), Pseudomonas aeruginosa (28%), Shigella dysenteriae(25%), Salmonella typhi(20%), and Aeromonas hydrophila (2%)Staph. aureus (35%), Staph.epidermidis (30%)resistance pattern against Cephalexin (80%), Erythromycin and Tetracycline (48%), Ampicillin(65%), Novobiocin(70%) Doxycycline (99%), Amoxicillin(41%), Ceftrizoxime (95%), Chloramphenicol (40%) , Gentamicin (60%), Ofloxacin (30%) and Ciprofloxacin( 20%).

Conclusions

Presence of E.coli indication of sewage or animal waste contamination, unfit for human consumption. high level of antibiotic resistance

Clinical Trial Registration (Please input N/A if not registered)

N/A
RETROPHARYNGEAL ABSCESS AS A RARE PRESENTATION OF KAWASAKI DISEASE

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Title of Case(s)

Kawasaki Disease presenting with Retropharyngeal Abscess

Background

The patient was an 8 year old girl who presented with left neck swelling with fever and found to have a retropharyngeal abscess on CT scan. Retropharyngeal abscess is a rare presentation of KD. Typical symptoms of KD may not be present at diagnosis and the diagnosis of KD requires a high index of clinical suspicion.

Case Presentation Summary

The patient was an 8 year old girl who presented with fever, cough, left neck swelling and reduced neck movement for 3 days. On examination, she was febrile with a 4x3cm left neck swelling. Investigations on seventh day of fever revealed hemoglobin of 12.7g/dL, WBC count 11.0x10^9/L, platelet count 275x10^9/L, CRP 319.4mg/L and ESR 80mm/hr. A CT neck revealed a retropharyngeal abscess and bilateral enlarged cervical lymph nodes, the largest 1.9x1.4cm. Intravenous ceftriaxone was commenced. Blood cultures and an extensive infective work-up returned negative.

Despite 3 days of intravenous antibiotics, the patient’s fever and neck swelling persisted. She subsequently developed bilateral conjunctivitis, strawberry tongue and rash on tenth day of fever. Investigations revealed WBC 9.56x10^9/L, CRP 252.2mg/L and ESR 120mm/hr. A diagnosis of KD was made in view of the constellation of symptoms and laboratory markers. She was commenced on intravenous immune globulin (IVIG) with resolution of fever and improvement of neck swelling within 24 hours. An echocardiogram performed on the fourteenth day of illness showed no coronary dilatation and the child was discharged well.
Learning Points/Discussion

1. Retropharyngeal abscess is a rare presentation of KD.
2. Typical symptoms of KD may not be present at the onset of fever.
3. Persistent fever in the presence of high inflammatory markers should alert clinicians to KD even in the absence of other symptoms.
Group B streptococcus (GBS) infection can cause considerable morbidity in neonates and infants. International guideline recommends universal screening for pregnant women and those found to be GBS positive or with risk factors are given intra-partum antibiotics. A trivalent conjugate vaccine (serotypes III, 1a and 1b) administered to pregnant women has been proposed to further decrease early onset disease (EOD) and late onset disease (LOD). We aim to examine the incidence of EOD and LOD, the causative GBS serotypes in our institution and to compare the risk factors between EOD and LOD.

Methods

In this retrospective study of 54 cases of infants <6 months old over a 6-year period, the influence of antenatal and perinatal risk factors were evaluated. The incidences of EOD and LOD were obtained using live births at KKH as the denominator. Invasive GBS isolates were serotyped by National Public Health Laboratory.

Results

There were 10 EOD and 44 LOD. The incidence of EOD and LOD ranged from 0.18 and 0.59 per 1000 live births per year respectively. The most common serotype was type III (65.7%), 1a (11.4%) and IV (8.6%). Chinese infants (p=0.019), normal birth weight (p=0.053) and maternal GBS status as unknown or negative (p < 0.05) are associated with LOD. In the multivariate analysis, LOD was associated with Chinese race (p=0.035, OR 18.6, 95% CI 1.24-280) and negative or unknown
Conclusions

The current guideline in our institution has reduced the EOD incidence which is comparable to international standards. A negative or unknown maternal GBS status without perinatal risk factors for sepsis was associated with LOD. The conjugate GBS vaccine may prevent up to 83% of invasive GBS disease.
PRIMARY IMMUNIZATION ACCORDING TO STIKO RECOMMENDATIONS AMONG CHILDREN WITH CONGENITAL HEART DISEASE
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Background

The Standing Committee on Immunisation (STIKO) recommends a standard vaccination program for children in Germany. For special subgroups, like children with congenital heart disease, even higher recommendation levels occur. However, little is known about the vaccination status of this group.

Methods

Children with congenital heart disease aged between 2 and 17 years were enrolled in a prospective study at the German Heart Center Munich, Germany. Vaccination and medical status were received by a specific questionnaire and patient survey. Excel and R was used for statistical analysis. Results were referred to the STIKO recommendations 2014.

Results

657 children with a mean age of 9.8 (SD+/− 4.8) years were enrolled. 41 (6.2%) had completed all recommended primary vaccinations within the recommended time frame and 179 (27.2%) within the maximum admissible time frame. Low immunization rates for pneumococci, meningococci and varicella led to the low coverage. Vaccination rates were significantly lowest for children consulting a general practitioner. Compared to the results of the German-wide inquiry on vaccination among children entering school (data collected by the Robert-Koch-Institut), children with congenital heart disease showed significantly lower individual vaccination rates for inactivated vaccines, while there was no difference for attenuated vaccines.

Conclusions

Children with congenital heart disease show inadequate immunization rates, both individually and compared to healthy children. It has to be discussed, why only every third child got adequate vaccination recommendations and why immunization rates were lower for inactivated vaccines.
02A. SCIENCE: ANTIMICROBIALS: RESISTANCE AND PHARMACOLOGY

ANTIMICROBIAL SCREENING OF WITHANIA COAGULANS AND NIGELLA SATIVA AGAINST CLINICAL SKIN INFECTION ISOLATES

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Background

The research focuses on the antimicrobial activity of *Withania coagulans* against *Nigella sativa*. *Withania coagulans* - also commonly known, as Paneer Doda in Pakistan, is a medicinal herb that is soon facing extinction. It has been used in indigenous medicine since ancient times. It works as a therapeutic agent that is used to cure various diseases including Diabetes and Small Pox. *Nigella sativa* – also generally called Black cumin or Kalonji, on the other hand is used in herbal medicine as well, to treat and prevent a number of diseases including Asthma and Diarrhea.

Methods

The methods that have been opted for the study are Disc Diffusion Method and Well Diffusion Method. It was observed that out of the two methods that were opted, the Well Diffusion method gave better results relative to the Disc Diffusion Method.

Results

The study of the research was fruitful in demonstrating the anti-microbial action of both *Withania coagulans* and *Nigella sativa*.

Conclusions

It was additionally helpful in distinguishing Agar Well Diffusion Method as the more definitive method that provided more reliable results.

Clinical Trial Registration (Please input N/A if not registered)

N/A
PATTERN OF MEASLES COMPLICATIONS IN CHILDREN


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Background

Measles is a contagious disease and there is no treatment. Complications affect in children some parts of body, such as: lungs, vocal cords, brain, ears, intestines and thrombocytes in blood.

The aim of this article is to show complications in children caused by measles as well as the incidence of complications.

Methods

Methods are based on data for pre-school children for five years from the beginning of 2013 to the end of 2017. Out of a total of 1019 registered children across Bosnia and Herzegovina through national medical data and data from pediatric clinics, pediatric primary services and pediatric hospitals. Sigma Stat 3.0 is used for electronic and statistical data processing.

Results

Pattern of complications were predominant as first inflammation of milder of respiratory system as bronchitis in 191 cases (18.74%) and laryngitis in 89 cases (8.73%) and severe inflammation as pneumonia in 73 cases (7.16%) and croup in 9 cases (0.88%), encephalitis in 2 cases (0.20%), ear infection in 114 cases (11.19%), low platelet count thrombocytopenia in 29 cases (2.85%), enterocolitis in 79 cases (7.75%) and hepatitis in 4 cases (0.39%) and subacute sclerosing panencephalitis (SSPE) and myocarditis were no reports in preschool children. There was only one death child from 1019 cases (0.10%) of measles and all together too high of 590 cases (57.90%) complications in measles.

Conclusions

Measles usually passes without causing serious damage to a child’s health but serious complications are common.

Clinical Trial Registration (Please input N/A if not registered)
GOOD COVERAGE OF IMMUNIZATION OF THE POPULATION IS NEEDED TO REDUCE THE RISK OF TRANSMITTING THE DISEASE TO SUSCEPTIBLE INDIVIDUALS WITHIN ONE POPULATION

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Background and Objective

The implementation of the immunization policy is essential to reduce the incidence and mortality of a number of infectious diseases and is a basic indicator of the health policy orientation towards preventive health care. The percentage of immunization against infectious diseases is high and over the past years it has been consistently above 95% in children up to one year old.

Methods

The descriptive epidemiological method is applied, the data are processed statistically and are presented in a tabular and graphical manner. The data are collected from the annual reports for vaccinated children by the calendar of vaccinations submitted to the Institute for Public Health of the Republic of Macedonia from the vaccination service of JZU "Health Center "Kocani" (period 2014-2016).

Learning Points Discussion

In the municipality of Kocani 2014, the coverage of Hepatitis B patients is 98%, in 2015 and 2016, the coverage is 99%, which is a higher percentage of coverage compared to the coverage in the Republic of Macedonia, which is for 2014 96.5%, for 2015 96.6% and for 2016 91.8%. In the municipality of Kocani and in the immunization against Haemophilus influenza type B is higher than 95% and is among the first municipalities according to the percentage of immunization for almost all types of vaccines. In 2014 and 2016, 99%, in 2015, one percent less coverage (98%). In the Republic of Macedonia there is a lower coverage ranging from 97.1% in 2014, 93.6% in 2015 and 88.6% in the last 2015. DiTer in the municipality of Kocani and R.M. in the period 2014-2016 year, it can be noted that the municipality of Kocani has a high coverage ranging from 99.4% (2014) and 98% to 2015 and 2016.
Background

This study aimed to isolate and identify probiotic lactobacillus and evaluate their effects on cholesterol levels.

Methods

Probiotic Lactobacillus was isolated from 3 samples butter milk, spinach and egg yolk. MRS agar and MRS broth were used for the growth of lactobacillus and identification of lactobacillus was confirmed by gram staining and various biochemical tests. Growth and survival of lactobacillus was evaluated by antibiotic resistance, acid tolerance in various pH (4, 7 & 9), Bile salt tolerance under different concentrations of bile salt (such as 0.1g, 0.2g, 0.3g, 0.4g & 0.5g) and in various temperatures such as (37°C, 50°C & 4°C). Cholesterol degradation capability of lactobacillus was determined under 3 different concentrations of cholesterol (200µg/ml, 400µg/ml, and 600µg/ml)

Results

Results of cholesterol assimilation were recorded by the percentage of cholesterol degraded. Out of all 3 samples, Lactobacillus isolated from butter milk showed the highest cholesterol degradation (26.68%) at concentration 600µg/ml.

Conclusions

The present study showed that the isolated probiotic LAB was able to assimilate cholesterol which in turn can reduce the risk of cardiovascular diseases.

Systematic Review Registration (Please input N/A if not registered)
Background

The antibiotic resistances is becoming a major hurdle in the field of medicine and necessitate the discovery of novel and natural therapeutic agents. Objective: The ambition of the present study is to evaluate the potential of Essential oils (EOs) as antimicrobial agents against five clinical isolates including Gram-negative and Gram-positive

Methods

The activity of eighteen different EOs on five clinical isolates including: Methicillin resistant Staphylococcus aureus (MRSA), klebsiella pneumonia (K. pneumonia), Staphylococcus aureus (S. aureus), Bacillus subtilis (B. subtilis) and Escherichia coli (E. coli) was investigated by well diffusion assay, minimum inhibitory concentration (MIC), time-kill assay, loss of cytoplasmic material and also bacteriostatic and bactericidal nature was determined.

Results

Among all EOs black seed and lemon grass was found to be effective against almost all clinical isolates except gram negative bacterias which showed high resistance against EOs as well as different antibiotics. They also showed best results in each parameter and are found to be bactericidal.

Conclusions

the current study highlights antibacterial activity of twelve out of eighteen EOs that showed spectrums at different extents. Two of twelve oils are considered the best and can be used in promotion of good health.

Systematic Review Registration (Please input N/A if not registered)

n/a
Background

Different studies show consistent predictable bacterial profiles in wound infections, antibiotic resistance and capacity to adapt to changing environment, which render the pathogens a matter of concern in hospital acquired infections. Therefore, periodical monitoring of bacterial profile and their antibiotic susceptibility pattern is important. The objective of the study is to determine the commonly encountered pathogens in pus samples along with their antibiotic susceptibility patterns.

Methods

Pus samples received for diagnostic microbiology were processed, and identified by standard protocols. Antibiotic susceptibility testing was done by Kirby-Bauer Disc Diffusion method.

Results

Among the isolated organisms from pus specimens, Staphylococcus aureus was the most common followed by Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Proteus species and Acinetobacter species. Quinolones, aminoglycosides and cephalosporins were found to be the most effective antimicrobials in vitro, whereas amoxicillin, minocycline and trimethoprim-sulphamethaxazole were least effective.

Conclusions

The resistance of organisms to antibiotics is increasing steadily as they are becoming more resistant to newer antibiotics, such as quinolones. Doctors and nurses spread awareness of antibiotic resistance, and it is their duty to keep themselves updated with the latest antibiograms of commonly encountered pathogens, so that appropriate antibiotics may be provided for the treatment of infections.

Systematic Review Registration (Please input N/A if not registered)
TROPICAL FEVER BURDEN AT A TERTIARY CARE HOSPITAL OF A DEVELOPING COUNTRY: CLINICAL PROFILE AND COMPLICATIONS

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Background

Tropical fevers are defined as infections that are prevalent in, or are unique to tropical and subtropical regions. Some of these occur throughout the year and some especially in rainy and post-rainy season. Major Concern about them is, high prevalence and morbidity and mortality caused by these infections, and overlapping clinical presentations, difficulties in arriving at specific diagnosis and need for early empiric treatment.

Methods

This was a prospective observational study conducted during the post monsoon season from September 2017 to November 2017 in the department of pediatrics,dayanand medical college and hospital ,Ludhiana,Punjab,India. All the children till the age of 17 years who came to the emergency with complaints of fever and who were provisionally diagnosed as cases of tropical fever were taken into the study.

Results

There were a total of 253 children with a provisional diagnosis of tropical fever. Most children were between age of 10-18 years(57.2%), with the youngest being 4 month old. Besides fever other common symptoms were pain abdomen(52.9%), vomiting(61.6%), loose stools(7.9%), bleeding(10.2%), rash(7.5%), itching(19.3%), and neurological symptoms(10.6%). Other signs were pallor(35.9%), skin hue(34.3%), prolonged capillary refill time (27.6%), cold extremities(8.6%), hepatomegaly(35.5%), ascites(14.2%), splenomegaly(7.5%) and hypotension(32.3%). Among various complications were Low platelet count (69.1%), leucopenia(36.3%), raised hematocrit(35.9%). Of all patients, 155(61.2%) were diagnosed as dengue fever, 17(6.7%) typhoid fever, 11(4.3%) scrub typhus, 3(1.1%) hepatitis A, 2(1%) leptospirosis and 42(16.6%) unclassified fever. Overall mortality rate was 3.9%.

Conclusions

Tropical fevers contribute a significant disease burden in children of developing countries. A practical approach is to group the symptoms and signs in a syndromic fashion so as to enable the clinician to have a plan to treat such patients.
Background

Resource-limited countries using the WHO HIV drug resistance (HIVDR) threshold survey suggests that transmission of drug-resistance strains is likely to be limited. However, as access to ART is expanded, increased emergence of HIVDR is feared as a potential consequence. We have performed a surveillance survey of transmitted HIVDR in the geographic setting of Accra, Ghana.

Methods

As part of a cross-sectional survey, 2 large voluntary counseling and testing centers in Accra enrolled 50 newly HIV-diagnosed, antiretroviral drug-naïve adults aged 18 to 25 years. Virus from plasma samples with >1,000 HIV RNA copies/mL (Roche Amplicor v1.5) were sequenced in the pol gene. Transmitted drug resistance-associated mutations (TDRM) were identified according to the WHO 2009 Surveillance DRM list, using Stanford CPR tool (v 5.0 beta). Phylogenetic relationships of the newly characterized viruses were estimated by comparison with HIV-1 reference sequences.

Results

Subtypes were predominantly D (39/70, 55.7%), A (29/70, 41.4%), and C (2/70; 2, 9%). Seven nucleotide sequences harbored a major TDRM (3 NNRTI, 3 NRTI, and 1 PI-associated mutation); HIVDR point prevalence was 10.0% (95% CI 4.1% to 19.5%). The identified TDRM were D67G (1.3%), L210W (2.6%); G190A (1.3%); G190S (1.3%); K101E (1.3%), and N88D (1.3%) for PI.

Conclusions

In Accra, the capital city of Ghana, we found a rate of transmitted HIVDR, which, according to the WHO threshold survey method, falls into the moderate (5 to 15%) category. This is a considerable increase compared to the rate of <5% estimated in the 2006-7 survey among women attending an antenatal clinic in Mamobi. As ART programs expand throughout Africa, incident infections should be monitored for the presence of transmitted drug resistance in order to guide ART regimen policies.

Clinical Trial Registration (Please input N/A if not registered)

N/A
CHEST WALL MASS – IS IT TB OR NOT TB?

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Title of Case(s)

CHEST WALL MASS – IS IT TB OR NOT TB?

Background

Musculoskeletal tuberculosis (TB) occurs in 1-3% of patients with the disease. However, cold abscess of the chest wall is rare and constitutes 1% to 5% of all cases of musculoskeletal TB. Patients are often young and have no comorbidity. Diagnosis is often delayed because of the atypical presentation and lack of awareness. We describe a case of anterior chest wall mass as the first presenting feature of tuberculosis.

Case Presentation Summary

A 15 year old girl presented with a 2 month history of a mass on the left anterior chest wall. She had a cough and intermittent fever for 2 weeks. There were no other systemic symptoms. She received BCG at birth.

On examination she had a 6cm x 4cm mass overlying the left 8th and 9th ribs. Chest x-ray and a subsequent MRI showed the mass eroding into the underlying 8th rib, hilar adenopathy and a small left pleural effusion.

The patient underwent a diagnostic biopsy to exclude malignancy. This revealed a fluid filled centre and a significant amount of pus was drained. A post-biopsy chest x-ray showed a markedly enlarged pleural effusion. The patient’s IGRA test was positive (16.05 iu/ml). The pleural fluid was smear negative and the culture confirmed drug sensitive Mycobacterium tuberculosis. The patient was treated with standard Anti-Tubercular Therapy and had an uneventful recovery.

Learning Points/Discussion

Tuberculosis is a great masquerader and atypical presentations are known to occur. TB should be considered in children presenting with a chest wall mass with hilar adenopathy. Other differential diagnoses include benign and malignant tumours. Prompt diagnosis and treatment of chest wall TB results in complete recovery and helps in preventing serious complications.
Background

The importance of antimicrobial stewardship is becoming increasingly accepted by other members of the MDT as a way of stemming antimicrobial resistance. There is very little published literature about the impact of antimicrobial stewardship ward rounds in paediatrics. Antimicrobial stewardship within paediatrics was identified as requiring improvement in the July 2016 Trust-wide antimicrobial prescribing audit.

To address these issues a joint decision made by the antimicrobial pharmacist team and the paediatricians to commence weekly multi-disciplinary ward rounds designed to improve antimicrobial stewardship and patient care.

Methods

Weekly ward rounds on a 25 bedded paediatric medicine ward were conducted by a paediatrician, a consultant microbiologist and an antimicrobial pharmacist. All patients receiving systemic antimicrobial treatment were reviewed by the team.

Results
Between February and June 2017, 46 patients and 59 prescriptions were reviewed by the team. 54.2% prescriptions did not have a documented duration and 10.2% did not have a documented indication. 67.8% prescriptions required the MDT to document a new duration on the drug chart or amend the existing duration in line.

This improvement in stewardship is anticipated to improve patient outcomes. Due to the lack of published studies investigating antimicrobial stewardship in paediatrics it is important for more work to be carried out. **Conclusions**

By conducting ward rounds, an improvement in stewardship was seen and this work forged better working relationships across different specialities. These results show that useful interventions can be made by undertaking targeted ward rounds. However, this approach is resource and labour intensive and investment should be considered for future programmes. We determined that 0.1 whole time equivalent band 8a antimicrobial pharmacist would need to be funded in order to maintain the ward round frequency.
Background

Metabolic profiling is a promising diagnostic and prognostic tool in the clinical setting through the analysis of urinary metabolites. Its non-invasive nature makes it ideal for studying pediatric conditions. A previous preclinical study has demonstrated that urinary metabolic profiling using nuclear magnetic resonance (1H-NMR) spectroscopy can predict congenital cytomegalovirus (CMV) infection. However, several sources of variation have been observed in children. The diagnosis and treatment of CMV infection, particularly asymptomatic congenital infections, remain a challenge. Our aim was to investigate the sources of variation in urinary metabolome of CMV-infected patients and controls and if it could be applied in the clinical setting.

Methods

Urine samples were collected in patients admitted at the neonatal unit of a tertiary centre for CMV screening using PCR (April 2016-July 2017). 1H-NMR spectra were obtained at 9.4T using a NOESYPR1D pulse sequence. Dataset was analysed using orthogonal projection on latent structures (OPLS-DA) to discriminate between CMV infection, sex, chronological age, gestational age, type of delivery, multiple birth and diet. OPLS-DA models were considered significant when CV-ANOVA <0.05.

Results

Nineteen cases of CMV infection (5 congenital, 11 postnatal and 3 of probable postnatal origin) and 18 negative controls were included. Age range was 0-115 and 0-122 days, respectively. Statistical significant discriminative models were obtained only for CMV infection (p=0.0299) and chronological age (p=0.0024). The responsible variables were N-acetytyrosine, propylen-glicol, betaine and succinate for CMV infection and propylen-glicol, myo-inositol and betaine for age.

Conclusions

Despite the high variability in metabolic profiles, its clinical application remains a possibility as shown in this study. Due to high variability and relatively low number of patients, multicenter studies are required to provide definitive answers.
Clinical Trial Registration (Please input N/A if not registered)

N/A
HIGH FLOW NASAL CANNULA THERAPY (HFNC) FOR INFANTS WITH RSV-BRONCHIOLITIS: RESULTING IN SHORTER LENGTH OF STAY, BUT NO DIFFERENCE IN ESCALATION OF CARE.

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Background

A large proportion of all infants are annually infected with respiratory syncytial virus (RSV) bronchiolitis, a lower airway infection. RSV-bronchiolitis is a severe burden on health care. Care is almost exclusively supportive and few evidence-based effective treatments exists. Heated, humidified, high flow nasal cannula (HFNC) is a promising new modality of respiratory support for infants with RSV. Rigorous safety data is lacking but its impact on health care and patient outcome seems promising.

The present study evaluates the usage of HFNC on a tertiary pediatric ward in Malmö, Sweden during two years (2014-15), setting it against standard care delivered the previous two years (2012-13).

Methods

A retrospective, comparative study reviewing all admitted cases (n=293) of infants younger than 1 year with RSV-bronchiolitis during 4 consecutive RSV-seasons. Two seasons without access to HFNC acted as control (n = 127) and two seasons with access to HFNC (n = 166) acted as the treatment group.

Results

Of the 166 children cared for 2014-15, 37 were treated with HFNC. No adverse events were registered. Having access to HFNC at the ward led to a shorter length of stay, 3,5 vs. 4,3 days (p < 0.01).

There were no differences in escalation of care 8,5% vs 8,9% (OR 0.82 95% CI 0.30-2.24), nCPAP usage 10 vs 11 (OR 0.53 95% CI 0.18-1.53), intubation rates (0% vs 0.6%, p > 0.05) or CO2-retention during care (OR 0.73 95% CI 0.37-1.42).

Conclusions

HFNC has been a safe treatment option without complications leading to a shorter stay at the hospital. Earlier results showing dramatic improvements in treatment outcomes could not be replicated in this study.
EARLY INFORMATION AND TRUST IN THE SWEDISH CHILD HEALTH CENTER NURSES INCREASED WILLINGNESS TO VACCINATE AGAINST ROTAVIRUS INFECTIONS

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Background

Rotavirus vaccines are effective against severe rotavirus infections, but have a modest impact on mortality due to these infections in high-income countries. In 2014, Stockholm was the first Swedish County to introduce the rotavirus vaccine to all newborns. In a near future the vaccine will be included in the Swedish immunization program. Parental knowledge and attitudes towards vaccines are crucial for high vaccination coverage. This study aimed to identify why parents refused to let their infant have the vaccination or were unsure.

Methods

This cross-sectional study was based on 1,063 questionnaires completed by the parents of newborn children in 2014, during four weeks in Stockholm. Stepwise logistic regression was used to identify the main predictors.

Results

Most (81%) parents intended to vaccinate their child against the rotavirus, while 19% were unwilling or uncertain. Parents with less education and children up to five weeks of age were more likely to be unwilling or uncertain about vaccinating their child. Other factors associated with a refusal or uncertainty about vaccinating were: not having enough information about the vaccine, no intention of accepting other vaccines, paying little heed to the child health nurses’ recommendations, thinking that the rotavirus was not a serious illness and not believing that the vaccine provided protection against serious forms of gastroenteritis.

Conclusions

Early information, extra information for parents with less education and close positive relationships between parents and child health nurses were important factors in high rotavirus vaccination rates.
This knowledge could facilitate the implementation of rotavirus vaccine in the Swedish immunization program in the near future.
USE OF CARBAPENEMS IN A FRENCH UNIVERSITY CHILDREN'S HOSPITAL: AN PROFESSIONAL PRACTICE EVALUATION

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Background

Carbapenems are used for severe infections that are resistant to other antibiotics. In recent years, the emergence of carbapenemase-producing bacteria has put us in a therapeutic stalemate. The objective of this study was to evaluate the complicity of prescriptions of carbapenems to recommendations as well as to assess the extent of re-evaluations of carbapenem prescriptions at 48-72h over two separate periods: before and after training was provided to prescribers concerning correct conduct in prescribing carbapenems.

Methods

This retrospective survey of professional practices concerned all children hospitalized at Bordeaux Children's Hospital of Bordeaux for whom a dispensation of carbapenems was registered by the local pharmacy during their hospitalization from the 1st January 2016 to the 30th of June 2016 and then after the intervention from the 1st January 2017 to the 30th June 2017. The conforming carbapenem prescriptions were evaluated by a pediatric infectious disease specialist on the basis of criteria from french organization (CCLIN/ARLIN and SPILF).

Results

Thirty-seven patients were included during the first period and twenty-three during the second period. The decision to initiate carbapenem therapy was justified in 46% of the cases during the first period and in 87% of the cases during the second period. The reassessment was found to be correct in 48% for the first period and 78% for the second period.

Conclusions

There was a decrease in the number of non-compliance of -70%, despite the increase in ESBL. We insist on the respect of the treatments' duration and the traceability of the systematic re-evaluation at 48-72h.
INVESTIGATION OF CEREBROSPINAL MENINGITIS OUTBREAK IN NIGER STATE, NIGERIA-2017

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Background

Cerebrospinal meningitis (CSM) is an epidemic prone vaccine preventable disease and remains a major public health challenge in the African meningitis belt. In March 2017, Niger State Ministry of Health reported outbreaks of meningitis in eleven out of the 25 local government areas (LGAs) of the state. We investigated to confirm the outbreak, describe its magnitude and institute appropriate control measures.

Methods

We conducted a descriptive study. We defined suspected case as any person with sudden onset of fever (>38.5°C rectal or 38.5°C axillary) or any of the following meningeal signs: neck stiffness, altered consciousness or other meningeal signs including bulging fontanelle in toddlers. A confirmed case was defined as a suspected case confirmed by isolation of Neisseria meningitidis from cerebrospinal fluid or blood. We carried out advocacy visits, active case search, data collection and public enlightenment. Cerebrospinal fluid (CSF) sample was collected and analyzed using Pastorex®. We analyzed the data using Epi info 7.2 and calculated frequencies and proportions.

Results

There were 123-suspected cases with median age of 12 years, seventy (56.9%) were males. Age group 10-14 (34.1%) were the most affected. The cumulative attack rate was 5.2/100,000 population with Magama LGA having the highest attack rate of 26.7/100,000 population. The peak of the outbreak was between 15 and 23rd March, 2017. Forty-three (43) CSF samples were collected and 12 (27.8%) were positive for Neisseria Meningitidis type C. Thirty-four (34) of the cases died giving a case fatality rate (CFR) of 27.6%.

Conclusions

An outbreak of CSM occurred in Niger State. We recommended mass vaccination of at risk individuals, intensified surveillance in the affected LGAs and continued health education.
LOW ADHERENCE TO THE CURRENT GUIDELINES FOR MANAGEMENT OF FEBRILE INFANTS IN A SWEDISH PEDIATRIC EMERGENCY DEPARTMENT

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Background

There are well-established international guidelines for the management of febrile infants under 2 months of age. They recommend lumbar puncture (LP), admission and antibiotic treatment for all infants <1 month old, and for ill-appearing infants 1-2 months old. In addition, blood and urine cultures are recommended for all patients. However, the management varies a lot and these guidelines have lately been questioned. The adherence internationally is quite low. In Sweden no official national guidelines exist, nor data regarding how febrile infants are managed.

Methods

Retrospective cohort study based on the medical records of infants ≤60 days presenting with fever at the PED in Malmö, Sweden, in 2015 and 2016. Only full-term infants without comorbidities were included. Laboratory testing, admissions, antibiotic treatment and revisit rates were analyzed.

Results

360 infants who met inclusion criteria were identified. Of the febrile infants ≤29 days old, 89% did not have an LP, 45% were not admitted, and 75% did not receive empirical antibiotic treatment. Of the ill-appearing febrile infants 30-60 days old only 17% had an LP performed. The rates of urine and blood cultures taken were low in both age groups, especially among those 30-60 days old. The prevalence of serious bacterial infection (SBI) was 8%. All cases of SBI were discovered upon the first visit.
Table. Variation in management of febrile infants ≤60 days of age at a pediatric emergency department.

<table>
<thead>
<tr>
<th>Laboratory testing</th>
<th>≤29 days (n=125)</th>
<th>30-60 days (n=235)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine + Blood + LP</td>
<td>13</td>
<td>0</td>
</tr>
<tr>
<td>Urine + Blood</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>Urine only</td>
<td>19</td>
<td>26</td>
</tr>
<tr>
<td>Other combination of Urine, Blood, LP</td>
<td>5</td>
<td>8</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Treatment</th>
<th>≤29 days (%)</th>
<th>30-60 days (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Third generation cephalosporin + Ampicillin</td>
<td>10 8.0</td>
<td>5 2.1</td>
</tr>
<tr>
<td>Third generation cephalosporin alone</td>
<td>18 14.4</td>
<td>14 6.0</td>
</tr>
<tr>
<td>Other IV antibiotic combination</td>
<td>3 2.4</td>
<td>0 0</td>
</tr>
<tr>
<td>No IV antibiotics</td>
<td>94 75.2</td>
<td>216 92.0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Outcome</th>
<th>≤29 days (%)</th>
<th>30-60 days (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospitalized</td>
<td>69 55.2</td>
<td>61 26.0</td>
</tr>
<tr>
<td>Discharged</td>
<td>56 44.8</td>
<td>174 74.0</td>
</tr>
<tr>
<td>Revisit within 10 days of those discharged**</td>
<td>22 39.3*</td>
<td>84 48.3*</td>
</tr>
<tr>
<td>SBI</td>
<td>17 13.6</td>
<td>11 4.7</td>
</tr>
<tr>
<td>SBI at hospitalization</td>
<td>17 13.6</td>
<td>11 4.7</td>
</tr>
<tr>
<td>SBI at revisit</td>
<td>0 0</td>
<td>0 0</td>
</tr>
</tbody>
</table>

*Percentages are based on the total number of infants who were discharged
**Most revisits were planned follow-ups.

Conclusions

The adherence to international guidelines was very low in both age groups. The rates for LP, admission and antibiotics were 11%, 55% and 25% respectively in the ≤29 days old group. Only 17% of the ill-appearing febrile infants 30-60 days had an LP. These rates are even lower than demonstrated in previous international studies. Despite the low adherence, no cases of SBI were identified with delay.
PREVALENCE AND ETIOLOGY OF SERIOUS BACTERIAL INFECTIONS IN FEBRILE INFANTS YOUNGER THAN 60 DAYS OF AGE, IN A SWEDISH PEDIATRIC EMERGENCY DEPARTMENT

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²Skåne University Hospital, Pediatric Emergency and Infectious Diseases Department, Malmö, Sweden

Background

Infants with fever without focus have a risk for a serious bacterial infection (SBI). The definition of SBI includes urinary tract infection (UTI), bacteremia and bacterial meningitis. Recent publications report an epidemiological shift of these infections with UTI accounting for 90% of SBIs and meningitis for no more than 2%. Around 3 decades ago, UTI accounted for 40-50% and meningitis for 0-14%. Escherichia coli is reported to be the main causative agent of SBIs while the prevalence of Group B Streptococcus (GBS) and Listeria Monocytogenes has decreased.

Methods

Medical records were reviewed of full-term infants <60 days of age without comorbidities who searched for care because of fever at the pediatric emergency department (PED) at Skåne University Hospital, Lund from the 1st of January 2014 until the 31st of December 2016. Reviewed factors were temperature, vital signs, blood, urine and cerebrospinal fluid (CSF) cultures, registered diagnose and outcome.

Results

Of the 256 infants included, 17 (6.7%) were diagnosed with an SBI. Thirteen (5.1%) had an UTI, 2 (0.8%) isolated bacteremia, 1 (0.4%) combined UTI and bacteremia and 1 (0.4%) combined bacterial meningitis and bacteremia. UTI accounted for 83% of all SBIs. E. coli was isolated in 11/14 (79%) of the positive urine cultures. GBS caused the only case of bacterial meningitis/bacteremia and was isolated in 2 urine cultures. No cases of L. monocytogenes were isolated.
Conclusions

This study showed that UTI was the predominant SBI among febrile infants, while the prevalence of bacterial meningitis and isolated bacteremia was very low. *E. coli* was the main pathogen while no cases of *L. Monocytogenes* were identified.

**Table.** Prevalence of SBIs in febrile infants <60 days of age presenting at the pediatric emergency department at Skåne University Hospital, Lund from 1\textsuperscript{st} of January 2014 until 31\textsuperscript{st} of December 2016.

<table>
<thead>
<tr>
<th>Age in days</th>
<th>Total Number of Infants N</th>
<th>UTI N (%)</th>
<th>Isolated Bacteremia N (%)</th>
<th>UTI + Bacteremia N (%)</th>
<th>Bacterial meningitis + Bacteremia N (%)</th>
<th>SBI Total N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-29</td>
<td>83</td>
<td>2 (2,4)</td>
<td>2 (2,4)</td>
<td>1 (1,2)</td>
<td>1 (1,2)</td>
<td>6 (7,2)</td>
</tr>
<tr>
<td>30-59</td>
<td>183</td>
<td>11 (6,0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>11 (6,6)</td>
</tr>
<tr>
<td>Total</td>
<td>256</td>
<td>13 (5,1)</td>
<td>2 (0,8)</td>
<td>1 (0,4)</td>
<td>1 (0,4)</td>
<td>17 (6,7)</td>
</tr>
</tbody>
</table>
Valganciclovir (VGCV) treatment of symptomatic cCMV infections for 6 months improves hearing and developmental outcome at 24 months modestly. 4 case reports on the emergence of CMV drug resistance in cCMV are available. We present a 5th case.

Case Presentation Summary

A mature infant with cCMV was diagnosed on his first day of life due to blueberry muffin signs, severe hepatosplenomegaly, anemia, thrombopenia, chorioretinitis-scars bilaterally; cerebral ultrasound showed periventricular calcifications. cCMV infection was confirmed by PCR from urine. IV ganciclovir was started from day 2. Due to a GFR around 25ml/kg/min dose adjustments were necessary, drug trough levels were too high several times. CMV UL97 genotyping from plasma, urine and throat swabs was initiated in week 7 p.p. due to elevated viral load (VL).

UL97 mutation C603W was detected from blood at week 7.

A switch to UL97 M460V and M460I mutations was observed in blood and urine two weeks later. In throat swabs, all three canonical UL97 mutations appeared and antiviral therapy was stopped. During antiviral therapy, levels of VGCV were always in the correct range. His further clinical course resulted in the need for bilateral cochlear implants due to deafness; several transfusions due to profound anemia, substitution of fat-soluble vitamins and UDC due to hepatic involvement. He has significant delay of motor functions so far at 14 months of age. Viral load was no longer present in throat swabs at 14 months of age.

Learning Points/Discussion

This case demonstrates the failure of VGCV therapy despite correct levels of VGCV. There is an urgent need for further therapeutic options in cCMV as well as for a good definition, which infants really profit from antiviral therapy.
Fatal Pneumococcal Meningitis in a vaccinated child

Background

2.4yr old boy presented to ER with febrile seizure, GCS 4/15, Past 2 days with cough, reduced intake, vomiting. He was initially seen by primary care doctor a 2am Dx viral illness and sent home, around 08.30am child noted to be limp. paramedics were at scene by 10.08am noted child actively seizing with temperature of 40°C. Buccal Midazolam administered twice in 10 minutes interval to control the seizure and reached ER

Past H/O LRTI, Bronchial asthma and Febrile Seizure. vaccination up to date including PCV13

Case Presentation Summary

ER vitals T 40°C , HR: 120/min, BP 139/97mmHg . BS 6.5 mmol/l. GCS 4/15 Eyes NR to light. unremarkable other systemic exam. He was intubated 10 minutes from arrival to hospital and septic workup was performed. Resuscitation fluids initiated with Normal saline 10 ml/kg and commenced on Intravenous Ceftriaxone and Acyclovir. and added Vancomycine later

WBC 25.1*10⁹, N 22.84*10⁹ with CRP 268.

CXR patchy consolidation LLL

VBG M+R acidosis with Lactate of 6.2 mmol/L.

CT Scan of Brain significant raised ICT, global hypoxic event with cerebral oedema.

started on Mannitol and Dexamethasone and transferred to Tertiary care for further management.

Blood Culture was positive for Strep. pneumoniae and susceptible to Ceftriaxone, Penicillin, Tetracycline and Vancomycin.

Pneumococcal PCR positive with Serotype 24 B Isolated in Sub typing.

MRI of Brain on following day revealed cerebral oedema with tonsillar herniation.
Child declared dead same day.

**Learning Points/Discussion**

Invasive Pneumococcal Disease in Ireland **Confirmed Q1-Q2, 2017**: 245, **confirmed Q1-Q2, 2016**: 233  
Increase in IPD compared with Q1-Q2, 2016: 5%

This case shows that despite the various strains of pneumococcal subtypes included in the PCV13 there are still strains outside the coverage that can cause fatal outcome to susceptible individuals.
Absence of skin tissue at birth

Background

Aplasia cutis congenital (ACC) is rare dermatological condition characterized by the absence of skin at birth. The lesion may affect the epidermis, dermis and subcutaneous tissue and can progress to involve the muscle, bone and other structures such as the dura.

The scalp is most frequently affected in approximately 90 percent of cases, but can be found in other parts of the body. It has a global incidence of 1 in 10,000 live births. This is the first to be reported from Sokoto, North western Nigeria.

Case Presentation Summary

ZM a female neonate delivered by a 21-year-old P3+0 mother at a peripheral hospital. She presented at 16 hours of life on account of absence of skin on both lower limbs.

The neonate appeared pink, afebrile, with bilaterally symmetric absence of skin tissue on the antero-medial surface of both lower extremities extending from the knees to the plantar area of the feet. She had no scalp lesion or bullae. Diagnosis/classification was Frieden type VII aplasia cutis congenita. Management was a multidisciplinary approach. Dressing with Eusol, povidone iodine cream and oral antibiotic (cefuroxime). Restoration of skin tissue was noticed 2 weeks later and the baby was discharged home for follow-up.

Learning Points/Discussion

Just over 500 cases reported worldwide. No gender and racial predilection. Few cases reported in Africa with one from Jos Nigeria by Mava Y et al. Etiology is unclear, Mutations of ribosomal GTPase BMS1 has been implicated in ACC with AD inheritance. Diagnosis mainly clinical and treatment is both conservative and surgical.
Absence of anterior abdominal muscle with renal complication in a new born

Background

Prune-Belly syndrome is a rare congenital disorder that affects males and is associated with high neonatal mortality. This is the first case in literature from North-western part of the country.

Case Presentation Summary

A 7-hour old term male neonate presented to the neonatal intensive care unit of our tertiary hospital with history of difficulty in breathing since birth. The mother, a 38-year old grand multiparous had history of maternal pyrexia at 4/12 gestation. She had no history of body rashes or exposure to radiation, and was not a known diabetic. The mother ingested traditional concoctions in early pregnancy in the form of powdered leaves for a febrile illness. An abdominal ultrasound did not reveal any fetal abnormality. No history of genetic anomaly in the family.

Examinations findings include respiratory distress, with wrinkling of the skin of the anterior abdominal wall, absence of anterior abdominal wall muscle and bilateral cryptorchidism. A diagnosis of Prune Belly syndrome with severe respiratory distress was made.

Abdominal ultrasound showed moderate hydronephrosis, with features of posterior urethral valve, bilateral polycystic kidney disease and non-demonstrable testicles. The patient had intra nasal oxygen, intravenous fluids and antibiotics. Patient developed features of acute urinary retention on account of which the urology team performed a vesicostomy. The baby was planned for dialysis due to worsening of renal function but the parents declined consent and requested for discharge on account of the fees. Patient died 18th day on admission following sudden respiratory distress.

Learning Points/Discussion

There is the need for routine early antenatal ultrasonography to help in detecting the condition and associated renal anomaly early, for effective prenatal and postnatal management.
PERINATAL ASPHYXIA AND FETAL OUTCOME IN A TERTIARY HOSPITAL: ARE WE WINNING?

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¹Usmanu Danfodiyo University Teaching Hospital, Paediatrics, Sokoto, Nigeria
²Paediatrics, Sokoto, Nigeria

Background

Poor Apgar score in newborns and the outcome

Methods

This two-year retrospective study was a review of all cases of attendant perinatal asphyxia admitted to Special Care Baby Unit (SCBU) of Usmanu Danfodiyo University Teaching Hospital, Sokoto, between March, 2005 and February, 2007. Data were obtained from maternal and neonatal case records. Results were analyzed and presented in simple percentages and frequencies.

Results

There was a total 5,224 deliveries during the study period. 174(3.3%) of the babies were admitted to the SCBU with various degrees of perinatal asphyxia. The overall incidence was 35.6/1000 and 31.2/1000 live births for the years 2005 and 2006, respectively. 100(57.5%) were males while 74(42.5%) were females, with M: F ratio of 1.4:1. 85 (48.9%) had severe perinatal asphyxia, 39(22.4%) had moderate perinatal asphyxia while 50(28.7%) had mild perinatal asphyxia. 108(62.1%) mothers attended antenatal clinic (ANC). Preterm deliveries were 64(36.8%), term babies: 108(58.6%) while, post term babies were, 8(4.6%). 54(31%) babies died, 41(75.9%) had severe perinatal asphyxia. 10(18.5%) had moderate perinatal asphyxia while 3(5.6%) were mildly asphyxiated.

Conclusions

Birth asphyxia remains a leading cause of neonatal morbidity and mortality in Nigeria. The incidence of 31/1000 live births in our study is slightly more than earlier figures of 26.5/1000 live births reported from two studies in Nigeria. The encountered rate could possibly represent the national average. There is the need, therefore, to improve on the present health care facilities especially in the areas of fetal monitoring and perinatal resuscitation.
EVALUATION OF AN ISOTHERMAL MOLECULAR POINT-OF-CARE METHOD FOR RAPID DETECTION OF RESPIRATORY SYNCYTIAL VIRUS AND INFLUENZA IN ROUTINE CONDITIONS

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¹Iris Hospitals South, Laboratory Medicine, Brussels, Belgium
²Iris Hospitals South, Pediatrics, Brussels, Belgium
³Scientific Institute of Public Health, Virology, Brussels, Belgium

Background

Respiratory Syncytial Virus (RSV) and Influenza are important respiratory pathogens. However, non-molecular diagnostic methods lack sensitivity, and PCR is not affordable for general labs due to the need of specialized operators and infrastructure. We aimed to evaluate the convenience and the performance of the isothermal point-of-care test Alere-i for the diagnosis of RSV and Influenza, comparing it to traditional methods.

Methods

Consecutive fresh nasopharyngeal specimens collected in children during the 2017 epidemic period were tested with the immunochromatographic BinaxNOW assay, SimulFluor direct immunofluorescence and Alere-i. In absence of PCR in our lab, we used a composite gold standard, with help of the National Influenza Reference Center (NRC) in order to determine the discrepant results.

Results

We collected 35 and 37 samples for RSV and Influenza respectively among children aged from 0 to 12.4y. 13 samples were RSV-positive with Alere-i vs 9 with BinaxNOW and SimulFluor. 7 were positive to Influenza-A with Alere-i (including 1 positive to both Influenza-A and B), vs 4 with BinaxNOW and 1 with SimulFluor. The NRC confirmed 1 discrepant RSV and 5 Influenza-A. The Influenza-B-positive sample was disproved. The estimated sensitivities of Alere-i were 100% for both RSV and Influenza, and its specificities were 88.0% and 96.8%.

Conclusions

Alere-i is easy to use and provides results for RSV and Influenza in less than 20 minutes. It lacks specificity comparing to traditional methods but has a high estimated sensitivity. Furthermore, if BinaxNOW and SimulFluor showed a good sensitivity for RSV (90.0%), it was very poor for Influenza (66.7% and 16.7% respectively). The limitation of our study is the absence of a real gold standard in our lab to allow the confirmation of the negative results obtained with Alere-i.

Clinical Trial Registration (Please input N/A if not registered)

N/A
CHALLENGES FACED BY TUBERCULOSIS PATIENTS DURING THEIR DOTS TREATMENT IN MAHOTTARI DISTRICT NEPAL

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²BPKIHS, SPH & Community Medicine, Dharan, Nepal

Background

TB is an infectious disease caused by the bacteria *Mycobacterium tuberculosis*. It ranks as the sixth leading cause of death in the country. If not treated, each person with active TB infects on average 10 people every year. **Objective** of the study to identify challenges faced by TB patients during their DOTS treatment.

Methods

Cross-sectional study was conducted among TB patients who were currently under treatment of DOTS at selected health facilities in Mahottari district. The patients were interviewed using a semi structured questionnaire. Chi-square test was applied for categorical data and Wilcoxon signed ranks test was applied to calculate difference between patient and family income before and during illness.

Results

Out of 109 TB patients median delay at DOTS three days, median patients delay 15 days and median health system delay in initiation of treatment was 30 days. Median work days lost of patients was 60 days and of care taker was 20 days respectively. Delay in initiation of treatment was found to be 97.3% among those who first contacted private health facility. This study shows 17.4% of respondents had to suffer from stigma, 22.9% of respondents suffered from catastrophic expenditure. To cope financial burden 55.96% respondents had taken loan and 44.04% had managed from savings.

Conclusions

Delay in initiation of treatment of TB was found to be high among those first contact at private health facility. Overall economic burden of disease hits catastrophic to nearly one fourth of respondent's total annual family income. Social stigma was found in significantly.
ADENOVIRAL DETECTION BY COMBINATION OF RECOMBINASE POLYMERASE AMPLIFICATION AND VERTICAL FLOW PAPER MICROARRAY; A POTENTIAL TOOL FOR POINT-OF-CARE VIRAL DIAGNOSTICS

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2Karolinska Institutet/Sachs’ Children and Youth Hospital, Department of Medical Epidemiology and Biostatistics, Stockholm, Sweden
3Karolinska Institutet/Sachs’ Children and Youth Hospital, Department of Public Health Sciences, Stockholm, Sweden

Background

Respiratory viral infections often mimic the symptoms of infections caused by bacteria, however, restricted and targeted administration of antibiotics is needed to combat the growing antimicrobial resistance. Conventional methods for diagnosis of viral infections can be time-consuming, although detection has moved towards PCR-based methods in clinical laboratories. However, PCR requires the use of a thermal cycler and thus isothermal amplification methods can be excellent alternatives for rapid point-of-care (POC) testing. In this work, we describe the validation and use of isothermal amplification of viral DNA at 37 °C coupled to a paper-based vertical flow microarray (VFM) setup that utilizes a colorimetric detection of amplicons using functionalized gold nanoparticles.

Methods

Two oligonucleotide probes, one in-house designed and one known adenoviral probe were tested and validated for microarray detection down to 50nM using a synthetic target template. Furthermore, primers were shown to function in a recombinase polymerase amplification reaction using both synthetic template and viral DNA.

Results

As a proof-of-concept, we demonstrate adenoviral detection with four different adenoviral species associated with respiratory infections using the paper-based VFM format. The presented assay was validated with selected adenoviral species using the in-house probe, enabling detection at 1ng of starting material with intra- and inter-assay %CV of ≤9% and ≤13%.

Conclusions

Combining RPA isothermal amplification, paper microarray analysis and nanoparticle-based colorimetric detection could be a useful strategy towards rapid and affordable multiplexed viral diagnostics that can be carried out at room-temperature.

Clinical Trial Registration (Please input N/A if not registered)
FACTORS ASSOCIATED WITH THE DEVELOPMENT OF CONGENITAL ZIKA SYNDROME IN INFANTS BORN TO MOTHERS WITH PROBABLE GESTATIONAL INFECTION: A CASE-CONTROL STUDY

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¹Universidade Federal do Rio de Janeiro, Preventive Medicine, Rio de Janeiro, Brazil
²Universidade Federal do Rio de Janeiro, Pediatrics, Rio de Janeiro, Brazil

Background

To investigate possible maternal- and pregnancy-related factors associated with the development of Congenital Zika Syndrome (CZS) in children of mothers with probable gestational infection.

Methods

This case-control study, we recruited mother-infant pairs between May 2015 and October 2017 in a pediatric infectious disease clinic in Rio de Janeiro. Inclusion criteria required either that the mother reported Zika infection symptoms during pregnancy or that the infant presented with clinical or imaging features of the CZS. Exclusion criteria included detection of an alternative cause for the patient's presentation or negative polymerase chain reaction assays for Zika in all specimens tested within 12 days from the beginning of maternal symptoms. Infants with CZS (CDC definition) were selected as cases and infants without CZS, but with probable maternal Zika virus infection during pregnancy, were selected as controls. Maternal and pregnancy-related informations were collected and their relationship to the presence of congenital anomalies due to CZS was assessed by Fisher exact or Mann-Whitney test.

Results

Out of the 42 included neonates, 24 (57.1%) were diagnosed with CZS (cases). The mean maternal age at the birth was 21 years old. The early occurrence of maternal symptoms during pregnancy was the only variable associated with CZS (odds ratio = 0.87, 95% CI: 0.78-0.97).

Case’s mothers presented symptoms until the 25th week of gestational age (GA), while control’s mothers presented until 36th weeks of GA. Income; illicit drug, alcohol, or tobacco use during pregnancy; other infections during pregnancy (including previous dengue infection) were not associated with CZS.

Conclusions

Our study corroborates the hypothesis that Zika virus infection earlier in pregnancy is a risk factor to the occurrence of congenital anomalies in their fetuses.

Clinical Trial Registration (Please input N/A if not registered)

n/a
Background: Hepatitis B Virus (HBV) is one of the most common chronic viral infections. Universal immunization against HBV is considered to be the best way of prevention of HBV infection. This study was conducted for the first time among Iraqi children below five years of age to determine the level anti-HBs antibody after primary vaccination.

Objectives: This study aimed to evaluate the level of the adequacy of seroconversion when hepatitis B vaccine is given at 0, 1 and 6 months as per WHO schedule among children under five years of age in Baghdad, Iraq.

Methods: A total 568 serum samples obtained from healthy children received three doses of recombinant Hepatitis B vaccine from Jan. to Nov. 2016, the serum samples were analyzed by VIDAS for the quantitative detection of anti-hepatitis B surface antigens.

Results: Results showed that (488) 86% children had protect anti-hepatitis B surface antigens (≥ 10 IU/L) and (80) 14% children had inadequate levels of antibodies (≤10 IU/L), the geometric mean titers for ant-HBs were 208 IU/L with standard deviation 147 IU/L, the Karkh district had no significant differences in the mean titer of anti-HBS antibody, the female had high titers of HBs against vaccination as compared that of males (P ≤ 0.05).

Conclusions: The vaccination program has been proven efficacy in children under five years of age living in Baghdad, the results showed that anti-HBS antibody titer may decrease over time after vaccination, finally, along with prevention and control strategies, ongoing investigation and monitoring antibodies level against HBV in children and other ranges are recommended.
ASSOCIATION BETWEEN ANTIBIOTIC EXPOSURE AND ANTIBIOTIC "RESPONSE FAILURE" IN PRESCHOOL CHILDREN WITH ACUTE RESPIRATORY TRACT INFECTIONS

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²Pharmatelligence, Research Fellow/Data Manager, Cardiff, United Kingdom
³Cardiff University, Wales School of Primary Care Research and the Department of Primary Care and Public Health, Cardiff, United Kingdom
⁴University of Southampton, Primary Care and Population Sciences, Southampton, United Kingdom

Background

Antibiotic use for self-limiting infections can have harmful consequences. These include the development of antibiotic resistance and disruption to the protective human microbiome. Preschool children with respiratory tract infections (RTIs) have the highest rate of antibiotic prescribing in primary care, although most RTIs in this age group are self-limiting. From routinely-collected primary care data, our aim was to explore whether higher levels of antibiotic exposure in children is associated with a greater likelihood of subsequent RTIs failing to respond to antibiotic treatment ("response failures").

Methods

Retrospective observational cohort study from the Clinical Practice Research Datalink 2009-2016. We selected a random sample of all acute RTI consultations in children under 5 years old where an antibiotic was prescribed. We estimated the odds with 95% confidence intervals using logistic regression between the number of antibiotic courses prescribed for RTIs in the preceding year, and a subsequent RTI not responding to antibiotic treatment ("response failure") adjusting for various confounders.

Results

Based on 114,254 children and 18,946 children with at least one antibiotic exposure in the preceding 12 months, children who received two or more courses of antibiotics for acute RTIs in the preceding year had greater odds of "response failure" (one antibiotic: adjusted odds ratio (OR) 1·03 [95% CI 0·88-1·21], p=0.67, n=230 children; two or more antibiotic courses: OR 1·32 [95% CI 1·04-1·66], p=0.02, n=97).

Conclusions

Relating the consequences of unnecessary antibiotic use to tangible and immediately relevant outcomes will help inform the development of more effective educational materials and awareness campaigns to promote appropriate antibiotic prescribing and use.
03A. SCIENCE: SEVERE BACTERIAL INFECTIONS

NEUROSURGERY IN CHILDREN WITH BACTERIAL MENINGITIS
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¹Infectious Diseases specialist, Infectious Diseases Clinic- UCCK, Prishtine, Kosovo

Background

Bacterial meningitis can be associated with life threatening neurological complications that require urgent neurosurgical treatment.

The aim of the study was to analyze neurosurgical treatment of children with bacterial meningitis.

Methods

This prospective study enrolled pediatric bacterial meningitis cases in two study periods: 277 children treated during years 1997–2002 and 77 during years 2009–2010.

Results

Of the 277 vs. 77 children treated for bacterial meningitis (BM), 60 (22 %) vs. 33 (43 %) patients developed early neurological complications (NC), while there were 15 (5.4 %) vs. 2 deaths (2.6 %). In both study periods, the majority of pediatric BM cases were caused by three most common meningeal pathogens, meningococcus, H. influenzae type B and pneumococcus (89% vs. 79%), while gram-negative bacilli caused around 10% of cases (8.9% vs. 10.5%).

Neuroimaging was performed in 39% (n=109) and 58% (n=45) of children with BM. Evident structural changes were recorded in 43% (n=47) vs 75% (n=34) of brain images. In both study periods, the most common NC confirmed by neuroimaging were: subdural effusions (35 vs 22); hydrocephalus (7 vs 2); cerebritis (1 vs 3); intracerebral bleeding (1 vs 3); subdural empyema (2 vs 1), spinal /cerebral abscess (1 vs 1), subdural hematoma (1 vs 1) and ventriculitis (0% vs 1). Due to a significant mass effect proved by neuroimaging and by clinical presentation, urgent neurosurgery was required in 5% vs. 4% of cases (9/38 vs. 2/24 cases with subdural collections, 5/7 vs. 1/2 of cases with hydrocephalus and 1 case of spinal abscess).

Conclusions

The neurosurgical treatment of children with bacterial meningitis was required almost equally in both study periods, with subdural effusions being the most common.

Clinical Trial Registration (Please input N/A if not registered)

N/A
Complicated pyelonephritis and pyonephrosis caused by Salmonella Type C: CASE REPORT

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Title of Case(s)
Complicated pyelonephritis and pyonephrosis caused by Salmonella Type C: CASE REPORT

Background

Salmonella species are considered a rare cause of UTI in children, usually associated with immunocompromised state or anatomic abnormalities. We present a case of a 14 month old boy with urosepsis and pyonephrosis caused by Salmonella Group C.

Case Presentation Summary

A 14 month old previously healthy boy presented to the emergency department with a 5-day history of weakness, fever (40.5°C), vomiting and diarrhea. Before admission, he was diagnosed with suspected bacterial gastroenteritis and was treated empirically with azithromycin, without improvement. At admission, urinalysis detected pyuria with moderate blood and microalbuminuria. Blood, feces and urine cultures yielded *Salmonella enterica* group C. Abdominal US revealed moderate-severe left hydrouretheronephrosis and pyonephrosis. Congenital obstructive megaureter was diagnosed. He was treated with ceftriaxone and subsequent blood, urine and stool cultures were all negative. An ureteral stent was inserted for drainage and within a few hours his symptoms improved dramatically. Treatment with oral trimethoprim-sulfamethoxazole was added. He is scheduled for ureteral reimplantation surgery to correct congenital obstructive megaureter secondary to ureteral vesicular junction stenosis.

Learning Points/Discussion

Salmonella species can cause pyelonephritis and pyonephrosis in a child with underlying urinary tract abnormalities, following gastrointestinal infection. Remittent fever should prompt abdominal imaging to evaluate for this possibility. Drainage should not be delayed in case of pyonephrosis.
Background

Recent incidences of involvement of *Plasmodium vivax* in severe malaria suggest a drastic shift in the clinical paradigm for vivax malaria. Mechanisms that trigger transition from non-severe (NSVM) to severe vivax malaria (SVM) are obscure. This multi-disciplinary study provides a comprehensive analysis of serum proteomics profile of NSVM and SVM to understand the itinerary during the ontogenetic advancement of the disease into severe forms and longitudinal analysis of the *P.vivax* infected children to identify surrogate markers of severity.

Methods

This prospective cohort study was conducted on 126 children of *P.vivax* malaria admitted from January 2017 to December 2017. The species diagnosis was made with peripheral smear and rapid diagnostic test and confirmed with polymerase chain reaction analysis. Severe malaria was defined as per WHO guidelines. Serum samples from children with NSVM (n=30) and SVM (n=30) were analysed by iTRAQ-based quantitative proteomic approach in comparison to healthy controls (HC) (n=50) and dengue illness as febrile control (FC) (n=45). The results were validated by employing immunoassay-based techniques.

Results

Comparative proteomics analysis of NSVM, SVM, HC and FC revealed evidences for the modulation of diverse physiological pathways including oxidative stress, cytoskeletal regulation, lipid metabolism and complement cascades in *P.vivax* malaria. Proteins like complement C3, alpha-2-macroglobulin, complement C5, hemopexin, plasminogen, alpha-1-antichymotrypsin, apolipoprotein A-IV, prothrombin, antithrombin-III, inter-alpha-trypsin inhibitor heavy chain H3, gelsolin & apolipoprotein A-I showed similar trends of differential expression. Proteins like Superoxide dismutase, C-Reactive Protein, Apolipoprotein E, Apolipoprotein A-1, Serum amyloid A, and Haptoglobin displayed significant (p≤.0001) correlation with the disease severity and therefore can be eventually used as powerful indicators for disease severity.

Conclusions

In this comprehensive multidisciplinary prospective study, 6 serum proteins were identified as potential predictive markers for *P.vivax* malaria severity.

Clinical Trial Registration (Please input N/A if not registered)
N/A
Title of Case(s)

Postoperative candidal mediastinitis in children: two case presentations.

Background

Previous reports indicate that postsurgical candidal deep sternal wound infections have an extremely high mortality rate. However, the incidence of such complication in pediatric cardiac surgery is unknown. Here we report two pediatric cases of candidal deep sternal wound infection after open-heart surgery.

Case Presentation Summary

Case 1. A 1-year 9-month old boy presented with prolonged fever that developed after total cardiopulmonary connection was performed. Pus discharge from the retrosternal space was observed on postoperative day 4 (POD4). MRSA was isolated from his blood and pus, and he was treated with vancomycin and surgical debridement. In spite of treatment, the wound condition gradually deteriorated. Candida parapsilosis was isolated from the sternal wound, and antifungal therapy with liposomal amphotericin B (L-AMB) was started. After treatment, the laboratory data improved and the wound culture was negative. The patient was discharged on POD132.

Case 2. Total cardiopulmonary connection was performed on a 3-year 10-month old girl with hypoplastic left heart syndrome. Postoperatively her sternal wound was left open to allow maintenance of blood pressure. Candida lusitaniae was isolated from the wound on POD8, and micafungin (MCFG) was started. Although blood culture was negative, C.lusitaniae was constantly detected from the sternal wound until POD34 in spite of addition of voriconazole (VRCZ), wound debridement and daily lavage. Cardiac function gradually deteriorated, and death occurred on POD55. Autopsy was not performed.

Learning Points/Discussion

Candidal mediastinitis is a rare but serious complication of cardiac surgery; some patients cannot be rescued in spite of early diagnosis and initiation of antifungal therapy. The choice and dosage of antifungal drugs depending on the type of pathogen and the status of the patient needs to be further investigated.
INCREASED CONSUMPTION OF ANTIFUNGAL AGENTS IN HIV NEGATIVE PEDIATRIC PATIENTS FROM TEACHING INFECTIOUS AND TROPICAL DISEASES CLINIC FROM BUCHAREST ROMANIA

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Background

An consistent body of evidences are currently documenting an increasing worldwide consumption of antifungal agents in health care suggesting the need for antifungal stewardship programs. In this paper we analyzed the trend of systemic antifungal agent consumption in our 500 beds clinic for infectious diseases as a prior phase of an antifungal agents stewardship program.

Methods

Yearly quantities of antifungal (AF) agents released by hospital pharmacy to wards were transformed in daily defined doses — consumption was standardized by expression of the amount of DDD used per 1000 patient days. Linear regression facility of Epi Info 7 software was used to generate correlation coefficients.

Results

Fluconazole was the most frequently prescribed antifungal. A strong significant positive correlation was found between AF consumption and yearly ranks only for pediatric wards (r: 90; p: 0.006). In these pediatric wards (124 beds) we found the followings:

- consumption of AF agents was correlated with yearly frequencies of oro pharyngeal candidiosis (r: 76,9%; p: 0.043) but not with yearly frequencies of systemic cases of Candida infections.

- further we found strong correlation between yearly consumption of AF agents and yearly consumption of Ceftriaxon (r:87.6 ; p: 0.010) but not with betalactam penicillin (p: 0.465), quinolones (p: 0.106) or macrolides (p: 0.825).

Conclusions

We can speculate that use of extended spectrum penicillins might favorised development of fungal upper respiratory tract infections and clinicians reacted prescribing Fluconazole. In this case our filling are that appropriateness of prescribing extended spectrum penicillins need to be assessed and merely replaced with ATC subgroup J01C. In different terms it appear that an antimicrobial stewardship program might improve proper AF agents use.

Clinical Trial Registration (Please input N/A if not registered)

N/A
Background

Zika Virus (ZikV) was identified in Africa seven decades ago. However, only in the current decade it appeared in Northeast Brazil, causing an explosive epidemic with increased rates of microcephaly and other serious birth defects, possibly being the worse severity spectrum of that infection in humans.

To describe clinical, neurophysiological and neuroradiological characteristics of children with congenital microcephaly diagnosed at birth potentially associated with congenital ZikV infection.

Methods

This was a retrospective study conducted at a reference Rehabilitation Centre in Salvador, Northeastern Brazil, from November 2015 to September 2016. Inclusion criteria were microcephaly diagnosed at birth and probable ZikV infection during pregnancy. Eligible patients were evaluated by trained paediatricians, physiotherapists, nurses and psychologists according to standardized procedures. Data were registered in pre-defined forms.

Results

The study group included 102 children, whose mean age was 4.1 ± 2.3 months. There were 56 (55%) girls and 46 (45%) boys. Cutaneous rash occurred massively (81%) during the first trimester of pregnancy. Mean gestational age at delivery was 38.4 ± 1.7 weeks and mean head circumference at birth was 28.6 ± 1.7 cm. Microcephaly was diagnosed during pregnancy in 65.7% of the cases. Microcephaly was mild/moderate (45.1%) or severe (54.9%). Abnormalities were observed in visual evoked potential (14.1%) and in auditory evoked potential (17.3%). The majority of the patients (56.3%) presented epileptogenic alteration in videoencephalogram. The most common findings in neuroimaging were: cerebral atrophy (92.1%), ventriculomegaly (92.1%), malformation of cortical development (85.1%) and cortico-subcortical calcifications (80.2%). Hypertonia was observed in 90.1%, hyperreflexia in 73.3% and arthrogryposis in 10.8% of the children.

Conclusions

In this group of patients which maternal cutaneous rash occurred predominantly early during pregnancy, neuroimaging findings were severe, neurosensory alterations were mild, and clinical alterations were common.
Title of Case(s)

AN AGGRESSIVE PRESENTATION OF PANTON VALENTINE LEUKOCIDIN POSITIVE STAPHYLOCOCCUS AUREUS AS OSTEOARTICULAR INFECTION IN A PREVIOUSLY HEALTHY 5-YEAR OLD

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Background

Panton Valentine Leukocidine (PVL) toxin is produced by some strains of Staphylococcus aureus. It causes severe necrotizing infections of skin, soft tissues, bones and joint. Infections caused by PVL-SA have not been well described in England.

Case Presentation Summary

A previously healthy 5-year old girl presented to a district hospital with right knee septic arthritis. She was started on Flucloxacillin and the wound was drained surgically twice with much improvement. She later deteriorated clinically, at which point she was referred to our tertiary facility. By then, blood and synovial fluid aspirate cultures had grown Methicillin Sensitive Staphylococcus aureus and further testing showed it was PVL positive. Linezolid and Clindamycin were added to her antibiotic regimen with good effect. 5 days later her wound was noticed to discharge pus and she was again taken to theatre. She needed two blood transfusions and had a total of five more knee wash-outs, at which point the wound failed to close primarily, requiring a transfer to a center for plastic surgery where she had soft tissue coverage of the defect. She got discharged on Ceftriaxone, Clindamycin and Rifampicin to complete an 11-week course of antibiotics in total. Three months after the initial infection, she came for a routine follow-up. Her wounds had healed and she was well in herself. Follow-up x-ray showed a moth-eaten appearance of her whole tibia. She is currently undergoing physiotherapy but will need long term follow-up to monitor for chronic osteomyelitis.

Learning Points/Discussion

Osteoarticular infections with PVL positive Staphylococcus aureus require aggressive medical and surgical treatment and could lead to potential long-term adverse effects.
Antibiotic resistance is an important societal health issue. There remains widespread public misconception about antibiotic use and resistance. Preschool children are at particular risk of receiving unnecessary antibiotics because they commonly present in primary care, and many childhood infections are self-limiting. Our aim was to explore parents’ perceptions and understanding of antibiotic use and resistance when considering how to manage their young child with an acute respiratory tract infection (RTI) and to explore what strategies parents would find acceptable to minimise antibiotic resistance for their families.

Methods

Semi-structured interviews with a purposive sample of 23 parents of preschool children who recently had an acute RTI across greater Oxfordshire during the 2016-7 winter. Thematic analysis was used to analyse the data.

Results

Parents had a sense of unrealistic optimism about how antibiotic resistance was likely to affect their family. They considered their families to be at low risk of antibiotic resistance because their families were “low users” of antibiotics. Most parents thought they acted morally responsible and were quite reticent about antibiotics for their children. Very few parents considered antibiotic resistance as a possible harm of antibiotics. Parents wanted future antibiotic awareness campaigns to have a universal and relevant message for their families that fits into their daily lives.

Conclusions

Future communication about the potential impact of unnecessary antibiotic use and antibiotic resistance needs to focus on outcomes that parents of young children can relate to, and in a format that parents will engage with to make a more informed decision about the risks and benefits of antibiotics for their child.
THE BURDEN OF HOSPITALIZATION OF MEASLES CASES IN CHILDREN AGED UNDER ONE YEAR DURING AN MEASLES EPIDEMIC IN BUCHAREST MUNICIPALITY – 2017

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Background

The current WHO strategy to prevent measles in children aged under one is to eliminate measles virus transmission based on very high immunity levels in whole population. During a measles epidemic that affected Romania starting with the fall of 2016 an important proportion of hospitalized cases in our 500 beds clinic were children aged under one. The aim of this work was to document the burden of hospitalized cases of measles in children aged under one.

Methods

The burden of hospitalized cases of measles in children aged under one (group A) was evaluated by statistically comparing of: (a) means of duration and cost of hospitalization, and (b) prevalence of cases with any type of measles complication and cases complicated with measles pneumonia, in this group with those calculated in preschool children, aged 1-5 years (group B).

For analysis the relevant information of all preschool (0-5 yrs) children hospitalized in our clinic during 2017 calendar year with the diagnosis of measles (n=424) were extracted from hospital electronic register and listed in MS Excel® format; Epi Info 7 software was used to perform statistic comparing for means and proportion.

Results

Prevalence of cases with any type of measles complications and the prevalence of cases with measles pneumonia were similar in both groups (p: 0.4231; p: 0.3625 ).

Means of duration and cost of hospitalization – were both significantly higher in group A than in group B (p: 0.0324; p.0005)

Conclusions

Although the complications were similar between the two group compared the burden of hospitalized cases of measles in under one children (duration and cost of hospitalization) is significantly higher than in over one preschool children. This represents a documented argument that measles control is cost saving.
18B. SCIENCE: ZOONOSIS, VECTOR-BORNE AND EMERGING INFECTIONS

RISK FACTORS FOR PERSISTENT BRUCELLOSIS IN CHILDREN

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Background

Brucellosis episodes may be complicated with relapse and chronic disease, necessitating prolonged duration of antibiotic treatment. While inadequate treatment is a known risk factor for persistent (relapse/chronic) disease, data regarding other risk factors associated with persistent brucellosis are scarce. We assessed childhood brucellosis episodes, differentiating between acute, single-episode disease and persistent episodes.

Methods

The medical files of first, acute brucellosis episodes from 2005 through 2014, identified from positive blood cultures or serology, were reviewed retrospectively. Persistent infections were defined as febrile episodes >1 month after the first episode necessitating treatment, and confirmed by bacteremia, serology or clinically.

Results

Of a total of 446 acute brucellosis episodes, 25% (n=111) had persistent disease, confirmed by bacteremia (35%), serology (46%) and clinically (19%).

Of all acute, first episodes, 99.6% were in Bedouin children and in 80% of them blood cultures were positive for Brucella melitensis.

In univariate analysis, fever (92% vs. 84%); lower mean neutrophil (*10^3/µl; 2.5±1.1 vs. 3.1±1.8) and platelet (*10^3/µl; 233±112 vs. 260±111) counts; IgG ≥1:160 (83% vs. 67%) and IgG ≥1:640 titers (26% vs. 17%) were associated with persistent disease. A trend toward higher bacteremia rates was observed in persistent infections (87% vs. 78%; p=0.051). In multivariate analyses, neutropenia (odds ratio, OR=2.704), bacteremia (OR=2.909) and IgG ≥1:160 titers (OR=2.236) were associated with persistent brucellosis.

Conclusions

Acute brucellosis episodes are commonly complicated by persistent disease, especially in bacteremic episodes with neutropenia and high IgG titers. Treating physicians may consider treatment regimen modifications in acute brucellosis episodes with those risk factors.
SEPTIC COSTOCHONDritis: DIAGNOSIS AND THERAPEUTIC PROPOSAL OF AN ATYPICAL ENTITY

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Title of Case(s)

Septic costochondritis: diagnosis and therapeutic proposal of an atypical entity

Background

Septic costochondritis is an uncommon clinical entity occurring spontaneously or secondary to trauma or thoracic wall surgery. Hematological spread is considered to be the major cause of primary costochondritis, being S.aureus, P.aeruginosa, E.coli and C.albicans the most frequently related microorganisms. Most of the described cases of costochondritis date from the last century, being mainly observed in intravenous drug abusers and patients with previous sternotomy, all of them of adult age.

Case Presentation Summary

We report the case of a 10-year-old girl who was admitted for evaluation of a painful mass in the lower chest wall, fever and general malaise. Ultrasound and later CT and MRI were performed, revealing the presence of a 2x2.5x3.3cm presumably chondro-cartilaginous nodular structure with necrotic center in the costal cartilage, with very little inflammation and associated to small pleural effusion. In the blood test, elevation of acute-phase proteins and leukocytosis were highlighted. Histological study was carried out: 1mL of purulent
material was obtained by puncture, revealing the presence of methicillin-susceptible S. aureus in the culture. Granulation tissue with fibroblastic reaction was observed by biopsy, with no signs of malignancy. Under the orientation of septic costochondritis, antibiotic treatment with intravenous cefazolin and oral rifampicin was performed for a week, adding 3 weeks of oral home treatment. After 4 weeks of antibiotic bitherapy, control ultrasound showed full resolution of the mass, being the patient asymptomatic.

Learning Points/Discussion

A case of costochondritis due to Staphylococcus aureus is described. It's a very rare disease from which we have clinical, analytical, morphological and anatomopathological characterization. We propose a successful therapeutic option based on the knowledge and experience we have about arthritis and osteomyelitis by the same microorganism.
Detours on the way to tuberculosis

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Background

Tuberculosis is rising in Germany. 5329 cases were reported to the RKI in 2016. Especially extrapulmonary forms of tuberculosis are often a diagnostic challenge.

Case Presentation Summary

Case We report a 23-month-old girl, who presented with local inflammatory signs in the area of the right medial malleolus. She was the 4\textsuperscript{th} of 4 children born to healthy, non-consanguineous German parents and had a history of mild developmental delay. She was initially treated in the surgery unit with abscess cleavage and antibiotic therapy for bacterial osteomyelitis. In the diagnostic workup osteomyelitis, meningitis with internal hydrocephalus and an infestation of the LVB 1 as well as a meningeal inflammation at the level of the sacrum due to tuberculosis could be demonstrated consistent with miliary tuberculosis. Treatment with INH, RMP, PZA and EMB in combination with dexamethasone was initiated. The cMRI showed an increase in the internal hydrocephalus, occasioning the tuberculostatic therapy to be extended by protonamide and amicacin and a Rickham reservoir to be implanted. In the absence of sufficient CSF drainage, a VP shunt was implanted after decontamination of CSF. This resulted in a gradual improvement of the condition and a marked improvement in motor skills. Since intracerebral granulomas persisted thalidomide was added. The remaining tuberculostatic therapy could be reduced and dexamethasone slowly tapered.

Learning Points/Discussion

Discussion
In addition to presenting the difficulties of diagnosing tuberculosis with a non-typical history, this case is particularly intended to stimulate discussion about the therapy of meningitis tuberculosa and its complications.
Background

The antimicrobials use has increased significantly, increasing antimicrobial resistance. Antimicrobials stewardship has been designed to combat it. Currently there are computer support strategies to optimize the results of these programs, and we locally developing an antimicrobials electronic request system (AERS). Purpose of this study is to determine the impact in antimicrobial consumption after 3 years of implementation of AERS.

Methods

Observational study performed at Roberto Del Río Children’s Hospital comparing: 2014 to 2016 (intervention) and 2013 (prior intervention). With AERS the physicians request restricted antimicrobials using the software tool. The electronic request warns infectious disease (ID) team in the hospital intranet. If it is approved, pharmacy is on line notified, and the antimicrobial is send to patient. In non-working hours, it is authorized automatically until the next available working day. We measured DDD/100 occupied days beds for vancomycin, cefotaxime, meropenem, imipenem, ertapenem, linezolid (restricted antimicrobial), amikacin, penicillin, amoxicillin and cloxacillin (unrestricted antimicrobial). No informed consent was needed. Descriptive statistical analysis was used.

Results

Cefotaxim is the most used restricted antimicrobial in our setting, after intervention decreased 28.8% in the pediatric unit and 35% in the ICU. Carbapenems consumption increased in ICU. Vancomycin decreased 2.8% in pediatric unit but increased 31.4% in ICU. Linezolid increased 520% in ICU and there was no change in consume in pediatric unit. Unrestricted antimicrobials had no change in the comparing two periods, except cloxacillin that increased 58.3% in pediatric unit and 45% in ICU.

Conclusions

Mainly impact of AERS was significantly decreased consumption in cefotaxim, the most used antimicrobial. Although there was an increased in use of vancomycin, linezolid and carbapenems, this was a minor effect. For us, AERS is a successful strategy for our antimicrobial stewardship.

Clinical Trial Registration (Please input N/A if not registered)

N/A
INFECTION ASSOCIATED HEMOPHAGOCYTIC SYNDROME IN CHILDREN: A RETROSPECTIVE ANALYSIS OF 17 CASES

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Background

Haemophagocytic syndrome (HPS) is a rapidly progressive, life-threatening syndrome of excessive immune activation. Early recognition of the clinical presentation and laboratory abnormalities associated with HPS and prompt initiation of treatment can be life saving. The aim of this study was to investigate the infectious etiologies, clinical and laboratory characteristics, and treatment outcomes of pediatric patients with infection associated hemophagocytic syndrome (IAHPS).

Methods

This is a retrospective record review of pediatric patients diagnosed to have IAHFS between December 2012 and January 2016.

Results

A total of 17 pediatric patients with IAHPS (10 boys / 7 girls; median age: 6 years, range 2-17 years) were enrolled in this study. Brucella (10 patients, 58%) was the most frequent infectious trigger of HFS. Other infectious triggers were Leishmania (3 patients), Salmonella Typhi (1 patient), Mycobacterium tuberculosis (1 patient), parvovirus B19 (1 patient), and influenza A (H3N2) (1 patient). Fever, bi/pansitopenia, hyperferritinemia, and elevated transaminases were present in all patients (100%), and splenomegaly in 13 patients (76%). The median duration of fever before diagnosis of HPS was 12 days (range, 5-25 days). All of the patients underwent bone marrow aspirations that confirmed hemophagocytosis. All patients received antimicrobial treatment for the underlying infections; 10 patients received intravenous immunoglobulin (IVIG) and 2 patients received IVIG+steroids due to persistent fever and progressively worsening clinical conditions. Recovery was noted in 16 (94%) patients. Mortality was only seen in 1 patient (5.8%) with influenza A (H3N2) pneumonia.

Conclusions

Physicians need to be aware of the occurrence of HFS in patients with prolonged fever, organomegaly, and cytopenias in the setting of an infectious process.
ETIOLOGY OF CHILDHOOD MENINGITIS IN NORTHEASTERN POLAND, 2017
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Background

In 2014 we observed an outbreak of enteroviral meningitis (EM) caused by Echo 30, which resulted in over 300 cases. In this study we aimed to evaluate the etiology of childhood central nervous system infections (CNS) infections 3 years after the outbreak.

Methods

A retrospective analysis of medical records of children with meningitis hospitalized in the Department of Pediatric Infectious Diseases at the Medical University of Bialystok in 2017. EM, varicella zoster meningitis (VZM), and herpes simplex encephalitis (HSE) were diagnosed based on the detection of viral genetic material in CSF. The diagnosis of Lyme neuroborreliosis (LNB) and tick-borne encephalitis (TBE) was confirmed by the detection of specific antibodies in serum and CSF samples. The diagnosis of bacterial meningitis (BM) was confirmed in CSF or blood culture.

Results

In 2017 there were 67 cases of CNS in children (33% girls, 77% boys) aged 1 month to 17 years. EM comprised the majority of cases (n=34, 51%). Vector-borne CNS infections were identified in 23 (34%) children: TBE was diagnosed in 14 children (21%), and LNB in 9 (13%). Six (67%) LNB cases presented with facial nerve palsy. BM was diagnosed in 5 children (7%). Other causes of CNS infections were rare (Figure 1a). In further analysis 11 different strains of enteroviruses were identified (Figure 1b). Remarkably, enterovirus A71 C2 was identified in one child, but the infection was mild and not associated with complications.

Conclusions

As opposed to 2014, in 2017 the etiology of childhood CNS infections was more diverse. As much as 34% of CNS infections were vector-borne indicating that clinicians need to include NB and TBE in differential diagnosis of aseptic meningitis.
15B. SCIENCE: GLOBAL CHILD HEALTH

REASONS AND REVIEW OF LATE DIAGNOSIS IN SICKLE CELL DISEASE – CASE REPORTS
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Title of Case(s)

DIAGNOSTIC CRISIS IN CRISSES OF SICKLE CELL DISEASE

Background

The age at presentation and clinical profile of Sickle cell disease (SCD) patients are extremely variable. The clinical manifestations of SCD result due to two key pathological processes- vaso occlusion and hemolysis. Infection can cause both specific and nonspecific effects on host and is common precipitating factor for crises.

Case Presentation Summary

Case 1: A seven year old boy with spastic para paresis was admitted for fever and abdominal pain. On examination, hepato splenomegalymegaly was present. Liver function tests - normal. Ferritin and Triglycerides were increased. Bicytopenia was present. Blood culture was positive for Streptococcus pneumoniae. A diagnosis of hemophagocytic lymphohisticocytosis (HLH) was made.

Case 2: A seven year old girl was admitted for anemia with severe pain in arm and spiking fever. She was treated with systemic antibiotics for fever and respiratory infection. Splenomegaly was present. Based on peripheral smear and Hemoglobin electrophoresis diagnosis of sickle cell anemia was made in both patients. In case 2, co inheritance of beta thalassemia was observed.

In both patients from rural set up, diagnosis of SCD was missed till age of seven years. In first case, the focus was always on spastic paraparasis. In the second patient, anemia was always symptomatically treated. Only occurrence of crises brought them to tertiary center. The clinical severity in co inheritance largely depends upon the nature of the β thalassemia mutations inherited.

Learning Points/Discussion

Early diagnosis of sickle cell anaemia is important because many complications can be prevented and treated. Education of the parents on complications requiring immediate care can be given. Both cases highlight the need for new born screening and locally appropriate model of care in India.
Background
Viral gastroenteritis is a major cause of hospital admissions in preschool children in high income countries. Childhood is a particularly important and vulnerable period in life in the development of health inequalities and disparities. Studies have shown that children in households with low socioeconomic standard have worse health than children of parents with high socioeconomic standard.

In this study the primary aim was to investigate socioeconomic determinants of hospital care caused by viral gastroenteritis, admissions as well as outpatient care in the emergency department in Sweden.

Methods
Register based study in a national birth cohort of 752 048 children below 5 years of age in Sweden during 2006-2012. Hazard ratios (HR) of time to first admission and first episode of outpatient emergency department (ED) care with a diagnosis of viral gastroenteritis were estimated with Cox regression.

Results
The adjusted HRs for hospital admission with a diagnosis of viral gastroenteritis were increased when the mother was <25 years; 1.30, (95% CI 1.24-1.35), had a short education, 1.18 (1.12-1.23), a psychiatric disorder, 1.34 (1.30-1.39), and/or when parents were born outside Europe, 1.23 (1.18-1.29). In contrast, the disposable income of the family was only marginally associated with hospital admissions because of viral gastroenteritis. The pattern of HRs for outpatient ED hospital care was similar. Hospital care incidences for viral gastroenteritis differed considerably between Swedish counties.

Conclusions
Parental indicators associated with a lower level of health literacy increases the risk for hospital care due to gastroenteritis in young children. Information about oral rehydration should be provided in ways that is accessible to these parents.
GANCICLOVIR-RESISTANT CYTOMEGALOVIRUS INFECTION IN PAEDIATRIC PATIENTS

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Background

Cytomegalovirus (CMV) infection is one of the leading causes of morbidity and mortality among haematopoietic stem cell and solid organ transplant patients. Recently, the emergence of CMV-drug resistance has been recognised among those who were treated with ganciclovir. However, there is still limited data in paediatric patients. We aimed to describe clinical characteristics and outcomes of CMV infection with ganciclovir resistance in paediatric patients.

Methods

We retrospectively identified 9 patients from 2013 to 2017 who had genotypically confirmed ganciclovir-resistant CMV infection. Genotypic assays for UL97 gene mutations were analysed by RT-PCR. Demographic data, clinical manifestations, virological data, treatment, and outcomes were collected from electronic records.

Results

The median age of the patients was 1.75 years (interquartile range [IQR], 0.73-10.35). Four transplanted recipients (3 liver, 1 kidney) and five oncologic patients (4 leukemia, 1 IAHS) were included. Ganciclovir resistance was tested at a median time of 23 days (IQR, 13.5-31) after initiation of treatment with ganciclovir with median CMV load of 46,700 copies/mL (IQR, 18,850-111,263) or log 4.67 (IQR, 4.26-5.04). All ganciclovir-resistant isolates harboured a UL97 mutation in codon 460. A median of maximum CMV load was 122,080 copies/mL (IQR, 75,400-1,449,756) or log 5.09 (IQR, 4.86-6.13). None of our patients had received ganciclovir for CMV prophylaxis. Five of 9 patients (55%) were successfully treated with high-dose ganciclovir (7.5 mg/kg twice daily). Others received foscarnet and cidofovir. Three patients died due to non-CMV-related problems.

Conclusions

Ganciclovir-resistant CMV infection is an emerging problem, not only in transplanted recipients but also oncologic patients. Therefore, screening for mutations should be considered in patients with persistent viremia, even though patients had not received ganciclovir prophylaxis before and treatment with high-dose ganciclovir could be an effective treatment modality.
Don’t forget the past – a sleeping disease can be awakened

Background

Congenital malaria is a rare disease, even in endemic countries. Compared to P. falciparum, P. vivax is more frequent in nonendemic regions because of its dormant asymptomatic hepatic stage in infected women.

Case Presentation Summary

A 24-day-old newborn female presented to our pediatric emergency department with a short history of fever, reduced feeding and irritability. Empiric antimicrobial treatment was started. Platelets were low (61 x 10^9/L). The mother had immigrated to Switzerland 2.5 years ago from Eritrea. Since then no travelling. The child’s fever persisted and thrombocytopenia worsened (min. 14 x 10^9/L). A manual differential WCC was performed, which, revealed, to our surprise, malaria parasites with a calculated parasite load of 8.4%. Intravenous Artesunate was started empirically. The child’s condition improved rapidly and fever defervesced within 24 hours. 48 hours after initiating treatment, Plasmodia were undetectable. Microscopic second look and PCR testing confirmed Plasmodium vivax. Treatment was adjusted to oral Chloroquin. The mother’s work-up revealed a negative malaria rapid diagnostic test, normal blood count and negative blood smear. The PCR was however positive for P. vivax. On further questioning, she disclosed that she had suffered from malaria in Eritrea 3 years ago. She had received Treatment (unknown agent) at that time. After the discharge of her child she was also treated with Chloroquine.

Learning Points/Discussion

Clinical findings of congenitally infected newborns are diverse and range from asymptomatic to late onset Sepsis spectrum. Although rare, malaria is an important differential diagnosis when evaluating febrile, thrombocytopenic or septic newborns of migrant mothers or those with a travel history to a malaria endemic country. The last malaria exposure of mothers may lie many years in the past.
CHARACTERISTICS OF POSITIVE BLOOD CULTURES, ANTIBIOTIC THERAPY AND OUTCOMES IN PAEDIATRIC BONE MARROW TRANSPLANT RECIPIENTS – A RETROSPECTIVE OBSERVATIONAL STUDY

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Background

Bone marrow transplantation (BMT) recipients are particularly susceptible to systemic infections. We aimed to characterize organisms leading to bacteriaemia in this group and map this to clinical data. In a retrospective observational study we analyzed the data of all post BMT patients with a positive blood culture to reflect on our current choice of antibiotics and removal of central lines.

Methods

Positive blood cultures were identified retrospectively from laboratory data between the period of February 2016 to March 2017 in a large paediatric BMT centre in London.

Clinical data included time of positivity compared to transplantation date, type of transplant, neutropenia, presence of a central venous catheter (CVC), community or hospital onset, type and length of antibiotic treatment clinical outcome and resistance patterns.

Results

35 positive blood cultures from 28 clinical episodes were identified. 68% presented in the first 90 days post transplantation, 79% of whom were neutropenic. An indwelling CVC was present in 89% of episodes. Coagulase negative Staphylococci (CONS) were the most common pathogen in 28%. 18% of the tested organisms were resistant to our first line piperacillin/tazobactam. 50% of CONS, 80% of non-CONS CVCs were removed within 7 days of bacteriaemia. 95% of CVC tips were cultured but only 1 cultured the organism same as the blood. The 30 day mortality rate was 14%.

Conclusions

Bacteriaemias are common complications of BMT. Identifying the responsible organisms allows targeted therapy and surveillance of regimens. We need to monitor the percentage of resistance to antibiotics and review our guidelines. We had a high rate of CVC removal with a low rate of positive line tip culture. Further study is needed as to whether early removal of CVCs in all bacteriaemic patients is necessary.
Severe Pertussis in a neonate – anticipate and treat hyperleukocytosis early

Background

Hyperleukocytosis, caused by pertussis toxin, is rare but life-threatening. In young infants this may lead to increased viscosity and vascular occlusion of vital organs, especially the lungs. Leukocyte depletion via exchange blood transfusion is an established treatment of hyperleukocytosis. The most effective prevention of pertussis in infants less than 3 months is immunization of women during second or third trimester in every pregnancy.

Case Presentation Summary

A 24 day old female neonate presented with a one-week history of afebrile rhinitis, paroxysmal cough and “turning dark” as reported by her mother. Both parents had a cough for 4 weeks. She appeared unwell with tachypnoea, paroxysmal coughing and apnoic spells. Pertussis was suspected and Azithromycin started. PCR from nasopharyngeal swab was positive. Day two the patient developed severe respiratory distress requiring oxygen. On Xray right upper lobe atelectasis. Laboratory: hyperleukocytosis (52.5 x10^9/L; 25.7 x10^9/L lymphocytes), hypercapnia (pCO2 7.79 kPa) and normal CRP (<5mg/L). Further increase of leukocytes to 63.5 x10^9/L 12 hours later. Exchange transfusion was performed after Intubation and ventilation. Significant leukocyte decrease to 22.5 10^9/L was achieved by the next day. Gradual improvement but oxygen supplementation for total of three weeks was neccessary. The mother had not been immunized against pertussis during pregnancy.

Learning Points/Discussion

Infants with severe pertussis and hyperleukocytosis benefit from early blood exchange transfusion to prevent respiratory failure. Repeated full blood count analyses in infants with pertussis help to detect hyperleukocytosis and anticipate the dynamics. Booster vaccination during pregnancy is key to protect young infants, the most vulnerable population. Gynaecologists should always take this intervention into their routine care bundle when consulting pregnant women.
Background

Despite identical treatment protocols during childhood ALL treatment, some children suffer from more frequent episodes of febrile neutropenia than others. The reason for this is still not fully known. Polymorphisms in the gene coding for MBL, called MBL2, have been correlated to infection susceptibility in a wide range of infections. However, the literature is showing conflicting results for the association between genetic variation in the MBL2 gene and infections in children with cancer.

Methods

Children diagnosed with ALL at Astrid Lindgren Children’s hospital, Stockholm, during 2004-2014 were enrolled in the study. Three different polymorphisms in the MBL2 gene were analyzed using pyrosequencing. The frequency of febrile neutropenia was retrospectively collected from medical records during the 2.5 years of treatment.

Results

Eighty-nine children were enrolled in the analyses. The median number of episodes of febrile neutropenia were 3 (range 0-9). Twenty-six children (29%) were heterozygote/homozygote for at least one polymorphism in the MBL2 gene. There were no statistically significant differences in frequency of febrile neutropenia when comparing those carrying polymorphism in the MBL2 gene and those that do not.

Conclusions

In this cohort, there were no correlation between polymorphisms in the MBL2 gene and risk for febrile neutropenia during the 2.5 years of treatment for ALL. Further statistical analyses and comparisons during specific time-points of the treatment and analyses for the gene coding for TLR4 will be added during the spring of 2018.
Background

Visceral Leishmaniasis is a neglected tropical parasitic disease caused by an obligate intracellular protozoan of the genus Leishmania, transmitted by the bite of infected sand flies (Phlebotomus species). VL is re-emerging disease in Armenia. Our goal is to describe the most common epidemiological, clinical and laboratory characteristics of VL in patients hospitalized in “Nork” Republican hospital.

Methods

We used the medical charts of patients with VL admitted to “Nork” hospital during the period July 2015-July 2017.

Results

Total number of patients 50, 96% of them-children with a mean age of 2.05, male 62%. 70% of cases were local, in Yerevan 20%, Tavush 20%, Lori 10%, Syunik 16%, Kotayk 2%, Armavir 2%. 14 patients had accompanying illnesses, from which RSV 1, Coxsackievirus 1, leukemia 1, malnutrition 4 and pneumonia 7. The majority of patients (94%) recovered, 3(6 %)-died. Relaps-2 cases.

Main clinical symptoms were general weakness(100%), pallor(100%), splenomegaly(100%), hepatomegaly(98%), fever(94%), lymphadenopathy(86%), hemorrhagic rash(22%), bleeding(22%), sleep disorder (20%), consciousness disorder (14%). Laboratory data: Anemia 100%, Hb mean value 71.68(g/L), 92.3(g/L), leukopenia 70%, mean value 2.82(10^9/L), 8.7(10^9/L), thrombocytopenia 82%, mean value 74(10^9/L), 276(10^9/L) at the time of admission and discharging respectively.

Diagnosis: bone marrow puncture was used for all patients, positive 92%, rK39 rapid test 25, positive 24 (96%), PCR 9, positive 8(88.8%), IFA 41, positive 36(87%).

Treatment: Glucantime received 90% of patients, Amphotericine B10%.

The mean duration of hospitalization-29.1 days.

Conclusions

The slowest recovered hemoglobin level of the laboratory data, the basis for additional research to detect nutritional deficits (iron, folic acid, vitamin B12).
All children with anemia, splenomegaly, pallor, general weakness (+/-fever) should be examined for VL in endemic areas. In the presence of typical symptoms, 1 or 2 negative laboratory tests—not enough to exclude the disease.

Clinical Trial Registration (Please input N/A if not registered)

N/A
A CASE OF AUTOIMMUNE HEPATITIS WITH EXTREMELY HIGH LEVEL OF ALPHA-FETOPROTEIN

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Title of Case(s)

A Case of Autoimmune Hepatitis with extremely high level of alpha-fetoprotein

Background

Autoimmune hepatitis (AIH) is a form of chronic hepatitis of unknown etiology. Two types of childhood AIH are recognized according to seropositivity: smooth muscle antibody (SMA) and/or antinuclear antibody (ANA), which is AIH type 1; and antibodies to liver-kidney microsome type 1 (anti-LKM1), which is AIH type 2. Our goal is to introduce rare case of patient with autoimmune hepatitis which developed after enteroviral infection and had extremely high level of alpha-fetoprotein (AFP).

Case Presentation Summary

The 5 years old boy admitted to hospital with fever, abdominal pain, weakness, jaundice, disorders of consciousness. A week before he had fever, diarrhea, vomiting. Laboratory data: CBC- Hb-102g/l (N120-140), RBC, WBC, PLT-normal, ESR-64mm/h. Liver enzymes, bilirubin and IgG levels were elevated as well, as AFP and ANA (ALT-2440 (N 0-42), AST-1640 (N 0-37), AFP 7685 ng/ml (N >7.02), total bilirubin-272.6 (N 8.55-20.5), direct 180.4, IgG - 22,96 g/l (N 7.0-16.0), ANA 1: 320 (N1:<10).

INR 3.29 (N 0.82-1.18), CEA-negative, Anti-ds-DNA, LDH-normal, Copper total 828ug/l (N900-1900), LKM 1:<10 (N1:<10), SMA 1:<10 (N1:<10). Serology and/or PCR for HCV, HBV, HAV, HEV, EBV, CMV, Parvovirus B19, Brucellosis, Yersiniosis, Pseudotuberculosis, Leishmaniasis, Leptospirosis were negative, stool test for Enterovirus - positive.

Liver biopsy showed autoimmune hepatitis (METAVIR Grade 2, stage 1).

Immediate therapy with high-dose prednisolone therapy was started, then we decreased prednisolone dose and add azathioprine. As a result, we had improvement of patients' condition, clinical findings and laboratory values.

Learning Points/Discussion

Autoimmune hepatitis followed by enteroviral infection. Extremely high level of alpha fetoprotein is not always marker of tumor.
Background

Viruses are the commonest cause of meningitis in children. We undertook a systematic literature review of long term outcomes following childhood viral meningitis.

Methods

A search was carried out using MEDLINE, Embase and Cochrane Review for studies from 1/1/1990 - 3/11/2017. The broad term “viral meningitis” was used in addition to specific viruses in combination with likely clinical sequelae and children or neonates. Studies were included where specific outcome measures were available beyond hospital discharge for children <16 years old with viral meningitis.

Results

In total, 3034 papers were identified and 10 deemed relevant.

Three single centre studies from the UK and USA were included. The U.K study showed no sequelae in 6 cases of infants <90 days old (4 enterovirus meningitis, 2 undefined) at 3-month follow-up. A US study demonstrated subtle language difficulties in 13 out of 16 infants <90 days old with enterovirus meningitis at 3 years. Conversely, a second US study identified no neurodevelopmental/cognitive sequelae in 53 infants at 30-months follow up.

Three studies evaluated outcomes in EV71 meningitis in China and Taiwan. One study demonstrated an increased risk of Attention Deficit Hyperactivity Disorder. The other two studies showed that children frequently recovered without sequelae.

Two out of 12 infants with EV meningitis in a study in Fiji and one out of six children in a study in Hong Kong developed sensorineural hearing loss. A study in Reunion island during a Chikungunya outbreak showed that 2 out of 4 children with meningitis had motor sequelae.

Conclusions

There are extremely limited data on the outcomes of viral meningitis in infants and children. Robustly conducted neurodevelopmental studies are warranted to inform the evidence based management of viral meningitis beyond hospital discharge.

Systematic Review Registration (Please input N/A if not registered)
TREATMENT EXPERIENCE WITH AMIKACIN IN PEDIATRIC PATIENTS WITH FEBRILE URINARY TRACT INFECTIONS CAUSED BY EXTENDED-SPECTRUM B-LACTAMASE-PRODUCING ESCHERICHIA COLI

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Background

Amikacin has shown promising in vitro activity against extended-spectrum β-lactamase (ESBL)-producing urinary isolates of *Escherichia coli*; however, clinical data are limited in children. We aimed to investigate the clinical and microbiological outcomes of febrile urinary tract infections (FUTIs) caused by ESBL-producing *E. coli* treated with amikacin in children.

Methods

A retrospective cohort study was performed on pediatric patients ≥3 months of age with FUTIs caused by ESBL-producing *E. coli*. Amikacin monotherapy (given at a dose of 7.5 mg/kg intravenously twice daily) was initiated as definitive treatment (after urine culture susceptibility results were available) of FUTIs in patients who failed to respond to the initial empiric treatment. Patients were excluded if they had impaired renal function and signs of sepsis.

Results

A total of 34 pediatric patients (22 females) were enrolled in this study. The median age was 16 months (range, 5-48 months). All *E. coli* isolates were susceptible to amikacin with MICs of ≤4 mg/L. The median duration of treatment was 7 days (range 3-10 days). Of the 34 patients, 33 (97%) improved clinically without requiring any additional antibiotics; repeat urine cultures on day 3 of amikacin treatment yielded negative results. The median time to resolution of fever was 2 days (range, 1-3 days). Treatment failure was only seen in 1 patient with concomitant bacteremia and persistent fever, who was then treated with intravenous ertapenem.

Conclusions

Our results suggest that amikacin might be a reasonable alternative to carbapenems for treating nonbacteremic FUTIs caused by ESBL producing *E. coli* in children with normal renal function, if the isolate is susceptible. To prevent the development of resistance, carbapenems should only be used in patients with severe infections with ESBL-producing Enterobacteriaceae other than UTIs.
Background

Community-acquired pneumonia (CAP) is the leading cause of death and hospitalization among children under-5 years worldwide. Information about seasonality and association of meteorological factors on the prevalence of respiratory viruses, particularly in tropical regions, is scarce. We investigated the seasonal distribution and the association of meteorological factors with the detection rate of respiratory viruses in children with CAP in a tropical region.

Methods

In a 54-month period, non-hospitalized patients, aged 2-59 months, were diagnosed with CAP in Salvador, Northeast Brazil, had nasopharyngeal aspirate samples collected and tested for 16 respiratory viruses by PCR (Anyplex [TM] II RV 16, Seegene, Seoul, South Korea). Data about rainfall, relative humidity, air temperature, and sunshine were collected. Time series analysis using Prais–Winsten generalized linear regression was used for identification of seasonality and association with meteorological factors.

Results

Out of 774 cases, 708 (91%) had ≥1 respiratory virus found. Seasonal features of rhinovirus, adenovirus, enterovirus, respiratory syncytial viruses A (RSVA) and B (RSVB), influenza viruses A (Flu A) and B (Flu B) were observed. Rainfall was inversely associated with rhinovirus, adenovirus, RSVB, Flu A, and coronavirus 229E occurrence. Relative humidity was directly associated with the incidence of rhinovirus, adenovirus, RSVA, RSVB, parainfluenza 2, human metapneumovirus (hMPV), Flu A, and coronavirus NL63. Air temperature was inversely associated with hMPV and directly associated with Flu A. Hours of sunshine were directly associated with hMPV detection rates.

Conclusions

Seasonality and meteorological factors probably interfere with circulation of respiratory viruses. This knowledge may help in planning of vaccine prevention strategies.
Background

Rotavirus is the leading cause of diarrheal disease and hospitalization in children <5 years. After natural/man-made disasters, contamination of water supplies results in the spread of enteric diseases. Consequently, immediate relief efforts focus on the transport of clean water or water purification systems to disaster areas at considerable expense. Since the efficacy of disinfecting Rotavirus-contaminated water using artificial UV- spectrum irradiation is well established, this study aimed at evaluating decontaminating drinking water in inexpensive, durable, and easily transportable plastic Ziploc™-bags exposed to abundant, natural, solar irradiation.

Methods

Water in Ziploc™-bags was contaminated with a simian rotavirus (10⁵ PFU/ml) during summer in Nashville, TN, USA. Starting at 9 AM, bags were then exposed for 6 hrs (10 experiments) to either direct ambient sunlight (SL-A), or to the same ambient atmospheric conditions but shielded in the dark as controls (D-A), or kept in a laboratory in the dark under a controlled room temperature of 25 C (D-RT). Serial hourly measures of the intensity of ambient UV-A levels (Fluence, defined as exposure time X UV-A intensity; h.W/m²), with triplicate samplings of viral counts and temperature of the contaminated water were then obtained. Fixed-effect ANOVA statistics were used to compare the survival rates.

Results

Rotavirus survival in the sunlight exposure experiments (SL) varied inversely to UV-A intensity in a significantly faster fashion than dark+ambient conditions (C-A), while dark+room temperature conditions (C-RT) had minimal attenuation of survival.
Conclusions

Durable, inexpensive Ziplock™- bags are useful for disinfection of Rotavirus-contaminated water using solar irradiation, and may have applications in disaster relief. Similar to reports on bacterial inactivation by sunlight, synergy between the optical and thermal inactivation processes EXISTS during solar disinfection of Rotavirus.

Clinical Trial Registration (Please input N/A if not registered)
MENINGOCOCCAL GROUP W OUTBREAK FOLLOWED BY THE MOST EXTENSIVE SWEDISH VACCINATION EFFORT
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Title of Case(s)
Management of a meningococcal group W outbreak in Sweden

Background
Meningococcal meningitis is a severe disease with high fatality. During March-May 2017 three children in the same living area in Nyköping, Sweden, presented with meningococcal (W) meningitis (1-11 years old). All cases were hospitalized at ICU, one case was fatal. We describe the events, medical decision and logistics of the most extensive vaccine effort to prevent meningococcal infection in Sweden.

Case Presentation Summary
The first case was handled according to antibiotic prophylaxis routine, to close household contacts. After the second case, antibiotic prophylaxis was extended to a wider group, including day-care centers and friends to the families. In total, 707 doses of antibiotics were administered through primary health care centers in the neighbourhood (mean age 18 years, range <1-85 years).

After the third case, it was decided by the Medical Officer to immunize all siblings and classmates of the three cases. The siblings of vaccinated children were also offered vaccination. 2600 doses of conjugated quadrivalent ACWY-vaccine were administered at child health care centers and schools in the neighbourhood within two weeks.

The total cost for vaccine was 1.5 million SEK and adding to this working hours and costs for antibiotic doses. No severe adverse events were recorded following vaccination. No further case of meningococcal meningitis has occurred after the immunizations.

Learning Points/Discussion
An extended antibiotic prophylactic to 707 individuals, mostly children, did not prevent further cases, indicating a high prevalence of meningococcal carriage in the area. Extensive efforts were made by and between different parts of the health care system and the municipality when antibiotic doses and vaccine were distributed. No further cases of meningococcal meningitis have been notified.
7-YEAR TREND OF COMMUNITY-ACQUIRED STAPHYLOCOCCUS AUREUS INFECTIONS IN A JAPANESE PEDIATRIC HOSPITAL


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Title of Case(s)

7-year Trend of Community-acquired Staphylococcus aureus Infections in a Japanese Pediatric Hospital

Background

In previous study held in 2010-2014, there found an apparent increase of hospitalized cases associated with community-acquired S.aureus infections in our hospital. Therefore this study was designed to reassess the trend of S.aureus infections after 2014.

Case Presentation Summary

We collected and reviewed the culture data and medical charts of inpatients associated with moderate to severe Staphylococcus aureus infections in Nagano Children’s Hospital, from January 2011 to December 2017.

Between 2011 and 2013, there had been only 3-4 cases of community-acquired S.aureus infections yearly, while 8 to 11 cases per year since 2014.

On the other hand, there had been no increase of health care-associated infections due to S.aureus (around 25-30 cases per year).

Majority of the community-acquired S.aureus infections were skin and soft tissue infections (lymphadenitis, abscess and cellulitis), but skeletal and blood stream infections were also found.

Among isolated strains, methicillin-susceptible S.aureus (MSSA) was predominant.

Learning Points/Discussion

Admissions associated with community-acquired S.aureus infections had increased in 2014, and this trend continued until 2017 in our hospital. The nation-wide, or at least, multicenter surveillance should be conducted for elucidation of the epidemiological trend of community-acquired S.aureus infections in Japanese children.
BONE HEALTH IN HIV INFECTED CHILDREN ON ANTIRETROVIRAL THERAPY – AN INDIAN STUDY

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Background

To determine the bone health in HIV infected children on antiretroviral therapy (ART).

Methods

31 HIV infected children aged 5-18 years underwent testing for serum calcium, phosphorous, alkaline phosphatase and 25(OH) Vitamin D. Bone Mineral Density (BMD) was done using a DXA scanner, Lunar iDXA system. Factors associated with low BMD such as age, gender, type of ART, duration of ART and vitamin D levels were analysed.

Results

Seven (22.6%) children had a low spinal BMD and 6 (19.4%) had low femoral neck BMD. Low serum calcium was seen in 6 (19.4%) patients and high alkaline phosphatase was seen in 15 (48.4%) patients. Low serum 25(OH)Vit D levels were present in 30 (96.8%) patients while all the patients had normal serum phosphorous levels. Duration of ART in those with low spinal BMD was 4.6±3.4 years as compared to 6.4±3.2 years in those with normal spinal BMD (p=0.235) and for low femoral neck BMD was 3.9±2 years as compared to 6.5±3.4 years for those with normal femoral neck BMD (p=0.031). Mean 25(OH)Vit D levels were 8.4±2.8 ng/ml in those with low femoral neck BMD as compared to 13.6±8.3 ng/ml in those with normal femoral neck BMD (p=0.015). Type of ART, gender, serum calcium and alkaline phosphatase did not have any association with low BMD.

Conclusions

Most of the HIV infected children on ART have normal BMD. Over 95% of HIV infected children have insufficient or deficient 25(OH)Vit D levels which tends to affect the appendicular BMD. BMD is affected more in children who have been on ART for a shorter time. Children who have been on ART for a longer time have normal BMD. No particular ART regimen is associated with low BMD.

Clinical Trial Registration (Please input N/A if not registered)

N/A
**15B. SCIENCE: GLOBAL CHILD HEALTH**

**HOW (IN-)EXACT ARE THE GRADUATED CUPS FOR ANTIBIOTIC SYRUPS IN AFRICA?**

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**Background**

Antibiotic syrups are among the most prescribed medications in pediatrics – not only in Africa.

Administration usually is using the small cup that comes with the bottle. Different measurement graduations are engraved in the transparent material and difficult to read, especially in dim light.

Pushed by the too often occurring discrepancy between attended and observed consumption of antibiotic syrups, we controlled the volumes indicated on the cups accompanying liquid childhood medications in Burkina Faso.

**Methods**

During November 2017 all 12 different cups from individual drugs present on the Pediatric Ward of the Hôpital St Camille in Ouagadougou were analysed.

Under perfect light conditions, the cups were put on a levelled table and filled according to their size up to the indicated lines for 2.5, 5, 10 and 15 mL. The cups were then emptied by aspiration into a syringe and the volume measured. The procedure was repeated by medical staff and lay care-givers.

**Results**

Overall only 5 out of 12 cups indicated the correct volume.

The 2.5 mL indicator line corresponded to an effective volume between 1.9 and 2.6 mL; the 5 mL indicator equaled between 3.5 and 7 mL, while the measured volume at the 10 mL-line yielded measured volumes between 6 and 11.5 mL.

Taking the 5mL-line 41.6% cups underdosed the drug for up to 50% and 16.6% of cups overdosed up to 40%!

**Conclusions**

The resulting dosing errors may have important consequences, not only in terms of cost but in terms of ineffective therapy, progressive infection and ultimately increasing resistance and ultimately death!

As immediate consequence we urge you to control the cups you use and, if necessary, switch to correctly graduated syringes!
Clinical Trial Registration (Please input N/A if not registered)

N/A
OUTCOME OF HOSPITALIZED SEVERELY MALNOURISHED CHILDREN PRESENTING WITH DIARRHEA AND VOMITING
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Background

Vomiting in diarrheal children especially with severe malnutrition is often associated with serious complication. However, data on outcome of vomiting in such children are lack. We evaluated outcomes of vomiting in children who were hospitalized with severe malnutrition and diarrhea.

Methods

In this chart review, we evaluated children with diarrhea aged 0-59 months, admitted to Dhaka Hospital of International Centre for Diarrhoeal Disease Research, Bangladesh, with severe malnutrition between April 2011 and August 2012. Comparison was made between the children with and without vomiting.

Results

Out of 306 enrolled children with diarrhea and severe malnutrition, 51 (17%) had vomiting and 255 (83%) admitted without vomiting. A total of 88 (29%) children experienced treatment failure, out of which 21 (41%) had vomiting and 67 (26%) did not have vomiting. The treatment failure was significantly higher in children who had vomiting than those without vomiting (relative risk [RR] 1.73, 95% CI 1.05 – 2.86; p=0.032). Simultaneously, a total of 31 (10%) children died, 12 (24%) of them had vomiting and 19 (8%) did not have vomiting. Death was significantly higher among the study children having vomiting compared to those without vomiting (RR 2.73, 95% CI 1.61 – 4.64; p<0.001). Using Log linear bi-nominal regression after adjusting for potential confounders such as metabolic acidosis and hypoglycemia, we found that death still remained significantly associated with vomiting in severely malnourished diarrheal children (RR 1.35, 95% CI 1.01 – 1.82; p=0.044).

Conclusions

The results of our data revealed that diarrheal children with severe malnutrition having vomiting during hospitalization had significantly poorer outcome compared to those without vomiting. The result underscores the importance of understanding the etiology and management of vomiting to reduce deaths in such children.
VALIDITY OF MODIFIED KENNETH-JONES’ CRITERIA IN DIAGNOSING TUBERCULOSIS IN SEVERELY MALNOURISHED CHILDREN PRESENTING WITH PNEUMONIA

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Background

Tuberculosis is common in children with severe acute malnutrition (SAM) presenting with pneumonia; however, it’s diagnosis is very difficult due to subtle clinical signs of TB in such population. Scoring system such as modified Kenneth Jones criteria (MKJC) that uses both clinical and simple laboratory data to assess the likelihood of tuberculosis in children might have greater value, especially in resource poor settings. However, there is limited information on the usefulness of MKJC scoring in the diagnosis of TB in severely malnourished children. To validate MKJC score compared to culture and Xpert MTB/RIF in the diagnosis of TB in severely malnourished pneumonic children.

Methods

In this prospective study, we enrolled under-five SAM children with radiological pneumonia after obtaining signed informed consent from respective care givers. We collected sputum (induced sputum and gastric lavage fluid) for microscopy (AFB), mycobacterial culture, and real-time PCR by Xpert MTB/RIF. Using culture and Xpert MTB/RIF as the reference, we compared the sensitivity and specificity, positive and negative predictive values, and the accuracy of MKJC score in diagnosing TB in this population.

Results

In total, 405 children were enrolled in our study. Sputum for microscopy (AFB) and mycobacterial culture was sent from 396 of them and Xpert MTB/RIF from the last 214 children. Compared to culture confirmed TB, the sensitivity and specificity (95% CI) of MKJC score were 60% (27-86%) and 84% (79-87%) respectively. Compared to culture and/or Xpert MTB/RIF positive TB these were 37% (20-58%) and 84% (79-87%) respectively.

Conclusions

Our data suggest that diagnosis of TB in SAM children with radiologic pneumonia using MKJC scoring is less sensitive but may minimize the chance of over treatment with anti-TB therapy especially in resource limited settings.
Background

Saudi Arabia is a destination to 4 million pilgrims annually and a host to a large expatriate population. It is also among the top consumers of antimicrobials globally, leading to soaring rates of antimicrobial resistance. Reports from the region highlight sporadic practices of antimicrobial stewardship programmes (ASPs) in healthcare organisations there. This study aimed to explore the level and process of ASPs adoption in Saudi hospitals, and provide recommendations to hospitals and policy makers on how barriers to ASPs adoption could be successfully overcome.

Methods

We conducted semi-structured interviews with healthcare professionals in three Saudi hospitals to explore barriers and facilitators to ASPs adoption. We then developed a questionnaire based on findings to investigate levels and factors affecting ASPs adoption at a national level. We further explored the process of ASP adoption in one of the few Saudi hospitals currently adopting ASPs, through in-depth interviews and a case study design.

Results

Only 26% of Saudi hospitals report ASPs adoption. Lack of expertise (infectious diseases specialists) is a major barrier to adoption; especially since they drive the formation of ASPs. ASPs adoption significantly reduces inappropriate antimicrobial use and the associated costs, and reduces resistance rates to certain microorganism-agent combinations, with a paradoxical increase in resistance rates to other combinations. In the absence of national surveillance programmes, the impact of ASP adoption remains unclear.

Conclusions

Despite the established benefits of ASPs, their adoption in Saudi hospitals remains low. Policy makers are urged to consider making ASPs adoption in hospitals a regulatory requirement, supported by national guidelines and surveillance programmes. Healthcare organisations are urged to invest in making available expertise and training, educational and development programmes if antimicrobial resistance is to be tackled in the region.
Patients Knowledge of and Attitudes to Antibiotics Use in Saudi Hospitals: The Institutional Role of Patients Education

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Background

Antimicrobial Stewardship Programmes (ASPs) are well-established initiatives to curb the inappropriate use of antimicrobials and reduce the emergence of resistance in healthcare organisations. Although prescriber-focused, the benefits of ASPs extend to patients through improving their use of antimicrobials and raising their awareness of antimicrobials resistance. This study aimed to assess patients’ knowledge of antimicrobials use and resistance in an ASP-adopting and a non-adopting hospital to evaluate the institutional role of patients’ education as part of ASP.

Methods

This is a cross-sectional study by means of a self-administered patient’s questionnaire in two Saudi hospitals; King Abdullah Medical city in Makkah; (1500 beds), one of the few Saudi hospitals adopting ASP, and King Fahad hospital in AlBaha, (380 beds) which is yet to adopt ASP. Patients’ responses were collected from May to August 2017. Data analysis included descriptive and correlation statistics.

Results

176 patients responded to the survey. 50.7\% of the responses were from the non-ASP adopting hospital. We identified a comparable lack of knowledge of appropriate antimicrobials use in both hospitals such that 68\% of participants agreed to share their antibiotics with family members, and only 31\% of participants believe that antibiotic resistance can result from not completing the full course of antibiotics. Only 26\% of patients think that antibiotic resistance is a problem in Saudi today, and only 27\% believe that their hospital stay improved their awareness of antibiotic resistance.

Conclusions

Patients awareness of appropriate antimicrobial use and resistance is low in Saudi hospitals. Successful adoption of ASPs should ensure that patients are counselled on correct antimicrobial use, and are aware of their potential contribution to antimicrobial resistance. Pharmacists can be more involved in patients counselling to ensure ASPs adoption outcomes are achieved.
HUMAN PARVOVIRUS B19: UBIQUITOUS BUT NOT NECESSARILY BENIGN

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²National Taiwan University Children's Hospital, Pediatric Infectious Disease, Taipei, Taiwan R.O.C.

Title of Case(s)

More than erythema infectiosum

Background

Since its discovery in 1975, human parvovirus B19 has been known to cause the largely self-limited erythema infectiosum. Recently, myocarditis and hemophagocytic lymphohistiocytosis secondary to parvovirus B19 have been reported, suggesting a wider cellular tropism besides erythroid progenitor cells. We describe a series of patients with parvovirus B19 infection presented with typical and atypical symptoms in our institution.

Case Presentation Summary

From 2009 to 2017, we identified 26 patients with positive human parvovirus B19 polymerase chain reaction in blood - 17 inpatients and 9 outpatients (Table 1).
Median age of diagnosis was 8.75 years with range from 0 days to 80.8 years. Eight (89%) of 9 outpatients and 5 (29%) of 17 inpatients were previously healthy. A preexisting medical condition was found in 12 (71%) inpatients. Outpatients presented predominantly with skin rash and fever; while

<table>
<thead>
<tr>
<th>Table 1: Characteristics of patients with positive parvovirus B19 polymerase chain reaction in blood from 2009 to 2017</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inpatients (n=17)</strong></td>
</tr>
<tr>
<td><strong>Gender</strong></td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td><strong>Age</strong></td>
</tr>
<tr>
<td>Infant (&lt;1 years)</td>
</tr>
<tr>
<td>Child (1 - 12 years)</td>
</tr>
<tr>
<td>Adolescent (12 - 18 years)</td>
</tr>
<tr>
<td>Adult (&gt;18 years)</td>
</tr>
<tr>
<td><strong>Preexisting medical condition(s)</strong></td>
</tr>
<tr>
<td>Hematologic disease</td>
</tr>
<tr>
<td>Immunologic disease</td>
</tr>
<tr>
<td>Cardiopulmonary disease</td>
</tr>
<tr>
<td><strong>Nil / Previously healthy</strong></td>
</tr>
<tr>
<td><strong>Initial presentation</strong></td>
</tr>
<tr>
<td>Fever</td>
</tr>
<tr>
<td>Fatigue / decreased fetal movement</td>
</tr>
<tr>
<td>Pallor</td>
</tr>
<tr>
<td>Jaundice</td>
</tr>
<tr>
<td>Shock</td>
</tr>
<tr>
<td>Seizure</td>
</tr>
<tr>
<td>Rash</td>
</tr>
<tr>
<td><strong>Sick contacts</strong></td>
</tr>
<tr>
<td>5</td>
</tr>
<tr>
<td><strong>Initial diagnosis</strong></td>
</tr>
<tr>
<td>Fever of unknown origin</td>
</tr>
<tr>
<td>Viral tonsillitis</td>
</tr>
<tr>
<td>Erythema infectiosum</td>
</tr>
<tr>
<td>Atypical infection</td>
</tr>
<tr>
<td>Scarlet fever</td>
</tr>
<tr>
<td>Fetomaternal hemorrhage</td>
</tr>
<tr>
<td>Viral myocarditis</td>
</tr>
<tr>
<td><strong>Disease course</strong></td>
</tr>
<tr>
<td>Self-limited</td>
</tr>
<tr>
<td>Cytopenia requiring transfusion(s)</td>
</tr>
<tr>
<td>Hemophagocytic lymphohistiocytosis</td>
</tr>
<tr>
<td>Extracorporeal membrane oxygenator</td>
</tr>
<tr>
<td><strong>Median hospital stay</strong></td>
</tr>
<tr>
<td>13 days (IQR 7 - 22.5; range 2 - 91)</td>
</tr>
<tr>
<td><strong>Death</strong></td>
</tr>
<tr>
<td>1 (6%)</td>
</tr>
</tbody>
</table>
inpatients presented mostly with fever, followed by fatigue, pallor, and/or jaundice. Six inpatients were initially diagnosed with fever of unknown origin, 4 with viral tonsillitis, 2 each with atypical infection and scarlet fever. In contrast, 5 outpatients was diagnosed with erythema infectiosum, and 3 with viral tonsillitis. All outpatients and 5 (29%) inpatients had a self-limited course. Nine (53%) inpatients required transfusion, 2 developed hemophagocytic lymphohistiocytosis, and 1 required extracorporeal membrane oxygenator for myocarditis. One mortality was reported - a 6 month old female with common variable immune deficiency who died of intraabdominal bleeding.

Learning Points/Discussion

1. In our series, human parvovirus B19 infection manifested as erythema infectiosum in most healthy children seen as outpatients.
2. A trend towards complicated disease was observed among inpatients with preexisting medical condition. Nevertheless, prognosis remains good.
3. Clinicians must bear in mind the variable symptoms and consider individual host factors when encountering suspicious cases.
NAZOPHARYNGEAL PNEUMOCOCCAL CARRIAGE IN HEALTHY TURKISH CHILDREN AFTER 13-VALENT CONJUGATED PNEUMOCOCCAL VACCINATION

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¹Ankara Hematology Oncology Children's Training and Research Hospital, Pediatric Infectious Diseases, Ankara, Turkey
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Background

The source of pneumococcal infections causing significant morbidity and mortality is mainly asymptomatic carriers. Along with the widespread use of conjugated pneumococcal vaccines all over the world, it is expected that the frequency of invasive pneumococcal disease will decrease in parallel with the decrease in proportion of carriers. The purpose of this study is to investigate the effects of pneumococcal conjugate vaccine (PCV13) on nasopharyngeal carriage rates of Streptococcus pneumoniae, and to determination the pneumococcal serotype distribution in healthy Turkish children.

Methods

The study was conducted on 500 healthy Turkish children between 0 month and 13 years of age. Samples were taken as nasopharyngeal swab samples from April to November 2014 from children who do not have a history of infection and antibiotic use within the last two weeks. Capsular serotyping by molecular method was performed on the isolates which were confirmed to be pneumococci.

Results

Nasopharyngeal pneumococcal carriage was detected in 49 (9.8%) of the 500 healthy children. Of the isolates, 26 (53%) were in PCV13 vaccine strains. Distribution of vaccine strains was as follows; serotype 3 18.3% (9/49), serotype 19F 14.2% , serotype 6A / B 8.2% , serotype 18C 4% , serotype 19A 2% , and serotype 9V% 2. Non-vaccine strains detected were serotype 11A , serotype 15B, serotype 23A , serotype 9L / N , serotype 15A , serotype 16F, serotype 31, serotype 35B, and serotype 35F. Six isolates was not identified.

Conclusions
Compared with nasopharyngeal carriage studies in Turkey conducted in the pre- and post-vaccine (PCV7) era, a significant decrease in carriage rates was detected in three years after the introduction of PCV13 (from 21.9% to 9.8%). However, the nasopharyngeal carriage is particularly high in PCV13 strains interestingly.
The development in the molecular biology techniques has helped researchers to study the effect of microbiome or the microorganisms in the human blood. Early onsets of the conditions caused by these microorganisms are bacteremia which could be followed by septicemia later resulting in septic shock. These microbes usually reside in the gut and could also be translocated from the oral cavity. We are interested in the presence of 28 microorganisms belonging to several genera (Acinetobacter to Staphylococcus) in the sterile blood. Various non communicable diseases as well as inflammatory and chronic disease could also be linked with the immunological modulations caused by the action of the dormant microbiota present in humans. Lipopolysaccharides (LPS) are the key molecules and master mind behind the alteration of host’s immune system, although these few microbial components could be curable through certain vaccines and antibiotics.

Methods

qPCR and different primers tested like CD200. Bacterial DNA to be tested first then we could device a new axiom on human sterile blood.

Results

Hypothesis: These microbes enter human body at different time frames and remain dormant for a long period of time, unless activated by some stimuli?

microbiome count:

<table>
<thead>
<tr>
<th>Microorganism</th>
<th>Count in patients with sepsis H/L (High or Low)</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. aureus</td>
<td>H</td>
</tr>
<tr>
<td>Enterococcus spp</td>
<td>H</td>
</tr>
<tr>
<td>S. pneumoniae</td>
<td>L</td>
</tr>
<tr>
<td>E. coli</td>
<td>L</td>
</tr>
<tr>
<td>Salmonella</td>
<td>L</td>
</tr>
<tr>
<td>Klebsiella</td>
<td>H</td>
</tr>
<tr>
<td>S. epidermidis</td>
<td>H</td>
</tr>
</tbody>
</table>

The primer binding action was noted in the initial phase of the research to move forth more capital is needed. Conclusions
Barriers occurring in the development of new promising vaccine may be crossed by studying the molecular and immunological patterns of other primate species like monkeys and baboons as these are known to be resistant to mutant LPS strain.
ABDOMINAL TUBERCULOSIS AND RAW MILK
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Background

Abdominal tuberculosis is rare in Western population and incidences declining in parts of India. In developed countries disease is largely limited to immigrants from world endemic for tuberculosis. Strict control of tuberculosis in dairy herds and pasteurization of milk have almost eliminated in India with tradition of boiling before consumption. But according to some raw milk enthusiasts, pasteurization or boiling milk destroys important nutritive properties, we witness few abdominal tuberculosis cases in these children with absence of associated pulmonary lesions.

Methods

Six children with under nutrition, pain abdomen, loss of appetite with history of consuming raw milk 2-3 times a day attending pediatric clinic were studied and investigated for tuberculosis.

Results

Six children, all males, between age 12-14 years were interviewed and investigated. There was strong history of family myth about consuming raw milk for good health believing factor for strong good physique manlihood. After investigations with blood, CT, MT, cytology X-ray it was bit difficult to isolate AFB with evidence of absent pulmonary lesions, associated abdominal lymphadenitis were with strong clinical and radiological suggestion for abdominal tuberculosis, all kids were given antitubercular treatment. After six month of follow up there was remarkable improvement clinically and radiological including CT studies.

Conclusions

The present study though not advance research oriented study but suggest that prevalence of consuming raw milk may be a trigger cause of under diagnose abdominal tuberculosis in children as even modern investigative methods also have limitations. I conclude that further more big, elaborative studies may be undertaken for the suggestion I lymphadenitis were strong suggestion for abdominal tuberculosis, with presence of strong clinical suspicion all kids were given antitubercular treatment. After six month of follow up there was remarkable improvement clinically and radiological including CT studies.
BACTEREMIA DUE TO KOCURIA KRISTINAЕ IN A CHILD: CASE REPORT

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2Istanbul Kartal Dr. Lütfi Kırdar Education and Research Hospital, Department of Pediatric Surgery, İstanbul, Turkey
3Istanbul Kartal Dr. Lütfi Kırdar Education and Research Hospital, İnfection Control Comittee, İstanbul, Turkey

Title of Case(s)
Bacteremia due to *Kocuria kristinae* in a Child: Case Report

Background

*Kocuria kristinae* is a catalase-positive, coagulase negative gram positive bacteria which belongs to Micrococcaceae family. It can be recovered from skin and oral flora and it rarely causes infections in humans.

In here, we described an infant with bacteremia due to *Kocuria kristinae* who have been hospitalized with the diagnosis of burn with boiled water.

Case Presentation Summary

A fifteen-month-old boy admitted to the pediatric emergency room with the compliants of %20 burn with hot water and hospitalized because of extension of deep tissues. In 48 hours of admission, he had fever. The laboratory results showed a white blood cell (WBC) count of 23.100/mm³, hemoglobin level of 13.7g/dl, platelet count of 419000/ mm³ and C-reactive protein levels of 127 mg/L (0-3.5 mg/L). Blood and urine cultures were obtained and empirical antibiotic therapy with ampicillin-sulbactam was started. The temperature decreased in normal range however two days after he had fever again. Blood and urine cultures were repeated and antibiotic therapy was changed to piperacillin-tazobactam. In 24 hours there was a signal indicating the growth of a microorganism in the peripheral vein blood culture. Gram-positive colonies were seen and teicoplanin therapy was added to the therapy. The microorganism was identified as *Kocuria kristinae* which was susceptible to teicoplanin. Echocardiography was normal. Control blood culture which was obtained on the third day of therapy, remained sterile and the infant was treated for 10 days.

Learning Points/Discussion

Patients who developed serious infections with *Kocuria kristinae* usually have an underlying facilitating condition such as immunodeficiency and central venous catheter use. In our patient the facilitating condition was deformation of skin integrity which led the skin flora invasion.
Background

Sapoviruses (SaV) belong to caliciviruses and are associated with acute gastroenteritis (AGE) but detected less commonly than related noroviruses. We examined the clinical significance and epidemiology of SaV gastroenteritis in Finnish children before and after the introduction of rotavirus (RV) mass vaccination.

Methods

1,437 stool samples from children <16 years old were collected in three hospital-based prospective 2-year surveillance studies of AGE conducted in Tampere, Finland. SaV findings from a 2-year period of 2006-2008, before the introduction of RV vaccination in the National Immunization Programme (NIP) in 2009, were compared to two 2-year periods in 2009-2011 and 2012-2014. SaVs were detected using a human calicivirus RT-PCR, and the partial RNA-dependent RNA polymerase region of the genome was sequenced for phylogenetic analysis. Clinical severity of AGE was estimated using the Vesikari Score for clinical severity.

Results

SaVs were detected in 60 sporadic cases, of which 53% were hospitalized and 47% seen in the outpatient clinic. The proportion of SaV cases of all AGE cases increased from 1.4% in pre-NIP years to 5.5% in post-NIP years. SaV AGE occurred mainly in winter and springtime but did not follow norovirus or RV epidemiology. The most commonly detected genotype was GII.1 with different predominant strain each year. Diarrhea and vomiting were detected in 92% and 76% of SaV AGE cases, respectively. Even though mild and moderate SaV AGE cases were also detected, the majority of SaV AGE cases were severe.

Conclusions

SaVs are detected sporadically but persistently in children and may cause severe AGE. The elimination of RV AGE by vaccination has increased the relative role of SaV AGEs.
THE NEGATIVE PREDICTIVE VALUE OF WHITE BLOOD CELL COUNT FOR PNEUMOCOCCAL INFECTION AMONG CHILDREN HOSPITALIZED WITH COMMUNITY-ACQUIRED PNEUMONIA

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¹Bahiana Foundation for Science Development, Bahiana School of Medicine, Salvador, Brazil
²Federal University of Bahia School of Medicine, Department of Pediatrics, Salvador, Brazil

Background

Community-acquired pneumonia (CAP) is a major cause of hospitalization and death among children under-5 years and Streptococcus pneumoniae remains the most frequent bacterial causative agent in this age strata. We assessed the role of white blood cell count (WBC) for prediction of pneumococcal infection in children hospitalized with CAP.

Methods

277 patients aged 2-59 months hospitalized with CAP in Salvador, Brazil, were recruited in this prospective study. Clinical data, nasopharyngeal aspirate and blood sample were collected upon admission; a second blood sample was collected 2-4 weeks after recruitment. Infection by 11 viruses and 9 bacteria was investigated. WBC was performed upon admission.

Results

Overall, 44 (15.9%) patients did not have WBC and 53 (19.1%) patients did not have at least one of the etiological tests performed. Thus, this study group comprised 180 cases. The median (IQR) age was 17.1 (9.2-28.9) months and 112 (62.2%) were male. Aetiology was established in 154 (85.6%) patients: viral (45.6%), viral-bacterial (23.3%), and bacterial (16.7%) infections were diagnosed. Typical and atypical bacterial infection was found in 48 (26.7%) and 27 (15.0%) cases, respectively. Pneumococcal infection was diagnosed in 36 (20.0%), being bacteraemic in 6 (3.3%) and positive in blood pneumolysin PCR in 5 (2.8%). Overall, the median (IQR) WBC was 15,850 (11,525-23,700)/mm³, being significantly higher among patients with pneumococcal infection (19,600 [13,525-29,350] vs. 15,150 [10,875-21,725]; P=0.02). According to the ROC curve, 15,650 was the cut-off with best performance (sensitivity 72.2%, specificity 53.5%, positive predictive value 28.0%, negative predictive value 88.5%).

Conclusions

Total WBC is a bad tool to predict pneumococcal infection among children under-5 years hospitalized with CAP. Conversely, it is a good tool to rule out pneumococcal infection in this group of patients.
Background

Frey syndrome, gustatory sweating and flushing of the involved skin, is usually depicted in context of iatrogenic or sequela after parotid gland region surgery or trauma. The syndrome is caused by damage to the auriculotemporal nerve, which contains both sympathetic and parasympathetic fibers and is named after polish-jewish neurologist Lucija Frey who described the syndrome pathophysiology in 1923. Although the condition and its management are well described in context of parotidectomy in adults, only few cases in children and particularly following herpes zoster infection were reported.

Case Presentation Summary

12-years old girl complained about red spots appearing on the left side of her face. The girl is usually healthy and fully vaccinated, including varicella vaccination. Six years prior to her presentation she suffered an episode of blister rash on the left side of her face, including lesions in the ear canal and buccal mucous membrane. The diagnosis of herpes zoster (Ramsay Hunt syndrome) was made and she was treated with Acyclovir with complete skin recovery. A hearing examination demonstrated mild-moderate left neurosensory hearing loss.

Since then, she is having short episodes of redness on her face without pain or sweating at the exact distribution of the zoster blisters 6 years ago. The appearance of spots is related to sour foods, such as sour flavored candies, yogurt and green apples. The diagnosis of post-herpetic Frey syndrome was
made and observational approach was adopted due to benign character of complains.

Learning Points/Discussion

The physician should inquire about the history of herpes zoster in the evaluation of unexplained flushing. Most children with Frey’s syndrome exhibit flushing without sweating. The acknowledgement with the phenomenon can prevent unnecessary allergy workup.
STREPTOCOCCUS PNEUMONIAE NASOPHARYNGEAL CARRIAGE IN CHILDREN UNDER 3 YEARS OLD ATTENDING DAY CARE CENTERS. CHANGES AFTER UNIVERSAL INTRODUCTION OF 13-VALENT CONJUGATED PNEUMOCOCCAL VACCINE IN ARGENTINA

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4Children Hospital of Posadas “Dr. Fernando Barreiro”, Epidemiology, Posadas, Argentina

5Rosario Childrens Hospital “Victor J. Vilela”, Infectology, Rosario, Argentina

6Rosario Childrens Hospital “Victor J. Vilela”, Bacteriology, Rosario, Argentina

7Childrens Hospital “Dr. Fernando Barreiro”, Bacteriology, Buenos Aires, Argentina

8Childrens Hospital “Pedro de Elizalde”, Bacteriology, Buenos Aires, Argentina

9Trelew Zonal Hospital, Epidemiology, Trelew, Argentina

10Trelew Zonal Hospital, Bacteriology, Trelew, Argentina

11Public Maternal and Child Hospital Of Salta, Infectology, Salta, Argentina

12Public Maternal and Child Hospital Of Salta, Bacteriology, Salta, Argentina

Background

The 13-valent conjugated pneumococcal vaccine (PCV13) was introduced to national immunization program of Argentina in 2012. Thereafter, an epidemiological study to describe Streptococcus pneumoniae (SPN) nasopharyngeal carriage (NC) prevalence and antimicrobial susceptibility was conducted, to compare these results with the ones of a previous-vaccinal carriage study conducted between 2007-8 (Gentile et al., unpublished data).

Methods

Between June-September 2015 a cross-sectional study among children <3 y.o. attending day-care centers in 5 cities of Argentina was performed. Nasopharyngeal samples were collected, SPN isolates were serotyped by means of the Quellung reaction, and antimicrobial susceptibility was determined by agar dilution method (CLSI). Results were compared with the previous study.

Results

A total of 359 toddlers were included. NC rate was higher when compared with previous study (61,6% (CI 95% 56.3-66.6) vs. 51,5%, respectively; p< 0.05). Non-PCV13 serotypes accounted for 90,9% (IC95% 86,3-94,3) of isolations. Most frequent serotypes found were 15B, 23B and 11A rather than 6A, 15B and 19F found in the previous study. Variables associated with carriage were city of residence (Rosario/Posadas), attending public day-care centers, and overcrowding.

Antimicrobial non-susceptibility was similar to previous study (Grafic1):
Main serotypes associated with penicillin non-susceptibility were non-PCV13: 23B(25%), 16F(13.6%), 15B(10.2%), 35B(4.5%) and 11A, 15C, 19A and 24F, 3.4% each.

Conclusions

NC of SPN was higher than previous study. Most isolates were non-PCV13 serotypes. Independent predictors for higher prevalence rates were: 1- Children living in Rosario and Posadas. 2- Children attending public day care centers and 3- overcrowding. Almost 40% of SPN isolates were resistant to penicillin, a result similar to pre-vaccine era and most of them associated to non-PCV13 serotypes. The serotype distribution in NC and its associated antibiotic resistance pattern, highlights the importance of surveillance in the post vaccine era.
OSTEOMYELITIS IN IMMUNOCOMPROMISED CHILDREN AND NEONATES

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Title of Case(s)

Osteomyelitis in Immunocompromised Children and Neonates

Background

Osteomyelitis (OM) is usually caused by bacteria but can be fungal, viral or parasitic in origin. OM in immunocompromised children and neonates is rare and has not been reviewed extensively. However, it can cause devastating sequelae, such as pathological fractures, growth disturbances and deformity, and must be managed quickly and aggressively. We aim to review the aetiology, clinical profile, treatment and outcomes of such cases.

Case Presentation Summary

Fourteen patients were identified. Of the 12 immunocompromised children, 6 of them (50%) had chemotherapy for underlying cancer, 2 had suspected Mendelian susceptibility to mycobacterial disease, and 1 each had bone marrow transplant for underlying Fanconi Anaemia, Bruton agammaglobulinaemia, familial haemophagocytic lymphohistiocytosis and type 2 diabetes mellitus. There were 2 neonates.

For causal organisms of OM, 2 were Staphylococcus aureus, 2 were Mycobacterium bovis (BCG), and 1 each was Mycobacterium tuberculosis, Pseudomonas aeruginosa, Stenotrophomonas maltophilia, Burkholderia pseudomallei and Rhizopus sp. One patient had both Clostridium tertium and Clostridium difficile isolated. In 4 patients, there were no causal organisms identified.

Treatment involved appropriate antimicrobials for durations ranging from 6 weeks to 1 year, as well as surgery (incision and drainage/curettage) in 11 patients (79%). Wherever possible, patients received treatment for their underlying immunodeficiency.

Only 3 patients (21%) recovered completely. Five patients (36%) had poor bone growth, 1 patient had recurrent bone discharge and 1 patient underwent palliative care for underlying osteosarcoma. Four patients (29%) died from their underlying conditions unrelated to OM.

Learning Points/Discussion
This study describes unusual pathogens in OM in immunocompromised children and neonates, and their devastating effects. Treatment involves prolonged administration of antibiotics and surgery. Outcomes are varied with immune recovery appearing to be important in bone healing.
DECLINE IN CHILD HOSPITALIZATION AND MORTALITY AFTER THE INTRODUCTION OF THE 7-VALENT PNEUMOCOCCAL CONJUGATIVE VACCINE (PCV-7) IN RWANDA

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Title of Case(s)

Decline in Child Hospitalization and Mortality after the introduction of the 7-Valent pneumococcal conjugative vaccine (PCV-7) in Rwanda

Background

Pneumonia is a public health problem in many developing countries where it takes many lives of children before the age of 5 years.

Case Presentation Summary

The aim of this study was to determine the impact of the PCV-7 on the rate of child hospitalization/mortality due to pneumonia in Huye District, Rwanda. A retrospective and comparative study was conducted on data recorded from archives of Kabutare District hospital located in Huye District in Rwanda. Hospitalization rates as well as death cases were compared between two periods i.e. before the introduction of PCV-7 (2007-2009) and after the introduction of PCV-7 (2010-2013). Statistical analysis showed a reduction in hospitalization of 53% (t=2.258; p=0.037) and a significant decline in death cases (t=3.002; p=0.015) following the introduction of the PCV-7 vaccine in Kabutare District Hospital. Interestingly, 30% of pneumonia positive children after the introduction of PCV-7 had also malaria, 11% had bronchiolitis, 7.4% harbored intestinal parasites, 2% were HIV positive and 6.7% presented signs of malnutrition.

The PCV-7 vaccine has significantly reduced the rate of child hospitalization and mortality in Rwanda but co-infections and malnutrition may be additional risk factors for pneumonia that need to be tackled.

Learning Points/Discussion

Overall, our study is consistent with studies by others that demonstrate a positive impact of the PCV-7 vaccination on the incidence and severity of childhood pneumonia. We also demonstrate that a high number of children hospitalized due to pneumonia had other important co-infections including malaria, HIV and intestinal parasites, which may favor the occurrence of pneumonia. It is therefore possible that the PCV-7 vaccination effort may be hindered by these other co-infections.
Title of Case(s)

CASE SERIES OF CHILDREN WITH CO-INFECTION WITH DENGUE FEVER AND TYPHOID FEVER IN DISTRICT HOSPITAL, CHANDIGARH INDIA

Background

Dengue fever and Typhoid fever are both endemic in India and concurrent infections can lead to serious complications. We report the case series of 3 patients admitted with acute febrile illness who were diagnosed with Dengue Fever. Since fever persisted, further workup was done which showed co-infection with Enteric fever.

Case Presentation Summary

Case 1. 5 year old girl admitted with history of fever from 15 days with cough, body aches, malaise, pain abdomen and poor oral intake and normal examination. Investigations showed thrombocytopenia and Dengue IgM and Widal test were positive (Titres - O: 1:160, H1:80).

Case 2. 7 year old girl presented with fever of 6 days duration with pain abdomen and presence of petechial spots. On Examination she had Hepatomegaly. Investigations showed thrombocytopenia. Dengue IgM and Widal test were positive (Titres - O: 1:160, H1:160).

Case 3. 8 year old girl with fever of 4 days duration with vomiting, pain abdomen and myalgia. On Examination she had hepatomegaly. Investigations showed leucopenia and thrombocytopenia. Dengue NS1 and IgM was positive and Widal test done later due to persistence of fever was positive (Titres - O: 1:160, H1:160).

All three patients were treated with parenteral Ceftriaxone and supportive measures and were discharged home.

Learning Points/Discussion

Dengue and Enteric fever both have overlapping signs and symptoms. In a febrile child with fever and thrombocytopenia both should be considered in endemic areas and investigations and management done accordingly to decrease the mortality and morbidity.
Evaluation of clinical, laboratory features and etiology of patients with febrile convulsion

Background

Febrile seizures are the most common type of benign seizures in childhood. In this study, it was planned to examine clinical characteristics, laboratory parameters and etiology of 233 patients with febrile seizures and to compare findings with control group consisting of 233 healthy children.

Case Presentation Summary

The mean age of the patients in the case group was 20.0 ± 11.2 months and the mean age of the patients in the control group was 24.5 ± 14.4 months. 78.1% of the patients were found to have simple febrile seizure and 21.9% of patients were found to have complex febrile seizure. 81.3% of the patients were found to have upper respiratory tract infection, 4% of the patients had lower respiratory tract infection, 9.4% of the patients had acute gastroenteritis, 4.5% of the patients had urinary tract infection and 0.9% of the patients had varicella infection. White blood cell count, neutrophil and creatinine values of the patients in the case group were significantly higher than those of the control group (p <0.001, p <0.001, p = 0.002) and hemoglobin (p <0.001), red blood cell count (p = 0.031), red cell distribution width, platelet (<0.001), mean platelet volume (p = 0.028), lymphocyte, sodium, potassium (p <0.001), AST (p = 0.01) and urea (p = 0.001) values were significantly lower than the control group.

Learning Points/Discussion

The iron deficiency anemia in the case group was found to be higher than the control group and mean platelet volume and sodium values of the case group were found lower than the control group. There is a need for more extensive prospective controlled studies in this area.
Upper respiratory tract infections (URTI) and lower respiratory tract infections (LRTI) are common in preschool children. Studies on respiratory tract infections (RTI) risk factors were performed some decades ago, statistical data are not exact because not all RTI are recorded - more studies are necessary. The aim of the survey was to evaluate the frequency and risk factors of acute respiratory infections among children under 6 years old.

Methods

The parents of 392 children completed questionnaires related to their child's yearlong health status and environmental factors. Statistical analysis was performed using Microsoft Excel, SPSS 21.0.

Results

The estimated mean of acute infections incidence was $6.21 \pm 4.49$ times/year. Boys had more frequent LRTI than girls ($p<0.05$). Children, not attending daycare, had less infections than children, who attended daycare or had contacts with siblings, who attended daycare ($p<0.05$). The increased rate of infections had children who attended daycare group of > 20 children; started attending daycare younger than 5 years old or spent >20 h/week in the daycare ($p<0.05$). Organic food and household cleaning products, sufficient time spent outdoors, adequate breastfeeding and house airing were related to the lower number of RTI ($p<0.05$).

Conclusions

The incidence of RTI among preschool children was 2 – 11 per year. The study showed the association between acute infections and the attendance of the daycare, sex, age and environmental factors. The later onset of daycare attendance, small number of children in the group and shorter time spend in daycare can decrease the incidence of RTI. Further studies on impact of organic food and household cleaning products on morbidity of RTI are preferred.
Background

Extended spectrum beta-lactamase (ESBL) gene is easily spread through plasmid among gram negative bacilli (GNB). ESBL producing GNB was detected in enterobacteriaceae among Japanese children as high as 13.6%. Although a wide variety of ESBL genes were known in each geographical region, few reports existed on distribution of ESBL genes in Japan. Our aim of survey was to describe types of ESBL genes in GNB isolated from Japanese children.

Methods

ESBL producing GNBs isolated from children were collected between June 2011 and April 2017 at Tokyo Metropolitan Children’s Medical Center. CTX-M and SHV genes were tested with conventional polymerase chain reaction. CTX-M genes were genotyped for CTX-M1, M2, and M9 group with a full-automated molecular testing by Genecube® (Toyobo, Osaka, Japan). Duplicated strains of same species from single patient were excluded. Demographic data from patients and bacteria were collected.

Results

Total of 253 isolates of ESBL producing GNBs were screened from 238 children. Among those, 244 strains were genotyped. Boys were 61.8%. Median age was 17 month-old (interquartile range; 3-85 month-old). Samples collected from inpatients were 63.6%. Cultured from urine, stool and sputum was 50.6%, 27.3% and 9.5%, respectively. *Escherichia coli*, *Klebsiella pneumoniae*, and *Enterobacter* spp. were 202 (79.8%), 23 (9.1%) and 10 (4.0%), respectively. ESBL genes of CTX-M9 group, SHV and CTX-M1 group were 153 (63.2%), 38(15.7%) and 34(14.0%), respectively.

Conclusions

This is the largest study reporting distribution of ESBL genes from GNBs among Japanese children. The most dominant ESBL gene was CTX-M9 group, followed by SHV. Although *Escherichia coli* ST131 clone producing CTX-M15 which belong to CTX-M1 group was prevalent worldwide, our study found CTX-M1 group gene was the third common ESBL gene, which was similar epidemiology of Japanese adults.
04B. SCIENCE: COMMUNITY ACQUIRED INFECTIONS: RESPIRATORY TRACT INFECTIONS

CLINICAL EVOLUTION AND ETIOLOGY IN CHILDREN HOSPITALIZED WITH COMMUNITY-ACQUIRED PNEUMONIA

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Background

Community-acquired pneumonia (CAP) remains an important cause of morbidity and mortality in children. Etiologic diagnosis is rarely established because lower respiratory tract specimens are difficult to obtain. Viral infection, however, is the most common one. Thus, empirical antibiotic therapy is probably over used. The aim of this study was to describe and compare the evolution and outcome in children hospitalized with CAP categorized in subgroups carefully defined by probable etiology.

Methods

A retrospective analysis of clinical signs and symptoms during hospitalization of 128 children admitted due to CAP was conducted. Etiology had been prospectively and thoroughly investigated. Patients were classified as sole or viral-bacterial co-infection; in the sole infection subgroup, the cases were further classified as viral, typical bacterial or atypical bacterial infection. Data on antibiotic therapy, length of hospital stay (LOS) and outcome were recorded.

Results

Overall, median age and LOS were 19.2(10.3-32.3; min 0.9; max 59) months and 6(4-9.8) days, respectively. Viral-bacterial co-infection (35.9%), viral sole infection (42.2%), typical bacterial sole infection (13.3%), and atypical bacterial sole infection (8.6%) were found. All patients received antibiotics and were discharged after improvement. Antibiotic was changed in 16(12.5%) and 23(18.0%) had fever on 3rd day of antibiotic therapy. No clinical difference was detected during evolution among the distinct etiological subgroups. Antibiotic change was associated with fever on 3rd day of treatment and was not associated with bacterial infection.

Conclusions

Antibiotic treatment is overused in children hospitalized with CAP, since sole viral infection is the probable cause of almost half of patients. These children evolve similarly, irrespective of the etiological agent and empirical therapy. Change in antibiotic therapy is not associated to bacterial infection, although is related to presence of fever after 48h of treatment onset.
CHILAIDITI SYNDROME & TETRALOGY OF FALLOT- A RARE CO- OCCURRENCE.
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Title of Case(s)
Chilaiditi syndrome & Tetralogy of Fallot a rare co- occurrence.

Background
Chilaiditi syndrome is the transposition of the large intestine winding in between diaphragm and the liver. This symptom is rarely recognized, 0.025-0.28% of the whole population. The Chilaiditi symptom can be examined without any serious abdominal pain indication. Tetralogy of Fallots is a cyanotic CHD which is common but not reported any case co occurrence with chilaiditi Syndrome.

Case Presentation Summary
A 7 years old, female child presented with abdominal pain, vomiting and respiratory distress. The child having no history of fever, PUD or taking any offending drugs but parents gave the history child was previously diagnosed as congenital heart disease & child becomes bluish on crying & running. On examination child is ill looking, cyanotic, precordial examination reveals ejection systolic murmur. Abdominal examination shows tenderness on epigastric region but no rebound tenderness & organomegaly. Plain abdominal radiograph showed colonic interposition between the anterior surface of the liver and the diaphragm which is Chilaiditi's sign & chest radiograph shows boat shaped heart & oligaemic lung field. CT scan of abdomen & Echocardiography of child performed which shows chilaiditi Syndrome & Tetralogy of fallot. Pneumo peritonium is D/D of chilaidi syndrome. Initial management of Chilaiditi syndrome was conservative with bed rest, intravenous fluid, bowel decompression, enemas, and laxatives. If the patient does not respond to initial conservative management, and either the obstruction fails to resolve or there is evidence of bowel ischemia, then surgical intervention is indicated. Fallot tetralogy managed conservatively propranolol, palliative shunt operation (B-T Shunt) and finally total surgical correction.

Learning Points/Discussion
Chilaiditi sign and Chilaiditi syndrome are rare entities, often misdiagnosed in clinical practice. Tetralogy of Fallots & Chilaiditi Syndrome is not the association, they are different entity. But both this condition present in our case. So, this is rare co-occurrence.
INFECTIVE ENDOCARDITIS ASSOCIATED WITH VENTRICULO-ATRIAL SHUNT ACCOMPANIED BY LUNG EMBOLI AND GLOMERULONEPHRITIS IN A CHILD

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Title of Case(s)

INFECTIVE ENDOCARDITIS ASSOCIATED WITH VENTRICULO-ATRIAL SHUNT ACCOMPANIED BY LUNG EMBOLI AND GLOMERULONEPHRITIS IN A CHILD

Background

There may be severe problems affecting multiple systems in infective endocarditis. The present case aims to report infective endocarditis associated with ventriculo-atrial shunt (VAS) accompanied by lung emboli and glomerulonephritis.

Case Presentation Summary

A 3-year old girl was referred to our hospital because the oxygen demand had not regressed, from another one where she had been monitoring for 10 days upon pneumonia diagnosis. Pre-birth meningomyelocele was detected, closure surgery was conducted after birth, a ventriculo-peritoneal shunt was replaced; a year ago a VAS was placed due to multiple shunt infection and functional disorders. Physical examination revealed fever, oxygen demand, tachycardia, wound scar at waist, leg-paralyses. Echocardiography showed vegetation starting at the end of the shunt at vena cava superior and reaching to tricuspid valve in right atrium. Acute phase reactants were high, C3 level low, C4 level normal. Erythrocyte-uria was detected and the patient was monitored with respect to nephritis. Vancomycin and meropenem were started after blood culture samples were taken. Chest tomography showed filling defects compatible with emboli, enoxaparin-sodium treatment started. Staphylococcus epidermidis growth was detected in blood cultures. The fever regressed to normal in the first treatment week, however, growth in blood cultures, oxygen demand and acute phase reactants were still high. In the third week of treatment, vegetation was surgically cleaned since dimensions were not changing, the shunt was changed. Antibiotic treatment was completed to 7 weeks. Hematuria continued, C3 level normalized; monitoring the patient with respect to glomerulonephritis and completing the enoxaparin-sodium treatment to 3 months was planned.

Learning Points/Discussion

Infecive endocarditis is rare in VAS cases; it is scarcely accompanied by lung emboli and glomerulonephritis.
03A. SCIENCE: SEVERE BACTERIAL INFECTIONS

BACILLE CALMETTE-GUÉRIN RELATED OSTEOMYELITIS AND SEPTIC ARTHRITIS OF THE ELBOW

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Title of Case(s)

Bacille Calmette-Guérin related Osteomyelitis and Septic Arthritis of the Elbow

Background

Osteoarticular tuberculosis is found in about 3-5% of patients with tuberculosis, with 2% of cases involving the elbow and wrist. Mycobacterium Tuberculosis is the main causative organism, and only a few cases are attributable to Mycobacterium Bovis. The International Union Against Tuberculosis and Lung Disease reports 0.39 cases of Bacille Calmette-Guérin (BCG) related osteomyelitis per million vaccinations. Here, we report a case of BCG related elbow osteomyelitis in a young boy.

Case Presentation Summary

An 8-year-old child presented with gradual elbow joint swelling and limitation of movement over the past 2 years. No fever or any other associated symptoms were reported. Plain X-ray showed lytic lesions in the proximal ulna with periosteal elevation. CT guided biopsy revealed granulomatous osteomyelitis. Cultures were negative for common bacteria, fungi and mycobacteria. He later developed further increase in swelling size associated with pain. MRI revealed interval development of large joint effusion with possible abscess formation consistent with septic arthritis. The patient was taken for debridement and biopsy. After 4 weeks of incubation, Mycobactrium Bovis was isolated. He was started on isoniazid, rifampicin, ethambutol, and moxifloxacin. He started to show improvement in swelling size and range of motion after 4 months, and was stepped down gradually to isoniazid and rifampicin to complete total of 23 months of therapy.

Learning Points/Discussion

BCG Osteomyelitis, although rare, could be a potential complication of BCG vaccination. Its insidious onset and low index of suspicion may result in a delayed diagnosis. Clinical suspicion, early diagnosis and early treatment are key to effective management. While BCG osteomyelitis shows favourable prognosis with oral chemotherapy, some cases may require surgical debridement.
DIPYLIDIDUM CANINUM INFECTION IN CHILDREN: CLINICAL PRESENTATION AND THERAPEUTIC CHALLENGES

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Title of Case(s)

DIPYLIDIDUM CANINUM INFECTION IN CHILDREN: CLINICAL PRESENTATION AND THERAPEUTIC CHALLENGES

Background

*Dipylidium caninum* infection is a relatively uncommon intestinal parasitic zoonosis. It is not well known to general practitioners and pediatricians in the developed countries which can lead to underdiagnosis. The transmission requires ingestion of the cysticercoid contaminating form of the parasite which is contained in dog and cat fleas. The course of the disease is quite benign but can occasionally pose significant diagnostic and therapeutic challenges. Prevention of the disease requires regular veterinary care of pet animals and addressing the problem of stray animals.

Case Presentation Summary

During the last two years ten cases of dipylidiasis (2 infants, 5 toddlers, 3 older children) presented in our Pediatric department and diagnosed in the Microbiology department in stool samples. Nine of them presented during a four month time period. There was a variety in clinical presentation (mainly gastrointestinal symptoms). In two cases there was a probable coinfection with another helminth (*Ascaris lumbricoides, Enterobius vermicularis*) as revealed from the patient history. Five of our cases did not report contact with animals and hence the mode of transmission was questioned, especially in infancy. Treatment with antiparasitics (praziquantel, niclosamide) was challenging in the two infants of our cohort which is relatively uncommon. We did not observe any serious intolerance or side effects to the administered drugs.

Learning Points/Discussion

There must be a greater clinical suspicion for diagnosis of dipylidiasis in children and preventative measures need to be taken to control the outspread of the parasitosis in humans.
04B. SCIENCE: COMMUNITY ACQUIRED INFECTIONS: RESPIRATORY TRACT INFECTIONS

RESPIRATORY VIRUS DETECTIONS AND BACTERIAL INFECTIONS AMONG NON-HOSPITALIZED CHILDREN WITH COMMUNITY-ACQUIRED PNEUMONIA TREATED WITH AMOXICILLIN: A PROSPECTIVE COHORT

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Background

Community-acquired pneumonia (CAP) imposes big morbidity and mortality in children and may be caused by several pathogens. Amoxicillin is the first-choice antibiotic to treat empirically non-hospitalized children with CAP. We described the frequency of virus detections and bacterial infections in non-hospitalized children with CAP treated with amoxicillin and compared the amoxicillin substitution rate due to treatment failure among children with or without typical bacterial infection.

Methods

Children aged 2-59 months with non-severe CAP (respiratory complaints plus radiographic pulmonary infiltrate/consolidation) were enrolled in a prospective cohort, in Salvador, Brazil. From 820 patients recruited in a clinical trial (ClinicalTrials.gov Identifier NCT01200706), 705 (86.0%) had nasopharyngeal aspirates (NPA) and serum collected upon admission and serum collected 2-4 weeks apart. NPAs were tested for 16 respiratory viruses by PCRs and bacterial infections were investigated by serology. Follow-up assessments occurred at 2, 5, and 14 days after enrolment.

Results

Respiratory viruses were detected in 643 (91.2%) cases, typical and atypical bacterial infections being diagnosed in 166 (23.5%) and 141 (20.0%), respectively. Typical bacterial infections comprised pneumococcal (18.3%), Haemophilus influenzae (5.8%), and Moraxella catarrhalis (2.7%) infections. The majority of the cases (55.6%) had only virus detection. Amoxicillin was substituted in 4 (0.6%) and in 19 (2.7%) patients due to adverse event or clinical failure, respectively. There was no significant difference when the amoxicillin substitution rate due to clinical failure was compared among children with or without typical bacterial infection (4.3% vs. 2.2%; P=0.2).

Conclusions

Respiratory viruses were detected in almost all cases and typical bacterial infection was found in approximately one fourth of them. It is crucial to distinguish children with from children without typical bacterial infection in order to rationalize antibiotic use.
16C. SCIENCE: TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

MANAGEMENT AND OUTCOME OF BACILLUS CALMETTE-GUÉRIN OSTEITIS/OSTEOMYELITIS IN CHILDREN: COMPARISON BY TYPES OF BONES

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Background

Osteitis or osteomyelitis is one of the rare but serious complications of Bacillus-Calmette-Guérin vaccination. Management and prognosis could be distinct when different region of bone is involved. The aim of this study is to compare management, and outcome of Bacillus Calmette-Guérin osteitis/osteomyelitis in children with different types of bones involved in order to institute an individualized management.

Methods

We reviewed all cases of Bacillus Calmette-Guérin osteitis/osteomyelitis registered to Taiwan’s vaccine injury compensation program during 1998-2014. Demographic, clinical, laboratory, treatment and outcome data were compared by the region of infected bone.

Results

Seventy-one patients were collected. The distribution for the types of bones was shown in figure 1. Among the seventy patients had chemotherapy, those with vertebral or multifocal infection received a longer duration of treatment (P < .001) and second-line antituberculous medications in addition to isoniazid, ethambutol, and rifampicin due to poor response (P = .02). Three patients (4.2%) had major sequelae with kyphosis or leg length discrepancy. Nevertheless, the outcome of patients with rib, sternum, and peripheral bones without multifocal involvement was good and the average time for functional recovery was 6.2 ± 3.9 months.

Conclusions

Children with Bacillus Calmette-Guérin osteitis/osteomyelitis in different types of bones have distinct outcome. Physicians should adjust the medical treatment to the affected sites. Patient with a single lesion at rib, sternum, and extremities could have a shorter duration of chemotherapy with isoniazid and rifampicin for 6-9 months. Meanwhile, those who have vertebral or multifocal lesions may need to receive a combination therapy including one second-line antituberculous agent as initial regimens and should be treated with a longer course for at least 12 months.
HEALTH SEEKING BEHAVIOUR FOR COMMON CHILDHOOD ILLNESSES AMONG CAREGIVERS OF UNDER-FIVES IN A KNOWN NIGERIAN COMMUNITY

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Background

Worldwide, the most common causes of death in children under the age of five years are pneumonia, diarrhoea, preterm birth complications and malaria. Among these, nearly all of child deaths due to pneumonia and diarrhea occur in sub-Saharan Africa and South Asia.

The aim of this study was to assess the health seeking behavior of care-givers of under-fives for common childhood illnesses in a known Nigerian Community.

Methods

This was a descriptive cross-sectional study conducted between March and October 2016. The sample size used was three hundred and thirty (330). Multi-stage sampling technique was used. Employed in this study was a structured interviewer administered questionnaire with 4-sections (A to D) addressing socio-demographic characteristics, knowledge and practices of health seeking behavior among caregivers of under-fives for common childhood illnesses.

The completed questionnaires were inputted and analyzed using the Epi Info Statistical software (version 7).

Results

Overall, most caregivers (77.13%) interviewed had poor knowledge. The most common known cause of childhood illnesses was organisms. Common symptoms mentioned were, fever and not playing well. The number of children below the age of 5 years in a household was found to be statistically significant when associated with taking child to a health facility, with a value of p= 0.029. Good knowledge of common childhood illnesses prompted good practice with a value of p= 0.024.

Conclusions

Health education programs and counseling should be given to members of the community, on the importance of identifying symptoms, and seeking timely and appropriate treatment for their children at health facilities.
Further research needs to be done to provide more knowledge and better understanding of factors that can be manipulated to enable the formation of community specific intervention programs that will improve health status.
ACUTE RHEUMATIC FEVER: AN UNEXPECTED CAUSE FOR FEVER OF UNKNOWN ORIGIN IN A CHILD

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Title of Case(s)

ACUTE RHEUMATIC FEVER: AN UNEXPECTED CAUSE FOR FEVER OF UNKNOWN ORIGIN IN A CHILD

Background

In acute rheumatic fever (ARF), the fever is explicit and recedes even in untreated cases. That ARF is the cause for fever of unknown origin (FUO) is almost unexpected.

Case Presentation Summary

A 10-year old boy was admitted with fever, continuing for 17 days and going up to 39.5°C. It was revealed that a pale red itchy rash which occasionally intensified occurred in the body and extremities on the 3rd day of the fever and that later abdominal pain and widespread muscle and joint pains developed. In physical examination, fever was 39.7°C, pulse was 140/min and the patient had difficulty in moving due to the pain. There was a pale macular rash, with pale erythema which was paler at the centre and became paler when pressed. Other findings were normal. In laboratory tests, ESR was 72 mm/h, CRP was 20 mg/dl. The haematology, urine, biochemical, radiology, serology and microbiology tests for the cause of the FUO were normal. In the electrocardiogram, PR elongation and in echocardiography moderate failures of mitral and aortic valves were determined. ASO was found to be 1.117 IU/ml. Upon ARF diagnosis, steroid treatment was started, benzathine penicillin was administered. On the second day of the treatment, fever and other findings disappeared. Treatment and follow-up were planned.

Learning Points/Discussion

ARF is not an expected cause in FUO cases. However, in moderate or high risk communities for ARF, the probability of ARF in FUO cases must be kept in mind.
PROGRESSIVE CYSTIC ECHINOCOCCOSIS WITH EXTENSIVE INVOLVEMENT IN A CHILD: HOW LONG AND HOW TO TREAT?
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Title of Case(s)
Echinococcosis

Background
Echinococcosis is a common zoonosis. The active agent in the majority of the cases in Turkey is *Echinococcus granulosus*. For treatment, albendazol and sometimes surgery is used. There is no consensus in the form and duration of drug administration. Our case is presented to highlight this issue.

Case Presentation Summary
A 9-year old boy was admitted with headache, diplopia in the left eye and convulsions. There were no particularities in physical examination findings. In cranial imaging, a 6.5X7.5 cm cystic lesion, without contrast involvement, shifting right at centre-line, without oedema around was identified in the parietal lobe. Thorax and abdominal imaging identified multiple cystic lesions, compatible with stage-2 and 3 cystic echinococcosis, some containing septa some lobular. Bone and cardiac images were normal. In serological examination, *Echinococcus* -IHA and -IgG were positive. Albendazol and anti-convulsive therapy was started. The cyst in the brain parenchyma was removed by surgery. Surgical treatment was not considered for the other cysts. 2-year albendezol therapy was continued at 28-day administrations with 10-day intervals. The lesions were followed-up every 6 months. *Echinococcus* - IHA and -IgG continued to be positive. At the end of the 2nd year of treatment, albendazol therapy was ceased since there was no radiological progress in the lesions. In the radiological assessment made after eight months, there was no change in size and stage of the lung cysts, however, there were numerous 5-7mm, stage-1 lesions in the liver. Uninterrupted albendazol therapy was re-started.

Learning Points/Discussion
Serological and radiological examinations are not helpful in determining the duration of treatment in echinococcosis cases. There is need for consensus in the form/duration of medical therapy and detailed guidelines on the follow-up of problematic cases.
Background and Objective

Background. Meningococcal meningitis (MM) in children is a serious public health problem as it can cause mortality and morbidity. MM is also responsible of high cost for the acute care and for the follow-up of affected patients.

Methods

Methods. In this report, we analyzed the real cost of pediatric MM hospitalization in the acute phase (HAP). For the purpose of the study, we analyzed the medical records of children hospitalized for a laboratory confirmed MM over a nine year period (January 2006-December 2016) at Bambino Gesù Children Hospital, Rome, Italy.


Learning Points Discussion

Results. Among all the children hospitalized in the study period, 32 fulfilled the inclusion criteria. The mean age of patients was 5.3 years (range 40 days-16.5 years). The mean cost of HAP was of 14874 euro (range from 9203 to 35050 euro). In children younger than 1 year old, the HAP costs were the highest. Comparing our data with the selected studies, we find out similar results of approximately 16750 euro (range 12000-20000 euro).

Conclusions. Hospital costs are an important end-point in health economic evaluation of the disease in order to implement preventive measures, promoting public funding decisions like immunization strategies and vaccination programmes.
Molecular typing of Staphylococcus aureus causing community-acquired severe infections in an Italian tertiary-care paediatric hospital

Background

Staphylococcus aureus (SA) causes a wide range of clinical manifestations, sometimes severe. Molecular typing of SA has been extensively used for epidemiological purposes, but often correlation between clinical findings and genotype is missing. Aim of this study is to evaluate the genetic background of SA causing community-acquired severe infections in a tertiary-care pediatric hospital in Rome, Italy, in the period January 2015 - August 2017.

Case Presentation Summary

SA isolated from clinical samples were retrospectively selected from community-acquired severe infections. Molecular analyses were performed for detection of genes encoding for mecA and Panton-Valentine leucocidin (PVL). MRSA strains were further investigated through the analysis of the SCCmec cassette and spa-typing. 24 SA strains were selected (source: blood 20; wound 3; nasopharyngeal aspirate 1). 14 strains were MSSA/PVL-; 5 MRSA/PVL+; 3 MRSA/PVL- and 2 MSSA/PVL+. Through spa-typing, the 16 MSSA were clustered in 11 groups. SCCmec IV-a was detected in 7 MRSA isolates. Interestingly, the 5 MRSA/PVL+ strains shared the same SCCmec (IV-a) and spa-type (t024). From a clinical perspective, among these five particular strains, 2 were responsible for severe WIs, one for necrotizing pneumonia, one for liver abscesses in a neonate, one for hip osteomyelitis complicated by septic shock, multiple intramuscular abscess and necrotizing pneumonia
Learning Points/Discussion

In our population, t024 was the most prevalent spa-type and was associated with MRSA/PVL+ strains, which caused severe diseases. It was not detected in MSSA strains. Molecular typing allows the monitoring of SA clusters and outbreaks, and in our experience it was also useful as a marker of severe disease. The circulation of this particular spa-type in patients not linked epidemiologically deserves further evaluation.
INFLUENCE OF VIT D PLASMA LEVEL ON PNEUMONIA SEVERITY AND OUTCOME IN INSTITUTIONALIZED CHILDREN

K. Gogberashvili

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Background

Study was aimed to assess the influence of vit D plasma concentration on pneumonia severity in children > 3 months of age placed in orphanages. The evidence on the effects of vit D supplementation on respiratory infections in children has not been assessed systematically.

Methods

Methods

The cross-sectional study was performed in Tbilisi Infant’s Orphanage. Study period 2011–2016 years. Participants were 42 children of both sexes at age >3 month to ≤4 years, hospitalized with clinical diagnosis of acute pneumonia. Every child received 400 IU of vit D up to 1 year. Pneumonia was defined as radiologically confirmed age-specific tachypnea along with local crepitations and with or without wheeze and fever. The study covered the following interventions: vit D plasma concentrations, monitoring the severity and outcomes from pneumonia, duration of illness, effectiveness of recommended treatment, quantity of cases with hospitalization. The calcidiol (25-OH-D) concentrations < 20 ng/mL was defined as vit D deficiency.

Results

Vit D deficiency was diagnosed in 84% of children hospitalized with severe pneumonia. There was no difference with the total lymphocyte and B-cells counts between investigated groups with different disease severity. However the total T-cell count and concentration of CD3 and CD4 were lower in groups with severe cases. There was elevated the number of CD8. Observed changes leaded to alteration in CD4/CD8 ratio with impact on morbidity.

Conclusions

Vitamin D has important functions other than Ca metabolism which include modulation of the innate and adaptive immune responses. It affects T cell maturation and facilitates the induction of T regulatory cells. It is recommended some modifications in accepted guidelines for management of CAP in institutionalized children with monitoring vit D level and supplementation if needed.
A CASE OF MYCOPLASMA ENCEPHALITIS
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Title of Case(s)
Mycoplasma Encephalitis

Background
M. pneumonia is a common cause of respiratory tract infections and can also lead to a wide range of pulmonary and extra-pulmonary manifestations. Neurological manifestations occur in approximately 0.1 percent of patients with M. pneumonia and most commonly affect children. We describe a case of mycoplasma encephalitis in a child with lower respiratory tract infection.

Case Presentation Summary
A 10-year-old boy presented with one week history of being general unwell and fever. The day before admission, he experienced severe lethargy, fatigue and he was unable to get out of the bed. On the day of admission he developed disorientation and confusion. There was no history of photophobia, neck stiffness or seizures.

Past history includes a vocal cord palsy needing tracheostomy which was reversed four years ago. On examination his GCS was 14/15, his speech was incoherent and he appeared confused. A detailed neurological examination was normal apart from inability to walk due to lethargy and fatigue.

Investigations – see table
Chest x-ray showed left upper and lower zone consolidation. EEG was suggestive of encephalopathy, CT and MRI brain was normal.

He was initially treated with IV Ceftriaxone, Aciclovir and Clarithromycin. Once the mycoplasma was confirmed, ceftriaxone and acyclovir were stopped. He started improving by day 4 of admission and did not have any further episodes of confusion. He went on to complete a 10 day course of IV clarithromycin and recovered completely.
Learning Points/Discussion

*M.pneumonia* associated central nervous system complications are rare but can cause significant morbidity and mortality if not treated promptly. The mechanism by which *M. pneumonia* causes encephalitis is still relatively unclear, and likely to be an immune mediated response.

It is important to consider mycoplasma in children presenting with chest symptoms and encephalopathy.
Background

Our aim was to assess diversity in the management of febrile children in Europe and to provide an overview of which aspects of local and regional emergency care can influence resource use and antibiotic use and thus have to be made available in future studies to aid in the interpretation of this diversity.

Methods

An electronic questionnaire was sent to 11 European hospitals. Three domains were studied: national/regional aspects of care (primary care, immunisation), local ED quality indicators (triage, supervision, guidelines, electronic health care records) and local factors influencing resource use (point-of-care tests (POCT) and admission rates).

Results
Primary care was available in all regions during office hours and in 55% during out-of-office hours. DTaP/IPV, Hib, PCV and MMR were part of the routine immunisation in all countries. Several countries offered additional routine immunisation such as meningococcal disease (n=6), rotavirus (n=5), varicella (n=4) and influenza (n=1). During office hours, the supervisor was present onsite in all settings, while this was the case in 45% settings during out-of-office hours. The supervising specialist was a paediatrician in 55% of the settings, while in the other settings care could also be delivered by a (paediatric) emergency physician. Guidelines for febrile children and sepsis were implemented in ten settings, however, settings differed in whether this was a NICE guideline, a national guideline or a local guideline. A POCT CRP was available in 6 ED's, a blood-gas analysis in 9 ED's. Admission rates ranged from 1-51%.

Conclusions

We observed differences in local quality indicators, regional and national aspects of care and resource availability. In studies regarding the management of febrile children and antibiotic use, this diversity has to be taken into account.
**Title of Case(s)**

**VACCINE-ASSOCIATED MEASLES IN AN 1-YEAR-OLD INFANT**

**Background**

Vaccine-associated measles has been rarely reported in children. We herein describe a case of vaccine-associated measles illness occurred 10 days after administration of the measles-mumps-rubella (MMR) vaccine containing the Enders attenuated Edmonston measles strain.

**Case Presentation Summary**

A previously healthy, 1-year-old girl presented to our hospital with the complaints of fever and diffuse maculopapular rash. The patient had received her first dose of MMR vaccine 10 days prior to the onset of rash (figure 1). Since measles is under enhanced surveillance according to the national action plan for measles elimination, an epidemiological investigation was initiated, and serum, urine and throat swab specimens for laboratory testing were obtained. The investigation found no similar cases among contacts of the patient. Measles virus infection was confirmed by both the detection of the measles-specific Ig M by ELISA method (Enzygnost®; Siemens, Germany) and the measles virus RNA in throat swab and urine specimen using real-time RT-PCR (Applied Biosystems). The measles virus was subsequently determined to be the vaccine strain by sequence analysis of the genome. The
patient was discharged from hospital in a good condition on hospital day 10.

Learning Points/Discussion

In order to maintain the accuracy of the measles surveillance system, it is critical to discriminate between measles vaccine and wild-type virus. Virus genotyping can be used to differentiate between wild-type and vaccine virus infection in those who have been immunized recently.
PNEUMOCOCCAL PERITONITIS DIAGNOSED BY RT-PCR IN A MALNOURISHED CHILD

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Title of Case(s)

Pneumococcal peritonitis diagnosed by RT-PCR in a malnourished child

Background

Spontaneous bacterial peritonitis caused by *Streptococcus pneumoniae* is infrequent and commonly occurs when underlying abdominal diseases are present. We describe a culture-negative pneumococcal SBP in a malnourished child diagnosed by RT-PCR.

Case Presentation Summary

A 2-year old girl was admitted to the ER with recurrent high fever (39.5°C), vomit and inappetence for 3 days. She was severely dehydrated, hypoactive, tachycardic, tachypneic and with distended and painful abdomen at examination – no peritoneal inflammation signs were evidenced. The additional parameters of the clinical examination were unremarkable. She had no underlying conditions or previous hospitalizations, however, she took a vegan diet, presented with failure to thrive, undernutrition and incomplete primary immunization series. Complementary evaluation evidenced severe leucopenia, C-reactive protein=40.1 mg/dL, bowel edema at abdominal X-ray and ultrasound, without free liquid in abdominal cavity. High dose ceftriaxone, metronidazole and ampicillin was empirically initiated, and she was transferred to the intensive care unit, where she required ventilatory support, multiple vasoactive drugs (noradrenaline, adrenaline, dobutamine, and milrinone), hemodialysis and several blood transfusions. An exploratory laparotomy was performed at the 2nd day of hospitalization, which identified a large amount of purulent secretion in the cavity, without signs of bowel perforation, acute appendicitis or any other apparent focus for the pyogenic infection. Sustained hemodynamic and ventilatory improvement occurred at the 15th day of antimicrobial course. The patient was discharged after 25 days of treatment, with no residual sequelae. Despite all negative cultures, RT-PCR collected from abdominal fluid five days after the laparotomy identified *Streptococcus pneumoniae*, which was negative in blood.

Learning Points/Discussion

RT-PCR is a useful tool for culture-negative infection and can improve the sensitivity of identification of invasive pneumococcal disease.
MOLECULAR EPIDEMIOLOGY AND GENETIC CHARACTERIZATION OF HUMAN RESPIRATORY SYNCYTIAL VIRUS DETECTED IN INPATIENT AND OUTPATIENT CHILDREN IN TEHRAN

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²School of Medicine- Tehran University of Medical Sciences, Department of Microbiology, Tehran, Iran
³Bahrami Children Hospital- Tehran University of Medical Sciences-, Infectious disease department, Tehran, Iran

Background

Human respiratory syncytial virus (HRSV) is the leading cause of acute lower respiratory tract infection in infants and young children. While no treatment is yet available, recent clinical trials on RSV vaccines are promising. Therefore RSV genotyping data before vaccine introduction are necessary. Limited information exists regarding HRSV genotypes in Iran.

Methods

In order to better understand HRSV strain diversity; we evaluated in-depth the genetic variability to the HRSV G and F protein detected in inpatient and outpatient children less than two years old with acute respiratory symptoms during 2015-2016 in a local area of Iran (Tehran). A total of 180 nasopharyngeal swabs specimens were evaluated. HRSV positive samples were genotyped based on G and F gene sequences using RT-PCR and sequencing methods. Genetic and antigenic characteristics of G and F genes were investigated in all selected sequences.

Results

Fifty-five out of 83 HRSV positive samples were sequenced in our survey. All of them were classified as subgroup A and belonged to the ON1 genotype. This study is the first report regarding the emergence of ON1 in Iran. The phylogenetic tree showed that ON-1 Iranian sequences clustered in 4 different lineages according to G and F genes. Fusion gene sequence analysis showed that all genetic changes in the Iranian isolates were base substitutions and no deletion, insertions, or frame-shift mutations were identified.

Conclusions

This study provided the first genetic analysis of HRSV F protein in Iran. The results of the present study highlight that standard molecular surveillance programs for early detection of circulating genotypes are necessary to improve the development of targeted therapies.
THE ROLE OF LIP氧化GENASES IN VIRAL INFECTIONS; HOW LIP氧化GENASE ENZYMES AFFECT VIRUS PATHOGENESIS?
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¹School of Medicine- Iran University of Medical Sciences, Department of Biochemistry, Tehran, Iran

Background

Lipoxygenases (LOXs) are members of non-hem iron–containing dioxygenases which categorized based on their positional specificity of fatty acid (substrate) oxygenation to 5,8,12 and 15 lipoxygenases. The cellular distribution of lipoxygenases is in platelets, leukocytes, keratinocytes and gastrointestinal epithelium. Their involvement in inflammatory disease onset and progression as well as respiratory diseases have received attention.

Methods

Because of the importance of the subject we performed a systematic review exploring how these enzymes affect virus pathogenesis. This study includes 175 published studies. We reviewed all published studies about lipoxygenases in viral infections identified by searching all databases, and related references from relevant articles.

Results

12-LOX causes polymorphonuclear cells (PMNs) migration and inflammation in Bacterial acute lung Infection. 15-LOX generates Eoxins as proinflammatory metabolites in eosinophils, mast cells, and nasal polyps cause elevated vascular permeability and inflammation. Also, 15-LOX expression in lung epithelial cells facilitates the release of chemokines likewise MIP-1, RANTES, and IP-10 and accumulation of inflammatory cells in inflammatory lung diseases. The mediatory effect of lipoxygenase pathway in viral infections which is the focus of this study can be considered as an effective pathway in pathogenesis of viral infection. The expression level of 5-LOX and its metabolite is increased in dengue virus, Hepatitis B virus, Epstein-Barr Virus (EBV), Human cytomegalovirus, Human rhinoviruses, Influenza virus, Kaposi's sarcoma-associated herpesvirus however decreased in HIV-1 infection.

Conclusions

The recent insights in the mechanistic role of lipoxygenase pathway in viral infection and possible therapeutic opportunities are reviewed in the presents study which support both favorable and unfavorable effects of lipoxygenase pathway on viral diseases based on virus type. Accordingly, lipoxyganase pathway can be considered as potential approaches for efficient therapies especially in children.

Systematic Review Registration (Please input N/A if not registered)

N/A
SURVEY ABOUT THE LOWER RESPIRATORY TRACT BACTERIAL INFECTIONS AMONG CHILDREN IN THE ICUS IN EGYPT

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²Natural Organization for Drug Control and Research NODCAR, Microbiology and Immunology, Giza, Egypt
³Faculty of pharmacy. Beni Suef university, Microbiology and Immunology, Beni Suef, Egypt

Background

The respiratory tract is one of the most common sites of infection. A 1.4 million children are died from acute Lower Respiratory Tract infections (LRTIs), pneumonia and bronchiolitis. This survey is aim to detect the the most prevalent causative bacteria for LRTIs among children in the Intensive Care Units (ICUs) from Cairo/ Egypt, and to detect the multi-drug resistant (MDR)bacteria. For farther protection by a trial to prepare a vaccine for the most prevalent bacteria of this cases.

Methods

Two hundreds clinical isolates from Lower Respiratory Tract infected children were collected from the Intensive Care Units (ICUs) in Cairo / Egypt, isolates were microbiologically identified, the antimicrobial susceptibility testing to different classes of antibiotics were done and the most prevalent causative bacteria for the LRTIs were determined.

Results

The survey revealed that there are five causative bacteria: Pseudomonas aeruginosa, Klebsiella pneumonia, E coli, Acinetobacter, Staph. aureus. The most prevalent Causative bacteria were found to be Pseudomonas aeruginosa with a percentage of 40% and Klebsiella pneumonia with a percentage of 36%. The antibiotic susceptibility tests appeared a high antibiotics resistance among Pseudomonas aeruginosa and Klebsiella pneumonia isolates to different antibiotics such as Vancomycin, Cefotaxim, Ceftriaxon, Cephradine and Clindamycin.

Conclusions

The survey included isolates from children with a case of Lower Respiratory Tract Infections in the ICUs in hospitals inside Cairo/ Egypt. The most causative bacteria were determined to be Pseudomonas aeruginosa and Klebsiella pneumonia. The high Multi Drug Resistance among isolates give us a good reason to start preparation of a combined vaccine against the most prevalent causative bacteria.
ESP18-0190  
E-POSTER VIEWING - MAY 28-JUNE 2 - EXHIBITION HOURS

19B. SCIENCE: OTHER

CHANGING PATTERNS OF ACUTE POST-STREPTOCOCCAL GLOMERULONEPHRITIS (APSGN) IN KOREA: THE FIRST LONG-TERM STUDY FOR 28 YEARS

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²Yonsei University College of Medicine, Pediatric Nephrology, Seoul, Republic of Korea

Background

The aim of this study was to investigate the changing patterns in clinical characteristics of acute post-streptococcal glomerulonephritis (APSGN) in Korean children.

Methods

We retrospectively analyzed the medical records of 131 children who were diagnosed with APSGN at Severance Hospital from the years 1987 to 2009. The patients were divided into two groups; Group 1 (n = 72, before the year 1998) and Group 2 (n = 47, after the year 1998). Clinical and laboratory findings were compared between the two groups.

Results

In group 2, vomiting (20.8% vs. 4.3%, \( P = 0.014 \)), oliguria (40.8% vs. 19.1%, \( P = 0.016 \)), generalized edema (86.1% vs. 63.8%, \( P = 0.005 \)), and pulmonary edema in chest X-ray (22.7% vs. 4.4%, \( P = 0.014 \)) were statistically less frequent than in group 1. Anti-streptococcal O (ASO) titers did not differ between the two groups, but the levels of C3 (21.7 ± 17.4 vs. 30.3 ± 22.2, \( P = 0.044 \)) were significantly higher in group 2 than those in group 1. In multiple logistic regression analyses, C3 was an independent predictive factor for APSGN patients with edema (odds ratio [OR]: 1.034, 95% CI: 1.010-1.060, \( P = 0.006 \)) and more than two acute nephritic symptoms (odds ratio [OR]: 0.974, 95% CI: 0.952-0.996, \( P = 0.020 \)). C3 negatively correlated with the increasing numbers of acute nephritic symptoms in APSGN patients (\( R = -0.182, P = 0.048 \)).

Conclusions

This is the first study to show that the severity of APSGN became milder since the year 1998 in Korea, which might be due to relatively less decrease of C3 levels against streptococcal infection in recent years. The level of C3 has a potential to predict the severity and prognosis of APSGN.
Liver failure in the course of tuberculosis in a boy treated with isoniazid

Background

Tuberculosis is a worldwide public health problem, caused by Mycobacterium tuberculosis. Current drugs such as isoniazid, pyrazinamide and rifampicyn used in the treatment of tuberculosis are potentially hepatotoxic and can lead to drug-induced hepatitis.

Case Presentation Summary

We present the case of a 5-year-old boy treated for tuberculosis. The family history revealed that the boy had contacted with his ill grandfather. On the basis of the radiological imaging and the results of laboratory tests, the diagnosis of lymph node tuberculosis was made. Anti-mycobacterial therapy with a 3-drug regimen (isoniazid, rifampicin, pyrazinamide in standard doses) was started. On the 6th day of treatment, vomiting and yellowing of the skin and the whites of eyes occurred. Laboratory tests revealed increased aminotransferase activity and elevated bilirubin levels. Due to increasing parameters of hepatic insufficiency (increased INR and elevated bilirubin levels), the boy was admitted to the Gastroenterology Unit of the Department of Pediatrics. Laboratory tests demonstrated: ALT 1888 U/L, AST 5517 U/L, total bilirubin 54.1 umol/L, INR 2.12. Tuberculosis treatment was discontinued. N-acetyl-cysteine, ursodeoxycholic acid, acyclovir and parenteral hydration were implemented. The patient was additionally diagnosed with Clostridium difficile infection, which was treated in a standard way. During the hospitalization, general improvement and gradual normalization of laboratory tests were observed. Currently, the boy has regular follow-up appointments in the outpatient setting; test results of liver cell functioning and damage parameters are normal.

Summary. In our paper we would like to draw attention to hepatotoxic effects of drugs used for the treatment of tuberculosis, also in the pediatric population.

Learning Points/Discussion

We would like to draw attention to hepatotoxic effects of drugs used for the treatment of tuberculosis, also in the pediatric population.
A RANDOMISED PROSPECTIVE STEP-WEDGE MULTICENTRE STUDY TO EVALUATE THE RELATIONSHIP BETWEEN PNEUMOCOCCAL COLONISATION DENSITY IN 2-YEAR-OLD CHILDREN AND RATES OF TRANSMISSION TO FAMILY CONTACTS.

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6Manchester University NHS Foundation Trust, Department of Paediatric Allergy and Immunology- Royal Manchester Childrens Hospital, Manchester, United Kingdom

Background

 Interruption of transmission of vaccine serotypes underlies effectiveness of pneumococcal conjugate vaccine programmes at population level. Nasal colonisation density varies widely between individuals and over time but its relationship to infectiousness is unknown. *Streptococcus pneumoniae* (Sp) nasal colonisation density is increased by upper respiratory viral infections and the live attenuated influenza vaccine (LAIV).

In a multi-centre prospective randomised stepped-wedge trial, we are using LAIV as a probe to increase density of pneumococcal nasal carriage in LAIV-naive 2-year-olds and then assessing the impact on transmission rates to household contacts.

Methods

500 families with an eligible 2-year-old index child will be recruited over 2 seasons. Families are randomised 1:1 for the index child to receive LAIV at visit 1 or visit 3 (4 weeks later); saliva and nasopharyngeal samples (NPS) are collected from participants every two weeks over 2 months. Samples are analysed for Sp using real-time quantitative PCR(lytA). Samples are considered positive when the threshold cycle (Ct) value is less than or equal to 35.

Results

Season 1 equating to 25% of total sample size

<table>
<thead>
<tr>
<th>Families enrolled</th>
<th>123</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants enrolled</td>
<td>421</td>
</tr>
<tr>
<td>Participants per family (average)</td>
<td>3.43</td>
</tr>
</tbody>
</table>
At Visit 1 (Bristol NPS data):

<table>
<thead>
<tr>
<th>Participant</th>
<th>Carriage rate</th>
<th>Median density of carriage (Log10 gene copies/ml (range))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Index child</td>
<td>82%</td>
<td>3.28 (0.68-4.13)</td>
</tr>
<tr>
<td>Sibling</td>
<td>50%</td>
<td>2.74 (0.79-4.81)</td>
</tr>
<tr>
<td>Mother</td>
<td>14%</td>
<td>1.06 (0.68-2.03)</td>
</tr>
<tr>
<td>Father</td>
<td>12%</td>
<td>1.19 (0.66-4.29)</td>
</tr>
</tbody>
</table>

Conclusions

These data confirm the feasibility of this study including high participation and completion rates per protocol. Pneumococcal carriage rates in all age groups are slightly higher than in our previous studies. This study exemplifies novel use of live attenuated vaccines as experimental probes in human challenge experiments to elucidate the biology of colonisation and transmission.

Clinical Trial Registration (Please input N/A if not registered)

N/A
A RARE CASE OF CHROMOBACTERIUM VIOLACEUM SEPSIS IN A CHILD IN FRENCH GUYANA

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²Centre Hospitalier Andrée Rosemon, Pédiatrie, Cayenne, French Guiana

A rare case of *Chromobacterium violaceum* sepsis in a child in French Guyana

**Background**

*Chromobacterium violaceum* is a facultative aero-anaerobic Gram-negative bacilli found in waters and soils of tropical and subtropical areas. Most often saprophyte, human infection is rare but responsible for severe sepsis with multiple location abscesses. Children appear to be at increased risk of developing this infection whether or not they have chronic septic granulomatous disease.

**Case Presentation Summary**

We report the case of a 2-year-old child with *Chromobacterium violaceum* induced sepsis revealed by a 40.6°C fever with hemodynamic disorders and fluid diarrhea. Multiple skin localizations gradually appeared: cellulitis of the right thigh, then left evolving towards an abscess, then a necrotic lesion of the foot and forehead. Clinical and biological evolution was unfavorable despite the antibiotic against *Staphylococcus aureus*. Repeated blood cultures were negative. The culture of superficial and deep skin abscesses samples revealed the presence of *C. violaceum*. The clinical course was rapidly improved with intravenous ceftazidime and ciprofloxacin relayed by oral ciprofloxacin for a total treatment period of 2 months. As predisposing factor, we found repeated bathing in rivers in the days before admission. The search for a hereditary immune deficiency is underway.

**Learning Points/Discussion**

This case highlights the importance of considering *Chromobacterium violaceum* infection in children with severe sepsis with multiple abscesses in tropical and subtropical areas. Moreover, the multiple cases reported in the literature suggest an emergence of this pathogen witch have a strong ability to adapt and communicate with its environment. Early bacteriological diagnosis could reduce mortality estimated at 50-60%. The most important predictors for mortality are presence of bacteremia, disseminated infection and use of ineffective antibiotics. Many questions still remain about the best therapeutic strategy to adopt.
16A. SCIENCE: TUBERCULOSIS

CHILDHOOD TB IN HIV ERA- IN SUB SAHARAN AFRICA

M. Anwar

*M. Anwar, Medical Manager, Department of Health, Richmond, South Africa*

**Background**

Childhood TB in HIV Era- in Sub Saharan Africa

TB is surging much of the Africa because of HIV epidemic, In South Africa out of all TB case 16% are children.

Childhood mortality is increasingly higher in sub-Saharan Africa. To know the reason of child mortality- is it because of TB or HIV or both?

**Methods**

TB & HIV infection in children in retrospective study was in our mind.

South Africa lucky to have Gene XPRT test kit available even in district hospital.

BCG vaccine and Tuberculin skin test and its results interpretation helps for diagnosis and prognosis of childhood TB.

In children, malnutrition, measles, and whooping cough increase the risk of progression to active TB disease.

**Results**

Present deaths Worldwide, HIV: 6000/day, TB: 5000/day

South Africa, TB case Incidence: 4 th in the world, Childhood TB- 16% of all TB cases.

In 2010, 8.8 million new TB cases globally, 1.1 million deaths (excluding HIV).

1.1 Million new HIV associated TB cases worldwide, Out of all 82% living in Sub Saharan-Africa.

About 50-60% of all HIV patients when start with ART, had TB in their life time.

Co-infection of TB &HIV – Globally- 13%, South Africa- are around 25-60% of amongst children.
Conclusions

Problem persists still on diagnosis of TB as 87% of the TB patients shows smear negative even with fluorescent microscope. It shows that smear negative TB patients have high mortality. It also observed that HIV patients having low CD4 count had low TB organism in sputum.

TB and HIV are correlated with each other; if we can decrease the incidence of HIV it decrease the incidence of TB both in morbidity and mortality, I will discuss all these issue and facts in this topic.

Clinical Trial Registration (Please input N/A if not registered)

N/A
A Paediatric Case of Meningitis with Bilateral VIIth Nerve Involvement

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Title of Case(s)

A Paediatric Case of Meningitis with Bilateral VIIth Nerve Involvement

Background

Lyme disease has a wide spectrum of clinical manifestations with potentially long-term neurological sequelae if left untreated. It is the most common tick-borne disease in the USA and Europe and is easily treated once recognised.

Case Presentation Summary

A previously well 10 year-old boy presented with evolving bilateral facial nerve palsy. He had been treated 10 days previously with prednisolone and aciclovir for a right-sided Bell’s palsy. He subsequently developed occipital headaches, fatigue, dizziness and pain in his right arm.

Clinical examination revealed isolated, dense bilateral facial nerve palsy, involving the forehead. Bloods revealed normal infection markers and a normal CXR. His MRI brain showed subtle enhancement involving the cranial nerves within the internal auditory meati, greater on the right.

Direct questioning revealed a possible tick bite in the groin region 4 weeks previously with no immediate sequelae. He regularly walks in Dartmoor National Park, an area endemic for Ixodes ticks.

Serological testing revealed indeterminate Borrelia IgG but positive Borrelia IgM. Lumbar puncture opening pressures were 34cm H2O and CSF microscopy showed 82x10⁶/l lymphocytes and 0 polymorphs. CSF protein was elevated at 0.62g/L.

He was treated with oral amoxicillin followed by IV Ceftriaxone for 21 days. At 3.5 months follow-up, he still had mild residual facial neurology.

Learning Points/Discussion

Many cases of Lyme disease result from unrecognized tick bites and in endemic areas, the absence of one does not exclude Lyme disease. Travel to endemic areas should be specifically addressed in any child presenting with facial nerve palsy. Where the palsy is bilateral, Borrelia serology should always be considered. Patients should also be counselled that any facial nerve palsy will take many months to resolve.
GenDisFinder - Exploring Text Mining of Biomedical Literature for Novel Gene-Disease Associations
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¹Bharathiar University, Bioinformatics, Coimbatore, India

**Background**

Most of the current laboratory research outputs are available online in the form of abstracts (e.g. PubMed/MEDLINE) and full text research articles (e.g. PubMED Central, BioMed Central). However, the growth in publications is exponential and at this rate of publication, it is difficult or impossible for biologists to keep up with the underlying hypotheses. Text mining is the application of techniques from machine learning in conjunction with natural language processing, information retrieval and statistical/mathematical approaches to extract useful knowledge from text.

**Methods**

We have developed a biomedical text mining tools named GenDisFinder (http://www.biominingbu.org/GenDisFinder/) to extract gene disease associations from biomedical literature to find novel gene disease associations not explicitly available in on-line databases. First as a text mining system it extracts and visualizes the gene-disease associations and related association networks from biomedical literature. Similarly it extracts and visualize protein-protein associations from literature. Finally as knowledge discovery tool it combines known Gene-disease relations and protein-protein interaction information and using network neighborhood analysis and find novel gene-disease associations.

**Results**

GenDisFinder tool and its associated algorithms and application to pediatric Infectious diseases will be discussed.

**Conclusions**

The linkage between the clinical and laboratory research domains is a key issue. Text Mining tools fill the gap and provide necessary linkage

**Clinical Trial Registration (Please input N/A if not registered)**

N/A
LAMINA PAPYRACEA DEHISCENCE: CAUSE FOR RECURRENT PRESEPTAL CELLULITIS, ORBITAL CELLULITIS AND ORBITAL ABSCESS IN A CHILD
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Title of Case(s)
RECURRENT PRESEPTAL- ORBITAL CELLULITIS AND ORBITAL ABSCESS

Background

Preseptal cellulitis, orbital cellulitis and orbital abscess are not frequent in children. In recurrent cases (extremely rare), the existence of congenital faults as well as primary immune system problems must be considered.

Case Presentation Summary

A 4-year old girl was admitted with redness/swelling in/around the right eye. In the past, she had frequent upper respiratory tract infections, and was treated for right orbital cellulitis, orbital abscess and after right preseptal cellulitis. In physical examination, the right eye would not open; its motion could not be assessed. There were no other particularities. Laboratory tests were normal except for elevation of acute phase reactants. MR imaging showed ethmoid and maxillary sinusitis, oedema in right preseptal/orbital areas and appearance compatible with abscess on the right orbital inner wall. Intravenous ampicillin-sulbactam and clindamycin administration was started.

On the third day of hospitalization, the orbital abscess was surgically discharged. There was no culture growth in the abscess sample. Immunological and sweat tests were normal. In MR imaging on the 14th day, the occasionally defective appearance of bilateral lamina papyracea was compatible with lamina papyracea dehiscence. Sinusitis findings continued and focal destruction areas were formed on the right ethmoid cellular lateral wall. On the 17th day, treatment was complete and patient was discharged. After 20 days, she came back with right preseptal cellulitis findings. Surgical correction of lamina papyracea dehiscence and the anatomic defect formed on the side wall of the ethmoid sinus was planned after antibiotic treatment.

Learning Points/Discussion

In recurrent preseptal cellulitis, orbital cellulitis or orbital abscess, the presence of congenital or acquired anatomical faults must also be investigated and the possibility of lamina papyracea dehiscence must be kept in mind.
STAPHYLOCOCCUS EPIDERMIDIS NATURAL VALVE ENDOCARDITIS IN A CHILD ENDING WITH MITRAL AND AORTIC VALVES REPLACEMENT

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Title of Case(s)

STAPHYLOCOCCUS EPIDERMIDIS NATURAL VALVE ENDOCARDITIS

Background

Coagulase-negative staphylococci lead to infective endocarditis mostly in patients with foreign matter such as catheter, bio-prosthesis or with immune system problems. *Staphylococcus epidermidis* is not an expected agent of endocarditis in previously healthy children. The present case is a scarce example of this.

Case Presentation Summary

A 13-year old girl was admitted with a fever, defatigation, tachypnea and vomiting. It was stated that she was examined three months ago for defatigation, diagnosed with iron deficiency anaemia, had been using iron medication since; the anaemia progressed nevertheless and she had a fever and vomiting for the last 4-5 days. In physical examination, her general condition was low, fever was 39°C, peak heart rate was 175/min; there was a 3/6 systolic murmur and a midsystolic click at the apex. Other findings were normal. Laboratory examination revealed 7.6 g/dl haemoglobin, 62 fl MCV, 24,000/mm³ leucocytes, 68,000/mm³ thrombocytes; acute phase reactants were high. Echocardiography showed vegetation and moderate failures in aortic and mitral valves. On the third day of ceftriaxone and gentamicin treatment upon infective endocarditis diagnosis, *S. epidermidis* growth was found in blood cultures, vancomycin was added. The patient's fever could not be controlled; there was no regression in acute phase reactants and septic emboli developed in the finger tips and soles. On the tenth day of treatment, vegetations were surgically cleaned, the mitral and aortic valves were replaced with bio-prosthesis valves. Antibiotic treatment was continued for 6 weeks and the healthy patient was discharged to be followed-up.

Learning Points/Discussion

The possibility of endocarditis must be considered in children with fever, defatigation and tachycardia. It must be kept in mind that in previously healthy children, severe *S.epidermidis* natural valve endocarditis may develop.
THE LINK BETWEEN VARICELLA AND IMMUNE SYSTEM: WHICH CHILDREN WILL DEVELOP ACUTE CEREBELLITIS?

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²Bambino Gesù Children Hospital, Lab Of Immunology And Immune Diagnosis, Roma, Italy

Background

Despite the public perception of varicella as a harmless childhood affliction, the clinical course can be severe in some children.

Methods

We included in the study patients admitted at Bambino Gesù Children Hospital, Roma, Italy for cerebellitis in varicella. Inclusion criteria was age between 3 and 18 years. Laboratory tests included: antibodies titles against vaccine antigens (tetanus, Haemophilus influenzae B, Streptococcus pneumoniae, Bordetella pertussis and Hepatitis B), serum immunoglobulin concentration, evaluation of lymphocyte subpopulations (CD3, CD4, CD8, CD19, CD16/56, central memory and effector memory T cells, B cell memory), in vitro antibody production.

Results

Twenty-five patients were included in the study. Immunological laboratory exams were altered in most of them. In order to avoid bias due to possible effects of the recent disease, we separately analyzed patients that were studied at follow up at least one year (Group 1, 13 patients) or between 1 month and 1 year after hospitalization (Group 2, 11 patients).

Most patients of either Group 1 (84.6%) and 2 (81%) had at least one immunological alteration.

In detail, in Group 1, 10 patients did not reach protective level of specific antibodies after vaccination for at least one of the evaluated antigens, 3 had reduced or absent in vitro antibody production and 2 had a decreased number of switched memory B cells. Five children had multiple defects.

In Group 2, insufficient response to vaccination was diagnosed in 8 patients, low/absent in vitro antibody production in 5 cases, switched memory B cells were reduced in 3 patients. Multiple defects were observed in 5 children.

Conclusions

Children who experience cerebellitis in varicella may have subtle alteration of the immune system, revealed by a detailed immunological work-up.

Clinical Trial Registration (Please input N/A if not registered)

N/A
16C. SCIENCE: TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

SHOULD WE BE SCREENING CHILDREN WHO ARE CONTACTS FOR PULMONARY AND EXTRA-PULMONARY TB CASES?

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²University Hospitals of Leicester, Paediatrics, Leicester, United Kingdom

Background

The United Kingdom has one of the highest incidences of Tuberculosis (TB) in Western Europe. The latest 2016 National Institute for Health and Care Excellence (NICE) guidance recommends screening of close contacts of people with pulmonary or laryngeal TB. We audited the management of paediatric TB in our centre and specifically looked at the management of pulmonary and extra pulmonary TB contacts.

Methods

We conducted a retrospective audit of children referred to our paediatric TB service in 2016. Data was collected for the first 50 children screened at each site. A structured proforma was used for data collection and results were compared between pulmonary and extra-pulmonary TB contacts, focusing on the number of children diagnosed with active or latent TB in each category.

Results

99/100 children (45 girls and 54 boys) had audit proformas included for analysis. 58/99 children were pulmonary TB contacts, (26 smear positive, 20 smear negative, 12 unknown smear status). 34/99 children were extra-pulmonary TB contacts. 7/99 were referrals for a combination of suspected TB and screening of asylum seekers. Results of screening are as follows:

<table>
<thead>
<tr>
<th></th>
<th>Active TB Diagnosis</th>
<th>Latent TB Diagnosis</th>
<th>Tested Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary TB Contacts, n = 58</td>
<td>3</td>
<td>9</td>
<td>46</td>
</tr>
<tr>
<td>Extra-Pulmonary TB Contacts, n = 34</td>
<td>1</td>
<td>1</td>
<td>32</td>
</tr>
<tr>
<td>Other, n = 7</td>
<td>0</td>
<td>0</td>
<td>7</td>
</tr>
</tbody>
</table>

Conclusions

The majority of children in this audit were pulmonary TB contacts with a significant number of extra-pulmonary TB contacts. We found one case of active TB and one case of latent TB in extra-pulmonary TB contacts. This reinforces the importance of screening all children who are exposed to TB irrespective of whether the index case has pulmonary or extra-pulmonary TB. We aim to re-audit our practice in the near future.
NDM-1 KLEBSIELLA PNEUMONIAE NEONATAL SEPSIS IN PREMATURE NEONATE – SUCCESSFUL TREATMENT AND NICU OUTBREAK STUDY

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Title of Case(s)

NDM-1 Klebsiella pneumoniae neonatal sepsis in premature neonate – successful treatment and NICU outbreak study.

Background

NDM-1-Carbapenemase-producing Enterobacteriaceae (NDM-CPE) outbreaks in NICUs are major threat and are increasingly reported worldwide. The optimal therapeutic approach for NDM-CPE sepsis in neonates is unknown. A comprehensive approach is necessary to control CPE outbreak.

Case Presentation Summary

A male premature infant, born after 28-weeks of gestation, presented at the age of six days with sepsis and pneumonia; the causative organism was NDM-CPE. The infant was treated with Fosfomycin, Tigecycline and Colistin for 18 days. Bronchoalveolar lavage was performed. After prolonged course the patient was discharged with moderate bronchopulmonary dysplasia but otherwise well outcome.

Outbreak investigation and control

4 out of 21 other exposed neonates were found positive by rectal screening. Carriers’ cohorting, designated area/staff/equipment, biweekly screening for NDM-CPE, environmental disinfection, temporary NICU closing for new admissions, observations on work processes were initiated to control the outbreak. Cross-transmission was not detected. The epidemiologic investigation revealed the outbreak source to be a neonate born in foreign country hospital after surrogate pregnancy. Alarmingly, the source neonate was screened on admission for CPE by rectal swab culture according to standard institutional practice, and was found negative. The original sample was tested by PCR and by enrichment culture, NDM-1-K.pneumoniae was detected by these methods. Learning Points/Discussion

A combined treatment with Tigecycline, Colistin and Fosfomycin was safe and effective in neonate with NDM-CPE LOS and pneumonia. A comprehensive infection control program can contain an outbreak of NDM-CPE in a NICU. If the risk for MDR-EB carriage is high, such as in patients from endemic to MDR-EB countries, PCR analysis and enrichment culture of screening samples are crucial.
Background

Antimicrobial resistance in Norway is among the lowest in the world, but to prevent an increase the Norwegian Government has launched a National Strategy including a 30% reduction of broad-spectrum antibiotics in hospitals within 2020. Broad-spectrum antibiotics are defined as second- and third-generation cephalosporins, carbapenems, piperacillin/tazobactam and quinolones. We are presenting a survey of antibiotic use in Norwegian hospitalized children and neonates. Our primary aim is to describe the use of broad-spectrum antibiotics in order to detect possibilities for optimization.

Methods

Data were extracted from eight national point prevalence surveys of systemic antibiotic prescriptions in Norwegian hospitals between 2015 and 2017. All neonates and children 0-19 years were included. The choice of antibiotics was various indications was compared with the empirical recommendations given in available Norwegian paediatric guidelines. In total, 1323 prescriptions were issued for 937 patients.

Results

Twenty-four percent of paediatric inpatients were given antibiotics. Adherence to guidelines was 48%, and 30% of all patients on antibiotics received broad-spectrum antibiotics. We identified only small variations in use of broad-spectrum antibiotics between hospitals. One third of the patients on antibiotic therapy received prophylaxis whereof 13% where given broad-spectrum antibiotics. In 30% of prescriptions with broad-spectrum antibiotics, no microbiological sample was obtained prior to treatment.
Conclusions

This study provides a vulnerable baseline for antibiotic prescribing in Norwegian hospitalized children and highlights the need for paediatric antibiotic stewardship in a country with low antimicrobial resistance. It indicates that diagnosis of infections and adherence to guidelines can be improved and that use of broad-spectrum antibiotics can be reduced both for treatment of infections and for prophylactic use.

Table 1) Use of broad-spectrum antibiotics and adherence to guidelines for various indications in Norwegian hospitalized children and neonates treated for infections (2015-2017). Neonates are only included when specified.

<table>
<thead>
<tr>
<th>Indication</th>
<th>Number of patients threatened (number of prescriptions)</th>
<th>Broad spectrum antibiotics(^1), number of patients (%)</th>
<th>Narrow spectrum antibiotics(^2), number of patients (%)</th>
<th>Adherence to the guideline(^3), number of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Community acquired pneumoniae</td>
<td>87 (106)</td>
<td>22 (25)</td>
<td>65 (75)</td>
<td>34 (39)</td>
</tr>
<tr>
<td>Hospital acquired pneumoniae</td>
<td>12 (15)</td>
<td>8 (67)</td>
<td>4 (33)</td>
<td>4 (33)</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>78 (109)</td>
<td>18 (23)</td>
<td>60 (77)</td>
<td>37 (47)</td>
</tr>
<tr>
<td>Neonatal sepsis</td>
<td>58 (100)</td>
<td>11 (19)</td>
<td>47 (75)</td>
<td>11 (19)</td>
</tr>
<tr>
<td>Sepsis and neutropenia</td>
<td>52 (85)</td>
<td>14 (27)</td>
<td>38 (73)</td>
<td>17 (33)</td>
</tr>
<tr>
<td>Intraabdominal infection</td>
<td>35 (49)</td>
<td>25 (71)</td>
<td>10 (29)</td>
<td>26 (74)</td>
</tr>
<tr>
<td>Infections in skin, soft tissue, bone and joint</td>
<td>67 (86)</td>
<td>21 (31)</td>
<td>46 (69)</td>
<td>38 (57)</td>
</tr>
<tr>
<td>Infection in ear, eye, nose and throat</td>
<td>51 (60)</td>
<td>10 (20)</td>
<td>41 (81)</td>
<td>45 (88)</td>
</tr>
<tr>
<td>CNS infections</td>
<td>23 (28)</td>
<td>17 (74)</td>
<td>6 (26)</td>
<td>13 (57)</td>
</tr>
<tr>
<td>Other infections(^4)</td>
<td>97 (143)</td>
<td>40 (41)</td>
<td>57 (59)</td>
<td>n/a</td>
</tr>
<tr>
<td>Other neonatal infections(^5)</td>
<td>17 (34)</td>
<td>4 (24)</td>
<td>13 (76)</td>
<td>n/a</td>
</tr>
<tr>
<td>Total</td>
<td>574 (810)</td>
<td>190 (33)</td>
<td>384 (67)</td>
<td>225 (48)</td>
</tr>
</tbody>
</table>

1 Second- and third-generation cephalosporins, carbapenems, piperacillin/tazobactam and quinolones. Monotherapy or in combination with any other antibiotic
2 Alone or in combination
3 Recommendation for first line empirical treatment in Norwegian paediatric guidelines
4 Surgical site infection (22), gastroenteritis (12) infection with unknown origin (10), infection in heart and blood vessels (5), gynaecological infection (1), prostatitis/epididymitis (1), unknown (45)
5 Pneumonia (2), infection with unknown origin (2), surgical site infection (1), unknown (12)
In South Korea, the number of cases of pertussis reported has increased in recent years. Despite effectiveness of maternal tetanus toxoid, reduced diphtheria toxoid, acellular pertussis (Tdap) vaccination, immunization rates of Tdap during pregnancy remain quite low. We assessed the knowledge, attitude and practice on maternal Tdap vaccination among pregnant women.

Methods

This study was a cross-sectional survey of pregnant women who visited obstetrics and gynecologic units in the Gyeonggi-do province of Korea. Individual questionnaires were administered to assess knowledge, attitude and practice on maternal immunization with Tdap.

Results

The questionnaires was completed by 184 pregnant women; 171 (93%) had not received information from doctors about pertussis and Tdap, and 164 (89%) did not know the need for Tdap vaccination. By multivariate analysis, the confidence that Tdap immunization is safe during pregnancy was a significantly important factor to subjects' intention to be vaccinated (OR 6.36, CI 1.75 to 15.2).

Conclusions

Most pregnant women seem to be neither recommended nor adequately informed about Tdap vaccination. Information given by health care professionals is very important to increase Tdap coverage among pregnant women.
IS PROCALCITONIN REALLY THE SPECIFIC MARKER FOR SERIOUS BACTERIAL INFECTION IN FEBRILE CHILDREN?

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Background

Early detection of serious bacterial infection (SBI) in febrile children is very important. Procalcitonin (PCT) is one of the useful inflammatory markers for early detection of SBI. However, the elevation of PCT is also observed in the cases without bacterial infections like Kawasaki disease. In this study, the PCT elevated cases were analyzed and the utility of PCT was evaluated.

Methods

The association between PCT level and the mean age, blood culture as well as final diagnosis was investigated in 280 children who were admitted to our hospital in 2016. The patients with significantly high PCT levels were classified into group A (PCT≥10ng/mL) and group B (10>PCT≥5ng/mL).

Results

Twelve children were in group A and median age was 6.9 months. Five (42%) had a positive blood culture. Six (50%) were diagnosed urinary tract infection (UTI) caused by extended-spectrum beta-lactamase (ESBL) producing E. coli. Of the 6, 2 children had bacteremia. On the other hand, 10 children were in group B and median age was 7.2 months. None had a positive blood culture and 6 (60%) were UTIs caused by ESBL producing E. coli.

Conclusions

Elevation of PCT was mainly observed in young infants. PCT≥5ng/mL suggested high possibility of UTIs caused by ESBL producing E. coli and PCT≥10ng/mL suggested high risk of bacteremia.
Vertical transmission of Mycoplasma pneumoniae infection

Background

Mycoplasma pneumoniae is a significant cause of pneumonia in school-aged children and young adults. We report a case of neonatal M. pneumoniae pneumonia in a preterm child manifesting in the first hours of life.

Case Presentation Summary

A preterm male neonate was delivered at 29 4/7 weeks of gestation by caesarean section because of recurrent vaginal bleedings and premature contractions. He developed a severe respiratory distress syndrome (RDS) in the first hour of life with an atypical presentation necessitating re-intubation twice within the first two weeks of life. Empiric antibiotic treatment was discontinued based on negative blood cultures and normal C-reactive protein on day of life (DOL) 2. The unclear situation led to a detailed review of the medical history during pregnancy: The mother recalled an untreated respiratory tract infection with intractable cough in 20 gestational weeks. The diagnostic work-up in the neonate was extended by PCR for M. pneumoniae, which was found positive in tracheal aspirate on DOL 3 and in a second sample from nasopharyngeal aspirate on DOL 4. Treatment with erythromycin was initiated on DOL 4 for two weeks and paralleled by clinical and radiographic improvement. M. pneumoniae-specific antibodies were found in the neonate on DOL 22 (IgG) and in the mother two weeks after birth (IgM and IgG, indicating a recent infection). Histologic examination of the placenta showed distinct chorioamnionitis and vasculitis. Placental tissues were tested positive for M. pneumoniae DNA by PCR and immunohistochemistry.

Learning Points/Discussion

This case demonstrates that M. pneumoniae can be considered as a cause of congenital pneumonia. The route of transmission of M. pneumoniae is vertical infection after dissemination of the bacteria following maternal respiratory tract infection.
MOLECULAR ANALYSIS OF STREPTOCOCCUS PNEUMONIAE STRAINS INVOLVED IN VACCINE FAILURE IN THE CZECH REPUBLIC

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Background

First conjugate pneumococcal vaccine registered in the Czech Republic was PCV7 in 2005. In following years PCV10 and PCV13 were registered and infants with underlying diseases were vaccinated. The conjugate pneumococcal vaccine was introduced into the National immunisation programme (NIP) for infants in 2010 in the scheme 3+1.

Methods

The surveillance of IPD started in the Czech Republic since 2008 and the EU case definition of IPD was adopted. The typing of S. pneumoniae was performed in the NRL by the classical Quellung reaction and from 2013 by the PCR method.

Results

All four isolates of serogroup 1 were classified into ST 306, which is one of the most frequent sequence types of this serogroup. Two isolates of serogroup 14 were both assigned to ST 124, a commonly identified sequence type of serogroup 14. Variability was observed in serogroup 3, with one isolate belonging to a relatively common sequence type, ST 505, and the other one to ST 124. The latter isolate is first case as the association of serogroup 3 and ST 124.

Conclusions

The methods of choice for a detailed identification were the Quellung reaction along with multiplexPCR and MLST. From the results of the analyses, it follows that all eight isolates of S. pneumoniae were assigned to the following three serotypes: 1 (n=4), 3 (n=2), and 14 (n=2).

Supported by Ministry of Health of the Czech Republic, grant nr.17-29256A. All rights reserved.
ETIOLOGICAL TRENDS AND PATTERNS OF ANTIMICROBIAL RESISTANCE IN RESPIRATORY INFECTIONS
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²Institute of Endemic Diseases, Pathology and Clinical Immunology, Khartoum, Sudan

Background
Respiratory infections are one of the commonest causes of morbidity and mortality related to infectious diseases worldwide. The emergence of antimicrobial resistance is a major global health problem which is well established in developing countries. Good clinical suspicion and correct laboratory identification of respiratory infection causing organisms followed by the appropriate management are needed to compact both community-acquired and nosocomial respiratory infections.

Methods
Respiratory isolates that have been morphologically identified and biologically characterized were subjected to antibiotic susceptibility testing.

Results
A total of 1481 respiratory specimens were examined, recovered 377 organisms from 350 culture positive samples [225(59.7%) sputum, 94(24.9%) broncho-alveolar lavage (BAL), 58(15.4%) Pleural fluid], the commonest organisms were Klebsiella ssp. (25.20%) and Mycobacterium tuberculosis (25.20%), followed by Staphylococcus aureus (19.89%) and Pseudomonas aeruginosa (8.49%). High rate of resistance of bacterial isolates was observed to Co-trimoxazole (BA), Ampicillin sulbactam (AS), Cefotaxime (CF) and Tetracycline (TE): 80%, 72.3%, 68.8% and 66.9% respectively, on the other hand very low resistance rate found to Amikacin (AK) and Levofloxacin (LE), 4.6% and 8.5% respectively.

Conclusions
Guided prescription of antimicrobial agents must be implemented and controlled to limit further spread of antimicrobial resistance.
A REVIEW OF PUBLISHED PNEUMOCOCCAL CARRIAGE STUDIES UNDERTAKEN IN THE UK HIGHLIGHTS A PAUCITY OF PUBLISHED DATA IN INFANTS AGED <12 MONTHS

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²Griffith University, School of Medicine, Gold Coast, Australia

Background and Objective

*Streptococcus pneumoniae* is a common commensal in the nasopharynx, with high prevalence in young children which subsequently declines with age. Carriage is asymptomatic and is an essential precursor to mucosal and invasive pneumococcal infections. Pneumococcal conjugate vaccines (PCVs) prevent nasopharyngeal acquisition of vaccine serotypes and reduce carriage density, generating indirect protection, but also allow increased carriage of non-vaccine serotypes. Published carriage studies undertaken in the UK were reviewed to synthesise findings and identify areas requiring further investigation.

Methods

Publications were identified through a PubMed search using “*Streptococcus pneumoniae*” OR “pneumococcal” AND “carriage” as search terms and also from a review of bibliographies/references from relevant articles. The search was primarily restricted to citations concerning data from the UK, though articles from a wider geographic scope and epidemiological significance relevant to carriage of the pneumococcus were included to support discussion.

Learning Points Discussion

27 articles were identified describing studies from the 1950s to 2015. Most were conducted in small local populations in southern England focussing on children aged 1-10yrs.

PCVs reduced carriage of vaccine serotypes but overall carriage prevalence appears stable.

Published carriage data in UK infants are particularly limited and reflect the pre-PCV era only. These indicate considerable carriage acquisition occurs during the first six months of life with significant exposure to circulating pneumococci. Carriage data in the elderly are also lacking.

There is a need for contemporary carriage studies in UK infants to better understand the current probability of their exposure to vaccine type pneumococci, particularly given the recent interest in reducing the number of infant priming doses from two to one in the UK.

More extensive longitudinal studies in larger geographic regions of the UK covering all ages using standardized methodologies are required.
THE INFLUENCE OF ANTIMYCOTICS ON THE ADHESION OF CO-CULTURE CANDIDA GLABRATA AND SACCHAROMYCES BOULARDII

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3Biotechnical Faculty, Microbiology, Ljubljana, Slovenia

Background

Following the widespread use of immunosuppressive therapy together with broad-spectrum antimycotic therapy, the frequency of mucosal and systemic infections caused by Candida glabrata has increased significantly. Due to increasing resistance of C. glabrata to existing drugs, it is very important to look for new strategies helping the treatment of such fungal diseases. An increasing number of potential health benefits are being attributed to probiotic treatments. The beneficial effect of probiotic yeast Saccharomyces boulardii in the case of C. glabrata infections have not been studied yet. Therefore, we tested the adhesion of C. glabrata in a co-culture with S. boulardii to polystyrene surface in the presence of antimycotics, namely fluconazole, itraconazole, and amphotericin B.

Methods

The method used to assess adhesion was crystal violet staining. The selection of antimycotics concentrations used in the adhesion assay was based on the minimum inhibitory concentrations (MICs) obtained by the preliminarily performed microdilution method according to Clinical and Laboratory Standards Institute (CLSI), standard M27-A2.

Results

The results showed that the lowest concentrations of antimycotics which significantly decreased the adhesion of C. glabrata in the co-cultures were generally higher than the MICs determined according to the CLSI method. We observed poor activity of azoles against C. glabrata. On the other hand, exposure to various concentrations of amphotericin B significantly reduced the adherence ability of C. glabrata strains or rather its growth in a single culture and in a co-culture with S. boulardii.

Conclusions

The results of our studies indicate that S. boulardii can have a significant inhibitory effect on the adhesion of C. glabrata. It can be speculated that S. boulardii could substitute the effect of antimycotics in some concentration range and with specific strain types.

Clinical Trial Registration (Please input N/A if not registered)

N/A
16A. SCIENCE: TUBERCULOSIS

TUBERCULOSIS MANAGEMENT AT A PEDIATRIC HEMATO-ONCOLOGY UNIT AFTER IN-HOSPITAL EXPOSURE TO A CASE WITH ACTIVE DISEASE

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Background

Risk of tuberculosis (TB) is increased in immunocompromised patients and children. There are no guidelines on how to study paediatric oncological population exposed to TB.

Aim: to describe our experience in the management of hemato-oncology children exposed to a patient’s mother with active TB.

Methods

Prospective study of hemato-oncology children with in-hospital exposure to TB in a tertiary hospital in Madrid in April 2017. Tuberculin Skin Test (TST), IGRA (Quantiferon®) and chest X-ray were performed initially and repeated 10-12 weeks after last exposure.

Results

From 32 patients studied, 24 formed circle 1 (shared >8 hours at day hospital) and 8 formed circle 2 (admitted simultaneously but different rooms). From circle 1, one patient was not studied (palliative care) and 3 were in other hospitals. Daughter of index case was treated for pulmonary TB. From 13 patients who required prophylaxis with isoniazid until second evaluation, 11 completed uneventfully. Two cases never received isoniazid due to hepatitis at that time. At second-time evaluation, one patient turned his TST from 0 to 6 mm, normal chest X-ray, and he was treated as a latent TB infection. In 2 cases, TB had to be ruled out because of pulmonary disease: lung nodule in a patient with Hodgkin lymphoma and pulmonary infiltrates in a case of fever and neutropenia. No test pointed to TB involvement. Finally, 210 hospital activities were necessary, including 84 interviews, from April to July 2017.

Conclusions

In our study, one oncologic patient presented latent TB infection after contact to index case. In 2 cases, TB complicated differential diagnosis of pulmonary condition. The approach to oncologic children exposed to TB involved a multidisciplinary team and a considerable use of resources in a short time.
INVASIVE MENINGOCOCCAL DISEASE IN THE CZECH REPUBLIC

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Background

Based on the 2017 surveillance data from the Czech Republic, 68 cases of invasive meningococcal disease (IMD) were diagnosed, i.e. 0.6 cases per 100000 population. This is an increase compared to 43 cases (0.4/100000) reported in 2016. In the Czech Republic, serogroup B is causing IMD mostly in the smallest children 0-11 months of age. IMD in adolescents is typically linked to serogroup C and recently also to serogroup B. Since 2016, cases caused by serogroup C are on the rise in children under five years of age as well.

Methods

The diagnosis was based not only on the conventional but also on the molecular methods (cultivation, agglutination, rt-PCR, MLST, WGS).

Results

In 2017, the causative serogroups were distributed as follows: B in 48.5 % of cases, C in 36.8 %, W in 4.4 %, and Y in 1.5 %; 2.9 % of cases were caused by non-groupable N. meningitidis, and the serogroup was not identified in 5.9 % of cases. The most frequently found hypervirulent complex was cc11, which has been on the rise in the Czech Republic since 2014. Sixty-nine percent of cases from 2017 were submitted to whole genome sequencing (WGS), and WGS data analysis is underway.

Conclusions

Acknowledgement

Supported by Ministry of Health of the Czech Republic, grant nr. 15-34887A from the. All rights reserved.
Background

Neonatal invasive candidiasis (NIC) is a leading cause of infection-related morbidity (with potential sequelae) and mortality in preterm neonates. Several studies have shown that (1,3)-beta-D-glucan (BDG) was accurate in detecting invasive fungal infection in adults and children, but studies in neonates are scarce. Our objective was to determine the diagnostic accuracy of BDG for diagnosing NIC.

Methods

We systematically searched MEDLINE and Google Scholar (inception to September 2017). We also conducted related citations tracking via PubMed, handsearched reference lists of included studies and relevant review articles, and screened all articles citing included studies. We included studies that compared BDG (Fungitell®) with any reference standard that included fungal blood culture in neonates. Two review authors screened titles and abstracts for relevance, assessed full texts for inclusion, and carried out data extraction and quality assessment using QUADAS-2. We used bivariate meta-analysis to estimate summary accuracy measures at a positivity threshold of 80 pg/mL.

Results

We included 6 studies in the review (359 participants). The overall methodological quality of included studies was good, the main source of concern being selection bias. Almost all studies used revised EORTC/MSG criteria to define NIC. At a positivity threshold of 80 pg/mL, the pooled estimates of sensitivity, specificity, positive likelihood ratio and negative likelihood ratio of BDG were 85% (95% confidence interval: 68% to 94%), 69% (95CI: 50% to 83%), 2.7 (95CI: 1.5 to 5.0), and 0.22 (95CI: 0.09 to 0.54), respectively.

Conclusions

BDG is a promising biomarker in the management of newborns with suspected NIC. Because of high sensitivity and low negative likelihood ratio, the BDG assay could be used as a screening tool to rule out NIC.
Systematic Review Registration (Please input N/A if not registered)

N/A
Background

Aim of this study was to investigate the rate of RSV-related hospitalizations in preterm infants of 35 and 36 weeks of gestational age (GA) during the first year of life and compare them to all other respiratory re-hospitalizations.

Methods

Single center cohort study including preterm infants of 35 +0 to 36+6 weeks of GA between 2005 and 2015 with follow-up during the first year of life.

Results

148 out of 1047 infants (14%) had been re-hospitalized 201 times due to respiratory diseases and 31 (3%) were tested RSV positive (RSV-H) representing 20.9% of all re-hospitalized preterm infants. A higher RSV-H rate was observed in children following discharge between October 1st and March 31st (4.2% vs. 2.0%, p=0.017), as well as in presence of older siblings (4.2% vs. 2.1%, p=0.023), Down syndrome (9.1% vs. 2.1%, p=0.11), and male gender (3.8% vs. 2.0%, p=0.003). Seventy-five percent of confirmed RSV-H occurred during the RSV season from November to April, with an incidence peak (20.8%) in January. RSV-H was associated with longer hospital stays (median 8 vs. 4 days, p=0.001), higher LRI scores (median 3 vs. 2, p=0.001) and more need for supplemental oxygen (33% vs. 10.1%; p=0.002) for a longer time (median 5.5 vs. 3 days; p<0.001). Mechanical ventilation was more often needed (12.5% vs. 1.2%, p=0.004) and admission to the ICU occurred more often (16.7% vs. 4.1%, p=0.018) and for a longer duration (median 10 vs. 6.5 days, p<0.001).

Conclusions

RSV-H rate was 3% presenting with a more severe course of disease compared to other respiratory diseases. Known risk factors were associated with a higher re-hospitalization rate.

Clinical Trial Registration (Please input N/A if not registered)

N/A
04B. SCIENCE: COMMUNITY ACQUIRED INFECTIONS: RESPIRATORY TRACT INFECTIONS

ARE RATES OF RSV HOSPITALIZATIONS LOWER IN HIGH-RISK INFANTS SINCE INTRODUCTION OF PALIVIZUMAB? AN OBSERVATIONAL COMPARATIVE COHORT ANALYSIS

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Background

Aim of the study was to compare RSV hospitalization (RSV-H) rates of 2 time periods from a single center with regard to rates of high-risk infants known for severe RSV disease within the first year of life.

Methods

RSV-H data of preterm born infants and infants with congenital heart disease (CDH) were compared between period 1 (1994-2000, without palivizumab prophylaxis) and period 2 (2009-2015, palivizumab prophylaxis).

Results

Between 1994 and 2000 303 RSV-H occurred and 745 between 2009 and 2015. The rate of preterm born infants was 9.9% (30/303) compared to 16.4% (122/745). 16/303 (5.28%) were born ≤ 32 weeks of gestational age (GA) compared to 36/745 (4.83%); relative risk reduction (RRR) 8.5%, p=0.831. Five of 303 (1.65%) were born ≤ 28 weeks of GA compared to 9/745 (1.21%); RRR 26.7%, p=0.286. In infants with CHD 18/303 (5.94%) had RSV-H during the first RSV season compared to 22/732 (3.04%); RRR 48.8%, p=0.011.

Conclusions

Rates of RSV-H increased, probably due to more RSV testing in period 2. Rates of preterm born infants exhibiting RSV-H did not decrease in contrast to rates of infants with CHD.

Clinical Trial Registration (Please input N/A if not registered)

N/A
THE REALITY OF OSELTAMIVIR PRESCRIPTION AMONG HOSPITALIZED CHILDREN IN A PEDIATRIC TERTIARY HOSPITAL

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Background

Oseltamivir is the most common antiviral used for treatment of influenza infection and its complications. It's use is currently recommended in all hospitalized children with influenza infection, regardless of the clinical status. The main goal of this study was to characterize children hospitalized with influenza after the influenza A pandemic, focusing on the treatment with oseltamivir and the factors that led to its prescription.

Methods

Observational study of inpatients with polymerase chain reaction–confirmed influenza from October 2012 to May 2016 at a pediatric university hospital in Portugal, between October 2012 and May 2016 (four consecutive influenza seasons). The primary goal was to evaluate oseltamivir use. Variables regarding demographics, underlying medical conditions, diagnoses, and outcome were also analysed. Statistical analysis with SPSS® 22 (p <0.05).

Results

Among the 83 cases diagnosed with influenza infection, 44 (53.0%) were treated with oseltamivir. The median age was 21.9 months (AIQ 12-61). There were 40 cases with risk factors for severe infection (48.2%). The most common clinical diagnosis was respiratory infection, namely pneumonia, in 34 cases (40.9%). There was a statistically significant association between the prescription of oseltamivir and the following variables: place of hospitalization (p=0.006), total days of hospitalization (p=0.002), changes in chest radiography (p=0.001), diagnosis of pneumonia (p=0.008), hypoxemia (p=0.001) and infection by influenza A(H1N1)pdm09 (p<0.001).

Conclusions

Although the prescription of oseltamivir was lower than recommended, it's use, in our hospital, has been increasing in the last influenza seasons. Treatment with oseltamivir was strongly associated with the identification of a specific subtype of influenza virus A(H1N1)pdm09. We believe it is important to promote strict adherence to the published guidelines for children hospitalized with influenza infection.
A 10-YEAR ANALYSIS OF RESPIRATORY SYNCYTIAL VIRUS ASSOCIATED ADMISSIONS TO A
PEDIATRIC INTENSIVE CARE UNIT

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Background

To evaluate population characteristics associated with respiratory syncytial virus (RSV) infection necessitating admittance to the pediatric intensive care unit (PICU).

Methods

Retrospective single-center cohort study including all infants and children admitted to the PICU due to RSV infection between 2006 and 2015. Data were collected regarding demographic characteristics, need for respiratory support, length of stay, selected laboratory parameters, medical treatment, presence of underlying/pre-existing disease, and mortality.

Results

The study population comprised 156 patients (57% male) with a mean age of 6.8 months (range 0 - 181) with confirmed RSV infection. Mean length of stay was 10 days (range 1 - 171). Respiratory support was given in 138 (88%) children of whom 26 (19%) needed intubation (1 case high-frequency oscillation, and none extracorporeal membrane oxygenation). Supplemental oxygen was given for mean 5.7 days (range 1 - 30). One or more underlying diseases were present in 65 (42%) children (41 congenital heart disease-CHD, 31 non-cardiac anomalies, 9 neurologic impairment, 6 bronchopulmonary dysplasia-BPD, and 5 chromosomal abnormalities); 52 (33%) were preterm born. Mortality rate due to RSV disease was 0.64% (1 child with CHD), another 2 died after becoming RSV negative due to their underlying disease (Jeune syndrome and CHD, respectively). Nosocomial infection was evident in 10 cases (6.4%). Thirty-eight children (24%) had diagnosis of bacterial superinfection with the most common pathogen being Haemophilus influenza (12 cases).

Conclusions

Prematurity and pre-existing disease were commonly associated with RSV infection necessitating admission to the PICU. RSV associated mortality rate was low.

Clinical Trial Registration (Please input N/A if not registered)

N/A
NEW ENTRANT TB SCREENING FOR CHILDREN - THE NEED TO IDENTIFY AND SCREEN
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Background

New entrant Tuberculosis (TB) screening for individuals from high incidence areas is part of the UK TB strategy (2015 - 2020) and only includes young people and adults aged 16 to 35 years. Latent TB Infection (LTBI) screening for new entrants from TB high incidence areas is an effective and cost-effective public health intervention and is recommended by NICE.

Methods

The children’s new entrant TB screening in Leicester is for children aged 0-16 years who are new to the UK. The majority of our referrals come from Leicester City Assist Practice which is a medical centre specifically designed to address the needs of asylum seekers with access to high quality healthcare. We reviewed our database over 4 years, from 2014 to 2017. Children were screened with a mantoux test and those tested positive were referred to Paediatric TB clinic.

Results

A total of 240 children were screened over four years with an average of 60 children per year. 14/240 (5.8%) were diagnosed with LTBI following a positive mantoux test. In addition 5/14 children had an IGRA (Interferon Gamma Release assay) test and all 5 were positive. All children with LTBI completed a 3 month course of Isoniazid and Rifampicin. 6 children were from India, 4 from Syria, 2 from Afghanistan, 1 from Somalia and 1 from Kenya.

Conclusions

Latent TB remains prevalent in the paediatric migrant population. The lack of commissioning for new entrant TB screening for children in the UK is unfortunate and has a risk of missing cases of TB in this group. Our service has demonstrated the importance of having local arrangements in high prevalent areas. Capturing all the eligible children remains an ongoing challenge for us.
PREVALENCE OF CONGENITAL INFECTION BY RUBELLA VIRUS AMONG INDIAN INFANTS WITH STRUCTURAL CONGENITAL HEART DEFECTS

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Background

Structural congenital heart defects (CHD) take a huge toll of congenital defects in children in India. Limited information is available regarding modifiable risk factors for its causation. This study was planned with an aim to determine the prevalence of congenital infection by rubella virus in Indian infants with structural CHD.

Methods

This cross-sectional, observational study was conducted at a tertiary care hospital in Northern India over one year period (Jul16-Jun17). Infants <6 months with structural CHD (both inpatient & outpatient) were enrolled after taking informed consent from their mothers. Blood samples were collected from mother-child binomials and tested for rubella IgM & IgG antibodies, using ELISA kits. Ethical clearance was obtained from Institute Ethics Committee, before enrolling subjects.

Results

A total of 80 infants (M:F=56:24), having mean age 69.4 (±56.5) days; were enrolled. In these screened infants, prevalence of congenital infection by rubella virus (either infants IgM rubella positive or infant’s IgG rubella titers more than mother’s) was 8.75 % (7/80). A total of 12.5% of studied mothers were seronegative for rubella IgG antibodies. Rubella IgM in all the mothers of babies, who had evidence of congenital rubella; disappeared by the time diagnosis was made; but maternal rubella IgG persisted. Transplacentally transmitted IgG rubella in uninfected babies was detected even up to 105 days of life. There was a statistical significant association between the occurrence of congenital rubella and cataract (p=0.0039), splenomegaly (p=0.007) and microcephaly (p=0.0084) in infants having structural CHD.

Conclusions

Congenital rubella still remains an important modifiable cause for structural CHD in India. Sincere efforts for rubella elimination using appropriate vaccination strategy would help in decreasing burden of structural CHD in India.

Clinical Trial Registration (Please input N/A if not registered)

N/A
Neisseria meningitidis most frequent serogroups varies in different countries worldwide. Since 2003 the predominant serogroups in São Paulo State are C and B. During this period cases from serogroups W and Y were also registered. Meningococcal C conjugate routine immunization for children under 2-years-old was introduced in 2010 in Brazil. The aim of this study was to evaluate serogroup W and Y incidence, case fatality and mortality in São Paulo State after vaccine introduction.

Methods

Neisseria meningitidis serogroups W and Y incidence, mortality and case fatality were compared with those in predominant serogroups C and B in São Paulo State from 2011 to 2017.

Results

Neisseria meningitidis incidence (cases/100.000 inhabitants) for serogroups W and Y were similar (median 0.06 vs 0.05, p=0.1). However, their incidence were significantly lower than serogroup B (median 0.2, p=0.002 and p=0.02, respectively) and serogroup C (median 0.6, p=0.02 and p=0.02, respectively). Mortality (deaths/100.000 inhabitants) for serogroups W and Y were similar (median 0.01 vs 0.007, p=0.07). Likewise, their mortality were significantly lower than serogroup B (median 0.03, p=0.006 and p=0.002, respectively) and serogroup C (median 0.1, p=0.002 and p=0.002, respectively). Otherwise, case fatality for serogroup W (median 22.2%) was significantly higher compared with serogroups Y (median 20.0%, p=0.04) and B (median 17.2, p=0.03), but not with serogroup C (median 19.6, p=0.05).

Conclusions

From 2011 to 2017 Neisseria meningitidis serogroups W and Y incidence, mortality and case fatality were quite diverse from that observed in predominant serogroups C and B.
CHOLECYSTITIS IN CHILDREN

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Background

The incidence of gallstones in children has increased in recent years. While some patients are admitted with the complaint of gallstone complications, the majority of patients are admitted with complaint of unspecified abdominal pain. The treatment of gallstones is still controversial. This study aims to investigate the impact of risk factors on gallstone complications and to identify surgical indications for gallstones.

Methods

Patients who were operated in the pediatric surgery clinic of Sakarya University, Faculty of Medicine between October 2011 and July 2017 were evaluated. Data including age and sex, body mass index (BMI), associated risk factors, gallstone-induced complications, postoperative complications, and pathological results were recorded.

Results

Thirty-six patients were included in the study. The mean age was 13.2 years with a female-to-male ratio of 2.27:1. Obesity was the most common risk factor. A total of 44% of the patients experienced a complication on admission. The risk factors had no effect on the complications (p=0.846). All patients underwent cholecystectomy. The pathology results of 94.5% of the patients who were operated were reported as chronic cholecystitis.

Conclusions

The incidence of gallstones increase in parallel with the risk factors. However, the risk factors have no influence on gallstone-induced complications. In our study, most patients who underwent surgery had signs of chronic cholecystitis. Therefore, we believe that patients who have recurrent abdominal pain and gallstone should also undergo surgical treatment.
Enteropathogens in Pediatric Gastroenteritis: Clinical Interpretation of New Tools Results

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Background

An issue in the study of acute gastro-enteritis (AGE) is the lack of sensitivity and specificity of available routine diagnostic methods (RDM), leaving >50% of patients without an identified pathogen. PCR-based methods are increasingly used for clinical purposes, but interpretation of their results remains complicated. What is the significance of a positive PCR result: true pathogen, contact with a dead organism, harmless colonizer? In this study we wanted to compare results obtained in symptomatic cases and asymptomatic controls using RDM and molecular methods.

Methods

Patients presenting to the pediatric emergency room of two university hospitals in Brussels with AGE were recruited prospectively from 05/2015 to 10/2016. A similar population of controls was recruited in the same hospitals. Stool analyses were done for patients and controls for common bacteria (culture), virus (immunochromatography) and parasites (microscopy). Stool were also analysed with Luminex Gastrointestinal Pathogen Panel (Luminex) which permits the detection by multiplex PCR of common enteropathogens.

Results
Stools from 178 patients and 165 controls were analysed by Luminex: in cases, excluding *Clostridium difficile*, a pathogen was detected in 56.2%, compared to 42.7% with RDM alone and 62.4% when combining the 2 methods. In controls, a total of 29.1% were positive for potential pathogens (10.3% by RDM and 24.2% by Luminex). High positivity percentages were found in cases (16.3%) and controls (11.5%) for *Salmonella*, only by Luminex.

### Conclusions

Molecular tools are an attractive method, providing rapid results and high positivity rates in cases with GEA. However, high rates of positivity in both cases and controls highlight the difficulty in interpreting those results, especially for *Salmonella* with Luminex. Laboratory stewardship will be key in streamlining patients in whom tests should be performed.
BACTERIAL MENINGITIS DUE TO HAEMOPHILUS INFLUENZAE SEROTYPE F IN A PATIENT WITH INNER EAR MALFORMATION: A CASE REPORT.
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Title of Case(s)
Bacterial meningitis due to *Haemophilus influenzae* serotype f in a patient with inner ear malformation: A case report

Background
Bacterial meningitis due to *Haemophilus influenzae* serotype f in a patient with inner ear malformation: A case report

Case Presentation Summary
The patient was a 3-year-old boy with left congenital deafness. He experienced headache and vomiting the day before hospitalization. At the time of hospitalization, he had symptoms of meningeal irritation, and cerebrospinal fluid tests showed pleocytosis. *Haemophilus influenzae* type f (Hif) was detected in his blood and cerebrospinal fluid cultures. He was diagnosed with bacterial meningitis due to Hif and treated with cefotaxime for 14 days. We performed thin-slice computed tomography (CT) scan as an additional investigation and found an inner ear anomaly with cerebrospinal fluid leak.

Learning Points/Discussion
Recently, an increased incidence of invasive non-type b *H. influenzae* infection, including Hif, has been reported in many countries. It is known that congenital inner ear anomalies increase the risk of recurrent bacterial meningitis. We suggested to his physician to consider surgical treatment for the inner ear anomaly in its early stage and to introduce 23-valent pneumococcal polysaccharide vaccine for him. Following this, he has not experienced recurrent meningitis for two years. Additional investigations such as thin-slice CT scan should be considered for patients with bacterial meningitis caused by rare microorganisms including Hif.
ANTENATAL VACCINATION AGAINST INFLUENZA AND PERTUSSIS IN GREECE

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Background

Pregnant women should receive influenza and pertussis vaccines according to the National Immunization Schedule in Greece. The purpose of the study was to assess the knowledge, attitudes, beliefs, and factors associated with the antenatal vaccine uptake of women in Western Greece.

Methods

A cross-sectional prospective survey was conducted on a random sample of pregnant women and women who have recently given birth at the antenatal clinics and maternal wards of 6 hospitals in Western Greece over a period of 3 months. The questionnaire included 28 questions on demographics, knowledge and attitude towards antenatal vaccination.

Results

432 women responded to the questionnaire (response rate of 86.4%), 108 (25%) had recently given birth. Although the majority of women were aware of both diseases (66.9%, 289), they admitted lack of adequate information offered from all sources about antenatal vaccination (73.4%, 317). Overall, there was poor awareness that the vaccination is safe to administer during pregnancy (95, 22 %). Few women even believed that maternal vaccination can cause birth defects (26, 5%) and autism (13, 2.5%). Moreover, only 76 (17.6%) of the study participants were aware that all pregnant women should receive influenza and pertussis vaccines according to the National Immunization Schedule. Worryingly, the majority of women (349, 80.8%) did not receive any recommendations from their obstetrician who is their major antenatal care provider. Only 26 (6%) of women had been offered the vaccines during current pregnancy.

Conclusions

The knowledge and uptake of influenza and pertussis vaccine among pregnant women in Greece is poor. There is substantial room for improvement among antenatal care providers in both patient education and offering the vaccine.
NEW INSIGHTS ON INVASION OF UROPATHEGENS IN ACUTE PYELONEPHRITIS IN CHILDREN
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Background

Precise mechanisms on invasion of uropathogens into the host in acute pyelonephritis (APN) remain to be solved. This study aimed to analyze the epidemiology and etiological pathogens of APN in children, and review 8 cases of APN presenting with no pyuria, previously known as acute lobar nephritis (ALN).

Methods

This was a retrospective observational cohort study of children below 16 years old, between 2006 and 2016. Electronic medical records and radiologic images were analyzed.

Results

A total of 359 patients fit the inclusion criteria; with 78.0% (n=280) below 12 months old. The male to female ratio was 5.3:1 in 0-2 months, 2.1:1 in 3-5 months; and 1.6:1 in 6-11 months old. Beyond 12 months, there was female predominance; with the female to male ratio 1.9:1 up to 4 years old, and over 17:1 beyond 5 years old. Escherichia coli was the leading cause of APN (83.8%) followed by Enterococcus species (6.7%) and Klebsiella pneumoniae (3.6%). Of the 8 patients diagnosed with APN without pyuria, the mean age was 9.8 years old, and 6 were female. Fever and severe abdominal pain with nausea and vomiting were the chief complaint in 5 of 8 patients. High while blood cell and C-reactive protein levels were observed (median, 17,900/mm³ and 13.1 mg/dL, respectively). Urine cultures were positive for E. coli in 3 cases. The computed tomography findings were compatible with complicated ALN.

Conclusions

There were marked male predominance in young infants, marked female predominance in older children, and a subset of patients without pyuria. These findings suggest that uropathogens may invade into the host through their colonized sites, not only urinary tract but also other sites of the host.
Background

The proper use of antibiotics is important to prevent antimicrobial resistance. Because of the individual difference in body weight, Day of Therapy (DOT) is commonly used in pediatrics. However, DOT is difficult to evaluate the influence of the hospitalized days such as the introduction of vaccine and outbreak of some infectious disease. Some studies analyzed the ratio of the consumption of broad- to narrow-spectrum (B/N ratio) of oral antibiotics for a quality indicator of antimicrobial stewardship program (ASP). The purpose of this study is to assess B/N ratio of intravenous antibiotics to the indicator of ASP.

Methods

We retrospectively investigated the usage of antibiotics with electronic medical records from 2011 to 2016 in pediatric wards at Juntendo Nerima Hospital. We calculated DOT and B/N ratio (Narrow spectrum: Ampicillin and Cefazolin, Broad spectrum: antibiotics except for Narrow) every two years.

Results

There were no significant differences between the total numbers of hospitalized patients in each period (1752, 1642, 1618). However, the number of inpatient and the rates of hospitalized days (19.1, 13.8, 12.2 %) due to bacterial infectious diseases decreased year by year. The total DOT (296, 190, 163 DOT/1000-patient days), and B/N ratio (1.32, 1.27, 0.93) also decreased significantly.

Conclusions

The quality indicators should be simple. However, DOT is susceptible to various factors such as vaccine policy and hygiene environment. It is difficult always to perform statistical sensitivity analysis. We can evaluate more accurately ASP with using plural marks (Mainly DOT and using B/N ratio by sensitivity analysis of institution). Further studies are needed.
Background: Water quality guidelines can be used to identify constituents of concern in water, to determine the levels to which the constituents of water must be treated for drinking purposes.

The aim of this paper is how to treat polluted drinking water.

Methods:

Methods: Fifty water samples representing different types of drinking water were collected and subjected for analysis chemically and microbiologically. Heavy metals were measured by atomic absorption spectrophotometer.

Results:

The results revealed that there were several areas polluted chemically by some heavy metals (Ni, Cd, Pb, Mn and Fe) and microbiologically by (Entamoeba Histolytica, Amoeba, Egg of Nematodes and total count of Bacteria).

Conclusions:

Conclusions and Recommendations: Membrane technology for the water cycle is playing an important role in the provision of safe water supply and treatment. Removal of some chemical constituents must be done and sewagesystem projects are implemented in all polluted areas of towns and villages.

Systematic Review Registration (Please input N/A if not registered)

N/A
Urinary tract infection is common bacterial infection in children. The changing pattern of antimicrobial sensitivity in UTI demands the use of appropriate antibiotics. Objective of the study was to detect culture & sensitivity pattern of bacteria implicated in UTI which will help to adopt more effective strategies in empirical of therapy.

Methods

It was cross sectional study conducted over children aged 6 month-5 year attending in OPD, department of Paediatrics Mymensingh Medical College Hospital from January 2016 to December 2016. Four hundred and fifty urine specimens collected from clinically suspected UTI children were examined by semiquantitative culture method & their sensitivity pattern were determined by disc diffusion technique.

Results

Of the 450 tested sample 99 samples showed growth of pathogens among which the most prevalent were E.coli 74(75%) followed by klebsiela pneumoniae 9(9.9%) and enterococci 6( 6%). Majority were isolate from female 70 (69%) while the remaining are from male. Imipenem, Meropenem, amikacin, nitrofurantoin, gentamycin and amoxyclav are found to be effective against 75-100% of the uropathogens. Most effective antibiotic in our study were imipenem, meropenem, amikacin and nitrofurantoin which show their efficacy against 91-100% isolates. More than 60% case show their resistance against amoxycillin, nalidexic acid, cefixime, ciproflaxacine, cotrimoxazole and cephalosporin which raises the question regarding rationality to empirically use of these antibiotics in UTI without culture & sensitivity reports.

Table 1: Prevalance of growth & overall sex distribution

<table>
<thead>
<tr>
<th>Sex</th>
<th>No. of tested (%)</th>
<th>No. of Growth %</th>
<th>No. of no growth %</th>
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</thead>
<tbody>
<tr>
<td>Male</td>
<td>200 (44.4%)</td>
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</tr>
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Conclusions
This study conclude that common urinary isolates were more sensitive to imipenem, meropenem, amikacin and nitrofurantoin in comparison to other antibiotics in this region.

Clinical Trial Registration (Please input N/A if not registered)

N/A
03B. SCIENCE: COMM.AQ. INVASIVE BACTERIAL INFECTIONS (NON-RESPIRATORY)

ANTIBIOTIC SENSITIVITY PATTERN & CAUSATIVE ORGANISM OF URINARY TRACT INFECTION IN CHILDREN IN A TERTIARY CARE HOSPITAL.
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¹Mymensingh Medical college Hospital, Department of Paediatrics, Mymensingh, Bangladesh
²Community Based Medical College- Bangladesh, Paediatrics, Mymensingh, Bangladesh
³Mymensingh Medical college Hospital, Department of Neonatology, Mymensingh, Bangladesh

Background

Urinary tract infection is common bacterial infection in children. The changing pattern of antimicrobial sensitivity in UTI demands the use of appropriate antibiotics. Objective of the study was to detect culture & sensitivity pattern of bacteria implicated in UTI which will help to adopt more effective strategies in empirical of therapy.

Methods

It was cross sectional study conducted over children aged 6 month-5 year attending in OPD, department of Paediatrics Mymensingh Medical College Hospital from January 2016 to December 2016. Four hundred and fifty urine specimens collected from clinically suspected UTI children were examined by semiquantitative culture method & their sensitivity pattern were determined by disc diffusion technique.

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Conclusions
This study conclude that common urinary isolates were more sensitive to imipenem, meropenem, amikacin and nitrofurantoin in comparison to other antibiotics in this region.

Clinical Trial Registration (Please input N/A if not registered)

N/A
Candidiasis is one of the leading causes of bloodstream infections (BSI) in neonatal intensive care units (NICUs) and is associated with high morbidity and mortality. It has been estimated that 2.4–9.0% of mortality and 25.0% of morbidity in the NICU setting may be attributable to Candida infections. Delay in recognition and in the initiation of appropriate antifungal therapy often leads to significant morbidity and mortality. Given the difficulty in establishing an early diagnosis, it is important to determine risk factors for Candida BSI and its impact on morbidity and mortality.

Methods

Retrospective Case Control Study between January 2014 and December 2017 in a Level III NICU in New Delhi. Study population included babies who grew Candida in blood culture. Data on patient demographics, medications, nutrition, ventilator use etc. was retrieved. For each case, one control neonate with negative blood culture matched for age, gender, gestational age, and birth weight was taken. Risk factors were evaluated from the time of admission until discharge or death. Variables that were significant on univariate analysis were entered into multivariate analysis.

Results

Thirty out of total of 8928 admitted newborns developed Candida BSI (3.36 per 1000). On univariate analysis factors associated with significantly higher risk of Candida BSI were apgar score<7 at 1 min, ventilation, vasopressor use, Total Parenteral Nutrition (TPN)
and prolonged hospital stay. Apgar score <7 at 1 min and vasopressor use were found to be independent risk factors on multivariate analysis. *Candida* BSI was associated with significantly higher mortality (33% v.s. 10% p<0.05)

**Conclusions**

*Candida* BSI is an important cause of mortality and morbidity in neonates. Apgar score<7 at 1 min and vasopressors use are independent risk factors for *Candida* BSI.
Background

Antimicrobial surveillance data is essential as a part of antibiotic stewardship program and assessment of the appropriateness of prescriptions. This study aimed to describe the antimicrobial prescribing in hospitalised neonates and children in tertiary-care centres in Thailand.

Methods

A standardised one day cross-sectional point prevalence survey (PPS), which is a part of the Global Antimicrobial Resistance, Prescribing, and Efficacy among Neonates and Children (GARPEC), was quarterly conducted in 2016. The surveys were conducted in 2 hospitals in Thailand. A standardised online data collection tool was developed using REDCap®. All inpatient neonates and children receiving an antimicrobial at 8:00 am on the day of the PPS were included. Denominators included the total number of inpatients.

Results

Of 866 patients during 4 cross-sectional surveys, 361 (42%) received antimicrobials. Of these, the antimicrobial consumption and type of treatment in neonates, children from general ward and intensive care unit (ICU) were shown in Figure 1. The indications were therapeutic 66% in neonates and 75% in children. The most common indications of antibiotic prescribing in neonates were sepsis (39%), followed by prophylaxis from newborn risk factor (13%). Common antibiotic uses in neonates were ampicillin (26%), gentamicin (25%), cefotaxime (9%), and meropenem (9%). In children, the most frequent indications were bacterial lower respiratory tract infection (20%) followed by sepsis (12%). The top 3 commonly prescribed antibiotics in children from general ward were meropenem (12%), ceftriaxone (9%), and cefazolin (6%), while in children from ICU were meropenem (19%), colistin (11%), and vancomycin (10%).
Conclusions

This surveillance study demonstrated highly use of meropenem in children in tertiary care centres in Thailand which may indicate caution of critical antibiotic use.
IMPACT IN IPD AFTER PCV 10 AND PCV13 INTRODUCTION IN CHILE

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²Hospital de niños Dr Exequiel González Cortés, Clinical pharmacist, Santiago, Chile
³Hospital de niños Dr Exequiel González Cortés, infection control program, Santiago, Chile

Background

Invasive Pneumococcal disease (IPD) is an important cause of morbidity and mortality. 19A serotype raise after PCV7 or PCV10 vaccination. Chile introduced PCV 10 into its national immunization program for infants in 2011 and during 2016 switched to PCV13 only in metropolitan region (MR) where almost 60% of cases occurred. The aim of this study is to describe the dynamic distribution of IPD in infants after PCV 10 and PCV 13 vaccination.

Methods

Ecological study of IPD cases from 2008 to 2017. Epidemiologic and microbiologic data was obtained from National Institute of Public Health; Poisson regression was used to estimate incidence rate ratio (IRR) and 95% confidence interval (CI) considering 2008-2010 as prePCVs, 2011 – 2015 as post PCV 10 and 2016-2017 as post PCV 13 periods.

Results

Overall IPD IRR decreased each year after PCVs implementation (IRR: 0,96; 95% CI: 0,96-0,97), being more protective in 2016-2017 period (IRR: 0,86, 95% CI: 0,77-0,95; p < 0,05); infants IRR was also protective each year focused on MR during 2016-2017 period (IRR 0,33; 95% CI:0,0,15- 0,74; p=0,007). From 2011 to 2017 IPD serotypes in infants included into PCV 10 were 24.6% and 49.3% belong to PCV 13. Non PCV 10 STs, specially 19A ST, steadily raised up with vaccine deployment in infants population, showing a decreasing trend before PCV 13 introduction in 2016

Conclusions

PCV 10 impact positively in overall Chilean population and infant’s IPD IRR but with a plateau higher than expected, showing a new reduction trend after PCV 13 introduction. Non PCV 10 STs, specially 19A ST, steadily raised up with vaccine deployment in infants population, showing a decreasing trend after PCV 13 implementation.
ACUTE DISSEMINATED ENCEPHALOMYELITIS IN CHILDREN AND ADOLESCENTS
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¹University hospital for infectious diseases "dr.Fran Mihaljevic"- School of Dental medicine- University of Zagreb, Pediatric Infectious Diseases Department, Zagreb, Croatia
²University hospital for Infectious Diseases "dr.Fran Mihaljevic", Pediatric Infectious Diseases Department, Zagreb, Croatia
³University hospital for infectious diseases "dr.Fran Mihaljevic"- School od medicine- University of Zagreb, Pediatric Infectious Diseases Department, Zagreb, Croatia

Background

Acute disseminated encephalomyelitis (ADEM) is a rare, usually monophasic inflammatory demyelinating disease of central nervous system. Nonspecific clinical manifestations and absence of reliable biochemical markers, makes the diagnosis based on clinical and paraclinical data.

Methods

We conducted retrospective study of 58 pediatric patients with ADEM treated in University hospital for infectious diseases diseases Zagreb in aim to identify distinguishing features of the disease which would facilitate early diagnosis.

Results

We treated 29 male and 29 female patients, median age 90 months (IQR 32.5-144 months). Half of our patients had anamnestic antecedent infection (respiratory illness in 72.41%). Most of patients presented during winter (34.48%) and spring (31.02%). Median of disease duration before admission was 4 days (IQR 2-8 days). Fever was present in 72.41% of patients. 23 patients had seizures during disease course. At admission, GCS was 15 in 66.67%, 14 in 15.69%, 10-12 in 9.8% and <10 in 7.84% of patients. Our patients had median (mononuclear) pleocytosis of 130 (IQR 23-281). Initial MRI was abnormal in 87.93% of patients. Predominantly affected regions wyere infratentorial region (37.25%), subcortical region (35.29%), deep gray matter – thalamus and basal ganglia (35.29%), periventricular area (33.33%), cortical (29.41%) and jucstacortical area (19.61%). 21.57% of patients had more than six lesions. Treatment regimens were as following: pulse doses of steroids in 64.29%, steroids+plasmapheresis in 12.5%, steroids+plasmapheresis+IVIG in 12.5%. At hospital discharge, 24 (41.38%) patients had sequele – most common was lower limb weakness (25%).

Conclusions

Patient age, history of antecedent infection, winter and spring seasonal peaks in disease presentation, clinical findings (fever, seizures, encephalopathy), laboratory findings (lymphocytic pleocytosis) and suggestive MRI findings are some of the findings commonly associated with this disease.
MICROBIOLOGICALLY CONFIRMED BONE AND JOINT INFECTIONS IN CHILDREN: A 7-YEAR RETROSPECTIVE STUDY IN A TERTIARY CHILDREN’S HOSPITAL

M. Petra¹, M. Daskalaki², T. Lagousi³, D. Mantakos¹, A. Spathis¹, A. Makri², I. Paspati¹, K. Filiopoulos¹, E. Staikou², E. Panagouli², S. Kostaridou³, P. Korovessi³, V. Tsagris³

¹Department of Orthopaedics, Penteli Children’s Hospital, Athens, Greece
²Department of Microbiology, Penteli Children’s Hospital, Athens, Greece
³Department of Paediatrics, Penteli Children's Hospital, Athens, Greece

Background

Bone and joint infections in children represent a diagnostic and therapeutic challenge, with causative agent identification being essential for targeted treatment. Here, we report a series of 21 children with microbiologically confirmed osteomyelitis (OM) and/or septic arthritis (SA) (out of 38 children with clinically and radiologically confirmed disease) admitted during a 7-year period.

Methods

We conducted a retrospective review of the medical records of children with microbiologically confirmed bone and joint infections, admitted to a tertiary Children’s Hospital in Athens, Greece, between January 2011 and December 2017. Children with predisposing factors were excluded from the study.

Results

Twenty-one children were included (8 OM, 9 SA, 4 combined SA and OM) aged 1.3-14.5 years. The commonest pathogen was Staphylococcus aureus (10/21), followed by Coagulase-Negative Staphylococci (4/21) and Streptococcus pyogenes (4/21); Pseudomonas aeruginosa, Kingella kingae, Bacillus licheniformis, Salmonella enterica, Clostridium novyi were identified in one case each. All, but one, patients were treated combining surgical irrigation with debridement and antimicrobials. Pus collected during surgery was additionally inoculated in blood-culture bottles. Treatment duration ranged from 4 to 41.7 weeks. Except from one short-term recurrence, all patients had an uneventful recovery at an average 27.5-month follow-up.

Conclusions

Bone and joint infection diagnosis and treatment in children remains a challenging and controversial issue. Since the causative agent was identified in the majority of bone and joint infections in our hospital (55.2%) through direct inoculation of aspirates into blood culture bottles, it appears that such an approach significantly increases the diagnostic yield. Notably, although Kingella kingae is recently considered an important pathogen in younger children, it is only rarely isolated in Greece. Our 2 SA cases of Kingella kingae and Clostridium novyi are the first ones described in Greece.
THE IMPACT OF ORGANIZATIONAL SUPPORT ON THE SPREAD OF NOSOCOMIAL INFECTIONS.

E. Kamunge

1Essex County College, Biology-Chemistry & Physics, NEWARK- NJ, USA

Background

Nosocomial infections (NIs) are new localized or systemic infections that develop in patients receiving medical care in healthcare facilities. NIs are recognized in hospitalized patients world-wide and are prevalent in all age groups. The infections are not present or incubating during a patient’s admission into the healthcare facility and are identified at least forty-eight to seventy-two hours following the patient’s admission. They are caused by pathogens such as bacteria, viruses and parasites present in the air, surfaces or equipment and are often transmitted by indirect and direct contact. The burdens of NIs include prolonged duration of hospitalization for patients resulting in increased costs of healthcare and, in some cases, deaths. It has been documented in the literature that at the time of their graduation from their professional education, healthcare professionals have sufficient knowledge to practice patient safety and infection control guidelines. However, the evidence suggests otherwise since healthcare workers are implicated in the transmission of NIs. With nurses having the most contacts with patients; understanding the impact of organizational support on their practice patterns with regard to the spread of NIs may provide one approach by which this health care issue would be addressed.

Methods

This was an exploratory, cross-sectional and descriptive study conducted using on-line survey responses from 352 registered nurses. Data was analyzed with descriptive and inferential non-parametric statistics.

Results

The results of correlation analysis indicated weak but significant positive correlation between organizational support and respondents’ attitudes and practices in respective categories.

Conclusions

The findings in this study suggest that organizational support plays pivotal roles toward reducing the spread of Nosocomial Infections.
Acute respiratory infection (ARI) imposes a considerable burden among children worldwide. Respiratory viruses are recognized to be the most frequent causative agents of ARI. However, the frequency of distinct viruses in tropical regions is scarce. We aimed to estimate the frequency of different respiratory viruses among children with ARI in a tropical setting.

Methods

This retrospective cross-sectional study was conducted in a Paediatric Emergency Room in Salvador, Northeast Brazil, between June 2014 and June 2017. Inclusion criteria included ≥2 of the following symptoms: fever for <7 days, cough, sore throat, myalgia, headache, arthralgia, running nose, or nasal blockage, besides age ≤ 18 years. As part of routine assistance, every patient who fulfilled the inclusion criteria had nasopharyngeal swab collected. Clinical data were retrieved from medical records. Respiratory viruses were searched by direct immunofluorescence and real-time polymerase chain reaction.

Results

The study group comprised 390 cases, whose median (IQR) age was 27.2 (11.0-51.3) months and 226 (57.9%) were male. The median (IQR) length of disease was 3 (2-4) days and the reported complaints were fever (100%), cough (96.3%), difficulty breathing (53.3%), running nose (25.3%), vomiting (20.3%), sore throat (15.3%), nasal blockage (11.6%), and headache (9.2%). Overall, 3 patients had undetermined results and respiratory viruses were found in 106 (27.4%) cases. Respiratory syncytial virus (RSV) was the most common one (19.5%), followed by influenza A (Flu A) (2.8%), influenza B (1.8%), adenovirus (1.3%), parainfluenza virus 1 (PIV 1) (1.3%), parainfluenza virus 3 (0.8%), and parainfluenza virus 2 (0.3%). Two samples had co-detections found: RSV + Flu A and Flu A + PIV 1.

Conclusions

RSV was the most frequently detected virus in this group of children with ARI in a tropical region.
LONG-TERM PRESERVATION OF MEASLES AND RUBELLA SPECIFIC-IGG ANTIBODIES IN CHILDREN WITH JUVENILE SPONDYLARTHritis ON ANTI-TNFα TREATMENT- A PROspective CONTROLLED STUDY

D. Maritsi, N. Spyridis, J. Kopsidas, M. Tsolia

"P. & A. Kyriakou" Children’s Hospital- Athens Medical School- National and Kapodestrian University of Athens, Second Department of Paediatrics, Athens, Greece

Background

Patients with autoimmune diseases are susceptible to infections due to their defective immune system and the receiving immunosuppressive treatment. Juvenile spondylarthritis (jSpA) often requires lifelong treatment with biologics, which manage to fully control the disease. However, data regarding response and long-term immunological memory to specific vaccines are lacking.

We aimed at a comprehensive assessment of how anti-TNFα therapy interferes with vaccine-specific-IgG titers in children with jSpA.

Methods

Prospective controlled study including 41 patients with jSpA and 149 matched-healthy controls. All patients had received two doses of MMR vaccine in early childhood. Samples were collected at diagnosis and at one and three years’ follow-up. Seroprotection rates as well as measles and rubella-IgG titers were measured and expressed as GMC’s. The Hospital’s Research and Ethics’ Committee approved the study; written informed consent was obtained.

Results

The two groups had similar demographic characteristics, vaccination history and immunization status. Seroprotection rates were adequate for both groups. The jSpA group had consistently inferior seroprotection rates. Both rubella and measles GMC’s were significantly lower in the jSpA compared to the control group (p<0.01) at one and three years’ follow up but not at diagnosis (p<0.05). During the follow-up period, the jSpA group had greater decrease in antibody levels as indicated from the significant interaction effect of analysis. Subgroup analysis showed that longer disease duration and prolonged treatment with anti-TNFα were directly correlated to lower antibody concentrations (p<0.01).

Conclusions

Anti-TNFα treatment seems to reduce measles and rubella-IgG titers. Further studies are required to assess long-term immunity conveyed by immunizations given at an early stage in children with rheumatic diseases, especially the ones receiving biologics. However, evaluation of immunization status against all vaccine preventable diseases in such patients may be beneficiary.
EPIDEMIOLOGY AND ETIOLOGY OF ACUTE ENCEPHALITIS IN COSTARICAN CHILDREN: A TERTIARY HOSPITAL EXPERIENCE

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¹Universidad de Costa Rica & Hospital Nacional de Niños “Dr. Carlos Sáenz Herrera”, Pediatrics Resident, San José, Costa Rica
²Hospital Nacional de Niños “Dr. Carlos Sáenz Herrera”, Neurology department, San José, Costa Rica
³Hospital Nacional de Niños “Dr. Carlos Sáenz Herrera”, Emergency department, San José, Costa Rica
⁴Hospital Nacional de Niños “Dr. Carlos Sáenz Herrera”, Molecular diagnosis division, San José, Costa Rica
⁵Hospital Nacional de Niños “Dr. Carlos Sáenz Herrera”, Infectious disease department, San José, Costa Rica

Background

Acute encephalitis results in substantial morbidity and mortality worldwide. Specific etiologies are identified in <50% of cases. The epidemiology and etiology of children hospitalized at the only pediatric tertiary referral hospital in CR, with acute encephalitis, was analyzed.

Methods

Prospective descriptive epidemiological study from March to October 2017. Case definition was defined according to the International Encephalitis Consortium.

Results

Forty patients were included. Average age at admission was 5 years; being children between 1-9 years the most affected (65.0%). 57.5% were male. Complications were seen in 26 (65.0%) patients; respiratory failure was the most common (70.0%), followed by status epilepticus (27.5%) and shock (27.5%). Nineteen children (47.5%) needed PICU support. Etiology was determined in 21 children (52.5%). Viral etiology was identified in 6 cases (15.0%) and bacterial etiology was identified in 6 cases (15.0%). A possible etiology was identified in 7 cases (17.5%). Autoimmune encephalitis was diagnosed in 2 cases (5.0%). Enterovirus and Pneumococcus were the most common confirmed agents. No cases of HSV were found. Despite extensive evaluation, the etiology of 19 cases (47.5%) remained undetermined. Sequelae were reported in 18 (45.0%) patients, being the most common: hypoacusia/deafness and oromotor dysfunction. The mortality rate was 15.0% (6 cases); 3 caused by viral agents (Adenovirus, HHV-6, Enterovirus), 2 by bacterial agents (Pneumococcus, Hib), and one of unknown etiology. Diffuse cerebral edema was the cause of death in all cases.

Conclusions

Acute encephalitis in costarican children is associated with significant morbidity and mortality. Although viral etiology has been considered the most frequent cause of acute encephalitis, we found similar cases of viral and bacterial agents. An early, aggressive antiviral, antibiotic and anti-edema treatment is suggested if acute encephalitis is suspected.
Clinical Trial Registration (Please input N/A if not registered)

N/A
PEDIATRIC INFECTIVE ENDOCARDITIS: CASE SERIES

N. Krajcar¹, L. Stemberger Marić¹, S. Roglić¹, Z. Barušić¹, G. Tešović¹

¹University Hospital for Infectious Diseases “Dr. Fran Mihaljević”, Paediatric Infectious Diseases, Zagreb, Croatia

Title of Case(s)

Pediatric infective endocarditis: case series

Background

Congenital heart disease (CHD) is the predominant underlying condition for infective endocarditis (IE) in children. Increasingly, IE develops in the absence of CHD, mostly in patients with indwelling catheters. In 8 to 10% of all cases there is no identifiable risk factor.

Case Presentation Summary

A total of 9 cases of IE in subjects <18 years of age were treated in University Hospital for Infectious Diseases in Zagreb in the past 13 years (2005-2017). There were 5 boys and 4 girls, aged 7 months to 17 years (median 7 years). 55% of cases were caused by common pathogenic bacteria (2 Coagulase-negative Staphylococcus, 2 Staphylococcus aureus, 1 Streptococcus sanguinis), while almost half of them (45%) were caused by relatively uncommon organisms in pediatric population: Enterococcus faecalis, Granulicatella adiacens, Haemophilus parainfluenzae and Abiotrophia defectiva (1 patient each). Although one (11%) patient didn’t have risk factor for IE, all of the others had CHD and one of them had central venous catheter as well. One patient (with IE due to S. aureus) had septic embolisation (meningoencephalitis) and two patients had relapse of IE (caused by KNS and Staphylococcus aureus). The most frequent antibiotic regimen for first 2 weeks of therapy was penicillin or its derivatives combined with gentamicin. Total duration of treatment was 6-8 weeks. Mortality rate was 22%, while others recovered completely.

Learning Points/Discussion

IE is a rare bacterial infection usually affecting children with CHD. Although IE is uncommon in children without risk factors, it should be suspected in patients with nonspecific clinical symptoms. In our case series Staphylococcus spp predominated as causative microorganism. We also noticed high proportion of cases caused by unusual bacteria and relatively low prevalence of streptococcal IE.
UMBELLIFERONE INHIBITS HIV – 1 INTEGRATES – A CLASSICAL INHIBITOR OF HIV REPLICATION

V. Kumar

Sam Higginbottom University of Agriculture- Technology and Sciences, Pharmaceutical Sciences, Allahabad, India

Background

Antiviral science or antiretroviral therapy despite of so much advances still faces new challenges from new HIV-1 infection, resistance still a major reason. Successful ART therapy cannot avoid infection associated morbidity with increase incidence of cardiovascular, bone and other cognitive disorder. Major drawback to the success of therapy with NNRTIs is the rapid development of drug-resistant HIV-1 variants and the cross-resistance between these structurally unrelated drugs. Following to the discovery of herbal based phyto-constituent as a class of novel, potent and selective compounds for NNRTI of HIV-1 RT, attention has been focused on the protective effect of umbelliferone (UF) nanoformulation, with potency against HIV-1 replication. The aim of the current study to developed a nanoformulation of UF potent anti-HIV agent via HIV-1 integrase inhibition.

Methods

Nanoparticles of UF embedded PLGA (UF-PLGA-NP) were prepared through emulsion evaporated technique for particle size, poly-disparity, zeta potential and drug release pattern determination. Molinspiration software program was used for elucidation of Lipiski’s Rule of 5. Molecular docking study was performed to scrutinize the binding affinity of UF at the HIV-1 integrase protein via using the 1QS4 PDB.

Results

The prepared formulation of UF showed the smooth spherical small surface with relative narrow size distribution. The molecular docking study of UF showed the considerable bioavailability. In the Anti-HIV assay, UF showed the utmost 87% inhibition of HIV-1 integrase catalytic with \( K_i = 85.56 \) nM. On the cytotoxicity assay, UF showed the lower percentage of cell viability. UF molecule extremely buried in the cavity of HIV-1 integrase catalytic domain via interacting with Thr66, Asn155, Asp116 and Glu152.

Conclusions

We can conclude that UF as potent inhibitor of HIV-1 via reduction of HIV-1 integrase with considerable bioavailability.

Clinical Trial Registration (Please input N/A if not registered)

N/A
10A. SCIENCE: FUNGAL INFECTIONS

PREDICTORS OF CANDIDA BLOOD STEAM INFECTION IN NEWBORNS ADMITTED IN LEVEL III NEONATAL UNIT NEW DELHI
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Background

Candida is one of the leading causes of bloodstream infections (BSI) in neonatal intensive care units (NICUs). The gross mortality of fungal infections ranges from 25% to 50%. In an Indian study, Candida attributed deaths occurred in 17% cases. The clinical presentation of invasive fungal and bacterial infection is similar causing diagnostic and treatment delay. Given the high mortality and difficulty in establishing an early diagnosis, it is important to determine predictors for Candida BSI. Objective was to find predictors for Candida BSI in newborns by comparing with Klebsiella BSI

Methods

Retrospective Case Control Study between January 2014 and December 2017 (48 months) in a Level III NICU in New Delhi. Study population included babies who grew Candida in blood culture. Data on patient demographics, medication use, nutrition, ventilation etc. was retrieved. For each case, one neonate who grew Klebsiella on blood culture was included. Their data were also extracted as previously described. Data analysis was performed using SPSS Version 20.0. Risk factors were assessed using Univariate analysis. All p values were two tailed and values<.05 were taken as significant.

Results

Thirty out of total of 8928 admitted newborns developed Candida BSI (3.36 per 1000). Examination of a standard battery of conditions associated with morbidity in both groups e.g. birth-weight, gestation, asphyxia, ventilation, vasopressors use, surfactant, steroid, parenteral nutrition etc did not reveal any notable differences. Candida BSI and Klebsiella BSI were associated with similar mortality (33% v.s. 43%)
Table 1. Univariate analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Candida (N=30)</th>
<th>Klebsiella (n=30)</th>
<th>O.R</th>
<th>Confidence interval</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male Sex</td>
<td>18</td>
<td>17</td>
<td>1.15</td>
<td>0.41</td>
<td>3.20</td>
</tr>
<tr>
<td>Gestation (weeks) Mean (SD)</td>
<td>31.7 (3.1)</td>
<td>32.5 (4.3)</td>
<td>0.94</td>
<td>0.82</td>
<td>1.08</td>
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<tr>
<td>Birth Weight (grams) Mean (SD)</td>
<td>1846 (507)</td>
<td>1572 (805)</td>
<td>1.09</td>
<td>0.99</td>
<td>1.00</td>
</tr>
<tr>
<td>Duration of stay (Days) Mean (SD)</td>
<td>39.5 (20.7)</td>
<td>27.3 (21.1)</td>
<td>1.02</td>
<td>0.99</td>
<td>1.04</td>
</tr>
<tr>
<td>Ventilation</td>
<td>22</td>
<td>16</td>
<td>2.41</td>
<td>0.82</td>
<td>7.09</td>
</tr>
<tr>
<td>Vasopressors</td>
<td>16</td>
<td>20</td>
<td>0.57</td>
<td>0.20</td>
<td>1.62</td>
</tr>
<tr>
<td>APGAR &lt;7 at 1 Min</td>
<td>17</td>
<td>11</td>
<td>2.26</td>
<td>0.80</td>
<td>6.36</td>
</tr>
<tr>
<td>Surfactant</td>
<td>9</td>
<td>8</td>
<td>1.18</td>
<td>0.38</td>
<td>3.63</td>
</tr>
<tr>
<td>Steroids</td>
<td>12</td>
<td>16</td>
<td>0.58</td>
<td>0.21</td>
<td>1.62</td>
</tr>
<tr>
<td>TPN</td>
<td>7</td>
<td>11</td>
<td>0.53</td>
<td>0.17</td>
<td>1.62</td>
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<tr>
<td>CPAP</td>
<td>23</td>
<td>18</td>
<td>2.19</td>
<td>0.72</td>
<td>6.69</td>
</tr>
<tr>
<td>Died</td>
<td>10</td>
<td>13</td>
<td>0.65</td>
<td>0.23</td>
<td>1.86</td>
</tr>
</tbody>
</table>

Conclusions

Newborns admitted with Candida or Klebsiella in BSI in level III neonatal units have similar epidemiological characteristics, morbidity and mortality.
Clinical Comparison of Influenza A and B Virus Infection in Hospitalized Children

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Background

The objective of this study was to compare the clinical characteristics of influenza A and B infections and analyze the effect of oseltamivir in hospitalized children.

Methods

We investigated children under the age of 15, who were diagnosed with influenza A/H1N1, A/H3N2, or B from January to April 2014. The subjects were admitted to the Changwon Fatima Hospital and diagnosed using a rapid antigen test from nasopharyngeal swabs. The medical records of the patients were retrospectively reviewed.

Results

A total of 302 pediatric patients with influenza were enrolled. Influenza B infection was the most common type (n=187, 61.9%), followed by A/H3N2 (n=100, 33.1%) and A/H1N1 (n=15, 5.0%). Compared to patients diagnosed with influenza A, patients diagnosed with influenza B were older (P =0.005), and the duration of fever was significantly longer (P =0.001). A total of 161 patients (53.3%) had been vaccinated against influenza during the season, before admission. Among the patients infected with A/H3N2 and B, the duration of fever was shorter in oseltamivir recipients compared to oseltamivir non-recipients (P =0.026 and P =0.004, respectively).

Conclusions

There were significant differences between influenza A and B groups in terms of age, demographics, and clinical course. Although the effectiveness of oseltamivir on influenza differs according to the type of influenza, our data provides evidence that oseltamivir is beneficial for both A and B infections.
VACCINE CONFIDENCE AND VACCINE HESITANCY: A PROSPECTIVE SURVEY AMONG PEDIATRICIANS
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2ICS Metropolitana Sud, CAP Sant Ildefons, Cornellà, Spain
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5Hospital Clinic - UB, Preventive Medicine, Barcelona, Spain

Background

Vaccine confidence and vaccine hesitancy are key components of any vaccination program. The real situation about this two components among practicing Pediatricians and their degree of basic knowledge about vaccines well as the prevalence of vaccine-hesitant parents, has seldom be studied.

Methods

We conducted a web-based survey of a 350 sample (95% confidence level, 5% error margin) of all 1,439 registered Pediatricians at the Barcelona College of Physicians. A total of 337 surveys were valid (23% of all population studied). Variables include demographic and professional practice data, basic knowledge about vaccines, perceived usefulness of vaccines, encounters with vaccine hesitant parents and main concerns related to this hesitancy, degree of confidence in several information sources and self-assessment of the personal knowledge about vaccination.

Results

The Pediatricians’ female/male ratio was 2:1; 54% had public practice, 20% private, 25% both. Nearly 100% agrees on the favorable risk/benefit ratio of vaccines. Vaccine hesitant parents were encountered by 94% of Pediatricians. The prevalence of vaccine hesitancy among parents is 3-5%. Most questioned vaccines were HPV and MMR. Fear of adverse events (78%) and doubts about the need (64%) are main reasons for hesitancy. Pediatricians trust official sources of information (95%) but not the Pharma Industry (70%). Up to 33% believe that their knowledge about vaccination should be improved.

Conclusions

The % of vaccine hesitancy in Barcelona is low, but nearly all Pediatricians face such a situation in their clinical practice. Pediatricians had a good knowledge about vaccines, but there is still room for improvement on the information they needed to answer properly questions posed by vaccine hesitant parents.
Background

Skin and soft tissues infections are frequent in pediatric age. Those can complicated with severe systemic infections if its putting of diagnose and treatment were not appropriate. In my country as the low social and economic conditions, we found a high prevalence of them. Purpose was to study epidemiological and clinical characteristics of the infections.

Methods

In the study were included all children presented in emergency room of our hospital with signs of the skin and soft tissues infections during the period January 2015-31 December 2015. The age ranged from 1 month -14 years. The diagnosis was based on clinical criteria. Epidemiological data analyzed were: sex, age, origin, risk factors and complications.

Results

During the period of study 124 children were presented with signs of skin and soft tissue infection. The most involved age group was 13 month-5years old with 83(70%)cases followed by age 1month -12months with 33(26.6%)cases and 6 years -14 years old with 8(6.4%)cases. About the gender, the male sex slightly dominates with 72(58%) cases. versus 52 female cases. The majority of cases originate from urban zone with 75(60%) presentations. July has had the majority of cases with 34(27.4%) children followed by August with 22(17.4%). The clinical presentations most frequent were: impetigo, piodermia, cellulitis. In the majority of cases we use oral antibiotics and topic ointment. There have been 2 cases of erysipelas which are admitted to the hospital.

Conclusions

Skin and soft tissues infections very frequent in Albania as a developing country. As long as they may lead to serious complication we should pay much more attentions about them particularly in improving of social and higenic conditions.
EPIDEMIOLOGICAL SITUATION OF ACUTE GASTROENTERITIS AND ITS COMPLICATIONS IN ALBANIAN CHILDREN.

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²University Hospital Center"Mother Theresa", Pediatric Emergency Department., Tirana, Albania

Background

Acute gastroenteritis is a common infection disease in pediatric age, and acute diarrhea is the most presenting symptom in Emergency Department of our Hospital. The aim of this study was to show the epidemiological data, risk factors, clinical characteristics, its complications and the tendency of this disease in our population.

Methods

In our study are included all children with signs and symptoms of acute gastroenteritis age from 1 month to 14 years old, presented in Pediatric Emergency room of University Hospital Mother Teresa, during the period 1 January to 31 December 2015. Epidemiological data analyzed were sex, age, origin, risk factors and complications.

Results

During the period of study 9401 children were presented with signs of acute gastroenteritis. Among them 9298 (98%) were not severe cases and 103 were severe cases which are admitted in the hospital. Age group most affected was 13m-5 years old with 5634 (59.9%) cases, followed by group age 6-14 years old with 1930 (20.5%) cases and age group 1m-12 month with 1837 (19.5%) cases. The male sex dominates with 5365 (57%) cases. Most of the cases (6142 (65%) came from urban zone. 3579 (38%) children were presented with acute diarrhea and 5822 (61.9%) cases with acute gastroenteritis (diarrhea and vomiting). The peak was in August. Some of the associating symptoms were fever, bronchitis, urticaria, abdominal colic, etc.. About the causative agent we have found mostly the rotavirus.

Conclusions

The well to moderate clinical situation of acute gastroenteritis can lead to severe forms and even death too. The high number of cases with this disease presenting to our hospital, raises the importance of Introduction in the routine immunization program, of the vaccination against the rotavirus.
Background

The success of combination antiretroviral therapy (cART) in the treatment of HIV infection has allowed an increasing number of HIV infected patients to survive childhood and to be now transitioning from pediatric to adult care. Little is known about the outcome in terms of clinical and social aspects of the transitioned patients.

Methods

We performed a transversal, retrospective study which included all HIV infected patients transitioned from pediatric to adult care in the last 6 years. The main aim was to assess retention in healthcare system. Virologic, immunologic parameters, ART background, adherence, resistance and socioeconomic status were also included. There is not a strict protocol, each case is treated individually.

Results

From 48 infected children, 12 transitioned to adult care. 11 had HIV-1 infection and 1 HIV-2; 11 had perinatal acquired HIV infection and 1 due to sexual transmission. The median age at transition was 19 (16-22) years-old, the median CD4 count was 780 (287-1091)/uL, with 10 patients (83%) with >500 CD4/ul and 3 with detectable viral load. 1 patient died from LIP-related bronchiectasis. All the others 11 were successfully linked to health care at transition (median 16 months), 8 (67%) presenting major resistance mutations to 1 or more drug class.

Conclusions

One of the highlights of this study is the fact that although these patients confronted many problems during their childhood and adolescence, including diagnosis disclosure, adherence and orphanage, we demonstrated their successfully retention to health care system. The pediatrician played an important role in the ART selections and in the good compliance of therapeutic. In adult care, it is still possible to provide appropriate regimes considering the drug mutations with good quality life and no adverse effects.
CASE OF TUBERCULOSIS MENINGITIS WITH ACUTE PRESENTATION

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Title of Case(s)

Case of Tuberculosis Meningitis with Acute Presentation

Background

Tuberculosis meningitis (TBM) is one of the common infections of central nervous system (CNS) in India. It poses challenges in diagnosis as symptoms can be non-specific initially, there is no single diagnostic test with high sensitivity and microbiologic yield is low. However, the outcome is directly dependent on the stage at which treatment is initiated. Early treatment can minimize complications therefore attempts at early diagnosis with clinical suspicion and appropriate laboratory tests is warranted.

Case Presentation Summary

A 7-year-old, presented with 2-day history of fever, headache and a generalized seizure on 2nd day of illness.

He was febrile, BP 96/62 mm Hg, drowsy at admission, had diplopia though extra ocular movements were normal and had terminal neck stiffness.

Blood counts were normal, CRP was negative. He had hyponatremia (127 mmol/L) requiring correction. Contrast enhanced CT scan was normal. CSF analysis showed 2 lymphocytes, glucose of 68 mg/dl, protein of 10.4mg/l, meningoencephalitis panel (PCR) was positive for TB, cultures were sterile.

He received sodium correction in view of hyponatremia with seizures following which his sensorium rapidly improved. After CECT brain which was normal a LP was done. 4 drug ATT with steroids commenced post CSF PCR reports. He completed ATT with complete recovery.

Learning Points/Discussion

• TB meningitis may present with a short febrile illness (< 7days). The clues for suspicion would be presence of altered sensorium and focal neurologic signs like cranial nerve palsies.

• Hyponatremia in the setting of CNS infection may be a clue for considering TBM.

• CSF TB PCR is invaluable in making a diagnosis especially in cases with short or atypical history.
CASE OF AUTOIMMUNE HEMOLYTIC ANEMIA IN A CHILD WITH NECROTIZING PNEUMONIA

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Title of Case(s)

A CASE OF AUTOIMMUNE HEMOLYTIC ANEMIA IN A CHILD WITH NECROTIZING PNEUMONIA

Background

Even though AIHA with Mycoplasma and Viral infections are common in children, AIHA associated with pneumococcal pneumonia is a rare presentation.

Case Presentation Summary

A 2 ½ years old child presented with cough and fever - 2 weeks with fast breathing. On evaluation, he was pale, tachypnoic and in respiratory distress with bronchial breathing on right side. Admitted in PICU and started on HFNC initially and later shifted to BIPAP in view of worsening distress. He was started on IV antibiotics, Meropenem and Vancomycin. Chest X-ray showed right upper and middle lobe consolidation. A complete blood counts showed leucocytosis with anemia (Hb - 7.9g/dl on admission and 5.9g/dl on next day). CRP was 338mg/dl. Peripheral smear showed normocytic hypochromic erythrocytes with few macrocytes, target cells and polychromatic cells. Coombs test was positive with anti IgG/C3d. Auto antibodies are present at 37 deg C as well as 4 deg C (both warm and cold antibodies). He was treated with IV Immunoglobulin (1g/kg) and later 1 unit of PRBC transfused. CT chest was done due to continuous fever spikes and persistently elevated inflammatory markers and it showed right necrotizing pneumonia with moderated empyema. Blood culture was negative, but PCR was positive for Streptococcus pneumoniae. Right thoracotomy and decortication with evacuation of empyema with lung debridement was done. IV antibiotics continued for 14 days and later changed to oral therapy.

Repeat Chest X-ray showed significant improvement.

Learning Points/Discussion

1. AIHA, though common with mycoplasma pneumonia can be seen with streptococcus pneumonia.
2. A short course of IVIG or Corticosteroids are beneficial for severe hemolytic anemia in acute phase.
3. Treatment of pneumonia itself reduces the hemolysis in due course.
CLOSTRIDIUM DIFFICILE INFECTION-ASSOCIATED REACTIVE ARTHRITIS MIMICKING SEPTIC ARTHRITIS OF THE KNEE

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²Gazi University School of Medicine, Department of Pediatric Infectious Diseases, Ankara, Turkey

Title of Case(s)

CLOSTRIDIUM DIFFICILE INFECTION-ASSOCIATED REACTIVE ARTHRITIS MIMICKING SEPTIC ARTHRITIS OF THE KNEE

Background

Clostridium difficile is an uncommon cause of reactive arthritis (ReA) in children. We herein present a rare case of C. difficile infection-associated ReA (CDIAReA) in a 10-year-old child, who developed severe diarrhea and a knee effusion following a course of oral antibiotic treatment.

Case Presentation Summary

A previously healthy 10-year-old boy was admitted to our hospital with a 3-day history of painful swelling in the left knee. Two weeks earlier he had completed a 7-day course of oral cefpodoxime. Five days after the discontinuation of antibiotic treatment, he developed watery diarrhea. On admission, the patient had fever up to 39°C. Physical examination revealed a warm, swollen, and tender left knee with decreased range of movement. Laboratory tests revealed a high leucocytosis (22,400/mm³) with 84% neutrophils. The erythrocyte sedimentation rate was 56 mm/h and C-reactive protein was 18 mg/dL. Magnetic resonance imaging of the left knee showed a large amount of joint effusion (Figure 1). After diagnostic arthrocentesis, empiric treatment with intravenous cefazolin was initiated for the presumptive diagnosis of septic arthritis. However, his fever and joint symptoms persisted. Gram stain and culture of synovial fluid were found to be negative. He continued to have large amounts of watery diarrhea in the hospital. Stool culture was negative, but C. difficile toxin B was detected by RT-PCR. On hospital day 4, oral metronidazole (30 mg/kg/day) was substituted for
cefazolin and continued for 10 days. Within 10 days his diarrhea and joint symptoms resolved.

Learning Points/Discussion

Our report emphasizes that CDIAREA should be considered in the differential diagnosis of children presenting with acute and painful arthritis that develops in the setting of postantibiotic diarrhea.
A POPULATION BASED OBSERVATIONAL STUDY OF THE AETIOLOGY OF INFECTION IN INFANTS UNDER THE AGE OF THREE MONTHS HOSPITALISED WITH A FEVER WITHOUT A SOURCE

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Background

Infants under the age of 3 months are often admitted to hospital with a fever without a source which could be a manifestation of an underlying invasive bacterial infection which, if left untreated, could result in significant morbidity or mortality. To arrive at a diagnosis and to administer the appropriate treatment, infants are investigated through a septic screen.

The aim of the study was to determine the aetiology of infection in infants admitted with a fever without a source.

Methods

A retrospective observational population study was performed at Mater Dei Hospital, the only hospital in Malta that provides paediatric inpatient services for all children living on the island. All infants under 3 months of age, admitted with an axillary temperature >38°C without a source who underwent a septic screen in 2016, were included. The results of microbiological and radiological investigations were analysed from each infant’s electronic results.

Results

During the twelve month study period, 102 infants hospitalised with a fever without a source underwent a septic screen. Significant bacteraemia was confirmed in 8.8% (Staphylococcus aureus and Streptococcus agalactiae being most prevalent) and 1% had bacterial meningitis. A urinary tract infection from Escherichia coli was diagnosed in 15.7% and 9.8% had radiologically confirmed pneumonia. Viral meningitis was confirmed in 18.6%. A diagnosis of upper respiratory tract infection was made by molecular analysis in 26.5%.

Conclusions

Although most infants with fever without source have a viral infection, a modest proportion may have a serious bacterial infection. A full sepsis screen remains an essential tool to identify and treat septic infants.
KAWASAKI DISEASE IN YOUNGER OF 90 DAYS, MULTICENTRE STUDY FROM SPAIN


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23Hospital General de Albacete, Pediatric Infectious Diseases, Albacete, Spain
24Hospital Clínico Universitario de Valladolid, Pediatrics, Valladolid, Spain
25Hospital Universitario de Burgos, Pediatrics, Burgos, Spain
26Hospital Universitario Río Hortega, Pediatrics, Valladolid, Spain
27Hospital General de Segovia, Pediatrics, Segovia, Spain
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Background

Kawasaki disease (KD) diagnosis is always challenging, but even more in younger than 1 year of life, when atypical or incomplete forms are more frequent. Moreover, in younger than six months an increased risk to develop coronary artery abnormalities (CAA), despite promptly administration of intravenous immunoglobulin (IVIG).

Our aim was to know the presentation and evolution of KD cases in population younger than 90 days of life.

Methods

Descriptive and retrospective study from infants younger than 90 days diagnosed of KD in Spain between 2011-2016, included in the multicentre study KAWA-RACE. Online database (REDCap) was reviewed and epidemiological, clinical, lab, treatment and sequelae data from patients was analysed.

Results

From 621 patients, 7 were <3months (1.13%). Three fulfilled criteria of complete KD; being rash the more consistent symptom (85%), and lymphadenopathy the least frequent (15%). Median of days
since the start of fever and IVIG was 8. Three patients presented viral infection: adenovirus, enterovirus, and coryzal symptoms. 57% developed CAA (3 aneurysms, 1 ecstasy), but no sequelae during follow-up. All patients responded to treatment, 6 just IVIG, 1 received also concomitant steroids.

Conclusions

Cases of KD younger than 3 months, represented 1.13% of our population. Despite 57% presented CAA, all responded to treatment and resolved from mentioned CAA. The delay in diagnosis wasn’t long, and treatment was initiated within recommended period in most cases. Viral infections may trigger KD and make difficult a correct diagnosis.
NECROTISING FASCIITIS DUE TO INVASIVE STREPTOCOCCUS PYOGENES INFECTION

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Title of Case(s)

NECROTISING FASCIITIS DUE TO INVASIVE STREPTOCOCCUS PYOGENES INFECTION

Background

Necrotising fasciitis (NF) is a rare and life threatening condition where early recognition and surgical intervention are essential factors for good outcomes. We present the first case of NF in Children’s Hospital during the last decade.

Case Presentation Summary

10-year-old boy was diagnosed with herpetic stomatitis. Five days later he presented to ED complaining of painful erythematous swelling of the left temporal area, photophobia, and persistent mouth lesions. At presentation he was febrile, drowsy (GCS 13), in pain, but haemodynamically stable.

Patient was admitted to PICU due to suspected NF. He was started on acyclovir, clindamycin, meropenem, and IV fluids. Laboratory workup showed highly elevated inflammatory markers and liver enzymes, coagulopathy. Head CT showed left side facial tissue oedema, parapharyngeal infiltration on the left and brain oedema. Despite treatment patient progressed to septic-toxic shock (TSS), and respiratory failure. He was started on vasopressors, mechanical ventilation, IV immunoglobulin.

The patient has undergone multiple life-saving surgical interventions. *S.pyogenes* was detected in the wound culture. Histological examination revealed skin, subcutaneous tissue and muscle necrosis. IV penicillin was added to antimicrobial treatment.

On the 7th day the patient was haemodynamically stable, vasopressors and mechanical ventilation were discontinued. On the 12th day he has recovered and was transferred to Paediatric Burn and Plastic Surgery ward for reconstructive surgery.

Learning Points/Discussion

1. Early recognition of NF and prompt surgical intervention are crucial and lifesaving.
2. Previous viral infection with breach of skin and mucosal barriers have possibly made patient more susceptible to NF.
3. *S.pyogenes* is a common etiologic agent of NF. Patients are always at risk of progression to TSS, and requires intensive care.
4. Role of IV immunoglobulin in the treatment of TSS is still under discussions.
04A. EDUCATION: SEVERE PNEUMONIA IN CHILDREN

12.33 YEARS ACTIVE SURVEILLANCE FOR PEDIATRIC PLEURAL EMPYEMA IN A MEXICAN HOSPITAL: EFFECTIVENESS OF PNEUMOCOCCAL 13-VALENT CONJUGATE VACCINE, AND EARLY EMERGENCE OF METHICILLIN-RESISTANT S. aureus

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Background

Previous publications from us and elsewhere have proved effectiveness of the 13-valent pneumococcal conjugate vaccine (PCV13) on Pneumococcal Pleural Empyema (PnPE) in children, with little emergence of other pathogens. We searched to see whether PCV13 reduces PnPE, and to identify other pathogens causing pleural empyemas (PE).

Methods

From Oct-2005 to Jan-2018 (12.33 years) we performed active surveillance for all cases of PE at the Hospital General de Tijuana, Mexico. Isolates from pleural fluid (PF) were identified by conventional culture, and since 2014 PCR was added for all culture-negative PF’s. \textit{S. pneumoniae} serotypes were detected by either Quellung Reaction (Statens Serum Institute\textsuperscript{®}) or PCR. Demographic, clinical, tomographic/radiologic, laboratorial and microbiological evaluation was performed on each patient prospectively. Statistical analysis was purely descriptive.

Results

A total of 64 PE were identified (5.28/year). Median age was of 51 months (1-191), hospitalization days of 18 (4-35). Decortication was performed in 42%, and two children died (3.2%). Bacterial identification was obtained from 51 (79.7%). \textit{S. pneumoniae} was the leading cause of all culture/PCR-confirmed PE (29=56.8%), followed by \textit{S. aureus} (14=27.4%), \textit{S. pyogenes} (3-5=9%) and others (5=9.8%). PCV13 was initiated on May/2012, and its effectiveness on serotype-specific PnPE was of 81%, for all PnPE of 56.1%, however, for all PE of -2.1% due to an increase of PE caused by \textit{S. aureus} (13 cases following PCV13 implementation, see Figure 1). All but one isolate of \textit{S. aureus} PE
Conclusions

Following 12.33 years of active surveillance, PCV13 has shown effectiveness on both serotype-specific and all PnPE, however, an increase of PE by MRSA has emerged. Continuous and close surveillance is mandatory to see whether this epidemiological behaviour is transitory or not.
VACCINE RESPONSE OF HIV-EXPOSED UNINFECTED INFANTS TO HEPATITIS B IMMUNIZATION

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Background

The efficacy of the hepatitis B vaccine is well demonstrated and since its inclusion in the national immunization programs, the prevalence of Hepatitis B infection and chronic disease in children has decreased especially in countries with high prevalence of Hepatitis B in adults. HIV–exposed uninfected infants represent a population with some altered immunity and susceptibility to infections in infancy. The aim of our study was to describe their antibody response to HBV vaccination.

Methods

Methods:

HIV-exposed uninfected infants are tested for the loss of HIV antibody around 18 months of life and HBV serology was measured at the same time. All children received at least three doses of the hepatitis B vaccine according to the Belgian vaccination program, and children whose mothers were Hepatitis B surface Antigen (HBsAg) positive received an additional dose at birth, together with HBV antibodies.

Results

143 infants born between January 2008 and December 2015 were studied. The measure of the anti-HBs antibody titers was performed 2 to 20 months after their last dose. The overall percentage of infants with anti-HBs antibody titers < 10µu/ml was 2.7%. Among the infants of HBsAg negative mothers, those who received 4 doses had significantly higher median antibody titers compared to those who received 3 doses (p=0.006).

Conclusions

HIV-Exposed Uninfected infants present a good vaccine response to Hepatitis B immunization after a completed vaccination program with the last dose administrated after the age of 6 months. Prospective studies are needed in order to determine the influence of the maternal infection to the immune response of the newborns, especially since in certain countries with high prevalence, the last dose is administrated at the age of 14 weeks.
KINGELLA KINGAE OROPHARYNGEAL CARRIAGE RATE AND DISTRIBUTION OF THEIR CAPSULE TYPE IN YOUNG CHILDREN IN FRANCE

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3ACTIV, Activ, St Maur des Fossés, France
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5Association Française de Pédiatrie Ambulatoire, Pédiatrie, Essey-les-Nancy, France

**Background**

*K. kingae* has become the leading pathogen of osteoarticular infections in several countries for young children under 4 years, but poor epidemiological data on the carriage in healthy children are available yet. We aimed to determine the rate of and the factors associated with *K. kingae* healthy carriage in young children in France.

**Methods**

Pediatricians prospectively enrolled healthy children aged 6-36 months during well baby visit. A throat swab was sampled and clinical and epidemiological data were anonymously collected. Carriage was defined by *K. kingae* positive throat culture and/or a combined result of 3 specific polymerase chain reactions (PCRs): positive *rtxA* and real-time *cpn60* PCRs were used to detect *K. kingae*, while a negative *groEL* PCR allowed excluding a *K. negevensis* carriage. Capsule types were determined by multiplex PCR.

**Results**

Between May 2015 and June 2016, 217 children were included (98 females [45.2%] and 119 males [54.8%]). *K. kingae* was detected by PCR in 11 (5.1%; 95% confidence interval: 2.6-8.9%) cases, but no strains were isolated by culture. Carriage rate was higher in children aged 18-23 months (4/35; 11.4%) and in children cared for out of home compared with those cared for at home (7/51; 13.7% vs. 4/166; 2.4%, respectively; p=0.004). Capsules a and b were identified in 4 samples each, whereas simultaneous capsules a and c were identified in one sample.

**Conclusions**

*K. kingae* healthy carriage rate in France was close to that described in other countries. Day-care centre attendance is an important associated factor. Capsules a and b, known to be associated with invasive infection, were commonly identified.

**Clinical Trial Registration (Please input N/A if not registered)**

N/A
04B. SCIENCE: COMMUNITY ACQUIRED INFECTIONS: RESPIRATORY TRACT INFECTIONS

SYSTEMIC CYTOKINE PROFILE ON ACUTE AND CONVALESCENT SERUM SAMPLES IN CHILDREN HOSPITALIZED WITH COMMUNITY-ACQUIRED PNEUMONIA

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Background

Community-acquired pneumonia (CAP) is the most frequent cause of death among children under-5 years worldwide. Serum interleukin-6 (IL-6) has been recently found to be independently associated with pneumococcal infection among these patients. However, information on the evolution of systemic cytokines is scarce. We aimed to fill this gap.

Methods

This was a prospective study at an Emergency Department in Salvador, Brazil. Children <5-years-old hospitalized with CAP in a 21-month period were investigated. On admission, clinical data and biological samples were collected to investigate 20 etiological agents and determine serum cytokine levels (IL-8, IL-6, IL-10) pg/ml. Every recruited child was re-evaluated 2–4 weeks after admission when the second blood sample and the follow-up chest radiograph were taken and a clinical examination was carried out. The same cytokines were measured in the convalescent serum samples.

Results

From 277 enrolled patients, serum sample was unavailable for cytokine measurement upon admission (n=61) or on follow-up (n=74). Therefore, this study group comprised 142 cases among which aetiology was detected in all. The median(IQR) age was 19(9-28) months and there were 83 (58.5%) male. Median(IQR) sampling interval was 18(16-21) days. Viral (52.1%), viral-bacterial (30.3%), and bacterial (17.6%) infections were diagnosed. Pneumococcal infection was found in 33(23.2%) patients. Overall, median IL-6 (11.6[4.68-30.63] vs. 21.00[20.20-21.70];P=0.03) and median IL-10 (3.50[3.00-4.43] vs. 20.10[19.80-20.33];P<0.001) were significantly higher in the convalescent serum samples, and median IL-8 was higher upon admission (81.25[33.05-226.15] vs. 66.40[25.48-166.70];P=0.1). The same evolution was observed for IL-8 and IL-10 among patients with or without pneumococcal infection. However, IL-6 decreased (30.60[12.40-50.80] vs. 20.80[20.30-22.20];P=0.07) in patients with and increased (9.20[4.15-22.65] vs. 21.00[20.20-21.70];P<0.001) in patients without pneumococcal infection.

Conclusions

Serum IL-6 evolves differently among children hospitalized with CAP with or without pneumococcal infection.
GLOBALIZATION AND ITS AFFECTS ON CHILD HEALTH

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Background and Objective

The aim of this literature review is to present the affects of globalization on child health and to figure out how to eliminate negative affects of it.

Methods

Globalization is the intensification of social relations in a global scale through the events that occur in one part of the world having direct or indirect effects on the other events happening in the other parts of the world. Globalization means global change in many subjects such as economy, politics, culture, health and social life. It leads to an increase in infectious diseases and global contagious diseases while contributes to generate policies related to health care services and to increase the disease prevention and intervention programs. Furthermore, globalization makes an increase in poverty. According to the World Bank reports, one fifth of world population lives below the poverty line. The most known and the most frequent affect of poverty is nutritional deficiency both directly in children or indirectly with lack of education of maternal. It is determined that nutritional deficiency has negative affects on immune system. This leads to emerge infectious diseases easily especially lethal diseases such as diarrhea and pneumonia. It is stated that infectious diseases are one of the important mortality reasons of neonates in the developing countries. In the conducted studies it is determined that infectious diseases in neonates (bacterial neonatal sepsis, acut diarrhea, acute lower respiratory infections etc) are related to poverty, emerge in developing countries and leads to mortality.

Learning Points Discussion

For he prevention of infectious diseases, negative affects of globalization should be considered, countries should have more comprehensive programs and health care providers should keep in contact.
PROCALCITONIN SEEMS TO BE BETTER THAN C REACTIVE PROTEIN DIAGNOSING BACTERIAL INFECTION, IN INFANTS WITH SEVERE BRONCHIOLITIS

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Background

Bronchiolitis is a common cause of Pediatric Intensive Care Unit (PICU) admission, because of the respiratory failure but also for the bacterial infection (BI) complication. The objective of the study was to describe the etiology of the BI in infants with severe bronchiolitis; and to define the procalcitonin (PCT) and C Reactive Protein (CRP) utility in order to diagnose this complication.

Methods

Prospective and observational study of infants who required PICU admission for severe bronchiolitis (September 2010-November 2016). The collected BI were sepsis, pneumonia and urinary tract infection (UTI). The applied severity score was the Bronchiolitis Score Severity of Sant Joan de Déu (BROSJOD). Statistical analysis was conducted by SPSS 20.0 program. Area under the curve (AUC) for PCT and CRP and cut of points were compared.

Results

705 infants recruited, 58.0% males, mean age 52 days, mean BROSJOD of 10 points. RSV was detected in 66.8%. An IB diagnosis was done in 32.2%: 22 sepsis, 54 pneumonias and 13 UTI. PCT values were significantly higher in BI cases compared with non-infected one, at admission and 48 hours, p= 0.032 and p= 0.048. CRP values were also higher in BI at admission. AUC for PCT was better than for CRP to diagnose BI, at two analyzed moments, p= 0.002 and p= 0.015 (optimal cut of value 1.5 ng/ml).

Conclusions

This study showed a relatively high frequency of BI in infants with severe bronchiolitis. The clinical diagnosis of BI is commonly completed with analytic parameters but sometimes these aren't especifics of bacterial complication. Biomarkers determination would improve the sensibility and specificity and PCT seems to be better than CRP for this purposes. It needs to be confirmed in other settings.
Acute bacterial meningitis remains a major health problem in children worldwide with higher mortality. This comprehensive study was executed to investigate the etiological profile and antimicrobial resistance patterns of bacterial isolates causing meningitis in admitted children in Bikaner, Northwestern India from January 2016 to December 2017.

Methods

A total of 209 children (≥29 days to ≤15 years age) were enrolled in the study with confirmed acute bacterial meningitis (defined as clinical meningeal syndrome and a positive bacterial agent isolated by cerebrospinal fluid culture (CSF) and/or positive CSF latex agglutination results). Isolated pathogens were identified using the Vitek-32 system. Gram stain results were used to guide subcultures and susceptibility testing. The antimicrobial susceptibility of isolates was determined using the disc diffusion method.

Results

Of the isolates, 52.8% were Gram-positive bacteria, and 47.2% were Gram-negative bacteria. *Streptococcus pneumoniae* (27.8%) was the most frequently isolated Gram-positive strain followed by *Staphylococcus epidermidis*, Group B Streptococcus, *Staphylococcus haemolyticus*, Group D Streptococcus and *Staphylococcus aureus*. Among the Gram-negative stains, *E. coli* (30.5%) was most frequently isolated followed by *Haemophilus influenzae* type b, *Klebsiella pneumonia* and *Pseudomonas aeruginosa*. Antimicrobial susceptibility tests indicated that for *E. coli* isolates, the susceptibility rates to aminoglycosides ranged from 66.8% to 100.0%; for cephalosporins ranged from 39.4% to 77.4%; and for piperacillin/tazobactam and imipenem were 93.3% and 100% respectively. Meanwhile, the susceptibility rates of *Streptococcus pneumoniae* isolates to penicillin G and ceftriaxone were 68.8% and 92.5% respectively. Gentamycin, ofloxacin, linezolid and vancomycin were identified as the most effective antibiotics for *Streptococcus pneumoniae*, each with susceptibility rates of 100%.

Conclusions

The emergence of resistant strains should be continuously monitored, and then provide reference for the selection of appropriate antibiotics.
STUDY OF OCULAR MANIFESTATIONS IN HIV/AIDS CHILDREN IN HIGHLY ACTIVE ANTI RETROVIRAL THERAPY (HAART) ERA FROM BIKANER, NORTHWESTERN INDIA

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Background

Human Immune deficiency Virus (HIV) has the capability to affect every organ system in the body. Ocular manifestations reflect systemic disease and may be the first sign of disseminated infection. This prospective study was executed to determine the spectrum of ocular manifestations in HIV positive children in Highly Active Anti Retroviral Therapy [HAART] era and to establish their correlation with CD4+T cells counts and stage of the disease.

Methods

This study enrolled 300 HIV positive children from February 2015 to December 2017. These children were evaluated, irrespective of the presence or absence of ocular symptoms and their treatment status. The ocular examination protocol included Visual Acuity [VA] Testing, color vision testing, ocular motility assessment, eye lid and adnexal examination, complete anterior and posterior segment examination.

Results

Ocular lesions were observed in 50.3% (151/300) children. Conjunctival microvasculopathy being the commonest finding seen in 9% (27/300) children followed by retinal microvasculopathy [7.3% (22/300)] and trichomegaly [6.3% (19/300)]. Herpes Zoster Ophthalmicus and Cytomegalovirus retinitis were observed in 1.33% and 1% children respectively. In this study 78.33% (235/300) children were on HAART. At the time of inclusion in the study, CD4+ cell counts ranged from 9 to 1838 cells/mm³ [mean±SD=375.6±249 cells/mm³]. In the study, 28 children had CD4+ cell counts ≤100/mm³, in whom 82.14% had ocular findings, while 71 children had CD4+ cell count ≥500/mm³ in whom only 35.21% children had ocular findings. The association between low CD4+ cell counts and ocular findings was statistically significant [p≤0.0001].

Conclusions

The pattern and severity of ocular manifestations was different than previous reports. Probably HAART has changed the pattern and severity of HIV related eye disease. Low CD4+ cell count and advanced stage of disease are the strong predictors of ocular involvement.

Clinical Trial Registration (Please input N/A if not registered)

N/A
Background

Infection is still the predominant cause of death in thalassaemic children after heart failure. Nonetheless, data relevant to the incidence and spectrum of the causal microorganisms are very limited, and do not reflect the long-term impact of modern treatment modalities. In this context, this prospective hospital based study revealed the incidence of infections causing hospitalisation and the role of potential risk factors for these infections.

Methods

A total 88 children with β-thalassaemia major and intermedia were followed for 4 years for all infections necessitating hospitalization. In most of them thalassaemia diagnosis was established by hemoglobin electrophoresis before the age of 2 years. Demographic and clinical information, with special emphasis on data related to infection, was collected. All infections were defined by the Centers for Disease Control and Prevention criteria.

Results

The overall adjusted rate of infection for the entire study group was 326 infections per 100 patient-years. The mean age at the time of infection was 5.9±2.6 years, with an increased incidence between the ages of 4 to 7 years. The distribution of infections were pneumonia (42.6%); pyrexia of unknown origin (19.2%); gastroenteritis (17.6%); upper respiratory infection included otitis media and sinusitis (14.2%); Urinary tract infection (10.1%); and Cellulitis (3.6%). Staphylococcus aureus was the major pathogen (28.4%) followed by Streptococcus pneumonia (18.7%), Klebsiella pneumonia (14.6%), Escherichia coli (9.9%) and other isolates. The infection rate in thalassaemia is affected mainly by the duration of the disease and is increased by splenectomy and, in the long term, by treatment with desferoxamine.

Conclusions

With current therapy and the resulting extended survival in thalassaemic children, more studies are needed in order to formulate up-to-date guidelines for prophylactic antibiotics and immune prophylaxis, adjusted for geographical differences.

Clinical Trial Registration (Please input N/A if not registered)

N/A
IMPACT OF ANTIMICROBIAL GUIDELINES ON ANTIBIOTIC UTILIZATION IN A CHILDREN'S HOSPITAL
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Background

Antimicrobial Stewardship Programmes (ASP) aim to optimize antimicrobial use. Point prevalence surveys (PPS) have been used in ASPs to characterize prevalence and indications of antimicrobials. As part of our ASP, empiric pediatric antimicrobial guidelines were implemented in our tertiary pediatric hospital in June 2013. We sought to evaluate the impact of these guidelines on antibiotic utilization and appropriateness in our hospital pre- and post- guideline implementation.

Methods

This was a retrospective point prevalence survey conducted in our hospital at 6 months pre- and post-guidelines implementation (2nd January 2013 and 2014). Details and indications of antibiotics prescribed in hospitalized paediatric patients were extracted from our hospital electronic records and classified in accordance to the different infective syndromes in our institution’s antibiotic guidelines. Appropriateness of antibiotics prescribed was evaluated if its indication was within the antibiotic guidelines. Patients receiving intra-operative and antibiotics for discharge were excluded.

Results

There were 244 and 212 paediatric inpatients on 2nd January 2013 and 2014, of which 150 (61.5%) and 108 (50.9%) were prescribed antibiotics respectively (p=0.019). There was a decrease in third-generation cephalosporins (16.4% vs. 9.3%, p=0.039) and an increase in β-lactam/β-lactamase inhibitor combinations (12.3% vs.14.5%, p=0.524). This was mainly attributed to the effects streamlining first-line empiric antibiotics. In addition, the increase in use of Piperacillin-Tazobactam was due to streamlining of first-line empiric antibiotics for febrile neutropenia to Piperacillin-Tazobactam. Pre-post guideline antibiotic appropriateness was 68.8% and 76.9% respectively.

Conclusions

This PPS provides an insight into antibiotic utilization in our institution pre- and post- antibiotic guidelines implementation and the impact of streamlining empiric antibiotic regimes. These findings and future PPS would be useful for identifying gaps in our institutional guidelines to inform future ASP initiatives.
PET HYPERMETABOLISM IN CHILDREN WITH EPILEPSY
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Background

Epilepsy is a chronic recurrent brain dysfunction syndrome. Clinical treatment on refractory epilepsy in children is more difficult. Preoperative precise positioning and the possible etiological factors of the refractory epilepsy is particularly important. The purpose of the study was to validate the children with epilepsy to investigate the possible etiological factors of F-18-FDG positron emission tomography (PET) hypermetabolism.

Methods

23 patients with childhood epilepsy of F-18-FDG PET cerebral brain studies for evidence of hypermetabolism were retrospectively reviewed. The metabolic abnormality, magnetic resonance imaging (MRI) findings and electroencephalography (EEG) were retrospectively reviewed, and the histopathology and surgical outcome of patients who underwent surgery were reviewed, respectively.

Results

PET hypermetabolism was identified in 23/396 (6%) of studies. Fourteen patients had seizures before or during their PET studies. Fourteen patients underwent surgery; in 9 patients, the site of resection was convergent with the region of PET hypermetabolism.

Conclusions

Regions of glucose hypermetabolism were observed most frequently in the frontal and parietal lobes, with or without hypometabolism. The hypermetabolism can occur during the ictal and interictal state. In the patients who underwent surgery, MCD is the most common histological type.
16C. SCIENCE: TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

PERFORMANCE OF GENOTYPIC AND PHENOTYPIC RESISTANCE TESTS IN THE DIAGNOSIS OF DRUG RESISTANT TUBERCULOSIS IN PEDIATRICS

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Background

Low organism burden compromises the yield of identifying children with drug-resistant tuberculosis (DR-TB). This study aimed to evaluate the rate of DR-TB cases and the diagnostic yield of diagnosis DR-TB by genotypic resistance testing in comparison to phenotypic resistance testing.

Methods

A retrospective study was conducted in children diagnosed with TB at the Department of Pediatrics, King Chulalongkorn Memorial Hospital. Phenotypic drug susceptibility testing (DST) was done using the mycobacterium growth indicator tube method. Genotypic DST was performed by Anyplex\textsuperscript{\textregistered} II MTB/MDR Detection of inhA, katG and rpoB.

Results

Between 2012 and 2016, 111 cases were diagnosed with TB. Median age at diagnosis (range) was 7 years (1 month – 20 years). Sites of infection included 32 (29%) pulmonary, 49 (44%) extrapulmonary and 30 (27%) both. Samples were sent for PCR (102 cases) and culture (103 cases). The yield of positive microbiologic tests was 29% for AFB smear, 45% for MTB PCR and 46% for mycobacterial culture.

Among the 57 cases of confirmed \textit{Mycobacterium tuberculosis} (\textit{Mtb}) by PCR and/or culture; 65% were diagnosed via both methods and 35% by either method. Any drug resistance was seen in 36% (95% CI 24-51) and 7% (95% CI 2-18) had rifampicin resistance. The yield of DR-TB by phenotypic DST was 38% (15/39) and genotypic DST was 37% (10/27). Among the 22 cases tested using both methods, isoniazid resistance was seen (5 cases katG, 2 cases inhA) as well as rifampicin resistance (2 cases). However, streptomycin (n=4) and pyrazinamide (n=1) resistance could only be
detected by phenotypic DST.

Table 1. Genotypic and phenotypic resistance tests for diagnosis of drug resistant tuberculosis in pediatrics

<table>
<thead>
<tr>
<th></th>
<th>Overall</th>
<th>Positive PCR</th>
<th>Positive culture</th>
<th>Both PCR and culture positive</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mycobacterium tuberculosis detection</strong></td>
<td>57/108 (53%)</td>
<td>47/103 (45%)</td>
<td>47/102 (45%)</td>
<td>37/97 (38%)</td>
</tr>
<tr>
<td><strong>DR-TB detection</strong></td>
<td>16/44 (36%)</td>
<td>10/27 (37%)</td>
<td>15/39 (38%)</td>
<td>8/22 (36%)</td>
</tr>
</tbody>
</table>

PCR: polymerase chain reaction; DST: drug sensitivity test; DRTB: drug-resistant tuberculosis

Conclusions

Utilizing PCR improved rates of confirmed MTB diagnosis. The yield of DR-TB detection by genotypic DST is similar to phenotypic DST.
01A. EDUCATION: PAEDIATRIC ANTIBIOTIC STEWARDSHIP

APPLICATION OF A DIAGNOSTIC AND THERAPEUTIC PROTOCOL OF BACTERIAL COINFECTIONS IN PATIENTS LESS THAN 6 MONTHS OF AGE WITH MODERATE TO SEVERE BRONCHIOLITIS

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Background

The use of antibiotics in bronchiolitis is controversial. Bacterial coinfection (BCi) increases mortality in these patients. Our aim is to describe the results of a diagnostic and therapeutic protocol of bacterial coinfection (BCi) in children less than 6 months of age with moderate to severe bronchiolitis admitted to the Paediatric Intensive Care Unit (PICU), as a part of our Paediatric Antibiotic Stewardship Program.

Methods

Epidemiological, clinical and microbiological data were collected from all successive cases of children less than 6 months with moderate to severe bronchiolitis (modified TAL score) admitted to our PICU between October 2016 and December 2017. Suspicion of BCi was defined as fever and/or compatible clinical or analytical features (procalcitonin (PCT) >0.5ng/dl). Seventy-six patients were included.

Results

Median age 41 days (ICR 28-73), 71% male. Sixty-eight patients had RSV infection. Fifty-nine (78%) received antibiotics (50% amoxicillin-clavulanate and 50% ampicillin plus cefotaxime). Lumbar puncture was performed in 12. BCi was confirmed in 13/59 (22%) by blood (1), urine (2) or tracheal aspirate (10) positive cultures. Protocol adherence was 76% for diagnosis and 85% for treatment. Median CRP and PCT values were 6,0mg/dl (4,0–10,0) and 1,5ng/dl (0,6–10,0) in confirmed BCi; 2,5mg/dl (0,9-4,5) and 0,8ng/dl (0,2-1,4) in suspected unconfirmed BCi; 0,9mg/dl (0,2-2,0) and 0,2ng/dl (0,1-0,2) in unsuspected BCi.

Conclusions

The use of a diagnostic and therapeutic protocol has allowed the detection of cases with higher risk for BCi, the optimization of antibiotic therapy and a decrease in the performance of invasive procedures (lumbar puncture) in a group of severely ill and especially susceptible to invasive bacterial infection patients.
A Case of Brucellosis Following Kidney Transplantation

Background

Brucellosis is one of the most common systemic zoonotic diseases transmitted by consumption of unpasteurized dairy products or by occupational contact with infected animals. Brucellosis is very rare in renal transplant recipients.

Case Presentation Summary

We report a 9-year-old Emirati girl who was diagnosed as brucellosis after her kidney transplantation surgery from her mother on Aug 23th 2017. The patient and her mother had a past history of consumption of raw camel milk with no direct contact with camels during May-June 2017. Her mother (donor) was diagnosed as brucellosis a month after donating her kidney to her daughter with the presentation of fever. After performing evaluation for etiology of possible infectious complications, blood culture grew Brucella melitensis. The mother was managed with doxycycline, rifampin, and ciprofloxacin. Two months following kidney transplantation surgery, the patient developed fever and blood culture grew Brucella melitensis. The patient was managed with oral doxycycline and rifampin for 6 weeks and recovered without complications.

Learning Points/Discussion

Although brucellosis very rare after kidney transplant, for both recipients and donors from endemic areas, it should be considered as it can mimic other infectious diseases.
**Interhemispheric abscess**

**Background**

Subdural abscess is defined as a purulent collection between dura-mater and arachnoids. It's an infrequent infection in Pediatrics, especially those situated at interhemispheric location.

**Case Presentation Summary**

14 years-old boy with 3-days-fever and headache. Neck stiffness and regular aspect. Blood analysis: Hb:11.2g/dl, leucocytes 8.42k/mcl (N: 89.5% and L: 4.4%) CRP of 25mg/dl and PCT: 59.71ng/ml. Spinal tap: glucose 63mg/dl; Proteins: 114.9mg/dl; RBC: 40cel /mcl; leukocytes 50cels /mcl.

Initially, was oriented as a meningitis, and ceftriaxone + vancomycin + steroids were started. Next day, empyemas on sagittal, frontal and lateral sides were observed on MR. Conservative treatment was done changing antibiotic to cloxacillin + ceftriaxone + metronidazole. After 48h, hemiparesis appeared and empyemas were drained. Bacterial culture and viral PCRs were negative.

Despite the good evolution and the decrease of CRP (3.35 mg/dl), new MR was done 2weeks after. It showed an increased size of the empyemas and a new interhemispheric one. Antibiotic was changed to meropenem and vancomycin.

Two weeks later, patient was improving till fever + itchy rash appeared. Red Man Syndrome was suspected. Antibiotics were changed to linezolid and meropenem. 24h after, lactic acidosis appeared with impairment of liver and kidney function, eosinophilia, headache and lethargy. Scan showed an increased interhemispheric empyma and edema. Dress syndrome and lactic acidosis were diagnosed. Abscess were re-drained and antibiotics were changed to levofloxacin and metronidazole.

Laboratory parameters and physical explorations were normalized. MR showed radiological improvement. After 10 days of treatment, he was discharged with Moxifloxacin as ambulatory treatment, completing 29days and recovering at all.

**Learning Points/Discussion**

Interhemispheric abscesses have a high morbidity-mortality. Treatment is a combination between antibiotic and surgery, requiring often, if the evolution isn't positive, the re-intervention, especially, if it's a complicated location.
16C. SCIENCE: TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

MYCOBACTERIUM BOVIS BCG OSTEOMYELITIS OF THE RIB: A RARE COMPLICATION PRESENTING YEARS AFTER IMMUNISATION

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Title of Case(s)

MYCOBACTERIUM BOVIS BCG OSTEOMYELITIS OF THE RIB: A RARE COMPLICATION PRESENTING YEARS AFTER IMMUNISATION

Background

Bacillus Calmette-Guérin (BCG) is one of the most commonly administered vaccines globally. BCG is used to prevent tuberculosis (TB) and contains live attenuated strains of \textit{Mycobacterium bovis}. In rare cases a distant complication such as osteomyelitis develops years after the immunisation. In countries where most children are non-BCG-vaccinated, diagnosis of these complications can be challenging. We present a case with BCG rib osteomyelitis.

Case Presentation Summary

A three-year-old Indian-born boy presented with a tender enlarging mass of the right lowest rib. Ultrasound imaging revealed an intramuscular tumour with central necrosis and led to a suspicion of sarcoma. A contrast-enhanced MRI showed a 3.7x2.4x2.8 cm mass in the rectus abdominis muscle. Abdominal MRI and thorax CT did not show signs of metastasis. Biopsy uncovered purulent material that was sent for further testing. PCR was positive for \textit{Mycobacterium tuberculosis} complex and histopathological examinations showed granulomatous inflammation. The boy had received BCG immunisation in India at infancy. The QuantiFERON-TB Gold Plus test was negative for TB and modified T-SPOT.TB test was highly reactive only to purified protein derivate stimulation. Hence, a BCG osteomyelitis was suspected and treatment with rifampin and isoniazid initiated. Further molecular methods identified the pathogen as \textit{Mycobacterium bovis} BCG with resistance to pyrazinamide confirming the diagnosis. In follow-up, the biopsy wound over the infected rib developed into a scrofuloderma that started healing well.

Learning Points/Discussion

BCG complications can develop years later and should be kept in mind when young immigrant children present with osteomyelitis. BCG strains have varying susceptibility to antituberculous drugs and reliable information on the worldwide use of different strains is important for choosing the correct regimen.
A 5 MONTH-OLD MALE INFANT WITH MULTIPLE SKIN AND LIVER ABSCESSSES DUE TO LEGIONELLA INFECTION

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Title of Case(s)
A 5 MONTH-OLD MALE INFANT WITH MULTIPLE SKIN AND LIVER ABSCESSSES DUE TO LEGIONELLA INFECTION

Background
Extrapulmonary legionella infections are rare and usually occur in immunocompromised hosts.

Case Presentation Summary
A 5 month-old male infant with history of recurrent oral thrush and candidiasis presented with multiple skin and liver abscesses. He was admitted for one month due to pneumonia and treated with intravenous meropenem and amikacin. Two weeks later, he developed multiple erythematous nodules with a high-grade fever and hepatomegaly. Chest radiography showed perihilar and left lower lung infiltrates. Abdominal computer tomography revealed several ring enhancing hypodense lesions, ranging between 0.5-1.9 cm in size in both hepatic lobes. Incision and drainage was done and cefazolin was given without improvement. Meropenem and vancomycin intravenous therapy was started. Gram stain of pus from skin abscesses revealed gram-negative rods with multiple polymorphonuclear leucocytes but aerobic culture was negative. DNA-based identification performed by partial 16S rRNA gene sequencing revealed *Legionella bozemanii* with 99.7% identity. The patient was also diagnosed with severe combined immunodeficiency (SCID) [CD4+ T cells 0 cells/mm³, low immunoglobulin]. Intravenous levofloxacin and immunoglobulin therapy were administered to the patient. He rapidly improved, becoming afebrile within 3 days and his abscesses healed within 2 weeks later. An abdominal ultrasound performed 3 weeks after levofloxacin therapy showed decreased size and number of lesions in both hepatic lobes. Levofloxacin was administered for a total of 19 weeks.

Learning Points/Discussion
- This case highlights the importance of considering infections caused by *Legionella spp.* where multiple skin and liver abscesses not improved by beta-lactam antibiotic therapy.
- Detection of *Legionella* DNA via PCR is a promising diagnostic technique.
- High index of suspicious for primary immunodeficiency should be kept in an unusual infection and/or severe manifestation.
Background

Our country has mandatory vaccination policy against the following diseases: tuberculosis, diphtheria, tetanus, pertussis, poliomyelitis, measles, parotitis (mumps), rubeola, hepatitis B and hemophilus influenza tip B. Polyvalent vaccines, hexavalent and pentavalent, were implemented for the first time in August 2015.

The aim of the study is to evaluate the vaccination coverage of preschool children before and after introducing polyvalent vaccine in Municipality of Bitola.

Methods

The survey was conducted in the Office for preventive health care of preschool children in Bitola. In retrospective epidemiological study the vaccination data were analyzed in the period of 2011 to 2017.

Results

Since 2015 the vaccination coverage rates increased.

- The coverage with the HB vaccine increased from 98% (2015) to 99.2% of children.
- Primary-vaccination against HiB in 2015 covered 93.3-99% of children, re-vaccination covered 89.7-99% (2015) and the coverage range of polyvalent vaccines was 98.3-99%.
- Primary-vaccination against DTP covered 91.1-98.3% (2015) while 98.3-98.7% of children were covered with polyvalent vaccine. Re-vaccination covered 97-99% (2015) of children while 98-99% were covered by polyvalent vaccines.
- OPV primary-vaccination coverage range was 91.1-98.7% (2015) while polyvalent vaccine's coverage range was 97.7-98.7%. Re-vaccination covered 98.5-99% (2015) of children i.e 98-99% after 2015.
- Only the coverage range of the vaccine against MMR has continuously decreased since 2011 (99.9%) but still, it is over 95%.

Conclusions

In Macedonia the implementation of multivalent vaccines increased the immunization coverage. The benefits for the parents are reduced number of visits to the doctor, less stressful conditions and side effects and increased trust in the quality and positive effects of the vaccination.
Molecular Epidemiology of Bordetella Pertussis in Iran from March 2015 to January 2018

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Background

Whooping cough is a contagious, acute respiratory illness of humans that is caused by the gram-negative bacteria Bordetella pertussis. Although pertussis is controlled by extensive vaccination programs, it is evident that the disease is re-emerging even in countries with high vaccination coverage. According to the WHO report, the diphtheria toxoid, tetanus toxoid and pertussis (DTP) vaccine coverage is estimated to be greater than 96% in Iran since the year 2000. In this study, we used PFGE to characterize B. Pertussis strains were isolated from pertussis patients and an investigation of pertussis toxin (PTX) and pertussis toxin promoter.

Methods

We studied 50 B. pertussis isolates collected in different provinces of Iran from patients and send to Pertussis Reference Laboratory, Institute Pasteur of Tehran, Iran between March 2015 - January 2018. Tohama I (ATCC BAA-589) as reference strain and two vaccine strains used in this study were Bp509 and Bp134. Information on age, gender and vaccination was available. Pertussis strains were confirmed by biochemical tests and molecular confirmation by specific primers targeting insertion sequence 481 (IS481), 100 (IS1002). PFGE-profiles were determined using a method based on single XbaI digest of the DNA.

Results

Among 50 patients, their age distribution were 31 case under 1 year, 13 case between 1-5 years and 6 case over 10 years old. The 50 isolates produced 17 distinct PFGE profiles, one PFGE profile IRII was dominant (45%) and representative ptxP3/ptxA1.

Conclusions

In Iran, pertussis remains an endemic infection. In recent years we had only the increasing incidence of infection in 2012 and 2013 with 1329 and 1415 cases. We found that our dominant cluster like Swedish dominant cluster (BpSR11) and ptx, ptxP allele are responsible for the clinical features of pertussis disease, our dominant cluster with ptxP3 have higher capacity to transfer between children and pathogenicity.
The Infectious Disease/Microbiology ward rounds at Great Ormond Street Hospital (GOSH) offer advice to the teams on the Intensive Care Units (ICUs) regarding antimicrobials and investigations that would be useful for patient management. Prendergast et al (2008) previously conducted an audit at GOSH finding that 82% of recommendations on these ward rounds were adhered to. This is an audit following that completed in 2008.

Methods

9 ICU ward rounds were audited and the recommendations were recorded. A total of 63 recommendations were given for 34 patients during the audit. The recommendations were placed into one of 3 categories: starting an antimicrobial, stopping an antimicrobial and ordering investigations. The careview system was accessed at a later date (mean 4.5 days) to assess whether recommendations had been followed.

Results

The ward round advised starting a total of 12 antibiotics, stopping a total of 23 antibiotics and recommended 25 investigations. 3 of the recommendations could not be followed up in the time period of the audit. 91.7% of the recommended antibiotics were started and 87.0% of the antibiotics were stopped appropriately but only 60.0% of the recommended investigations were ordered. In total 76.7% of the 60 recommendations were followed.

Conclusions

Despite the small sample size, results indicate that the ICUs follow recommendations relating to antimicrobials well, with some scope for improvement. However, planned investigations are not always completed. There could be valid reasons for uncompleted investigations: including the instability of the child or prioritisation of alternative investigations based on clinical need and availability of samples. Next steps will be to work with a newly implemented antimicrobial stewardship programme to implement new strategies to improve practice and re-audit.
EXOME SEQUENCING REVEALS NEW CANDIDATE GENES IN HOST GENOMIC SUSCEPTIBILITY TO RESPIRATORY SYNCYTIAL VIRUS DISEASE

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Background

Respiratory syncytial virus (RSV) is an important cause of serious lower respiratory tract disease in infants. Several studies have shown evidence pointing to the genome of the host as an important factor determining susceptibility to respiratory disease caused by RSV.

Methods

The complete exomes of 54 patients infected by RSV that needed hospitalization due to development of severe bronchiolitis was sequenced. The Iberian sample (IBS) from The 1000 Genomes Project (1000G) was used as control group.

Results

The study points to SNP rs199665292 in the olfactory receptor gene OR13C5 as the best candidate variant ($P$-value = $1.16 \times 10^{-12}$; OR = 5.56). Genetic variants at HLA genes ($HLA$-DQA1, $HLA$-DPB1), and in the mucin 4 gene ($MUC4$) also emerge as susceptibility candidates. By collapsing rare variants in genes and weighing by pathogenicity, we obtained confirmatory signals of association in the olfactory receptor gene OR8U1/OR8U8, the taste receptor TAS2R19, and another mucin gene
Conclusions

The associations observed between RSV patients and olfactory and taste receptors are of special interest; and this finding is in line with recent evidence pointing to their role in viral infectious diseases.

Clinical Trial Registration (Please input N/A if not registered)

N/A
12A. SCIENCE: NON-INVASIVE GASTROINTESTINAL AND MUCOSAL INFECTIONS

CHANGES OF THE INCIDENCE AND ETIOLOGY OF ACUTE GASTROENTERITIS AFTER THE INTRODUCTION OF ROTAVIRUS VACCINE IN STOCKHOLM, SWEDEN

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Background

In Stockholm vaccination against rotavirus began in 2014. In this survey, we investigated changes in admission rates, etiology, age and characteristics for children 0-4 years of age admitted for gastroenteritis in our catchment area during eight seasons 2008-2016.

Methods

We included patients with a clinical diagnosis of gastroenteritis. Stool examinations for viruses were obtained in 80%. The frequency of underlying disease was about 26% for children infected with rotavirus and 39% for children infected with other viruses.

Results

The admission rate roughly halved over the study period (figure). The reduction mainly corresponded to fewer rotavirus infections. There was no increase in other viruses. The median age of children infected with rotavirus increased from 13.7 to 18.5 months after vaccination was introduced. Interestingly, there were also fewer children aged 2-4 admitted. 8% of the children with rotavirus and 6% with other viruses developed a complication. Children infected with both noro- and rotavirus (5% of tested children) did not have a more severe disease than those with a single infection.
Conclusions

Rotavirus vaccination reduced the number of children admitted for gastroenteritis. No replacement with other viruses was observed. There was a trend of reduced numbers of admitted children even before vaccination was started and also in older children not covered by the vaccination program.
Background

Despite several immunization efforts, China saw a resurgence of measles in 2012. It probably due to a change of measles epidemiology over time, particularly before and after the provincial supplementary immunization activities (SIAs). In addition, monitoring of age-specific transmissibility should be conducted for planning adequate disease control strategies.

Methods

Totally 22,362 clinically and laboratory confirmed measles cases from 2009 to 2016 were extracted from the National Infectious Disease Monitoring Information System (Guangdong Province, southern China). The changes on epidemiological characteristics between the 2009-11 and 2012-16, as marked by the end of province-wide SIA and start of resurgences were compared. Reproduction numbers ($R_s$) were estimated for different age groups.

Results

Children cases, especially for infants aged 0-8 months had replaced the 7-25 years old in having most measles cases during the resurgence after 2012 ($p<0.01$). Compared to the 2011 level of 32 cases (10.3% of all cases), the number of cases among infants of 0-8 months old surged to 2306 (32.8% of all cases) in 2013 and decreased back to 333 (26.3%) in 2016. The major driving force of the outbreak was children aged 0–6 years (peak $R$ values $>1$). Nevertheless, adult cases had an increasing proportion over years in Guangdong and replaced the 0-8 months old infants in being the highest-incidence group in 2016 (28.7% of all cases). Adults aged 26–45 years demonstrated the highest transmission (peak $R$ of 1.24 and 1.20 in 2014 and 2015, respectively).

Conclusions

Although Guangdong province has implemented province-wide routine immunization, we showed that the benefits of the SIAs were short-lived. Disease control strategies should target children and adult groups that carry high potential for measles transmission.
MICROBIOLOGICAL FINDINGS IN CHILDREN WITH KAWASAKI DISEASE. RESULTS OF A NATIONAL STUDY (KAWA-RACE 2011-2016)


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13 Hospital Clínico Universitario Lozano Blesa, Pediatrics, Zaragoza, Spain
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Background

Kawasaki disease (KD) is a multisystem vasculitis associated with coronary artery abnormalities in children. The relationship between infection and KD is still unclear.

Methods

Retrospective study performed within the KAWA-RACE network (2011-2016). We analysed patients with positive microbiological findings (PMF) and those with a previous recent infection (PRI) during the 4 weeks preceding KD.

Results

A total of 621 children with KD were included. PMF was found in 101 (16%) patients and PRI in 107 (17%). We found significant less cardiac abnormalities in the group with PRI when compared to those without PRI, yet no differences in the group with a PMF. We found a significant higher ESR level in the PMF group (82 vs 72 mm/h) (table1). Throat infection was the most common proven acute infection
Conclusions

Clinical presentation of most childhood infections may overlap with KD diagnostic criteria making diagnosis challenging. We found a lower incidence of cardiac abnormalities in the group with a PRI meaning that KD may be overdiagnosed and overtreated, but this practice seems justified because of the risk of developing CAA. A positive microbiological result should not rule out KD and should not delay treatment if KD is highly suspected.
PAEDIATRIC INVASIVE PNEUMOCOCCAL DISEASE- 5 YEAR RETROSPECTIVE ANALYSIS OF SEROTYPES AND ANTIMICROBIAL SUSCEPTIBILITIES AT A SCOTTISH TERTIARY REFERRAL HOSPITAL

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Background

Invasive pneumococcal disease (IPD) remains an important cause of morbidity and mortality worldwide. In the UK the 13-valent pneumococcal conjugate vaccine (PCV 13) was introduced in 2010 as part of the NHS childhood vaccination programme. Despite vaccination invasive disease still occurs and early detection with prompt management including appropriate antibiotics is required.

Methods

Retrospective analysis of laboratory electronic records for 5 years, 01/01/13-31/12/17. Data retrieved from Clinical Portal and Telepath systems included age, sex, date of specimen, specimen type, and serotype of invasive Streptococcus pneumoniae. Isolates sent to the Scottish Haemophilus, Legionella, Meningococcus and Pneumococcus Reference Laboratory (SHLMPRL) analysed for serotype, MLST and antimicrobial sensitivities; data then cross referred with patient data.

Results

A total of 40 IPD episodes were recorded: 33 (82.5%) bacteraemias, 6 (15%) cerebrospinal fluids (CSFs), one (2.5%) pleural fluid. There was no temporal pattern detected nor serotype commonality. Children aged ≤5 accounted for 27 (67.5%) cases, with overall sex ratio 21 males: 19 females. Eleven (27.5%) IPD episodes were caused by serotypes contained in 13-valent PCV whereas 33 (82.5%) were caused by serotypes contained in 23-valent PPV. All isolates had penicillin MIC<2 mg/L (within EUCAST non-meningitis values) and two had MIC 0.25mg/L, outwith EUCAST values for meningitis. Both were bacteraemias caused by serotypes not found in any pneumococcal vaccines

Conclusions

This review confirmed that the burden of IPD occurs in those aged ≤5 and predominantly by serotypes not contained in PCV 13. Reasons for IPD due to serotypes present in PCV 13 include failure to receive vaccine, or failure to mount adequate immune response. Ongoing surveillance of serotypes and antimicrobial susceptibilities is required both locally and nationally to ensure appropriate vaccine serotype coverage and vigilance concerning emerging antimicrobial resistance.
Background

Blood stream infection (BSI) is an important cause of morbidity and mortality in pediatric patients. Prompt and appropriate antimicrobial therapy can make the difference between cure and death or disability. Emergence of antimicrobial resistance, particularly methicillin resistance, in *S. epidermidis* is a serious problem. The aim of our study was to evaluate the causative agents of BSIs and antimicrobial susceptibility patterns of *S.epidermidis* strains, retrospectively.

Methods

Blood samples were collected from neonatal intensive care unit and pediatric services of Okan University Hospital from January-December 2017. Samples were evaluated with BacT / ALERT (Biomérieux, France) blood culture system. Catalase and coagulase tests (Plasmatec, England) were initially performed for the isolates associated with bacteremia. Vitek 2 Compact (Biomérieux, France) system was used to identify coagulase negative staphylococci and to determine their susceptibility to antimicrobials.

Results

Out of 398 blood samples, growth was detected in 47 (11.8%). 42 (89.4%) samples were considered to be associated with bacteremia, and 5 (10.6%) as contamination. The most frequently isolated microorganism was *S.epidermidis* (64.3%), followed by Candida spp. (11.9%). All *S.epidermidis* isolates were identified as MRSE and 37% were samples sent from Neonatal Intensive Care Unit. Resistance rates of *S.epidermidis* strains to other antibiotics were as follows; erythromycin 85.2% , inducible clindamycin 92.6% , clindamycin 85.2% trimethoprim / sulfoxethoxazole 85.2% phosphomycin 92.6% and fusidic acid 96.3%.

Conclusions

Rapid initiation of antimicrobial therapy is of high importance in bloodstream infections. Knowing the frequencies and susceptibility patterns of common microbial pathogens is crucial for selecting appropriate empiric therapy or prophylaxis. In our study high prevalence of methicillin and multi-drug resistance in *S.epidermidis* strains isolated from pediatric patients, emphasized the importance of continuous screening for antibiotic resistance in pediatric care units.
INDIRECT IMPACT OF PNEUMOCOCCAL CONJUGATE VACCINATION AGAINST INVASIVE PNEUMOCOCCAL DISEASE IN THE NETHERLANDS IN OLDER ADULTS

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Background

The 7-valent pneumococcal conjugate vaccine (PCV7) was introduced in the Dutch National Immunization Program in 2006 and replaced by PCV10 in 2011. We evaluated the impact of PCV7/10 in 2016-2017 on invasive pneumococcal disease (IPD) in older adults.

Methods

We used Streptococcus pneumoniae isolates from cases with IPD that were submitted to the Netherlands Reference Laboratory for Bacterial Meningitis for serotyping by nine sentinel laboratories, covering 25% of the Dutch population. We compared (serotype-specific) IPD incidence in the last epidemiological year (June 2016-May 2017) to the pre-PCV7 period (June 2004-May 2006) and pre-PCV10 period (June 2009-May 2011) in 50-64 year olds and 65+ year olds.

Results

In 50-64 year olds, no significant change in IPD incidence was observed in 2016-2017 (16.4/100,000) compared with pre-PCV7 (17.9/100,000). In 65+ year olds, IPD incidence decreased significantly in 2016-2017 (51.1/100,000) compared with pre-PCV7 (62.7/100,000), but not compared with pre-PCV10 (49.2/100,000). PCV10-specific IPD incidence decreased significantly from 5.0/100,000 pre-PCV10 to 1.3/100,000 in 2016-2017 in 50-64 year olds and from 9.0/100,000 to 2.7/100,000 in 65+ year olds. Non-PCV10-type IPD incidence increased significantly from 7.2/100,000 pre-PCV7 to 15.1/100,000 in 2016-2017 in 50-64 year olds and from 22.6/100,000 to 45.5/100,000 in 65+ year olds. PCV13-specific IPD incidence (including 19A) did not increase significantly in 2016-2017 compared with pre-PCV10 (4.0/100,000 vs. 3.1/100,000 in 50-64 year olds, 10.9/100,000 vs. 9.6/100,000 in 65+ year olds).

Conclusions

Introduction of PCV7 and PCV10 has had a limited impact on the burden of IPD in older adults due to replacement by non-vaccine serotypes. Continuous surveillance is warranted to monitor IPD disease burden and to estimate the potential impact of future vaccines.
INCIDENCE OF TUBERCULOSIS INFECTION IN CHILDREN TRAVELLING TO COUNTRIES WITH HIGH PREVALENCE OF TUBERCULOSIS (PRELIMINARY RESULTS)

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Background

children residing in low-incidence countries of tuberculosis (TB) travelling abroad to endemic TB regions for visiting friends and relatives (VFR) are at risk of latent TB infection (LTBI). The identification of risk factors associated with TB infection would allow us to improve screening programmes pre-post travel. The aim of this study was to determine the incidence and risk factors associated with LTBI in VFR children travelling to countries with high-incidence of TB.

Methods

a multicentric prospective cohort study is being developed since 2017, including different health-care levels, of a cohort of VFR children <15-year-old travelling to high-incidence TB countries of >50 cases/10⁵ inhabitants. Children were screened before travelling with a tuberculin skin test (TST), LTBI was defined as a TST conversion and/or a positive QuantiFERON-TB Plus® (QFT) performed after the trip. Statistical analysis was carried out through Stata®v13. Ethical approval was obtained from all the participating centres.
Results
two-hundred sixty-four children were recruited, 252 analysed (12 not TST-screened). Median[IQR] age was 5.83[2.84-9.02] years; 50.8% female; 86.7% autochthonous; 4.8% BCG-vaccinated; 41.3%(104/252) travelled to Africa, 36.9%(93/252) to Asia, 20.6%(52/252) to America/Caribbean, and 1.2%(3/252) to Eastern Europe. Median[IQR] travel duration was 1.3[1.0-1.8] months. TST was performed at a median[IQR] of 16[7-22] days before departure's date; 4/252(1.6%; 95%CI:0.6-4.2%) were TST positive: 3/252(1.2%; 95%CI:0.4-3.6%) LTBI, and 1/252(0.4%) because of BCG vaccination. Among 187 children visited after travelling, TST and/or QFT were performed in 74.9%(95%CI:68.1-80.6%) of them at a median[IQR] of 74[53-95] days, and no LTBI were detected due to travel itself.

Conclusions
no LTBI cases were detected after travelling in these preliminary results. However, 3 children with LTBI (1.2%, 95%CI:0.4-3.6%) were diagnosed before the trip, two previously visited high-incidence TB countries. VFR children could be a high-risk group for LTBI and should be screened.

Clinical Trial Registration (Please input N/A if not registered)
N/A
TRENDS IN ANTIMICROBIAL RESISTANCE OF URINARY TRACT PATHOGENS IN CHILDREN IN CRETE, GREECE: A SINGLE CENTRE EXPERIENCE

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Background

Urinary tract infection (UTI) constitutes a common cause of antibiotic use in childhood. Nowadays, there is a growing concern about increasing resistance to antibiotics and emergence of extended spectrum beta lactamase (ESBL) producing uropathogens. The aim of the present study was to report the most common UTI pathogens and their antimicrobial resistance patterns among children in Crete and compare the results in the region with those reported ten years ago.

Methods

This 5-year (2012-2016) retrospective study records the uropathogens and their susceptibility patterns among children 30 days to 16 years old, who were discharged with the diagnosis of UTI from a District General Hospital in Crete. After identification of the bacteria, resistance patterns and presence of extended spectrum beta lactamases (ESBLs) were detected.

Results

UTI was diagnosed in 284 children (62.0% female; mean age 26 months). The occurrence rates of isolated pathogens were: *Escherichia coli* (E. coli) 75.4%, *Klebsiella spp* 9.15%, *Proteus spp* 5.29% and *Enterobacter spp* 3.87%. Antimicrobial resistance of *E. coli* was most common to piperacillin (38.9%), ampicillin (30.3%), trimethoprim-sulfamethoxazole (TMP-SMX) (16.4%) and ampicillin/sulbactam (13.3%). 4.20% of *E. coli* strains were ESBL-producing. Interestingly, a significant decrease in *E. coli* resistance to ampicillin and TMP-SMX was observed compared to the previous study. Resistance to ampicillin, TMP-SMX and piperacillin was noted for 46.4%, 16.9% and 46.5% of the total uropathogens, respectively, making these agents inappropriate for empirical treatment of febrile UTI in our region. On the other hand, more than 94% of microorganisms were susceptible to cefuroxime, ceftriaxone/cefotaxime and piperacillin/tazobactam, which seem to be effective for treatment of paediatric UTIs.

Conclusions

The antibiotic resistance, although decreasing, is still high in hospitalized children with UTIs in the study area.

Clinical Trial Registration (Please input N/A if not registered)

N/A
Background

“Fever without source” (FWS) is a common diagnostic challenge in infancy. However, few infants with FWS have a serious bacterial infection (SBI) and most non-toxic appearing can be managed using low risk laboratory and clinical criteria.

Objectives: To analyze our management approach of FWS in infancy over a ten-year study period.

Methods

This was a retrospective registry-based cohort study of the management of all infants 30-90 days with FWS admitted in the paediatric department over the 10-year study period (January 2008-December 2017). The infants considered as low risk for SBI were those fulfilling the ‘Rochester criteria’: 1) appeared well; 2) were previously healthy; 3) had no focal infection; 4) had white blood cell (WBC) count 5.0-15.0 x 10^9 cells/L, band form count ≤ 1.5 x 10^9 cells/L, ≤10 WBC per high power field (HPF) on microscopic examination of spin urine sediment, and ≤5 WBC per HPF on microscopic examination of a stool smear (if diarrhea).

Results

Of the 219 infants (46.6% male) enrolled in the study, 193/219 (88.1%) were well appearing and 145/219 (66.2%) met all low risk criteria. 193/219 (88.1%) received intravenous antibiotics, with third generation cephalosporins being by far the most frequently administered antibiotics (98.4%). Among the infants that met the low-risk criteria, the high majority (93.8%) underwent complete sepsis evaluation, including a lumbar puncture and 84.8% of them were treated with intravenous antibiotics. The management decision was not significantly affected by the gender, age, previous NICU admission or vaccination status.

Conclusions

Our results reveal the need to reinforce medical education in order to avoid inappropriate use of antibiotics in low risk infants with FWS, given that antibiotic resistance is a growing public health concern worldwide.
Title of Case(s)

Title: Diphtheria: down but not out yet!

Background

We report a case of severe tonsilopharyngeal diphtheria in an unimmunised Indian child which was complicated by renal failure, myocarditis, palatal palsy and polyneuropathy.

Case Presentation Summary

An 11-year old unimmunized boy presented with gradually progressive dysphagia and noisy breathing for last 5 days. On examination, the child had bull neck, stridor, and bilateral grade II tonsillar hypertrophy with overlying grayish white membrane which bled to touch. His Albert stain and throat swab culture for Corynebacterium diphtheriae was negative. Blood investigations revealed acute kidney injury (AKI). During the second week of hospitalisation, he developed hypotension, tachycardia and grade II systolic murmur consistent with myocarditis which was confirmed by Creatine phosphokinase-MB levels, electrocardiogram and 2-D echocardiography. Two weeks post admission, he developed dysarthria, nasal twang of voice along with nasal regurgitation of liquids suggestive of palatal palsy. At 4 weeks, the child developed bilateral lateral gaze palsy along with paralysis of accommodation and diplopia. His clinical course is detailed in Fig. 1.

Given his clinical presentation and unimmunised status, we considered the possibility of tonsilopharyngeal diphtheria. One lakh units of diphtheria anti-toxin and erythromycin was given for 14 days after which his bull neck, stridor amd pseudomembrane resolved. His worsening AKI required hemodialysis and hypotension necessitated the use of vasopressors. He was started on tube feeds in view of palatal palsy. His condition improved and presently at 7 weeks he is accepting orally and is kept under observation for onset of any muscle weakness.

Learning Points/Discussion
As *Corynebacterium diphtheria* is a fastidious organism, it is imperative that even in the absence of culture negativity, prompt treatment with diphtheria antitoxin and antibiotics should be initiated in suspected cases.
MANDATORY VACCINATIONS IN EUROPEAN COUNTRIES AND THE FAKE NEWS

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2USL, Vaccine Department, Benevento, Italy

Background

High rates of vaccination coverage in childhood are important to prevent infectious diseases. Lack of information and fake news are actually recognised among the main factors contributing to low immunization coverage. Enforcing mandatory vaccinations is one of the strategies that some countries adopted and others are considering in order to face this issue. Recently, compulsory vaccination has been introduced in Italy. People who had been asked to vaccinate their children have often been scared by fake news and by the false information that Italy is the only one country with mandatory vaccination policy.

Aim of the study is confronting vaccination policies in children under 12 months against diphtheria, tetanus, pertussis, hepatitis B, poliovirus and Haemophilus influenzae type b among different European countries.

Methods

Information on policies of mandatory or recommended vaccinations were gathered by ECDC and were taken from the official website (https://vaccine-schedule.ecdc.europa.eu/)

Results

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Conclusions
Not only in Italy, some vaccinations are mandatory in childhood. Other countries adopted the compulsory policies in order to prevent the spread of infectious diseases.
Title of Case(s)

This can’t just be RSV! A miliary tuberculosis case

Background

Miliary tuberculosis is rare in industrialized countries and in vaccinated populations. It results from a massive lymphohematogenous dissemination of Mycobacterium tuberculosis and it can have variable and nonspecific clinical manifestations.

In 2016 Portugal fulfilled the WHO/UNICEF criteria to be considered a low-risk country for tuberculosis and switched from a BCG universal vaccination to a risk group strategy. Case Presentation Summary

GMMF, a 3 month-old boy of gipsy ethnicity, was hospitalized with a hypoxemic RSV acute bronchiolitis. His clinical condition deteriorated and he was sent to an intensive care unit (PICU) for mechanical invasive ventilation. On day seven he returned to the ward. Two days later, his clinical condition worsened and he was transferred to our PICU. The chest radiograph showed bi-apical opacities. Despite ventilatory support, he maintained hypoxemia, weight loss, diarrhea, neurologic abnormalities (poor visual behavior, irritability), and hyponatremia.

A Chest CT revealed apical lobes consolidation, several nodular and cystic formations and enlarged mediastinal lymph nodes. Mycobacterium tuberculosis complex was isolated (PCR and culture) in a bronchial sample; meningeal involvement was confirmed (CSF low glucose, high protein and pleocytosis). Anti-TB therapy was immediately started (INH+RIF+ETB+PZN) and Prednisone with a favorable evolution. The family was screened. His grandmother has a longstanding cough, being the probable source; she refuses screening, as there are prejudices against TB in her community.
Learning Points/Discussion

Miliary TB is fatal if untreated and early initiation of specific anti-TB treatment can be lifesaving. Since vaccination strategy changed in 2017 in Portugal, it is essential that risk groups are correctly identified and vaccinated shortly after birth, as it should have happened with this infant. Screening of contacts must be done thoroughly, despite existing prejudices against this disease.
CEFTRIAXONE-RELATED BILIARY OBSTRUCTION: NOT SO BENIGN AFTER ALL

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Title of Case(s)

CEFTRIAXONE-RELATED BILIARY OBSTRUCTION: NOT SO BENIGN AFTER ALL

Background

Ceftriaxone is known to cause benign self-resolving biliary pseudolithiasis in up to 43% of children. This is rarely clinically significant. We present a child with Pott’s puffy tumour who developed symptomatic ceftriaxone-related gallstones >1 month after ceftriaxone discontinuation, requiring surgical intervention.

Case Presentation Summary

A 9-year-old boy with chronic atopy presented with 9 days of fever, headache, and a progressively enlarging, tender forehead swelling. CT and MRI imaging showed frontal sinusitis with frontal bone osteomyelitis and adjacent epidural collection. Pott’s puffy tumour was diagnosed. He underwent functional endoscopic sinus surgery; cultures grew *Streptococcus anginosus*. He completed 6 weeks of ceftriaxone 82mg/kg/day with improvement in radiological findings and inflammatory markers. Over 6 weeks, liver biochemistry done weekly was unremarkable. He recovered uneventfully.

5 weeks later, he presented with epigastric pain and vomiting. Blood investigations showed conjugated hyperbilirubinemia (total bilirubin 36 µmol/L, conjugated bilirubin 23 µmol/L) with transaminitis (ALT 300 U/L, AST 94 U/L, ALP 288 U/L, LDH 319 U/L, GGT 235 U/L). Ultrasound revealed multiple gallstones in the gallbladder and a gallstone in the common bile duct with mild prominence of the upstream biliary tree. Choledocholithiasis was diagnosed. He had no other risk factors for gallstone formation.

He remained symptomatic despite fasting and analgesia. He underwent endoscopic retrograde cholangiopancreatography to remove the obstructing gallstone. Abdominal pain and liver biochemistry resolved after 2 weeks.

Learning Points/Discussion

Ceftriaxone-related biliary pseudolithiasis typically occurs up to 14 days after initiating ceftriaxone and is reversible within 2 weeks of antibiotic cessation. Risk factors include young age and high ceftriaxone doses. We highlight a case of late-onset ceftriaxone-related gallstones requiring surgical removal. Clinicians should be vigilant for this complication even after cessation of therapy.

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Background

Purpose of this study is to review trends in vertical HIV transmission over a thirty-year period at our centre. We retrospectively analysed epidemiological and clinical data (including pregnancy, childbirth, mother and first-degree relatives information) of all children born from HIV-positive women at the Parma Children's Hospital between 1984 and 2017.

Methods

A total of 230 patients were included and divided into two groups according to perinatal HIV prevention strategies. Outcomes of 149 children (group-A) born between January 2004 and April 2017 were compared with those of 81 children (group-B) born between 1984 and 2003.

Results

Considering maternal outcomes, sexual transmission was the way of infection for 73% of women from group-A as compared to only 35% in group-B. The HAART therapy scheme was adopted for 56% of women among group-A. Conversely, this treatment had been provided to group-B mothers in only 14% of cases, whereas majority of them were being receiving single-drug therapy during pregnancy. ZDV was administered for prophylaxis in 87% of neonates from 2004 onwards, while only 56% of children from group-B benefited from the same treatment. The overall vertical transmission rate was 8 (group-A: 2; group-B: 6).

Conclusions

The development of personalized prevention strategies (including caesarean section, artificial feeding, neonatal prophylaxis with ZDV) correlates with a transmission rate of less than 1%, which is in line with other reports in the literature. The study support the use of a combination of prevention measures, preconception counselling, assistance to HIV-positive couples and access to treatment for all infected women in order to ensure a high level of protection against HIV vertical transmission in pregnant women.
Background

Hyperbilirubinemia is a well described side effect of piperacillin in adults. In our NICU we changed second line antibiotic treatment from Vancomycin and Amikacin to piperacillin-tazobactam due to the insurgence of aminoglycoside-resistant Pseudomonas strains.

Case Presentation Summary

A male term neonate born by vacuum extraction after prolonged labor needed mask ventilation followed by nCPAP. Clinical findings and chest x-ray were consistent with meconium aspiration syndrome. After intubation and surfactant administration first line antibiotics were started. The baby was extubated on day 5 and needed nasal CPAP until day 7. Since on day 10 the infant was still tachypnoeic and inflammation markers increased, antibiotic therapy was switched to piperacillin-tazobactam. On day 13 stools were hypocholic, direct bilirubin was 4.91mg/dl (total 5.88mg/dl), gGt 359 U/L, AST and ALT in normal range. Ultrasound scan showed signs of cholestasis. After withdrawal of piperacillin-tazobactam, direct bilirubin returned to near normal values, ultrasound scan was normal. Liver function tests after discharge were within the normal range.

Learning Points/Discussion

In adults, this side effect occurs in about 1-5%. We found only one controlled study in neonates, which did not report safety data. The largest case series of 353 consecutive neonates with sepsis did not report any altered liver function. Another case series of preterm infants did not report high direct bilirubin.

Resistance to antibiotics is a problem in NICUs. Direct hyperbilirubinemia after piperacillin is surprisingly not described in the case series analyzed, although one would expect it more common in neonates. More safety data for antibiotics in neonates are urgently needed.
13A. SCIENCE: PUBLIC HEALTH | EPIDEMIOLOGY

DIPHTHERIA OUTBREAK IN EAST JAVA, INDONESIA 2011-2015: IS THERE ANY DIFFERENCE RISK FACTORS BETWEEN CARRIERS AND CASES?

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¹Dr Soetomo Hospital, Child Health Department, Surabaya, Indonesia

Background

The re-emerged of diphtheria cases in East Java, Indonesia counted about 3000 cases during 2011-2015 developed a thought to find out the risk factors for this outbreaks. Whether a carrier has a role or not for this outbreak has never been evaluated. We analyzed the differences of risk factors between carriers and cases in children with confirmed positive culture of toxigenic Corynebacterium diphtheria strain from throat swab.

Methods

An observational cross sectional study was conducted. We retrieved data of diphtheria patients and their close contact from Health office and East Java Regional Centre of Laboratory during outbreak 2011-2015. Carrier defined as person with positive throat swab culture of toxigenic Corynebacterium diphtheria without any clinical signs and symptoms. The age, sex, immunization history and nutritional status between patients and carriers aged 1-18 years old were compared and analyzed.

Results

In total, 147 diphtheria cases and 34 carriers were included. One hundred and one samples (56 %) were ≤ 9 years of age, and 80 (44 %) were ≥ 9 years of age. There was no significant differences of risk factors between groups from the multivariate analyses. The most age in both group is 3 ≤ 9 year old. Male is dominant (51.8 %) in patients group but in carriers are female (58.8 %). Both group have good nutritional status (p=0.63) and received complete basic immunization (p=0.45).

Conclusions

Age, sex, nutritional status and immunization history between cases and carriers were not different during diphtheria outbreaks in East Java, Indonesia.
Acquired recto-vaginal fistula as a presenting feature of an infant with SCID.

Background

Acquired recto-vaginal fistula in infancy is rare. There are case reports in the literature of acquired recto-vaginal fistula in infants born of asymptomatic HIV infected mothers. However, such a presentation in SCID is very unusual.

Case Presentation Summary

A 5 ½ month old girl was admitted with history of passing stools per vaginum of 3 days duration. Well thriving child with no preceding trauma, fever or systemic symptoms. First born of a non-consanguineous marriage, term AGA (birth weight - 3100 gms). Mother was HIV negative. No adverse reactions to vaccines (OPV, BCG, DTP, Hib and Hep B). No contact with TB patient. Had no lymphadenopathy or organomegaly. BCG scar was normal. Weight and length were normal.

Course: She underwent diversion colostomy. Developed multiple cutaneous abscesses and later, burst abdomen on post operative day 10.

Differential diagnoses for acquired rectovaginal fistula and cutaneous abscesses: Immunodeficiency – SCID/ CGD, Neutrophilic dermatoses and IBD.

Labs:
Whole genome sequencing - JAK 3 mutation (autosomal recessive).

Outcome: She developed severe pneumonia/ARDS and succumbed to the illness. Parents have been counselled regarding carrier testing and prenatal diagnostics.

Learning Points/Discussion

1. Consider immunodeficiency in acquired rectovaginal fistulas in infancy.

2. Not all SCIDs have failure to thrive, adverse reactions to vaccines and lymphopenia.
3. Ask for Gene Xpert MTB on tissue or pus samples when clinically indicated. Gene Xpert clinched the diagnosis as even HPE was non-specific due to the severe T cell deficiency.
USE OF ANTIBIOTICS IN PEDIATRIC PATIENTS: A PREVALENCE-SURVEY CONDUCTED IN FOUR ITALIAN CHILDREN’S HOSPITALS

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Background

To measure antibiotic use among inpatient children is useful to plan actions aimed at improving appropriateness of antibiotic prescribing. Defined Daily Doses (DDDs) are the most commonly used metrics to estimate antibiotic consumption in adults, but its use in children is not recommended. This study aimed at assessing prevalence of antibiotic use in Italian pediatric hospitals; moreover, alternative measurements for antibiotic use in children as days-of-therapy (DOTs), length-of-therapy (LOTs) and prescribed daily doses (PDDs) were estimated.

Methods

Prevalence survey was conducted in four Italian pediatric hospitals during a one-week period between November-December 2016. Antibiotic therapies (ATC: J01) and reasons for treatment were collected by reviewing medical charts of all hospitalized patients. Antibiotic consumption on the survey date was expressed as prevalence of use. DOTs, LOTs and PDDs were computed considering antibiotic treatments administered in the 30 days preceding the survey date. DOTs and LOTs per 100 patients-days were calculated for therapeutic treatments only. The median PDDs by age groups and type of molecules were compared to DDDs (PDD:DDD ratio).

Results

Among 810 surveyed children, 380 (46.9%) received one or more antibiotic(s) on the survey date. Patients received antibiotics mainly for prophylaxis (217/810; 26.8%) whereas the prevalence of antibiotic treatments for infections was 20.6% (167/810). DOTs and LOTs were 33.1 e 19.1 per 100 patient-days, respectively. The median PDDs approached to DDDs only in children aged ≥10 years old; moreover, the PDD:DDD ratio was highly variable among antibiotic molecules in this age group.

Conclusions

Our data confirmed that DDDs cannot be used to measure pediatric antibiotic use. Prevalence of antibiotic use represented a good proxy of LOTs especially in a context where computer-based prescribing has not yet been developed.
Background and Objective

Background:

Tuberculosis is an infectious disease which is both curable and preventable. Extra-pulmonary TB refers to tuberculosis involving organs other than the lungs. Tuberculosis is still a major public health problem in our country. In 2010, TB was ranked the 6th leading cause of mortality across all ages.

OBJECTIVE: To describe the prevalence of extrapulmonary tuberculosis among pediatric patients aged 1-18 year old in a tertiary government hospital.

Methods

This is a Retrospective, descriptive study. The study includes patients aged 1-18 years old admitted at Ospital ng Maynila Medical Center with the diagnosis of EPTB from year 2014-2016. The patient’s files were reviewed. Clinico-demographic profile, clinical findings, treatment and outcome were obtained. Data were arranged in tables expressed as proportions and percentages.

Learning Points Discussion

This study revealed a prevalence rate of 0.35% for EPTB among all pediatric admission for the years 2014-2016. Majority of the cases were children aged 1-5 years old, (64%) mean age 10 years old. There are no sex predilections. Majority of cases have no known TB disease and TB exposure. Cases of EPTB include TB meningitis (84%) presenting with changes in sensorium. Gastrointestinal TB (8%) presented with abdominal distension and a case of TB Uveitis presented with whitish lesion in the eye. Among these patients 33% were discharged as improved and 42% died all of which are TB meningitis patients.

CONCLUSION: There is a need to strengthen our TB program in terms of active case finding to further decrease the transmission of TB and initiate early treatment. It is important to educate health professionals to identify possible cases of EPTB and prevent fatal outcomes.
NUTRITIONAL, CLINICAL AND IMMUNOLOGICAL STATUS AT HIV DIAGNOSIS IN A PEDIATRIC HIV REFERRAL UNIT IN BATA, EQUATORIAL GUINEA

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Background

HIV infection has an important morbidity and mortality in Equatorial Guinea, with a prevalence increased in the last decade (6.2% in 2014), with 200 new infections among <15 years-old children in 2016 (UNAIDS). The objective is to evaluate the nutritional, clinical and immunological status at the moment of HIV diagnosis in the pediatric population of an HIV referral unit in Equatorial Guinea.

Methods

Children <18 years-old diagnosed with HIV between April 2009 and September 2017 were included. Clinical, immunological and nutritional data were collected. Weight-for-height-Z-score, Weight-for-age-Z-score and height-for-age-Z-score were calculated using the WHO Child Growth Standards. The population was classified according to the moment of diagnosis in 2 equal periods (April 2009-June 2013 and July 2013-September 2017).

Results

A total of 213 children with HIV were diagnosed (49.3% males), median age 3.8 years (IQR: 1.5-8.2). The most frequent transmission route was vertical (65.3%). Clinical stage (WHO) III in 121 cases (56.8%) and IV in 53 (24.9%). Coinfection with HBV in 12/133 (9%) and pulmonary tuberculosis in 6/213 (2.8%). Immunological stage (CDC) II in 51/130 (39.2%) and III in 44/130 (33.8%). Nutritional data at the table. Higher prevalence of underweight in <5 years (64.4% vs 46.7%, p=0.01). Moderate-severe immunodeficiency was associated with severe underweight: OR 3.9 (95%CI 1.4-11.1, p=0.01). In the second period, prevalence of moderate-severe immunodeficiency decreased (87.2% to 67.0%, p = 0.018), without significant differences in nutritional status or prevalence of advanced disease (clinical stage III-IV).
Conclusions

Malnutrition and immunosuppression should be evaluated at HIV diagnosis and managed promptly since HIV diagnosis. There is a need for a training for nurses and doctors to make HIV diagnosis earlier in Equatorial Guinea.
Background

Bacterial meningitis (BM) still causes many deaths and long-term sequelae, especially in developing countries. Angola, a Sub-Saharan country, launched *Haemophilus influenzae* type band 13-valent pneumococcal conjugate vaccines in 2006 and 2013, respectively. Previously Luanda Children’s Hospital (HPDB) treated approximately 800 patients with probable BM yearly.

Methods

HPDB is a teaching hospital which attends 300 new patients daily. Spinal tap (ST) was performed for children presenting with altered consciousness, prostration, convulsions, meningism, bulging fontanelle and neonatal sepsis. Cerebrospinal fluid (CSF) leukocyte count, glucose and protein were measured routinely. Gram-stain and culture were performed if CSF leukocytes were >10/μl, or glucose <25 mg/dL, and for all neonates’ CSF. This prospective surveillance study collected data of all STs in HPDB during one year (21.10.2016 – 20.10.2017).

Results

STs were performed on 2472 children of whom 1370 (55%) were male. BM was probable in 343 children, of whom 155 (45%) aged ≤30 days. Bacteria were detected in 226 CSF samples, causative agents being *Streptococcus pneumoniae* (n=33), *Klebsiella* sp. (n=23), *Streptococcus agalactiae* (n=16), *Escherichia coli* (n=15), *Staphylococcus aureus* (n=13) *Neisseria meningitidis* (n=11), *Haemophilus influenzae* (n=8), other Gram-positive (n=54), and Gram-negative (n=53) bacteria. At discharge, the other diseases diagnosed were malaria (31% of 1838), neonatal sepsis (26%), convulsions/epilepsy (7.9%), encephalitis/viral meningitis (2.9%), and tuberculous meningitis (1.8%).

Conclusions

Of all children presenting at HPDB, 2% had ST performed and of them, 14% were diagnosed with probable BM. Almost half of those were neonates. After introduction of conjugate vaccines in Angola, the number of BM in HPDB has lowered about 60%. Still, pneumococcus, meningococcus, and *Haemophilus* remain important causes of BM.
FOLLOW-UP OF CHILDREN BORN TO MOTHERS WITH VIRUS ZIKA INFECTION DURING PREGNANCY: SITUATION TWO YEARS AFTER THE WORLDWIDE ALERT

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Background

Zika virus infection (ZVI) is a significant public health problem due to its association with neurological pathology, especially in children born to mothers with ZVI during pregnancy. Objective: to analyze the characteristics and development of children born to mothers with ZVI during pregnancy in a Spanish National Referral Centre for Tropical Diseases after two years of follow-up.

Methods

We reviewed the medical records of infants born to mothers with laboratory confirmed or probably ZVI during pregnancy from January 2016 to December 2017.

Results

Sixteen term newborns born to mothers from endemic areas were included. Nine mothers reported ZVI symptoms during pregnancy, mean gestational age at diagnosis of 18 weeks (rank: 8-34). All presented anti-Zika IgG antibodies, but only one IgM antibodies; 8/16 positive anti-Zika antibodies by plaque-reduction neutralization test, the remaining were indeterminate. During pregnancy, Zika PCR was positive in: 1/8 in blood and 1/11 in urine. Prenatal ultrasounds were pathological in 2/17 cases. Children were evaluated at birth, and at one, three, six and nine months. All physical examinations, anthropometry, psychomotor development, eye fundus and hearing screening test were normal. Cerebral ultrasound at birth showed lenticulostriate vasculopathy in one and mild periventricular echogenicity in two. Zika serology performed at birth were IgM-IgG+ in all cases. Zika PCR was negative in: 15/15 in blood and 2/2 in CSF. IgG antibodies become undetectable at one month in 5/17, 4/17 at three months and 1/17 at six months, with the remaining being followed-up.

Conclusions

No child born to mother with ZVI during pregnancy developed congenital infection nor significant adverse outcomes during follow-up. Maternal antibodies in a half of the children became negative at the first and third months.
Background

The aim of this study was to evaluate antibiotic resistant rates and prescribing patterns in hospitalised children with febrile and afebrile urinary tract infections (UTIs) in a district hospital in central Greece.

Methods

Data was collected retrospectively, including information on clinical diagnosis, antibiograms and antibiotic prescriptions. Patients were included based on clinical and microbiological criteria, while sensitivity to antimicrobials was determined using the Kirby-Bauer disk diffusion method.

Results

A total of 236 pathogens were isolated from 230 patients. The main causative organism was *Escherichia coli* (79.2%) with high reported resistance rates to ampicillin (42.0%), trimethoprim-sulfamethoxazole (26.5%) and amoxicillin-clavulanic acid (12.2%). Lower resistance rates were identified for 3rd generation cephalosporins (1.7%), nitrofurantoine (2.3%), ciprofloxacin (1.3%) and amikacin (0.9%). *Klebsiella* sp. isolates were highly resistant to cefaclor (27.3%). 459 hospital prescriptions were identified for UTIs. Amikacin (31.2%) was the most common antibiotic prescribed in this population, followed by amoxicillin-clavulanic acid (17.4%) and ampicillin (13.5%). Children received prolonged intravenous treatments for febrile (5.4 days; SD 1.45) and afebrile UTIs (4.7 days; SD 1.34).

Conclusions
The establishment of specific UTIs antimicrobial stewardship programs could help to minimise inappropriate prescribing in Greek hospitals. The routine national surveillance of antimicrobial resistance in children could better inform clinical practice for specific infectious syndromes.
Background and Objective

Pneumococcal disease burden represents one of the largest burdens of vaccine preventable disease in countries without a pneumococcal vaccine program. China has recently approved the use of PCV13 to protect against pneumococcal disease caused by 13 serotypes of S. pneumoniae. The objective of this study is to estimate the clinical and economic impact of introducing city expanded program for immunization (EPI) in Chongqing.

Methods

A 1-year decision analytic model was used to estimate costs and outcomes of vaccinating 85% of the 330 thousand infants born annually in Chongqing from a payer perspective. PCV13 was compared to no-vaccination in preventing cases and associated costs of invasive pneumococcal disease (IPD), community acquired pneumonia (CAP), and acute otitis media (AOM). Inputs were derived from the China Health Insurance Research Association (CHIRA) database and the published literature. The vaccine was evaluated in a 3+1 schedule assuming the average list price of 698 RMB per dose.

Learning Points Discussion

In the base case, assuming indirect effects for IPD and hospitalized CAP, PCV13 is projected to prevent more episodes and deaths, and is highly cost-effective compared to no vaccination (Table 1). PCV13 remained cost-saving or highly cost-effective across a number of scenarios.

If Chongqing were to fund an EPI with PCV13, our model predicts a remarkable public health and cost-saving impact in China. While further research is needed to understand the national burden of disease, our model suggests that consideration should be made to scale up pneumococcal vaccination in Chongqing and across China.
<table>
<thead>
<tr>
<th></th>
<th>No Vaccine</th>
<th>PCV13</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cases</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IPD</td>
<td>582</td>
<td>351</td>
<td>-231</td>
</tr>
<tr>
<td>CAP</td>
<td>1,375,345</td>
<td>1,248,831</td>
<td>-126,514</td>
</tr>
<tr>
<td>AOM</td>
<td>248,351</td>
<td>229,181</td>
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<tr>
<td><strong>Deaths</strong></td>
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<td></td>
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<tr>
<td>QALYs Lost</td>
<td>565,418</td>
<td>511,532</td>
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CHALLENGES WITH UNUSUAL INFECTION OF UNSUAL SEVERITY - METHICILLIN RESISTANT STAPHYLOCOCCUS AUREUS INFECTION

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Title of Case(s)

CHALLENGES WITH UNUSUAL INFECTION OF UNSUAL SEVERITY - METHICILLIN RESISTANT STAPHYLOCOCCUS AUREUS INFECTION

Background

MRSA is an important cause of morbidity & mortality. Recently, CA – MRSA infections are on the rise. Hence, a strong index of suspicion is important to diagnose and treat early.

Case Presentation Summary

A 4 yr old child presented with h/o pain in the right shoulder for 6 days and hip which was later followed by generalized body pain associated with fever for 4 days. He was toxic, febrile and unable to walk and move his right hand. He had generalized swelling of the above limbs which were tender. With possibility of polymyositis, MRI of the right upper limb showed features of osteomyelitis in the right humerus and consolidation involving the right lung. Investigations showed leukopenia, thrombocytopenia, high CRP (237mg/dl). Whole body MRI was done which additionally showed myositis of both thigh muscles. CT chest confirmed bilateral lung consolidation. Blood culture grew MRSA. He was treated with vancomycin and linezolid. He was intubated on day 4 of admission when surgery was done (Curettage, Saucerisation). Nearly 200 ml pus was drained from the right upper arm. Right chest drain was also inserted. A course of IVIG was given for persistent toxemic symptoms.

Learning Points/Discussion

Invasive MRSA infections associated with the production of PVL toxins have high mortality despite adequate treatment. This case is presented to discuss the issues with CA-MRSA infections, clinical clues to early recognition and appropriate treatment and when to suspect infections due to strains producing PVL toxin, empirical choice of antibiotics, interpreting cultures of MRSA bacteremia, role of various antimicrobials, role of IVIG, ideal investigation and treatment for osteomyelitis, Community level prevention strategies and carrier detection issue with MRSA infections.
17E. SCIENCE: VACCINE DEVELOPMENT, IMMUNOGENICITY AND SAFETY

VACCINATION IN THE WORLD AND IN TURKEY
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¹Adana State Hospital, Nursing, Adana, Turkey
²Çukurova University, Child Health and Diseases Nursing, Adana, Turkey

Background and Objective

Aim of this review is to emphasize vaccination programs and historical process and practicing guidelines of them applied both in the World and in Turkey.

Methods

Infectious diseases are one of the biggest problem of public health especially in developing countries. Those diseases leads to morbidity and mortality by causing epidemics in different regions termly. Vaccination applied in primary healthcare services is the most effective method to prevent from morbidity and mortality. Vaccination takes a prior place between interventions of child health care. In the world millions of children continues to die because of vaccine preventable diseases. World Healthcare Organization (WHO) developed Expanded Programme on Immunization (EPI) and recommended it in 1974. The EPI launched at that time recommended the use of vaccines to protect against six diseases: tuberculosis (BCG), diphtheria, tetanus, pertussis (DTP vaccine), measles and poliomyelitis. EPI was started in Turkey in 1981 and accelerated with vaccination campaigns in 1985. Recommendations of WHO’s recommendation is also effective for generating and performing vaccination programs of the countries besides country’s own national data. It takes an important place in health policies to change the vaccination calendar in need. For example; Maternal-Neonate Tetanus Elimination Program was performed within the scope of EPI as of 2009. Additionally, according to data of WHO starting with the arrival of Syrian immigrants some infectious diseases (polio, tuberculosis, measles) eradicated before has been seen in Turkey therefore some additional changes were made.

Learning Points Discussion

Consequently, primary health care providers takes an important place in vaccine preventable diseases. They should follow current information about vaccination programs and determine to apply additional vaccines in need.
02A. SCIENCE: ANTIMICROBIALS: RESISTANCE AND PHARMACOLOGY

ANTIBIOTICS AND CURE RATES IN CHILDHOOD FEBRILE URINARY TRACT INFECTIONS IN CLINICAL TRIALS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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2St George’s University of London-Institute for Infection and Immunity, Paediatric Infectious Diseases Research Group, London, United Kingdom
3Institut National de la Santé Et de la Recherche Médicale- Université Paris Diderot, Infection- Antimicrobiens- Modélisation- Evolution- Unité Mixte de Recherche 1137, Sorbonne Paris Cité- Paris- France, France
4University Children’s Hospital Basel, Paediatric Pharmacology, Basel, Switzerland
5University of Pennsylvania School of Medicine, Department of Pediatrics, Philadelphia- Pennsylvania, USA

Background

Urinary tract infections (UTIs) are common among children, with an increased incidence in infants. Their prompt and appropriate treatment is of critical importance in order to minimise acute or long-term complications. In this systematic review, we assessed the antimicrobials used for febrile urinary tract infections in pediatric clinical trials and meta-analyzed the observed cure rates and reasons for treatment failure.

Methods

We searched Medline, Embase and Cochrane central databases between January 1, 1990, and November 24, 2016, combining MeSH and free-text terms for: “urinary tract infections”, AND “therapeutics”, AND “clinical trials” in children (age range 0–18 years). Two independent reviewers assessed study quality and performed data extraction. The major outcome measures were clinical and microbiological cure rates according to different antibiotics.

Results

We identified 2,762 published studies and included 30 clinical trials investigating 3913 cases of pediatric febrile urinary tract infections. Children with no underlying condition were the main population included in the trials (n=2,602; 66.5%). Cephalosporins were the most frequently antibiotic studied in trials (22/30, 73.3%). Only a few antibiotics active against resistant urinary tract infections have been tested in randomised clinical trials, mainly aminoglycosides. The summary point cure rate of all investigational drugs was estimated to 95.3% [95% CI 93.5-96.9%]. Among 3,002 patients for whom cure and failure rates were reported, only 3.9% (3.9%; 118/3,002) were considered clinically to have treatment failure, while 135 (4.5%; 135/3,002) had microbiological failure.

Conclusions

We observed high treatment cure rates for childhood urinary tract infections in clinical trials, regardless of the investigational drug chosen, the route of administration, duration and dosing. This suggests that
future research should prioritise observational studies and clinical trials on children with multi-drug resistant infections.

**Systematic Review Registration (Please input N/A if not registered)**

N/A
ENTERIC MYOCARDITIS: A CASE SERIES IN CHILDREN FROM BIKANER, NORTHWESTERN INDIA

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¹S.P. Medical College, Pediatric Medicine, Bikaner, India

Title of Case(s)

Enteric myocarditis in children

Background

Majority of this enteric illness follow a benign self limiting course but recently rare atypical manifestations like cardiac involvement are increasingly seen due to rising burden of disease and increased awareness. We present 14 children found to have clinical evidence of myocarditis out of total 156 children with bacteriologically or serologically proven typhoid fever in tertiary care hospital from January 2015 to December 2017.

Case Presentation Summary

Diagnosis of enteric illness was made on isolation of the organism in blood culture [87.8% (137/156)], stool culture [7.1% (11/156)] and urine culture [4.5% (7/156)]. Median age was 9 years (range 3-11 years). Median duration of fever was 6 days (range 3-13 days). Common cardio-respiratory symptoms at time of admission were shock (54.55%), heart failure (27.27%) and chest pain (18.18%). Chest X-ray showed cardiomegaly (63.64%), pleural effusion (54.55%) and pulmonary edema (18.18%). Cardiac biomarkers creatinine kinase MB isoenzyme (mean±SD=141±55.91 U/l) and Troponin I (mean±SD=7±2.92 µg/l) were elevated in all these children. The commonest ECG abnormality encountered was prolongation of the QT interval (63.64%); widespread ST segment elevation and/ or T wave inversion (27.27%), bundle branch blocks, first degree atrioventricular block and arrhythmias were also noted. The Transthoracic echocardiographic findings were ranged from depressed left ventricular ejection fraction (100%), abnormal left ventricular wall motion (54.55%) and pericardial perfusion (18.18%). Cardiac MRI was done in 7 children revealing myocarditis. All these children were treated according to standard protocols and all recovered well.

Learning Points/Discussion

• Typhoid fever is a rare cause of acute myocarditis.
• Possibility of enteric myocarditis should always be considered if a dengue fever patient has refractory shock and congestive heart failure.
• Most patients with acute (typhoid) myocarditis have an excellent long-term prognosis.
05A. SCIENCE: NEONATAL INFECTIONS

FACTORS PREDICTING DEVELOPMENT OF SEPTIC SHOCK AMONG NEONATES PRESENTING WITH SEPSIS

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²Post Graduate Institute of Medical Education and Research, Medical Microbiology, Chandigarh, India

Background

Sepsis is the second most common cause of neonatal mortality. Nevertheless factors predicting development of shock among septic neonates have not been scientifically studied. We evaluated factors predicting development of shock within 14 days of onset of neonatal sepsis.

Methods

This cohort study was performed from June 2016 to June 2017. We enrolled consecutive neonates with probable or proven sepsis. Their demographic factors, antenatal/obstetrical factors, factors related to perinatal transition and immediate neonatal period, clinical risk factors at onset of sepsis, hematological factors, metabolic factors (acid base parameters) and immunological factors (lymphocyte subsets/CD markers) were recorded at the baseline. We followed these neonates for development of shock within 14 days of enrollment.

Results

We enrolled 137 neonates. Twenty nine neonates developed shock (Shock group). Remaining neonates were labelled as control group. On univariate analysis following variables were significantly different between shock and control group [demographic (birth weight, small for gestational age (SGA)); antenatal (pregnancy induced hypertension); intrapartum (Apgar scores); immediate postnatal (Downe’s score >6, hyaline membrane disease); clinical signs of sepsis (temperature, apnea, oxygen requirement, mandatory ventilation, pallor, hypoglycemia, encephalopathy, hypotonia, seizures, sclerema, clinical risk index of babies score); metabolic parameters (pH, standard base excess, standard bicarbonate); hematological parameters (need for transfusion, total lymphocyte counts (TLC), platelet count), immunological (CD-3 and CD-56 lymphocyte subsets). On multivariable logistic regression analysis birth weight <1500g, SGA status, need of mandatory ventilation, encephalopathy, sclerema, lower total leukocyte counts independently predicted development of septic shock.

Conclusions

Among neonates presenting with sepsis birth weight <1500g, SGA status, need of mandatory ventilation, encephalopathy, sclerema, lower total leukocyte counts independently predicted development of shock within 14 days of onset of sepsis.

Clinical Trial Registration (Please input N/A if not registered)

N/A
A NEW MANAGEMENT STRATEGY (NMS) FOR SUSPECTED INVASIVE FUNGAL DISEASE (IFD) IN PEDIATRIC HAEMATO-ONCOLOGY PATIENTS; A PROSPECTIVE STUDY.

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\textsuperscript{3}Sophia Children's Hospital, Paediatrics, Rotterdam, The Netherlands
\textsuperscript{4}Sophia Children's Hospital, Paediatric Infectious Diseases, Rotterdam, The Netherlands
\textsuperscript{5}Emma Children's Hospital- Academic Medical Center-, Paediatric Infectious Diseases, Amsterdam, The Netherlands
\textsuperscript{6}Wilhelmina Children's Hospital, Paediatric Infectious Diseases, Utrecht, The Netherlands
\textsuperscript{7}Radboud UMC, Paediatric Infectious Diseases, Nijmegen, The Netherlands

Background

Increased prevalence of azole resistance in \textit{A. fumigatus}, voriconazole underdosing problems in children and a changing epidemiology of IFD, have led to the development of a NMS to achieve standardized diagnostic work-up and therapeutic intervention for suspected IFD in paediatric haemato-oncology patients in the Netherlands.

Methods

We collected demographic, clinical, diagnostic and outcome data in the PedMyc database from pediatric haemato-oncology patients (<18 yrs) with a clinical suspicion of IFD in four university hospitals in the Netherlands. Management strategy is shown in the flow diagram.

Results

From 2013-2016, 104 patients were included. ALL was the most common underlying condition, 42.3% (44/104), followed by AML, 23% (24/104) and NHL with 11.5% (12/104). 11/ 104 (10.6%) were HSCT recipients. The NMS was carried out in 77% (80/104) of which 68 (85%) were started on L-AmB and 12 (15%) on L-AmB + voriconazole. CT-thorax was performed in 82.5% (66/80) with abnormalities in 81.8% (54/66). 71.2% (57/80) underwent a broncho-alveolar lavage resulting in 33.3% (n=19) positive cultures. MRI-cerebrum was performed in 43.8% (35/80) with abnormalities in 40% (14/35). Diagnosis after diagnostic work-up: proven IFD 17.5% (5 aspergillosis, 5 candidiasis, 3 other mycoses), probable 23.7%, possible 42.5%. No treatment changes were made in 60% (48/80) of the patients. From those started on L-AmB, 33.8% (23/68) changed to voriconazole monotherapy, 10.3% (7/68) were changed to combination therapy. Only 2 out of the 12 patients started initially on combination therapy, were switched to monotherapy. Complete and partial response was seen in 77.3%, death was reported in 21.2%.

Conclusions

The NMS proved to be a feasible strategy with a favourable outcome allowing 42% patients to be categorised as proven/probable IFD by employing a standardized diagnostic work-up.
ACUTE FLACCID PARALYSIS IN YOUNG CHILDREN - ‘WATCH THEIR BACK’

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¹Post Graduate Institute of Medical Education and Research, Pediatrics, Chandigarh, India
²Post Graduate Institute of Medical Education and Research, Radiodiagnosis, Chandigarh, India
³Post Graduate Institute of Medical Education and Research, Neurosurgery, Chandigarh, India
⁴Medanta Medicity, Pediatrics, Gurugram, India

Title of Case(s)

Acute flaccid paralysis in young children: “Watch their Back”

Background

Congenital dermal sinus is a developmental malformation which may be associated with sinus tract between the skin and the deeper tissues, even spinal cord. Hence, can have complicated presentations like gait abnormalities, infections, urinary symptoms or mass lesions. We hereby describe a series of six children with spinal abscesses complicating dermal sinus.

Case Presentation Summary

Of a total of 111 children of acute flaccid paralysis admitted during this period, six had spinal abscess associated with dermal sinus. (The other diagnosis were Guillain Barre syndrome, myositis, myelitis). The median age of diagnosis and median duration of symptoms was 8.5 months and 33 days. All six children presented with progressive weakness of lower limbs; fever and urinary symptoms were present in two children. In none of the children was spinal cord infection kept as an initial differential diagnosis. All children had evidence of intra-medullary abscess, cord edema and spinal arachnoiditis. One child had holocord involvement, while rest had involvement of dorso-lumbosacral spine. Four children needed spinal laminotomy and drainage. The offending organism was isolated in two children (E.coli). All except one (parents declined treatment) were treated with intravenous antibiotics for 6-8 weeks. All children had motor improvement after treatment but all were left with severe neurological motor deficits and residual neurogenic bladder

Learning Points/Discussion

The infection of the spinal cord and meninges due to a dermal sinus is rare cause of paralysis and can present without fever. In any child with flaccid paralysis, a careful examination of back for dermal sinus is critical to suspect this diagnosis. Significant residual neuro-deficits in our series underline the importance of early diagnosis of a congenital dermal sinus and prevention of complications.
Invasive Pneumococcal Disease at University Medical Centre LJUBLJANA before and after introduction of routine pneumococcal vaccination in Slovenia

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2University Medical Centre LJUBLJANA, Children’s Hospital, LJUBLJANA, Slovenia
3National Laboratory of Health Environment and Food, Department for Public Health Microbiology, LJUBLJANA, Slovenia

Background

In Slovenia, surveillance of invasive pneumococcal disease (IPD) in children has been performed since 1993. All isolates are sent to the National Reference Laboratory for serotyping. In 2015, the 10-valent pneumococcal conjugate vaccine (PCV10) was introduced (no catch-up) in the immunization programme with 48.4% coverage in 2015 and 49% in 2016. The aim of the study was to assess features of IPD and pneumococcal serotypes in children <15 years treated at the University Medical Centre LJUBLJANA (UMCL) in a two-year period before and after introduction of PCV10 vaccination.

Methods

Data on clinical features of IPD in children <15 years treated at UMCL from 2013 to 2016 were collected. All isolates were serotyped and antimicrobial resistance was assessed.

Results

Throughout the study period there were 100 IPD cases, 67 in 2013-14 and 33 in 2015-16. After PCV10 introduction, there was a 85% reduction of IPD cases in infants (13 vs. 2), followed by 75% in 24-59 month olds (20 vs. 5) and a 24% in those 12-23 months old (21 vs. 16). The most common syndrome in both periods was bacteremia, followed by pneumonia. Among pneumococcal isolates, in both periods vaccine serotypes prevailed. An increase in serotype 3, 6A and 19A cases was not observed. The majority of isolates were penicillin-susceptible (87% in 2013-14, 90% in 2015-16), others demonstrated intermediate resistance. All isolates were cefotaxime-sensitive.

Conclusions

After PCV10 introduction in 2015 with roughly 50% vaccination coverage, a 50% decrease in number of IPD cases was observed at UMCL with vaccine serotypes predominating. The majority of isolates remain penicillin-susceptible. Further surveillance is needed to monitor changes in IPD epidemiology.
ANTI-RABIC IMMUNIZATION IN ABIDJAN FROM 2012 TO 2014

H. Attoh Toure¹, R.T.K. Akpégni¹, R. Oussou¹, N. Konan², I. Tiembre¹, B.V.J. Benie¹
¹Felix Houphouet Boigny University, Public Health, Abidjan, Ivory Coast
²National Institute of Public Hygiene, Information, Abidjan, Ivory Coast

Background

On average 20 cases of human rabies are reported annually in Côte d'Ivoire. As a result, preventive measures remain the most effective way to pre-empt this disease and post-exposure care, including immunization, remains a key element. In this context, we conducted a study whose objective was to describe post-exposure immunization in Abidjan, from 2012 to 2014.

Methods

We carried out a descriptive cross-sectional study over a period of 5 months in three Anti-Rabies Centers (ARCs) in the city of Abidjan. The dataset came from files of victims of bites, scratches or licking by suspected animals received from 2012 to 2014 in the aforementioned ARCs and was analyzed with the Epi info 3.5.4 software.

Results

We counted 10,477 victims in care during the period of our study. In terms of socio-demographic characteristics, 57% were male and 45.8% were under 15 years of age. Regarding the type of lesion, almost all (99.66%) had WHO class II or III, lesions for which post-exposure immunization was required. The most incriminated animal species was 89.3% dog and the majority of exposures took place at home (55.1%). Of these animals, only 23% were immunized against rabies and 21% of them were subjected to full veterinary surveillance. More than half of the victims (55%) had initiated the Zagreb protocol and 58.8% had abandoned the treatment initiated. These dropouts were related to the type of protocol used. Indeed, patients were more likely to quit the Essen protocol than the Zagreb protocol.

Conclusions

Accessibility of immunization is one of the three essential measures recommended by the global framework for rabies elimination. From this perspective, free vaccination could be an effective response to this public health problem.
FUSOBACTERIUM NECROPHORUM ACUTE OTITIS MEDIA IN INFANTS AND YOUNG TODDLERS: PRESENTATION OF CASE AND REVIEW OF THE LITERATURE

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²Penteli Children’s Hospital, Microbiology Laboratory, Athens, Greece
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Title of Case(s)

FUSOBACTERIUM NECROPHORUM ACUTE OTITIS MEDIA

Background

_Fusobacterium necrophorum_ is an anaerobic Gram-negative bacillus which comprises the flora of the oral cavity, the gastrointestinal and female genital tract. It may cause a wide range of age independent head and neck infections. Most common infection in children less than 2 years old is acute otitis media (AOM) with serious complications such as mastoiditis, osteomyelitis and Lemierre syndrome.

Case Presentation Summary

An otherwise healthy eighteen-month-old girl presented to our department in good condition, with fever and right ear otorrhea. History of 2-3 episodes of recurrent AOM the last few months was also mentioned.

The clinical examination revealed tympanic membrane rupture and fluid presence in the ear canal without mastoiditis. Fluid was obtained for culture and the child was discharged on empiric amoxycillin-clavulanate.

_F. necrophorum_ was isolated from fluid culture, identified by colony morphology, gram staining and resistance phenotype to antimicrobials (susceptible kanamycin, colistin, penicillin, rifampicin and resistance in vancomycin) and confirmed by BD BBL-Crystal semiconductor identification system.

Follow-up was uneventful and after completion of 10-day course, a complete resolution of symptoms and restoration of the tympanic membrane anatomy and function were noted.

Learning Points/Discussion

Anaerobes, are responsible for less than 1% of the middle ear infections, with _F. necrophorum_ being very rare among young toddlers (12 cases in a 40-year literature review), with an increasing trend during the last decade. These age groups are more vulnerable to serious complications such as mastoiditis, which occurs to the majority of _F. necrophorum_ AOM, with higher incidence than other pathogens. Since in our case there was no complication, it appears that prompt initiation of antimicrobial treatment in cases of otorrhea, might be of importance in order to avoid complication in cases of _F. necrophorum_ AOM.
THROMBOCYTOPENIA AS A RARE COMPLICATION OF ACUTE GASTROENTERITIS IN CHILDREN

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¹School of Medicine in Katowice- Medical University of Silesia- Katowice- Poland, Department of Pediatrics, Katowice, Poland
²Upper-Silesian Child Health Care Centre- Katowice- Poland, Gastroenterology Unit, Katowice, Poland

Background

Thrombocytopenia is a complication that may occur during gastrointestinal infections. The purpose of the study was to evaluate the incidence and severity of thrombocytopenia in children with acute gastroenteritis according to etiology.

Methods

The study group consisted of 4409 children hospitalized in the Gastroenterology Unit due to acute gastroenteritis: 1588 children with rotavirus infection and 2821 children with another cause of gastroenteritis. Of the study group, 97 patients with thrombocytopaenia (platelets<140 K/ul)were isolated and divided into two groups: children with rotavirus infection RV(+) and children with infection of another etiology RV(-). Thrombocytopenia was divided into 3 stages: mild(139-100K/ul), moderate(99-50K/ul) and severe(49-0K/ul). The structure of sex, age, hospitalization time, inflammation parameters, stage of thrombocytopenia and etiological factor were analyzed. Results were analyzed using Statistica 13.1.

Results

<table>
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<tr>
<th>Stage</th>
<th>Patients with thrombocytopenia</th>
<th>Male</th>
<th>Severe</th>
<th>Moderate</th>
<th>Mild</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td>4409 (100%)</td>
<td>97</td>
<td>8</td>
<td>34</td>
<td>55</td>
</tr>
<tr>
<td>RV(+)</td>
<td>1588 (36,01%)</td>
<td>47</td>
<td>3</td>
<td>18</td>
<td>26</td>
</tr>
<tr>
<td>RV(-)</td>
<td>2821 (63,99%)</td>
<td>50</td>
<td>1</td>
<td>16</td>
<td>29</td>
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Thrombocytopenia was more common in RV(+)group and among boys. Children with mild thrombocytopenia in the RV(+) group were younger than children in the RV(-)group with the same platelets level (average age 3 vs. 5.15 years old). In children with thrombocytopaenia, there was a positive correlation between age/CRP level and hospitalization time.

Conclusions

Thrombocytopenia is a rare complication of acute gastroenteritis. Especially boys, with rotavirus infection are more likely to develop thrombocytopaenia than children with gastroenteritis of different etiology. The presence of rotavirus infection doesn't affect the severity of thrombocytopenia. Younger children were more likely to be hospitalized due to rotavirus infection than due to gastroenteritis of
different etiology. Attention should be paid to thrombocytopenia <50K/ul, because of the direct risk of internal bleeding.
KAWASAKI DISEASE IN ARMENIA

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**Title of Case(s)**

KAWASAKI DISEASE IN ARMENIA

**Background**

Kawasaki disease (KD) is an acute vasculitis of childhood. Serious complications can occur in 15-25% of patients if untreated. With prompt IVIG therapy this percentage decreases to 1-5%.

We report cases of KD ever diagnosed in paediatric hospital in Armenia - “Arabkir” Medical Center between 2013-2017.

**Case Presentation Summary**

KD was diagnosed on the basis of clinical criteria established by the American Heart Association. 34 patients with KD were included (16 males/18 females, mean age 42 month) in the study.

**Clinical findings:** Median duration of fever on admission was 7 days. Non-suppurative conjunctivitis was documented in 28 (82%), rash in 27 (79%), lymphadenopathy in 24 (71%), arthritis in 8 (23%), edema of the hands/feet in 18 (53%) patients. All children developed skin desquamation at the subacute stage.

**Laboratory results:** 25 (74%) patients showed elevation of CRP >48 mg/dl (mean 96, max 235), 27 (80%) - ESR >15 mm/h (mean 35, max 62). High platelets (mean 600\(\times\)10\(^9\)/l, max 1300\(\times\)10\(^9\)/l) was documented at the second week of the disease in 22 (65%). 10 (29%) children had elevated ALT (mean 132 IU/l) and AST (mean 66 IU/l). 5 patients (15%) had coronary artery aneurysms (CAA), of them 1 showed giant aneurism.

**Treatment:** 28 patients (82%) received single, 2 children (6%) - double doses of 2g/kg IVIG. All had aspirin 50-80 mg/kg/day followed by low dose regimen. 6 patients (18%) did not get IVIG because of late referral. Follow-up echocardiography was normal in all children except 1 who developed CAA.

**Learning Points/Discussion**

KD should be considered in the differential diagnosis of children with unexplained prolonged (> 5 days) fever. The disease is under-diagnosed in our country and requires an increased awareness among paediatric specialists.
Background

According to WHO, the only way to reduce infant-juvenile mortality due to vaccine-preventable diseases is to increase the vaccine coverage of the Expanded Program on Immunization (EPI). Despite considerable efforts in recent years, a significant proportion of children are unvaccinated. In the Diapé health area, vaccination coverage has never reached 90% during the last three years. This study aimed to identify the factors associated with the immunization of children aged from 12 to 23 months.

Methods

We conducted a cross-sectional study from the 15th to the 27th of August 2017 in the villages of the Diapé health area. Our study population consisted of children aged from 12 to 23 months and their mothers selected using a random WHO cluster sample (30 clusters of 7 children). The data were collected using a standardized questionnaire administered face-to-face in households.

Results

A total of 210 mothers of children were included in the survey. Mothers’ average age was 26 years ± 2.3 years and 32.4% had no grade level. Immunization coverage of all EPI antigens in children aged from 12 to 23 months was 74.3%, of which 35.8% received the full schedule on time. The bi-varied analyzes showed that low immunization coverage was associated with the animist mother religion (OR = 5.8, 95% CI [2.2-14.9]), low knowledge of EPI target diseases (OR = 6.1, 95% CI [1.8-20.8]), ignorance of the age of the last vaccine (OR = 12.8, 95% CI [5.2-31.7]) and the poor quality of services (OR = 7.2, 95% CI [3.7-13.9]).

Conclusions

There is a need to strengthen maternal awareness-raising activities on the immunization schedule and the benefits of immunization with the participation of community and religious leaders.
SYSTEMATIC LITERATURE REVIEW AND DATABASE ANALYSIS ON EPIDEMIOLOGICAL BURDEN OF MENINGOCOCCAL DISEASE IN BRAZIL

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Background

Meningococcal disease (MD) is endemic in Brazil. Epidemiology data are necessary to guide future prevention and control strategies. This study aims to evaluate MD epidemiological profile in Brazil.

Methods

A systematic literature review was conducted from January 2005 to January 2017, including studies with epidemiological information on MD in Brazil for any population group, data concerning serogroups and its relation to disease course. Governmental documents and databases were analyzed to provide annual incidence, absolute number of diagnosed cases and identified serogroup, relative cases distribution per identified serogroup by region and age group, and lethality rate.

Results

Relative distribution of serogroups by age (2015)

Sixteen studies showed median age from 3 to 8 years, predominant male population, and incidence rate from 0.88 to 5.3 cases/100,000 inhabitants/year (peak of 8.1 in 1995). According to secondary data, MD annual incidence in 2015 is higher in male patients <1-year-old (57/100,000), and in southern and southeastern regions. A significant reduction in diagnosed cases was observed over the
years (Figure). MD lethality presented a variation between 20.0 and 50.0%, higher for serogroup W (17.8%), followed by B and C. Data from Ministry of Health showed an absolute reduction in meningitis attributable deaths between 2007 and 2015, however, with constant lethality rate (9.5%). In 2015, serogroup W showed higher lethality rate. Serogroup B was the most prevalent in nine studies and C in five. Recent studies show an increase in serogroup W. Secondary data showed majority of serogroup C. However, in 2015, only 3.9% presented serogroup identification.

Conclusions

Despite reduction in cases reported by literature and databases, lethality remains stable, mainly that associated with serogroup W.

Systematic Review Registration (Please input N/A if not registered)

N/A
EB18-0374
E-PAPER VIEWING - MAY 28-JUNE 2 - EXHIBITION HOURS

08B. SCIENCE: INFECTION AND IMMUNOLOGY

IMMUNE RESPONSE FEATURES DURING VIRAL DIARRHEA AS A RISK FACTOR FOR THE DEVELOPMENT OF FUNCTIONAL GASTROINTESTINAL DISORDERS IN CHILDREN

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Background

Immune response in viral gastroenteritis (VG) is of considerable importance, as immune mechanisms can be involved in visceral hypersensitivity chronic inflammation in the mucosa formation in patients with functional gastrointestinal disorders (FGD). Purpose of the study: to establish immune response features in VG in children, promoting the development of FGD.

Methods

The study included 147 children aged 1-7 years with rotavirus (n=60, group I), norovirus (n=57, group II) and rota-norovirus infections (n=30, group III) approved with PCR in feces. Immune status (definition of the main subpopulations of leukocytes, evaluation of interferon status, determination of the concentration of serum immunoglobulins) was carried twice in the 3rd-5th and 18th-21st days of the disease. The convalescents of viral gastroenteritis were observed outpatients in Pasteur Research Institute medical center for 12 months (with clinical examinations 1 time in 3 months) with the purpose of revealing FGD in accordance with Rome IV criteria.

Results

FGD were diagnosed in 30 convalescents of VG, 14 (23.3%) in group I, 9 (16.4%) in group II and 7 (25, 0%) in group III (p = 0.4). Children with FGD in acute period of VG more frequently had virus-induced IFN production suppression (p=0.02), and CD8 lymphocytes level decrease (p=0.03). The most pronounced changes in these indicators were found in children in III group. In the 2nd period (18-21 days) children with FGD had an increase in the level of CD25 + lymphocytes (p=0.05), and relatively lower levels of serum IgA (p=0.04).

Conclusions

An increased risk of FGD formation is observed in children after VG if detecting suppression of virus-induced IFN production, decrease in CD8 lymphocytes in acute period of VG, an increase of CD25 lymphocytes during the reconvalescence period of VG.

Clinical Trial Registration (Please input N/A if not registered)
N/A
CENTRAL VENOUS CATHETER-ASSOCIATED FUNGEMIA DUE TO RHODOTORULA MUCILAGINOSA IN A PREMATURE INFANT

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Title of Case(s)

CENTRAL VENOUS CATHETER-ASSOCIATED FUNGEMIA DUE TO RHODOTORULA MUCILAGINOSA IN A PREMATURE INFANT

Background

A few cases of Rhodotorula mucilaginosa fungemia have been reported in premature infants. We hereby present a case of central venous catheter (CVC)-associated fungemia due to R. mucilaginosa in a premature infant.

Case Presentation Summary

A male infant was born weighing 1,450 g at 31 weeks with cesarean section due to premature rupture of membranes. Therapy including ampicillin and gentamicin was initiated at birth. The patient had a CVC inserted on day 3 for administration of total parenteral nutrition. He developed signs of sepsis and necrotising enterocolitis on day 14, so empiric treatment with vancomycin, meropenem and fluconazole was started. After a period of clinical improvement lasting ~2 weeks, the patient's clinical condition deteriorated again, and both peripheral and CVC blood cultures yielded yeasts. Blood culture drawn from the CVC demonstrated positive result 1 hour earlier than the peripheral culture, and the patient diagnosed to have CVC-associated fungemia. The strain was identified as R. mucilaginosa by API 20C AUX (Biomerieux, Marcy l'Etoile, France). Susceptibility test was performed with E test strips, and MICs were the following: 0.25 mg/L for amphotericin B, over 64 mg/L for fluconazole, 1 mg/L for voriconazole, and over 64 mg/L for micafungin. Vancomycin and meropenem were discontinued, and fluconazole was switched to amphotericin B deoxycolate. The catheter was removed on the sixth day of the antifungal treatment. The patient improved clinically and blood culture became negative. Amphotericin B was discontinued 14 days after the first negative blood culture.

Learning Points/Discussion

R. mucilaginosa can cause catheter-related fungemia in premature infants. Correct identification is mandatory for appropriate management, as Rhodotorula spp are resistant to antifungal agents, such as fluconazole and echinocandins.
ACUTE CYTOMEGALOVIRUS INFECTION IN PRETERM BORN INFANT

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Title of Case(s)

Acute cytomegalovirus infection in preterm born infant

Background

Cytomegalovirus (CMV) infection is one of the most common viral infections of the newborn. Common mechanisms of the infection include perinatal exposure to infected genitalia secrete during birth or ingestion of breast milk containing CMV. Not always perinatal exposure to CMV are associated with clinical manifestation of disease. However, to premature infants perinatal infection can result in severe, disseminated infection, associated with end-organ damage and death.

Case Presentation Summary

Preterm born infant (28th week of gestation, weight 1.320g) was admitted to neonatal Intensive care unit. Due to respiratory distress, she received respiratory support with CPAP, surfactant application, antibacterial therapy and parenteral nutrition. At the 9th day of life her condition deteriorated with respiratory insufficiency and lung bleeding secondary to hypocoagulation. Mechanical lung ventilation was started. Since 14th day of life, thrombocytopenia progressed. She received multiple platelets transfusions. Despite of broad spectrum antibacterial therapy, blood component transfusions, repeated surfactant application, the condition continued to deteriorate with pneumonitis on x-ray examination progressing and increasing the hyperbilirubinemia (at the expense of direct bilirubine). She had unexplained episodes of fever with rising of CRP and II-6. All the blood cultures were negatives. At the 38th day of life CMV antigen was confirmed in urine sample, which was considered to be the cause of pneumonitis, hepatitis and thrombocytopenia. The therapy with ganciclovir was started. Despite of treatment, hepatic failure progressed, ascites appeared. The hypocoagulation with repeated gastrointestinal bleeding repeated. Respiratory insufficiency and hemodynamic problems increased and patient died.

Learning Points/Discussion

In conclusion, CMV infection must be kept in mind if child have pneumonitis, hepatitis and unexplained thrombocytopenia.
LACTOCOCCUS LACTIS CAUSED SEPTICEMIA IN TOTAL PARENTERAL NUTRITION DEPENDENT CHILD WITH ULTRA-SHORT BOWEL SYNDROME – CASE REPORT.

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Title of Case(s)

Lactococcus lactis caused septicemia in total parenteral nutrition dependent child with ultra-short bowel syndrome – case report.

Background

Lactococcus does not normally colonize human tissue and is classified as non-pathogenic. Lactococcus lactis is a spherically-shaped, facultative anaerobe, gram-positive, lactic acid bacterium widely used for industrial production of fermented dairy products. There are few reports, where the bacterial infection has been caused by Lactococcus species in children, the mechanism of the infection is unclear.

Case Presentation Summary

We report a case of a 3.3 years old girl with ultra-short bowel syndrome, duodenocoloanastomosis, Broviac catheter, portal hypertension and who is on a long-term home parenteral nutrition (with chronic liver changes, cholestasis and cholelithiasis, chronic pancreatitis). She was presented with fever 38°C and no other symptoms, with a high risk of catheter related infection. Blood cultures from two hands and Broviac catheter were taken before the treatment and on the 18th day of hospitalization. CRP on the 1st day was 76,57mg/L. Immediate antibacterial treatment with cefuroxime was started but changed to Vancomycin for 14 days as the fever continued and CRP raised to 112mg/L. Positive blood culture identified Lactococcus lactis. In retrospective analysis, we managed to find out that she has been given some unknow probiotics.

Learning Points/Discussion

The case report suggests that we should be aware of mostly non-pathogenic bacteria causing serious infection in patients who are immunocompromised or who have a long term intravenous catheter.
Background

The incidence and severity of viral respiratory infections in children undergoing hematopoietic cell transplantation (HCT) may vary according to NK cells reconstitution patterns. Our aims are to describe viral respiratory infections and to characterize NK cells in these patients.

Methods

Prospective single-center study including patients <18 years undergoing HCT and matched healthy controls. Nasopharyngeal aspirates (NPA) were collected in the pre-transplantation week, on transplantation day and during the post-transplantation period (days 10, 20 and 30). Respiratory viruses (influenza, parainfluenza 1–4, coronavirus 229E-OC43, enterovirus, rhinovirus, RSV, metapneumovirus, bocavirus, adenovirus) were studied by PCR and NK phenotype by flow cytometry.

Results

Fifteen HCT recipients (100% allogenic) and 13 matched controls were recruited. Viral infections were detected in 2/12 (17%) valid control samples (1 rhinovirus, 1 adenovirus) and in 9/49 (18%) patient samples (5 rhinovirus, 2 parainfluenza, 2 adenovirus). All viral infections were caused by a single pathogen. Both controls with positive viral detection were asymptomatic. In the patient group, respiratory viruses were identified before HCT in 6 patients (2 symptomatic) and after HCT in 3 (1 symptomatic). The percentage of NK cells at HCT in NPA was higher in patients than in controls, whereas the percentage of T cells at HCT was lower in patients. We observed an increase in T cells and a decrease in NK cells after HCT. The NCR and NKG2D receptor expression on NK cells was high in patients with positive viral detection except for NKp44 at day 10 after HCT.

Conclusions
Asymptomatic infection by respiratory viruses is common in HCT recipients. Immune cells in NPA differ in HCT recipients and in controls, and change over time. These results should be validated in a larger sample.

Clinical Trial Registration (Please input N/A if not registered)

N/A
ROLE OF HEALTH CARE PROVIDERS IN PREVENTING NOSOCOMIAL INFECTION IN NEONATAL INTENSIVE CARE UNITS

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Background and Objective

Aim of this literature review is to state the role of health care providers in preventing nosocomial infection in neonatal intensive care units (NICU).

Methods

World Health Organisation (WHO) defines nosocomial infection as infectious which is nonexistent in the patient when applied to the health unit or infectious that are not in the incubation period. Those infections increase mortality and morbidity of hospitalized individuals, extend the hospitalization period and they place significant burdens on the country's economy in terms of health expenditures. Nosocomial infections which 15% of them are preventable infections appear to be a serious health problem. Firstly, health care providers working in NICU should be knowledgeable and experienced about NICU to prevent infectious in this area. The skin, the first defense against infections, has not fully developed in newborns, particularly in preterms. Babies with low birth weight should only be wiped with warm water and cotton and staff should use gloves while contacting neonates. Umbilical cord should be keep clean and dry and just be wrapped with sterile sponge as recommended by WHO. Risky patients should be defined, isolation methods should be applied in every patient carefully, guidelines both for antibiotic using and surveillance programs should be generated. Enteral probiotic using is regarding with decreasing in morbidity rates of infection and Necrotizan Enterocolit (NEC). In a conducted study, it is stated that there is a decrease in incidence of nosocomial infections and NEC due to nutrition pattern combined with probiotic agents (Lactobacillus acidophilus ve Bifidobacterium infantis).

Learning Points Discussion

Health care providers working in NICU should be conscious and educated for preventing nosocomial infections.
AN UNUSUAL CASE OF LATE ONSET DISSEMINATED STAPHYLOCOCCAL SEPSIS IN A PRETERM INFANT

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Title of Case(s)

AN UNUSUAL CASE OF LATE ONSET DISSEMINATED STAPHYLOCOCCAL SEPSIS IN A PRETERM INFANT.

Background

Percutaneous central venous catheters (PCVC) are commonly used in the neonatal intensive care unit. Preterm infants are more predisposed to develop catheter related blood stream infection (CRBSI) which happens to be the most common complication associated with PCVC.

Case Presentation Summary

30 weeks male baby recovering in the neonatal unit was noted to be have increasing oxygen requirement and was ventilated on 10th day of life. SepTIC screen revealed a rising C Reactive protein along with thrombocytopenia. Blood culture grew *Staphylococcus aureus* (SA) and was positive for Panton Valentine Leukocidin (PVL) toxin. Within 24 hours he developed a dusky 4th toe on his right foot and an abscess overlying the antero-medial aspect of his left elbow and another overlying his Xiphisternum. Echocardiography and ophthalmological examination was normal. Magnetic resonance imaging of whole body showed cavitating lesions in the right upper lobe, right lung base and also in the left lung. He had a multi loculated collection in the left ante cubital fossa measuring 33x17mm and a lower pre-sternal collection measuring 13x4mm. Baby had a long line in his right arm which was removed as it was believed to be the source of dissemination of the bacteria. He was initially started on Cefotaxime and Vancomycin and later changed to Flucloxacillin and Linezolid as per culture sensitivity. Baby responded well to antibiotics and was discharged without any sequelae

Learning Points/Discussion

Sepsis due to PVL toxin producing SA can cause significant morbidity and mortality in neonates. Proper screening should be done to rule out septic foci in neonates. MRI is a good non-invasive tool to demonstrate multiple septic foci in a patient with disseminated sepsis.
VACCINE-PREVENTABLE AWARENESS IN ROMANIAN PARENTS VIA SOCIAL MEDIA – THE PERTUSSIS CASE

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Background

In the difficult setting of a constant decrease of vaccine coverage in Romania, medical education on vaccine-preventable diseases could reach parents by means of new tools. Parents are using on-line resources when they experience a health issue in their children. A research on patient behavior documented in our country a particular approach in solving health-related aspects: 74% of urban patients go on-line before asking their GP and 31% use Social Media about diseases. Our study aims to evaluate the impact of a Social Media tool in this particular setting.

Methods

Retrospective analysis of educational activities regarding vaccine-preventable diseases (with a special focus on Pertussis) in a large representative group of parents and doctors [more than 68 000 followers] called SVC [“Spitalul Virtual de Copii” – Virtual Children’s Hospital].

Results

13 different posts or notes were related to Pertussis, counting more than half a million views. A slow and progressive increase of interest and awareness has been observed during 12 months. First posts proved a significant preference for documents presented entirely in Romanian language, being seen 4 times more often and having more than two-fold share rate. Highest impact had a short video of a typical pertussis case in a 5 years old girl admitted in our department (>220000 people have seen this post and >1300 shared the document). This approach impacted also on physicians. Disease awareness generated an increase of referrals and testing for pertussis in clinic.

Conclusions

New tools should address the patient-doctor communication paradigm. Parents and patients are prone to individual on-line search of data regarding diseases. We are now building a complex Social Media network in order to increase disease awareness and decrease vaccine hesitancy in our country.
A COMPARISON OF VIRAL BRONCHIOLITIS HOSPITAL MANAGEMENT PRE AND POST NATIONAL GUIDELINE PUBLICATION IN THE UK

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Background

This study aimed to prospectively survey the management of viral bronchiolitis in hospital trusts in the UK after the publication of NICE Guidance in 2015 and compare this to similar data collected prior to the guideline’s publication.

Methods

An electronic, structured questionnaire was sent to hospital paediatricians across the UK in March 2015, prior to, and May 2017, after the publication of, the NICE bronchiolitis guideline. The questionnaire contained questions relating to the management of infants with viral bronchiolitis in the hospital setting. Participants were identified via the Royal College of Paediatrics and Child Health contacts system.

Results

A total of 111 trusts in 2015 and 100 trusts in 2017 had a paediatrician provide a response. Compliance to various aspects of the NICE guidelines ranged from 43-100% in 2015 to 52-97% in 2017. Improvements were seen in the appropriate use of supplemental oxygen (58% to 66% compliance), prescription of antibiotics (46% to 52% compliance), nebulised adrenaline (78% to 87% compliance), hypertonic saline (45% to 66% compliance) and provision of written guidance to parents (47% to 78% compliance). The percentage of trusts fully compliant with the guideline was 18% in 2015 and 19% in 2017 (P=0.9).

Conclusions

Improvements were seen in reported compliance in certain areas of the guideline, however the number of trusts who were 100% compliant has not changed significantly. This may be in part due to the short period of time between publication of the guidelines and re-assessment and differences in the hospital doctors responding in each year.
EVALUATION OF CYTOMEGALOVIRUS (CMV) IMMUNE RESPONSE IN CHILDREN DURING THE FIRST YEAR AFTER HEMATOPOYETIC STEM CELLS OR SOLID ORGANS TRANSPLANTATION

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Background

CMV specific immune response is altered in transplant recipients. Antivirals are associated with resistance, toxicity and need for viral load monitoring. QuantiFERON-CMV® is able to detect CMV specific T lymphocytes against CMV, but there is limited information in children. Objectives: to describe CMV immune response and CMV viral load in pediatric hematopoietic stem cell transplant (HSCT) and solid organ transplant (SOT) patients.

Methods

Children with risk of CMV infection undergoing HSCT were enrolled 6 weeks post transplant and 3 months after SOT. They were followed up to 12 months. QuantiFERON-CMV® was performed monthly in HSCT and every 2 months in SOT. CMV viral load (AmpliPrep/COBAS®), lymphocyte count and immunosuppressant levels were recorded.

Results

Sixteen patients were included (14 finished follow up), median age 9,2 years, 50% men. Eight received TPH (5 umbilical cord, 1 related donor, 2 unrelated donor), 6 with high risk of CMV reactivation and 6 with acute graft versus host disease. Eight were TOS (4 heart, 3 liver, 1 kidney), two with high risk of CMV reactivation. Lymphocytes at 3 months were 850 and 2050 cel/ml in TPH and TOS, respectively (p=0,04). In both groups 5 patients had reactive QuantiFERON-CMV®. In SOT 4/5 had detectable CMV viral load, none of them needed antiviral therapy after reaching a reactive QuantiFERON-CMV® level. In HSCT 2/5 had CMV infection, both occurred before reaching a reactive QuantiFERON-CMV®.

Conclusions

Patients with CMV detectable viral load and a reactive QuantiFERON-CMV® did not required antiviral therapy. QuantiFERON-CMV® can be useful after the suspension of antiviral prophylaxis in SOT. In HSCT, CMV infection was less frequent, so it is difficult to make recommendations, it could be useful in patients that already have had a positive CMV viral load.
09C. SCIENCE: INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS

ANTIBIOTIC PROPHYLAXIS IS EFFECTIVE FOR NEUTROPENIC PATIENTS WITH PEDIATRIC CANCER FOLLOWING INTENSIVE CHEMOTHERAPY

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Background

It is yet well understood whether prophylactic antibiotics are effective for neutropenic patients with pediatric cancer during chemotherapy. This study aimed to investigate the efficacy of prophylactic antibiotics in the pediatric cancer patients who were treated with different intensity chemotherapy regimens.

Methods

Medical records of neuroblastoma patients and brain tumor patients who were treated with three different chemotherapy regimens (regimen NB for neuroblastoma and regimens A and B for brain tumors) in our hospital between May 2007 and July 2017 were retrospectively analyzed. Piperacillin sodium (PIPC) was used for prophylaxis during neutropenic period since July 2014.

Results

104 neutropenic periods from 26 eligible patients were analyzed. 14 patients received PIPC prophylaxis and 12 patient received no prophylaxis. First we confirmed that both no-prophylaxis and prophylaxis group experienced comparable levels of myelosuppression. During neutropenic period following chemotherapy, PIPC prophylaxis significantly reduced frequency of febrile neutropenia (FN) (35% vs 64%, p=0.006), maximum body temperature (37.9 ± 0.49 vs 38.3 ± 0.80, p = 0.002), fever duration (°C) (0.6 ± 1.0 vs 1.9 ± 2.4, p = 0.001), and maximum serum CRP levels (mg/dl) (2.5 ± 2.8 vs 1.0 ± 1.7, p < 0.001). We next asked whether different intensity of chemotherapy affects the efficacy of prophylactic antibiotics. Consistent with overall analysis, significant reductions of frequency and severity of FN were observed following high- (NB) and intermediate- (A) intensity regimen. In contrast, after moderate intensity chemotherapy (B), no significant reduction was observed in the frequency of FN by prophylaxis.

Conclusions

Our results suggested that prophylactic antibiotics with PIPC were effective to reduce frequencies and severity of febrile episodes following high intensity chemotherapy. Conversely prophylaxis may be less effective following moderate intensity chemotherapy.
A girl coming back from Madagascar. Is that pneumonic plague?

Background

Plague is a zoonotic disease caused by *Yersinia pestis*, that can lead to a bubonic, septicemic and pneumonic form (less common). The bacteria is transmitted to humans by the bite of an infected fly (*Xenopsylla cheopis*) or by airborne droplets from a human/animal case of pneumonic disease. From August 2017, there is an outbreak of pneumonic plague in Madagascar with 1791 cases and 202 deaths.

Case Presentation Summary

A 6 years old girl presented with 12h of fever (pitch 38.5ºC) and history of 3 days with cough with blood-tinged sputum. Six days ago, she arrived from Madagascar, where she lived for 6 months (cooperators' daughter). They lived in Antananarivo, were cases of pneumonic plague had been diagnosed during the present outbreak. She had suffered from croup before.

She was isolated after identification and was given a surgical mask. Respiratory precautions were taken by all health staff (gloves, glasses, coat, FFP3-mask).

On physical examination, her overall status was good, with aphonia and barking cough.

Blood test: hemoglobin 14.4g/dl, leucocytes 9.900/mm3 (granulocytes 65.5%, lymphocyte 25,8%), platelets 227.000/mm3, CRP<2,9 mg/L, procalcitonin 0,1 ng/mL.

Microbiology: thick smear and *Plasmodium Ag*: negatives. Serology and dengue Ag: negatives. A blood sample was taken for culture and PCR for *Yersinia*. A nasal swab was sent for respiratory viruses and parainfluenza virus type 3 was detected.

Learning Points/Discussion

Due to the increase in international travelling and adoption, tropical diseases are spreading worldwide. All health practitioners should be updated in international alerts, as they have a high impact on Public Health. Suspicious patients should be isolated. However, common diseases must be discarded. High level isolation units are crucial for the management of these diseases.
Background

Congenital cytomegalovirus infection (cCMV) has been described to be more frequent in Spain among HIV-exposed uninfected infants. Estimated prevalence in the general population is 0.3%, pre-ART 9.2%; post- HAART 1.3%. The aim of this study was to analyze the prevalence of cCMV among children born to HIV-infected mothers, and identify risk factors for infection.

Methods

Retrospective, descriptive study (2014-2017) including HIV-exposed uninfected infants. cCMV was ruled out by means of Shell vial culture in urine sample, within the first two weeks of life, according to national recommendations. Epidemiological and clinical data were recorded.

Results

A total of 40 mother-to-infant pairs were included. 92.5% of women had been diagnosed with HIV before pregnancy and all were on ART. Median CD4-T cell count at delivery was 650.5/mm3 (IQR:177-1700) and HIV-viral load: undetectable 32/40, if detectable, median 258 copies/mm3 (IQR: 37-486). CMV serology test was performed in the first trimester in 89.5%, with 100% positive IgG seroprevalence. However, there were no reported cases of vertical transmission of HIV and/or CMV.

Median gestational age was 38.5 weeks [IQR:32.8-40.3], weight 2.980 gr (IQR:1525-3760), length 48 cm (IQR:32-51), and head circumference 34 cm (IQR:28-45). Not a single patient presented with signs or symptoms of cCMV and no cytopenias were found. Otoacoustic emissions were normal in 95%.

Conclusions

cCMV prevalence was 0% in our series of infants born to HIV-infected mothers, lower than the prevalence reported before in Spain. If these results are confirmed by larger multicenter studies, national guidelines may contemplate to remove the screening for cCMV among asymptomatic HIV-exposed uninfected infants.
PREVENTING HIV MOTHER TO CHILD TRANSMISSION. THREE YEARS OF EXPERIENCE IN A TERTIARY HOSPITAL IN SPAIN

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Background

Thanks to access to antiretroviral treatment (ART), HIV- vertical transmission (VT) has dramatically decreased in the last years in Spain, and is situated today below 1%. The aim of this study was to describe the clinical and epidemiological features related with VT.

Methods

Retrospective, descriptive study (2014-2017) including all newborns to HIV infected mothers in a tertiary hospital in Spain. Epidemiological and clinical data related to the mother and newborn were recorded.

Results

40 neonates were included, 92.5% born to mothers diagnosed with HIV before pregnancy. Median CD4-T-cell at delivery was 650,5/mm3 (IQR: 177-1700) and HIV-viral load: undetectable 32/40, if detectable, median 258 copies/mm3 (IQR: 37-486). CDC-2014 mother's stage was: A1 (10%), A2 (35%), A3 (7,5%), B2 (7,5%), B3 (2,5%), C3 (20%), no data (12,5%). All women received treatment along pregnancy: 2 NRTIs + 1 NNRTIs (37%), 2 NRTIs + 1 PIs (45%), 2 NRTIs + 1 II (10%), other schemes (8%). The most commonly used regimen was Tenofovir-disoproxil-Fumarate+Emtricitabine+Rilpivirine (25%). 81,5% received Tenofovir as NRTI. 6/40 mothers received Raltegravir during the last weeks of pregnancy. The delivery was eutocic in 57,5%, and all cases received Zidovudine intrapartum. Median gestational age was 38.5 weeks (IQR: 32.8-40.3). All newborns were given prophylaxis for 28 days: zidovudine alone 80% and triple therapy (AZT+3TC+NVP) 20%. No newborn was breastfeeding. All children were follow up, and no cases of VT were documented.

Conclusions

There were no cases of vertical transmission of HIV between 2014 and 2017 in our hospital. Most women knew her HIV-status and received treatment before pregnancy. During pregnancy, most regimens are based on Tenofovir, with an increase in the use on integrase inhibitors, specially to achieve viral suppression before delivery.
THE HIDDEN TRUTH BEHIND INVASIVE PNEUMOCOCCAL DISEASE

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Background

Pneumococcal conjugate vaccines (PCV) have reduced the incidence of invasive pneumococcal disease (IND). However, there are vaccinated children who develop IND, some of whom suffer from an undiagnosed immunodeficiency.

The aim of this study was to describe immune disorders in children with IND.

Methods

Retrospective, descriptive, single-center study (2003-2015). All children <14 years of age that suffered from IND (confirmed by culture/PCR of sterile body fluid samples) were included.

Results

127 patients were analyzed. Median age was 33 months (IQR;12-59). Most frequent clinical presentation was bacteremic pneumonia (56/127;44%), followed by pneumonia with empyema (33/127;26%), meningitis (12/127; 16%) and sepsis (3/127;2%). Vaccination status: 84/121 (69%) had received ≥2PCV doses and 68/121 (56%) ≥3 doses. From the 84 children who received ≥2 doses, in 5 (6%) the infection was caused by vaccine serotypes. Immune response to vaccine had not been evaluated in any of them.

Underlying health conditions that could predispose to IND affected 33/127 patients (25%): 9/127 frequent respiratory infections, 5/127 prematurity, 4/127 Down syndrome, 2/127 lymphangiectasia. Other comorbidities (affecting one patient each) were: cardiopathy, prior S. pyogenes myositis, prior meningococcal sepsis, acute lymphoid leukemia after IND, neutropenia, coagulopathy, esophageal atresia and celiac disease and hepatic-haemangioendothelioma. Immunological evaluation had been conducted only in 38/133 (28%): 21% hypogammaglobulinemia, 6% C2 deletion, 31% CD4/CD8 inverted ratio; 50% children who received ≥3 PCV doses had no antibody response to tetanus (4/8), 50% (4/8) to diphtheria. Abdominal ultrasound was performed in 38/127, 4/38 (11%) were abnormal.

Conclusions

Immune disorders are frequent in patients with IND. Careful medical history taking and immune tests would have been useful. Abdominal ultrasound and a basic immunological evaluation are advisable in children with IND, especially in severe cases.
TUBERCULOUS LYMPHADENITIS WITH PHLYCTENULAR KERATOCONJUNCTIVITIS AND ERYTHEMA NODOSUM. A RARE ASSOCIATION

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Title of Case(s)

Tuberculous lymphadenitis with Phlyctenular keratoconjunctivitis and Erythema nodosum. A rare association.

Background

Primary tuberculosis (TB) are usually pulmonary, TB as cervical lymphadenitis has been reported frequently. Phlyctenular Keratoconjunctivitis (PKC) and Erythema nodosum (EN) may rarely be associated with this, but usually found separately. In the recent past we have not found any case report with these association which prompt us to present this case.

Case Presentation Summary

An eight years girl presented with low grade evening rise of temperature for three months, swelling of right mandibular area for two months, some red colored painful lesion on shins and continuous watering and redness of both eyes for last fifteen days. She lived in the dormitory where she exposed to a TB patient six months ago.

On examination, the child had cervical lymphadenopathy in right jugulodigastric node (2.5×2.5 cm), soft, rounded, non-tender and matted without any discharging sinus. Other Lymph nodes were not palpable. Eye showed bilateral PKC. Skin survey revealed EN on both shins.

Other systemic examinations were normal. CBC was normal, ESR 49 mm in 1st hour. Chest X-ray was normal, MT was 28mm. FNAC lymph nodes showed features of TB. Gen Xpert was positive. Diagnosis of primary TB was made and started anti tubercular drugs with isoniazide, rifampicin, pyrazinamide and ethambutol for two months followed by isoniazide and rifampicin another four months. EN and PKC disappeared within two weeks. Lymph nodes become normal within five months treatment.
Learning Points/Discussion

Matted firm, non-tender cervical lymphnode in a child is suspicious of tubercular origin, if it is associated with EN it is highly suspicious and if EN and PKC are present it is highly suggestive of tuberculosis.
MYCOPLASMA PNEUMONIAE: MORE THAN PNEUMONIA

N. Smith

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Title of Case(s)

Mycoplasma pneumoniae: more than pneumonia

Background

M. pneumoniae is endemic in many areas throughout the world and is a common cause of respiratory tract infections, particularly in children of school age. However, the bacterium can also cause serious neurological disease. As the incidence of this is low, and pathogenesis poorly understood, such infection may be inappropriately omitted from a differential diagnosis. Yet even if a high index of suspicion for M. pneumoniae CNS disease is maintained, challenges with diagnostic techniques and a paucity of resources to help guide management can lead to uncertainty within clinical practice.

Case Presentation Summary

A 6-year-old girl initially presented with general malaise and lower respiratory tract symptoms. After commencing treatment for atypical community-acquired pneumonia her condition worsened and she developed focal seizures. Multiple investigations were performed, with serological results indicating likely M. pneumoniae infection. A diagnosis of M. pneumoniae meningoencephalitis was ultimately made. The patient received a number of antimicrobial agents and her symptoms gradually resolved. Subsequent to this initial admission, she has displayed personality change and cognitive impairment.

Learning Points/Discussion

This case highlights the diagnostic challenges in M. pneumoniae meningoencephalitis, uncertainty surrounding treatment protocols, and the potential long-term sequelae of this condition. More evidence is required to help elucidate optimal management of this condition. Until this is available, raised awareness among paediatricians, along with adherence to currently recognised best practice for diagnostic testing, and a pragmatic approach to treatment may lead to improved outcomes.
FACTORS ASSOCIATED WITH UPTAKE OF INFLUENZA AND PERTUSSIS VACCINES AMONG PREGNANT WOMEN IN SOUTH AUSTRALIA

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Background

Maternal immunization is an effective strategy to protect pregnant women and their infants from vaccine-preventable diseases. Despite the recommendation of maternal influenza and more recently pertussis immunization in Australia, uptake of these vaccines has been suboptimal. A midwife delivered immunization program for pregnant women at the Women's and Children's Hospital in South Australia commenced in April 2015. Monitoring the uptake of the current funded vaccine programs for pregnant women is limited. The study aimed to estimate maternal vaccine uptake and assess factors associated with influenza and pertussis vaccine uptake among pregnant women.

Methods

This prospective study was undertaken between November 2014 and July 2016 at the Women’s and Children’s Hospital. Demographic details and vaccination history for South Australian pregnant women who attended the antenatal clinic were collected. A standardised self-reported survey was completed during pregnancy with a follow up telephone interview at 8-10 weeks post-delivery.

Results

Of the 205 women consented, 180 pregnant women completed the study and received 76% and 81% maternal influenza and pertussis vaccines respectively. The adjusted odds of women receiving maternal vaccines during pregnancy were significantly higher for women delivering after the implementation of the midwife delivered program compared with women who delivered babies prior to the program for both pertussis vaccination (AOR 21.1, 95% CI 6.14-72.9; p<0.001) and influenza vaccination (AOR 5.95,95% CI 2.13-16.6,p<0.001). Women receiving a recommendation from a health care provider and first time mothers were significantly more likely to receive influenza vaccination during pregnancy.

Conclusions

High uptake of vaccines during pregnancy can be attained with health care provider recommendation and inclusion of maternal immunization as part of standard antenatal care. A midwife delivered maternal immunization program is a promising approach to improve maternal vaccine uptake.
SIMILAR GENOMIC PATTERN TO VACCINE STRAIN AMONG BORDETELLA PERTUSSIS ISOLATES IN IRAN

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Background

Despite a long history of vaccination with high coverage in children, a resurgence of pertussis has been observed in many countries. Adaptation of \textit{B. pertussis} isolates is one of the major reasons for pertussis reemergence. To identify the discrimination between local and vaccine strains, the genomic patterns and allele types of \textit{B. pertussis}, vaccine and circulating strains isolated from clinical specimens in Iran were analyzed in this study.

Methods

A total of 100 \textit{B. pertussis} strains collected from nasopharyngeal samples from 2008 to 2014 were studied. Biochemical tests, slide agglutination and real-time PCR were done to detect \textit{B. pertussis} strains. Sequencing of \textit{ptxP}, \textit{ptx} and \textit{prn} genes was carried out to determine the allele types of these virulence factors. Ultimately, the genomic patterns of \textit{B. pertussis} strains were investigated by PFGE using XbaI restriction enzyme. Vaccine strains \textit{B. pertussis} 134 and 509 were also analyzed.

Results

The results of PFGE showed 24 PFGE patterns that clustered into 17 PFGE groups. We found only one strain with the genomic pattern similar to vaccine strain \textit{B. pertussis} 134 with the same virulence profile except \textit{ptxA} (\textit{ptxP1}, \textit{ptxA1} and \textit{prn1}). However, \textit{B. pertussis} 509 showed the distinct PFGE pattern.

Conclusions

Of all 100 studied isolates until 2014, we found only one isolate showing the genomic pattern like vaccine strain. However, the clonal spread with different virulence profile from vaccine strains has been observed among the circulating strains. It may be suggested that strain variation between vaccine and local isolates may have an important effect on pertussis persistence and outbreaks in Iran like other parts of the world.

Clinical Trial Registration (Please input N/A if not registered)

N/A
UNUSUAL COMPLICATION IN A DIFFICULT TO DIAGNOSE CASE OF CNS TUBERCULOSIS

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Title of Case(s)

UNUSUAL COMPLICATION IN A DIFFICULT TO DIAGNOSE CASE OF CNS TUBERCULOSIS

Background

Tuberculosis (TB) is endemic in India and often affects the CNS in young children. Childhood TB being paucibacillary, presents a diagnostic challenge, especially with isolated central nervous system (CNS) involvement. This case documents the unusual complication of localized hemophagocytic lympho-histiocytosis (HLH) in the CNS due to TBM.

Case Presentation Summary

1 year old boy presented with 2 weeks of fever, cough, and convulsions, altered sensorium and left sided weakness for 3 days. Initial blood count showed anemia and lymphocytic leukocytosis 48,200/cu. mm. CSF: proteins - 99 mg%, normal glucose, 5 lymphocytes.

Examination: Stable vitals, pallor, moderate hepatomegaly. Bilateral wheeze and crepitations. CNS: GCS 9/15, Cranial nerves and pupils normal; left hypotonic hemiparesis with hyperreflexia.


Repeat CSF: Proteins 81 mg%, Glucose 94 mg% WBC 114 cells (P 45%, L 55%). CSF PCR for TB negative.

MRI brain: Granulomatous lesion in basal ganglia - etiology.

Stereotactic brain biopsy: Increased cellularity, reactive glial cells, large number of CD68 +ve histiocytes. No caseation, granulomas, organisms. Probable diagnosis: HLH.

No evidence of HLH elsewhere on biochemistry – no hypofibrinogenemia, hypertriglyceridemia or increase in Ferritin levels. Bone marrow – no hemophagocytosis seen. ATT omitted and started on HLH protocol. Clinical improvement in sensorium, motor deficit but fever persisted. Then brain biopsy tissue grew M. tuberculosis! ATT re-started with further improvement.

Learning Points/Discussion

TBM is common and with myriad forms of presentation and complications.
Diagnosis of TBM is difficult.

TBM can induce (localized) HLH requiring additional therapy.
IMMUNIZATION COVERAGE, IN CHILDREN 12 YEARS OLD, IN WESTERN GREECE 4 YEARS EXPERIENCE

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Background

Immunization coverage in children in Greece has achieved high levels during the previous years. However, recent poor economic situations in the country may have influenced children's admissions to pediatric surgeries, especially for preventive medicine. The main purpose of our study was to investigate the immunization coverage in children who live in Patras.

Methods

There were randomly selected 41 from 87 public primary schools in Patras, all in urban areas. All children who were born between 2003 and 2004, and whose parents gave consent, were included in the study. Immunization data were collected through the National pediatric vaccination cards. The sampling took place between September 2015 and December 2017.

Results

There were 1350 subjects enrolled in the study. The mean age was 12 years and 46.5% were boys. Children were fully vaccinated against Hepatitis B (98.9%), Tetanus, Poliomyelitis, Diphtheria, Pertussis and Haemophilus Influenzae (98.3%). Additionally, they were fully vaccinated against Measles, Mumps, Rubella (98.4%), Varicella (82.4%), Hepatitis A (84.7%) and Meningitidococcus type C (97.1%). The vaccination coverage was low for Streptococcus Pneumoniae (55.2%), Mycobacterium (BCG, 24%) and Meningitidococcus type B (3.6%).

Conclusions

Immunization coverage in children (12 years old) in Patras remained in high levels. A lower vaccination coverage was observed against Streptococcus Pneumoniae. Greek children were almost not vaccinated against Mycobacterium and Meningitidococcus type B. The reasons of this low vaccination coverage should be explored. We should mention that the Meningitis B vaccine is not yet included in the National Vaccination Program. There is a need for a national strategy plan in order to increase vaccination, especially against Streptococcus Pneumoniae, Mycobacterium and Meningitidococcus (type B).
Background

The inappropriate use of antimicrobials is one of the main factors for the emergence of antimicrobial resistance. Antimicrobial stewardship programs have been innovated in many hospitals to optimize the use of antimicrobials. In order to effectively enforce, appropriate assessment of antibacterial procedure is needed. This study aims to describe antimicrobial prescribing patterns at a tertiary care children’s hospital in Japan.

Methods

As part of the GARPEC (Global Antimicrobial Resistance, Prescribing and Efficacy in Neonates and Children) study, one-point prevalence surveys (PPSs) were carried out in three periods at Tokyo Metropolitan Children’s Medical Center in Japan: in May-June 2016, September-October 2016, and December 2016-February 2017. Data collected included antimicrobial agents prescribed, dose, frequency, route of administration, and reasons for treatment. The surveys included children and neonates receiving antimicrobials on the day of PPS.

Results

A total of 414 patients were surveyed, of whom 94.2% (n=390) were children and 5.8% (n=24) were neonates. The most frequently prescribed antimicrobials for treatment were ampicillin (14.0%), cefotaxime (12.2%) and ampicillin/sulbactam (10.5%). Overall, 181 prescriptions (43.7%) were the prophylaxis for medical problems. The most commonly used for prophylaxis was SMZ/TMP (34.3%) and fluconazole (33.1%). Cefazolin (25.1%) was the most commonly prescribed parental antimicrobials, followed by ampicillin (15.2%). The most frequently prescribed oral antimicrobial was SMZ/TMP (43.0%).

Conclusions

The study showed that penicillins and 3rd generation cephalosporins were widely prescribed for treatment at a tertiary care children’s hospital in Japan. More than 40% of all prescriptions were prophylactic administration, mostly SMZ/TMP and fluconazole. The most commonly prescribed parental antimicrobials were penicillins and 1st generation cephalosporins, which were prescribed mainly for treatment. The oral antimicrobials were SMZ/TMP and fluconazole, mostly for prophylaxis.
ESP18-0402
E-POSTER VIEWING - MAY 28-JUNE 2 - EXHIBITION HOURS

04B. SCIENCE: COMMUNITY ACQUIRED INFECTIONS: RESPIRATORY TRACT INFECTIONS

DIFFERENT CLINICAL MANIFESTATIONS AND ANTIVIRAL-RESPONSE BETWEEN INFLUENZA SUBTYPES
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Background

Several observational studies demonstrated that Oseltamivir had a beneficial effect during 2009-A/H1N1 pandemics, but there are still controversies about its use, especially with seasonal subtypes.

Methods

The aim of this observational retrospective study was to detect clinical and antiviral-response differences among the current circulating viral subtypes during two consecutive seasons (2015/16-2016/17). Seventy-five hospitalized patients were recruited in a tertiary hospital: 25 influenza A/H1N1-2009, 25 A/H3N2 and 25 influenza B. All patients received oseltamivir.

Results

Children with influenza-B infection were older than those with A/H1N1 and A/H3N2 (168 months (p25-27: 59-196) vs 39 (18-64) and 27 (16-85), respectively; p<0.01). 45/75 had preexisting conditions, mainly neurological. Rates of pre-existing conditions did not differ between subtypes.

The leading cause of hospitalization was respiratory insufficiency (39/75), with similar proportion between the groups. Digestive manifestations were frequent (24/75), but diarrhea was only described in A/H1N1 (5/25;p=0.03). Neurological symptoms tended to be more frequent in patients with influenza A (11/50 A vs 1/25 B;p=0.06). Acute myositis only occurred with influenza B infection (5/25;p<0.01).

Bacterial co-infection (mainly pneumococcal) was more frequent in patients with influenza A (11/50 vs 1/25;p=0.06).

9/75 patients required intensive-care. No differences between subtypes were found. Nevertheless, none of the 5/9 previously healthy patients had influenza B. No mortality was found.

There was a correlation between the delay in starting oseltamivir treatment and the duration of the disease for all subtypes (rho-Spearman A/H1N1:0.58, p<0,01; A/H3N2:0.51, p=0,01; B:0.49, p=0.04).

Conclusions

Extra-pulmonary symptoms and severity of influenza disease may vary depending on the subtype, especially in previously-healthy patients. Delays in starting oseltamivir treatment increased length of symptoms, regardless of the subtype.

Clinical Trial Registration (Please input N/A if not registered)
IDENTIFICATION OF Streptococcus agalactiae ISOLATED FROM DISCHARGE IN PREGNANT WOMEN USING 16S rRNA PRIMERS COMPARED WITH CONVENTIONAL METHODS.

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Background

Group B streptococcus (GBS) is a part of many women’s vaginal and also gastrointestinal tract normal flora, but it can cause life threatening. The aim of this study was to evaluate PCR assay targeting 16S rRNA primers compared with conventional culture method for direct detection of GBS in vaginal specimens of pregnant women at 35–37 weeks of gestation in Hamadan.

Methods

203 vaginal specimens of pregnant women at 35–37 weeks of pregnancy from June 2014 through February 2015 were evaluated for detection of GBS using culture method and PCR assay. The species were identified by biochemical and serological methods. Data was gathered through a questionnaire and analyzed using SPSS 13 software.

Results

Prevalence of GBS in 203 collected samples was 7.39% using culture method and 19.70% using PCR assay. 25 specimens resulted positive by PCR and negative by culture; 2 specimens resulted positive by culture and negative by PCR. Generally, a total of 42 specimens (20.69%) were considered true positive. PCR results in comparison to culture (as gold standard) revealed sensitivity of 88.24%, specificity of 87.44%, positive and negative predictive value of 35.71%, 98.95%, respectively, and accuracy of 87.50%.

Conclusions

The study data demonstrated that performing only culture method leads to missed false negative carrier individuals. Thus, it is recommended that both the PCR assay and conventional culture method perform routinely in order to detect GBS.
Background

The most common reason for the development of intestinal dysbiosis in children can be the use of antibiotics, which could lead to antibiotic-associated diarrhea that can be linked to the negative impact of waste products Clostridium difficile.

Methods

The study included 120 children with enteric infections, from them children till 6 months, there were 20 cases (16.7%); from 6 months to 1 year -60 (50.0%), over the year - 40 (33.3%). The diagnosis of intestinal infection from all the sick children were confirmed bacteriologically: Ps. Aerogenosa in 1(0,8%), Salmonella Enteritidis - 2(1,7%), Proteus Vulgaris - 3(2.5%), Enterobacter cloacae - 7(5,8%), Citrobacter diversus - 7(5,8%), Klebsiella pneumoniae - 8(6,7%), Morganella Morganii - 9(7,5%), Proteus Mirabilis - 10 (8,3%), Citrobacter former - 12 (10%), acute enteric infection unspecified etiology in 61(50.8 percent). The rotavirus antigen in the feces -12 (10%). Treatment scheme with Enterol (saccharomyces boulardii): for children up to one year 1 sachet 1 time, over one year 1 sachet 1-2 times a day.

Results

At admission all studied sick children was expressed intoxicating syndrome and dyspeptic syndrome. Dyspeptic syndrome in the form of vomiting before treatment was observed in 52 (43.3%) sick children, and after treatment the symptoms completely was stopped. Bloating in the form of flatulence was before treatment in 112 (93.3%)children and after treatment the abdomen was soft, painless in all examined children. Thin stool with pathological impurities was before treatment in 109 (90,8%) sick children and after treatment in 2 children (1.7%), (p≤0.05).

Conclusions

The use of Enterol had a positive impact on the duration of basic clinical symptoms in diarrhea. The use of Enterol in the age dosages within 5 days prevents the development antibiotic-associated diarrhea in children.
A CASE OF CONGENITAL TUBERCULOSIS BORN FROM A MOTHER WITH PULMONARY TUBERCULOSIS

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Title of Case(s)

A Case of Congenital Tuberculosis Born from a Mother with Pulmonary Tuberculosis

Background

Congenital tuberculosis is a rare disease with a high fatality rate. Congenital tuberculosis is thought to be infected through the placenta from the infected mother.

Case Presentation Summary

We report a case of congenital tuberculosis in a 15-day-old male infant who presented with fever and vomiting. The baby was born by vaginal delivery from a mother who had a history of salpingectomy due to unknown cause. Physical examination revealed distended abdomen with engorged superficial vein and hepatomegaly. Abdominal sonography revealed multiple microabscesses on liver, spleen and kidney. Tuberculin skin test found to be negative. Gene Expert PCR of gastric aspirate was positive. Smears of intra-abdominal LN specimens contained acid-fast bacilli, and cultures were positive for *Mycobacterium tuberculosis*. There were no pulmonary lesions on chest CT. Nodular enhancing lesions in the bilateral cerebral and cerebellar hemisphere on brain MRI suggested tuberculous granuloma. The baby’s mother had no apparent clinical symptoms but her chest radiograph showed micronodular infiltrates on the left upper lobe. Sputum specimen revealed acid-fast bacilli, and *M. tuberculosis* was cultured from sputum. The baby was managed with isoniazid, pyrazinamide, rifampicin for 12 months. During the course of management, the baby developed massive ascites.

Learning Points/Discussion

Congenital tuberculosis should be considered in infants with fever and intra-abdominal microabscess.
ASSOCIATION BETWEEN METEOROLOGICAL VARIATIONS AND INFLUENZA ACTIVITY ACROSS DIFFERENT CLIMATE ZONES

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Background

While influenza A and B cause annual epidemics worldwide, they exhibit remarkably distinct seasonality across different climate zones. However, studies examining the association between meteorological factors and influenza seasonality across different climate zones within the same period are scarcely available to date.

Methods

This study analyzed the marginal effects and interactions of meteorological variations on activity of influenza A and B in 11 sites spread over different climatic zones. Data regarding daily mean temperature, relative humidity, wind speed and daily precipitation amount were acquired. The daily numbers of laboratory-confirmed influenza A and B cases from January 1, 2011 to December 31, 2015 were collected from each study site. The boosted regression tree was employed to analyze the marginal effects, whereas interaction effects were assessed via Friedman’s H-statistic and visualized via three-dimensional plots.

Results

Cold temperature was a major determinant that favored both influenza A and B in temperate and subtropical sites. The temperature-to-influenza A, but not influenza B, exhibited a U-shape association in subtropical and tropical sites. In the temperate zone, both influenza A and B were favored by high relative humidity but not extremely wet conditions. Positive interaction effect from cold and wet conditions on influenza activity was observed in most temperate sites.

Conclusions

Meteorological variables, particularly temperature and relative humidity, are strongly associated with influenza activity, and association patterns varied between influenza A and B and among climate zones. Further modelling studies to predict the impact of global warming on the disease burden of influenza and to understand the potential differences across climate zones are needed. A meteorology-based alert system for influenza epidemics might assist in public health response.
08D. SCIENCE: IMMUNOLOGY AND HOST-PATHOGEN INTERACTIONS

IMMUNE REHABILITATING THERAPY IN SEVERE FORMS OF SALMONELLOSIS IN CHILDREN.
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Background

Nowadays great attention is paid to medicines of vegetable origin. In this regard, interest is the study of the antioxidant and immunomodulatory action of the drug "Kyzylmay with propolis" in combination with antibacterial therapy.

Methods

The study included 45 children aged 6 months to 3 years who received "Kyzylmay with propolis" in suppositories.

Results

In the analysis of T-system immunity in patients with salmonellosis was detected the decrease of populations with phenotype CD 3 in 1.9%, phagocytic activity of neutrophils in 1.45 (p < 0.01) in comparison with healthy children. A decrease in the percentage of CD 8 (T-helper cells), CD 8 (T-suppressor) and adhesive capacity of neutrophils, respectively in 1.5, 1.7 and 1.2 times (p < 0.01) and increased of CD 56 (NK lymphocytes) in 1.7 times (p < 0.01). Was observed decrease in the percentage of B-lymphocytes in 1.6 (9.37±1.11) times (p < 0.05). Indicators of spontaneous and induced NST-test with the Salmonella was reduced in 3.9 and 2.6 times (p < 0.05), and the stimulation index in 2.1 times, which indicated disturbances in the immune status and reflected low functional reserve of phagocytes. The treatment of severe forms of salmonellosis "Kyzylmay with propolis" contributed to the decline in body temperature to normal values, the relief of symptoms of toxicosis with exsicosis, neurotoxicity and infectious toxic shock. Stool frequency decreased to 5-7 times a day and has acquired a doughy form. Populations with phenotypes reached a level control.

Conclusions

The use of Enterol had a positive impact on the duration of basic clinical symptoms in diarrhea. The use of Enterol in the age dosages within 5 days prevents the development antibioticassociated diarrhea in children.
The authors declare that they have no competing interest. Sponsors had no role in study design, or collection, analysis and interpretation of data.

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Background and Objective

Schistosomiasis is a tropical disease caused by Schistosoma. It is one of the most prevalent, though neglected, of the tropical infectious diseases. More than 240 million people in 78 countries are infected. The advent and proliferation of mass drug administration programmes using the single drug praziquantel is resulting in increased numbers of people, mainly children aged 6-14 years. However, such reliance on praziquantel represents a precarious situation, and some studies have confirmed isolates of Schistosoma have reduced susceptibility to praziquantel. So more strategies are needed to prevent and control schistosomiasis.

Methods

Gene-chip technology are used to uncover the gene expression of females at three time points (before pairing, pairing, after pairing), and thereby identify genes that likely contribute to pairing and reproduction. We also observed the morphological changes of reproductive organs of 

S. japonicum by Confocal Laser Scanning Microscopy (CLSM) and the egg production of 

S. japonicum using light microscopy after Sjfs800 gene silence.

Learning Points Discussion

Among the most interesting genes identified here was fs800, which play an important role in development of vitellarium and egg production. This study makes us better understand regulatory features of genes before and after pairing in 

S. japonicum female, and provides some new clues for the prevention and treatment of schistosomiasis.
01A. EDUCATION: PAEDIATRIC ANTIBIOTIC STEWARDSHIP

POINT-OF-PRESCRIPTION INTERVENTION TO IMPROVE THE CHOICE OF ANTIBIOTIC IN ACUTE OTITIS MEDIA IN CHILDREN

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²Hospital Beatriz Ángelo, Quality Improvement, Loures, Portugal

Background

Misuse of antibiotics is a serious problem and is directly related to the increase of bacterial resistance. Antimicrobial Stewardship Programs can have a significant impact on the choice of antibiotic. This study evaluated the impact of a simple intervention on antibiotic prescribing in the pediatric emergency department.

Methods

Prospective study that included all children admitted to the emergency department for a year. The intervention consisted in placing a warning with information about the recommended antibiotic in children with the diagnosis of acute otitis media. The prescription of antibiotics in this disease was monitored before, during and after the intervention in different age groups and for several professional groups.

Results

During the study period, a diagnosis of acute otitis media was made in 5,695 children. The percentage of Amoxicillin prescription increased significantly after the intervention. This increase occurred due to an increase in prescription by pediatricians especially in the age group between six months and two years. The percentage of amoxicillin prescription was lower in the group of GPs than in other groups (p <0.01). Those significantly increased the percentage of Amoxicillin prescription during the intervention but this returned to the previous values after the intervention.

Conclusions

A very simple measure can have a significant impact on the type of antibiotic prescribed in a pediatric emergency department. The impact of Antimicrobial Stewardship Programs is not the same in different professional groups. These programs should be prolonged otherwise their results will be lost over time.
LOW MICROBIAL TRANSLOCATION DESPITE GASTROINTESTINAL INVOLVEMENT IN HENOCH-SCHÖNLEIN PURPURA

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Background

Henoch-Schönlein purpura (HSP) is the first cause of systemic vasculitis in childhood, characterized by immunoglobulin A deposits in the small vessels. Two-thirds of children have abdominal involvement with at least abdominal pain due to sub-mucosal hemorrhage and edema of the intestinal walls. We report data on microbial translocation in pediatric Henoch-Schönlein purpura.

Methods

Children, aged between 3 and 15.6 years old, were included in 3 groups: A, acute HSP (n=30), B, remission HSP (n=30), C control, healthy children matched on age (n=38). Bacterial translocation on plasma samples was studied by bacterial 16S rDNA levels (qPCR), LBP (LPS Binding Protein) and sCD14 levels (ELISA); intestinal permeability and damages were assessed by Zonuline and I-FABP level (ELISA); intestinal permeability and damages were assessed by Zonuline and I-FABP level (ELISA) on plasma samples.

Results

For A and B, gastrointestinal involvement occurred respectively in 63% and 73% of children. 16S rDNA levels was lower in A (7.90 [Sd 3.72] cp/µl) and B (9.84 [Sd 5.11] cp/µl) than in C (12.45 [Sd 8.1630] cp/µl), not statistically significant. LBP levels in A (41.47 [Sd 19.19] µg/ml) were significantly higher than in B (27.02 [Sd 16.34] µg/ml) and C (16.57 [Sd 12.59] µg/ml). sCD14 levels in A (6.85 [Sd 2.54] µg/ml) and B (6.22 [Sd 2.09] µg/ml) were significantly higher than in controls (4.43 [Sd 1.98] µg/ml). I-FABP level in A was significantly higher than in C group. No statistic difference was found on Zonuline levels between the 3 groups.

Conclusions

While intestinal involvement was prevalent in HSP patients, bacterial translocation (16S rRNA plasma PCR) was lower than in healthy subjects. However, the host response to components of bacteria was stronger in HSP patients. The role of HSP mucosal Immunoglobulin A will be studied in the future to understand this phenomenon.
CEREBROSPINAL FLUID AND BLOOD CULTURES IN A PAEDIATRIC POPULATION
R. Saunders¹, S. Hewson¹, S. Bandi²
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²University Hospitals of Leicester NHS Trust, Paediatrics, Leicester, United Kingdom

Background

Leicester Children’s Hospital serves a population of approximately 200,000 children. The aim of this retrospective survey was to evaluate the activity of the Hospital in terms of microbiological investigation of suspected invasive bacterial infections, in order to understand local epidemiology and inform future service development and training needs.

Methods

The microbiology laboratory results database was searched for all cerebrospinal fluid (CSF) samples and blood cultures taken from paediatric patients (age <16) over a 1-year period (1 March 2016 – 28 February 2017). Samples referred for testing from other Trusts and post-mortem samples were excluded, as were any discarded samples (e.g. leaking, unlabelled). Data recorded included demographic data, requesting location and microbiology result.

Results

777 CSF and 5702 blood culture samples were analysed. Sample requesting locations and main results are listed in the accompanying table.

9 CSF samples were sent away for meningococcal/pneumococcal PCR, with 1 positive result for N. meningitidis serogroup B. PCR testing of blood revealed a further 2 cases of N. meningitidis and 5 cases of S. pneumoniae. Antimicrobial resistance in this population was not problematic; there were
no MRSA or carbapenem-resistant Enterobacteriaceae cases.

<table>
<thead>
<tr>
<th>Origin of samples</th>
<th>CSF</th>
<th>Blood cultures</th>
</tr>
</thead>
<tbody>
<tr>
<td>General paediatrics</td>
<td>352</td>
<td>2139 (38%)</td>
</tr>
<tr>
<td>Neonatal units</td>
<td>336</td>
<td>1766 (31%)</td>
</tr>
<tr>
<td>Paediatric intensive care</td>
<td>35</td>
<td>480 (8%)</td>
</tr>
<tr>
<td>Emergency Department/other</td>
<td>59</td>
<td>1317 (23%)</td>
</tr>
<tr>
<td><strong>Total number of samples</strong></td>
<td><strong>777</strong> (100%)</td>
<td><strong>5702 (100%)</strong></td>
</tr>
<tr>
<td>Number of source patients</td>
<td>758</td>
<td>3679</td>
</tr>
</tbody>
</table>

**Results**

- Elevated white cell count: 40 (5.1%) N/A
- Positive Gram stain/culture: 9 (1.3%) 316 (5.5%)

**Organisms seen or isolated**

- **CSF**
  - Coliforms (2)
  - Streptococcus infantarius (1)
  - Viridans group streptococci (4)
  - Coagulase-neg staphylococci (2)

- **Blood cultures**
  - Skin/oral commensals (220)
  - Enterobacteriaceae (48)
  - Enterococcus spp. (17)
  - Staphylococcus aureus (11)
  - Pseudomonas spp. (7)
  - Group B streptococcus (5)
  - Haemophilus influenzae (5)
  - Neisseria meningitidis (5)
  - Salmonella ser Typhi (3)
  - Streptococcus pneumoniae (3)

**Conclusions**

The yield of significant culture-positive results from sterile sites in children is very low, with the majority of organisms isolated from paediatric CSF and blood being skin/oral commensals and thus potential contaminants.

Nevertheless, the information obtained from significant positive cultures remains clinically valuable. PCR-based methods appear successful in identifying further cases, but pose logistical and financial challenges, and do not yield information on antimicrobial sensitivity. Education aimed at reducing contamination rates should be considered.
ORGANISMS ISOLATED FROM URINE IN A MIXED PAEDIATRIC POPULATION

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²University Hospitals of Leicester NHS Trust, Paediatrics, Leicester, United Kingdom

Background

The Leicester Microbiology Laboratory serves a population of approximately 200,000 children, and receives urine samples from Leicester Children’s Hospital and community general practices. UK-wide antimicrobial resistance surveillance data that is specific to children is not routinely published. The aim of this retrospective survey was therefore to focus on paediatric urine cultures in order to inform local empirical paediatric antimicrobial prescribing.

Methods

The microbiology laboratory results database was searched for all urine samples taken from paediatric patients (age <16) over a 1-year period (1 March 2016 – 28 February 2017). Any discarded samples (e.g. leaking, unlabelled) were excluded. Data extracted included demographic data, requesting location (hospital/community) and microbiology result including organism name and antimicrobial susceptibilities.

Results

Data for 5928 paediatric urine samples were analysed from 4458 unique patients. 1826 (31%) were taken within the acute hospital setting, with 4102 (69%) being sent from community sources. Overall, 2530 (43%) urine samples were culture-positive, although 404 samples had mixed bacterial flora (≥3 organisms) consistent with faecal contamination. Therefore 2126 samples (36% of total) had susceptibility testing carried out. 1687 (79%) of these grew *Escherichia coli*, with sensitivity test results shown in the table.

Conclusions

Empirical antimicrobial therapy for urinary tract infection should adequately cover the predominant organism, *E. coli*. Our current first-line antibiotic is trimethoprim. At first glance, it appears that this is a suboptimal choice. However, there may be sampling bias as (despite current guidelines) urine sampling in practice is more likely to be carried out when first-line therapy has failed. In addition, clinical response and in vitro testing are not always directly correlated. Moreover, empirical therapy also needs to take into account other organisms, as well as safety and cost.
URINARY ANGIOTENSINOGEN IN CHILDREN WITH URINARY TRACT INFECTION

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²Juntendo university, Department of Pediatrics, Tokyo, Japan

Background

Urinary tract infection (UTI) is one of the most common diseases in children and in some cases, kidney injury occurs. On the other hand, urinary angiotensinogen (U-AGT) is a new effective biomarker that reflects intrarenal renin-angiotensin system (RAS) and gathering attention in many renal diseases. There are many reports on U-AGT and kidney disease. However, there is no study about U-AGT of children with UTI.

Methods

All children younger than 4 months who came to Toshima Hospital with fever between January 2015 and December 2015 were included. The patients diagnosed to have UTI were divided into a UTI group and the others were divided into a non-UTI group, and U-AGT levels were measured using a human total angiotensinogen assay kit: a sandwich enzyme-linked immunosorbent assay (ELISA) kit.

Results

A total of 18 patients were included in this study. There were 7 patients in UTI group and 11 patients in non-UTI group. The patents in non-UTI group were diagnosed as viral infection, meningitis, and pneumonia. Patient’s mean age had no significant difference between two groups. U-AGT levels were higher in patients in UTI group compared to them in non-UTI group (0.78 ± 0.99 ng/dL and 0.18 ± 0.20 ng/dL, respectively, p < 0.05).

Conclusions

U-AGT was elevated in UTI patients. As U-AGT reflects the intrarenal RAS, activation of RAS was suggested in UTI patients and not only vesicoureteral reflex contribute to renal scarring after UTI but also activation of RAS may contribute to renal scarring. However, the number of patients is small and serum AGT was not able to measure and further study is needed.
BACKGROUND

Retrospective study

Updated data on paediatric health service utilisation is a prerequisite for the evaluation of interventions. We describe the nationwide development in health service utilisation against infections in the Danish child population 1999-2016. In a period with decreasing child mortality potentially increased rates of hospitalisation and use of antibiotics may not be beneficial. This abstract involves data up to 2014.

METHODS

We followed the population of all Danish children until 5 years of age in the public health registers for the outcomes hospitalisation for infection, use of local and systemic antibiotics, and vaccine coverage. Using 1999 as reference year, results are presented as rates and incidence rate ratios until 2014 (IRR2014). Updated data from 2015 and 2016 will be available soon.

RESULTS

The age and sex distribution was stable. The percentage of chronically-diseased children increased.

Hospitalisation rates for infection increased (IRR2014 = 1.31), mostly among neonates. Rates were highest in chronically-diseased children, higher in boys and declined with age.

Systemic antibiotics use declined (IRR2014 = 0.78) albeit not for neonates (IRR2014 = 1.45).

Vaccination coverage was stable. At 13 months, 50-60% of children had 3 DTP-vaccines; 30-40% had 3 DTP + 1 MMR at 16 months. MMR1-coverage was higher among girls; lower in chronically-diseased children.

CONCLUSIONS

Rates of hospitalisation for infection increased, especially among neonates; decreasing use of systemic antibiotics, except among neonates; and stable vaccination coverages. Children often received their child vaccination with delay. Sex and chronic disease were risk factors for MMR-vaccination.
Mortality decreased in all age groups, thus the increased rates of hospitalisation and antibiotics use among neonates may not be beneficial. The trends may be explained by changed clinical practice towards intervention in high-risk groups. Future studies of this effect are warranted.
17A. SCIENCE: VACCINE UPDATES

ESTIMATING THE VARIABLE IMPACT OF IMPLEMENTING A REDUCED DOSING SCHEDULE IN THE UNITED KINGDOM

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²Pfizer Inc, Patient & Health Impact, New York, USA
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⁶Pfizer Inc, Patient & Health Impact, Philadelphia, USA

Background

7- and 13-valent pneumococcal conjugate vaccines (PCV) have been an effective part of routine immunization using a 2+1 schedule in the United Kingdom (UK) for the previous 11 years. Studies are ongoing to evaluate effects of removing a dose from the primary series. The objective of this study is to evaluate the local and regional relative impact within the UK of implementation of a 1+1 schedule given variation in vaccination rates.

Methods

A dynamic transmission model was developed using UK serotype-specific invasive pneumococcal disease (IPD) surveillance data from 2001-2016. Vaccination adherence rates were varied to understand the potential disparities and impact across different regions and cities given the reliance of a reduced schedule on booster dose effectiveness.

Results

When comparing the impact of a 1+1 schedule in London, where booster dose adherence ranged from 67 to 91% (mean=84.5%), to average booster dose compliance in the UK (94%), the change in incidence with a 1+1 schedule was 30% higher for all IPD in London when compared to the average UK adherence rate. Specifically for serotype 19A, the UK on average saw an 18% increase in disease caused by serotype 19A with a 1+1 schedule compared to a 2+1 schedule, while London saw a 33.3% increase (RR=1.85).

Conclusions

Results suggest that removal of an infant priming dose would increase pneumococcal disease cases and medical costs compared with maintaining a 2+1 schedule. This has important policy implications specifically for underserved populations in cities and regions with lower booster dose adherence who will be at a particular disadvantage when considering a change in vaccination schedule.
Background

Intussusception is the invagination of an intestine segment within a more distal one and it is the most common cause of bowel obstruction in children. Association with viral gastrointestinal infection is discussed in many years, but it is different from studies. In this study, we conducted multiplex PCR from stool specimens in patients with intussusception. To evaluate the relationship intussusception with viral gastrointestinal infection, we conducted viral testing on stool samples from patients with intussusception.

Methods

Stool samples were collected 1-2 days after air reduction in patients with intussusception from September 2013 to August 2017. Samples were tested for enteric adenovirus, norovirus GI, norovirus GII, rotavirus, astrovirus, sapovirus by multiplex polymerase chain reaction.

Results

198 patients with intussusception were got air reduction. 153 (77.2%) stool samples were tested multiplex PCR. 53 samples of 153 (34.6%) were positive results. Enteric adenovirus was detected in 32 (60.4%) cases, norovirus GII in 12 (22.6%), norovirus GI in 6 (11.3%), astrovirus in 3 (5.6%), rotavirus in 3 (5.6%) cases. Coinfection of enteric adenovirus and norovirus GII in 3 cases was detected.

Conclusions

Our results show that intussusception is associated with enteric adenovirus infections, and norovirus GII infections. We can not find the association of intussusception with rotavirus infection. We suggest that after vaccine era, rotavirus is no more origin of intussusception.

Clinical Trial Registration (Please input N/A if not registered)

N/A
03B. SCIENCE: COMM.ACQ. INVASIVE BACTERIAL INFECTIONS (NON-RESPIRATORY)

INTRA VENOUS VERSUS ORAL ANTIBIOTICS FOR CHILDREN TREATED IN THE EMERGENCY DEPARTMENT FOR UTI/PYELONEPHRITIS: WHAT ARE THE DIFFERENCES IN CLINICAL CHARACTERISTICS AND OUTCOMES?

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²Murdoch Children's Research Institute, Paediatrics, Melbourne, Australia
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⁶Royal Children's Hospital, Anaesthesia, Melbourne, Australia

Background

Febrile UTI/pyelonephritis is a common diagnosis for children presenting to the Emergency Department (ED). A Cochrane review of the management of pyelonephritis in children suggests no difference in outcomes between intravenous (IV) and oral antibiotics (PO). Despite this, many children are treated with at least one dose of IV antibiotics. The reasons are often unclear and it is uncertain whether this is appropriate as the Cochrane review excluded children at the more severe end of the clinical spectrum. Our aim was to compare presenting characteristics of the children treated with IV vs PO antibiotics.

Methods

A prospective observational study of children presenting to the ED at a tertiary children’s hospital in Australia with UTI/pyelonephritis from May 2016 – Apr 2017. Data collection included demographic, clinical features, microbiology, treatment and outcomes. Key outcomes were compared.

Results

Of 541 children included, 378 (70%) received antibiotics PO, 143 (26%) IV and 20 (4%) intramuscular route (analysed in the IV group). Patients were significantly more likely to receive IV antibiotics if they presented to ED with fever, vomiting, rigors or lethargy, had a history of previous UTI, or were pre-treated with PO antibiotics (Table). Patients with a known history of a previous resistant organism were not more likely to receive IV antibiotics. Those treated with IV antibiotics were more likely to receive IV fluids. There was no difference in the age of the patients in each group, or the proportion of representation/admission.
Table

<table>
<thead>
<tr>
<th>Initial antibiotic route</th>
<th>PO No. (%)</th>
<th>IV No. (%)</th>
<th>Odds Ratio (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total patients</td>
<td>378 (70)</td>
<td>163 (30)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>5.4</td>
<td>5.2</td>
<td></td>
<td>0.64</td>
</tr>
<tr>
<td>SD</td>
<td>4.2</td>
<td>5.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinical features</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fever</td>
<td>197 (52)</td>
<td>133 (81)</td>
<td>4.1 (2.6-6.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Rigors</td>
<td>16 (4)</td>
<td>27 (17)</td>
<td>4.5 (2.4-6.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Vomiting</td>
<td>130 (34)</td>
<td>85 (52)</td>
<td>2.1 (1.4-3.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lethargy</td>
<td>70 (19)</td>
<td>47 (29)</td>
<td>1.6 (1.2-2.7)</td>
<td>0.007</td>
</tr>
<tr>
<td>None of above</td>
<td>127 (34)</td>
<td>11 (7)</td>
<td>0.1 (0.1-0.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Prior to presentation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Previous UTI</td>
<td>105 (30)</td>
<td>66 (44)</td>
<td>1.8 (1.2-2.7)</td>
<td>0.003</td>
</tr>
<tr>
<td>Prior antibiotics</td>
<td>71 (19)</td>
<td>51 (32)</td>
<td>2.1 (1.3-3.1)</td>
<td>0.001</td>
</tr>
<tr>
<td>Prophylaxis</td>
<td>11 (3)</td>
<td>12 (8)</td>
<td>2.6 (1.1-6.8)</td>
<td>0.023</td>
</tr>
<tr>
<td>Known resistant organism</td>
<td>27 (8)</td>
<td>18 (13)</td>
<td>2.6 (1.1-6.8)</td>
<td>0.116</td>
</tr>
<tr>
<td>Treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluid bolus</td>
<td>1 (0.3)</td>
<td>25 (16)</td>
<td>65 (12-100)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Maintenance fluids</td>
<td>7 (2)</td>
<td>59 (37)</td>
<td>31 (14-68)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Outcome</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Represent to ED</td>
<td>26 (7)</td>
<td>15 (9)</td>
<td>1.1 (0.5-2.0)</td>
<td>0.97</td>
</tr>
<tr>
<td>Readmitted</td>
<td>8 (2)</td>
<td>4 (2)</td>
<td>0.9 (0.2-3.6)</td>
<td>0.89</td>
</tr>
</tbody>
</table>

Conclusions

IV antibiotics are currently used in 30% of patients with UTI/pyelonephritis. The IV group have different characteristics and some receive additional management with fluid therapy. Indications for IV vs PO treatment of UTI need to become more evidence based.

Clinical Trial Registration (Please input N/A if not registered)

N/A
Paediatric cancer patients face an increased risk of nosocomial bloodstream infections. In most cases, these infections are associated with the use of a long-term central venous catheter. This study describes the epidemiology and the profile of microorganisms responsible for catheter-related bacteriemia in paediatric cancer patients.

Methods

Retrospective analysis of medical records of patients hospitalized at Pediatric Hematology and Oncology Department between 2010 and 2015, who had central venous catheter. Most of them (56.8%) were diagnosed with hematological malignancies. Data on patient demographic, diagnosis, timing and type of catheter associated complication were collected. Blood cultures were taken in suspected blood stream infections - fever, chills, increase of inflammatory markers.

Results

Overall 241 children with 276 long-term central venous catheters were evaluated between January 2010 and 2015. There were 106 positive blood cultures in this group. Although coagulase-negative staphylococci were the pathogens most commonly isolated, Gram-negative microorganisms were also prevalent (24/106) 22.6%. Candida was cultured from 3.8% blood samples (4/106). Bacteria resistant to standard antibiotic treatment were detected in 33% (35/106) blood samples.

Conclusions

The most frequently encountered pathogens in catheter-associated infection are coagulase-negative staphylococci.

The organisms associated with catheter related bacteriemia represents mostly the normal resident flora of the skin at the insertion site.

Bacteria resistant to standard antibiotic treatment are important causative agents of bacteriemia.
INTER PENETRATING POLYMER NETWORK(IPN)BASED MULTI PARTICULATE SYSTEM FOR CONTROLLED DELIVERY OF INFECTIVE AGENT
K. Ghosal*  
*Dr. B C Roy College of Pharmacy & AHS, Pharmacy, Durgapur, India

Background and Objective

To prepare and evaluation of Interpenetrating network (IPN) based beads for controlled delivery of Norfloxacin-complex.

Methods

The drugs that are hydrophobic in nature are difficult to deliver to the desired parts of the body. The objective of this study was to develop controlled release delivery of Norfloxacin-complex though bead. Bead will be formulated by ionotropic gelation technique using sodium alginate, poly vinyl alcohol and xanthan gum as release retarding polysaccharides and calcium chloride as cross linking agent. This delivery system may enhance the solubility of Norfloxacin as a subsequent effect, absorption and bioavailability of the drug will be improved.

Learning Points Discussion

Solid state characterization by Fourier transform infrared spectroscopy (FT-IR) and differential scanning calorimetry (DSC) analysis, XRD will be carried out to determine any incompatibility between the drug and other components used in the formulations. Surface image will be done by SEM. In vitro release study, particle size will be measured to see the suitability of this system.

The beads were enough mechanically strong. The method used here to prepare bead was very easy and reproducible. The majority of the work is pending to see the suitability of his dosage form to achieve our aim.
A FRENCH COMPUTERIZED NETWORK IN AMBULATORY PEDIATRICS AND INFECTIOUS DISEASES RESEARCH

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²AFPA, Ambulatory Pediatric Network, Saint Germain en Laye, France

Background

Infectious diseases account for 50-70% of pediatric daily practice. In order to improve the diagnostic performance of pediatricians by providing real-time data on epidemiology of several infectious diseases, we have set up a national surveillance network, PARI (Pediatric and Ambulatory Research in Infectious diseases), with 2 characteristics: 1) first of all, specific trainings in infectious diseases of participating pediatricians and use of rapid diagnosis tests, and 2) automated data extraction from the primary-care pediatricians’ computer.

Methods

Since September 2017, we prospectively collect anonymized data (age, sex, height, weight, daycare attendance, vaccines, diagnosis and prescriptions) of children with infectious diseases, in 82 primary-care pediatricians of the French Ambulatory Pediatric Association (AFPA) using the same software (Infansoft®, CompuGroup Medical). No additional data than those required in the daily practice of the pediatricians are requested.

Results

During the first 4 months of this study, data on 9,818 consultations, 53,467 vaccines, 13,353 diagnoses and 41,342 drug-prescriptions were collected. Mean age was 2.8 ± 2.5 years and boys accounted for 57.4% of children. Data were daily and automatically provided on a dedicated website as graphs for all pediatricians, to allow them to monitor the epidemiology of different diseases, locally as well as at national level: beginning in late November for influenza, a peak in mid-October for enteroviruses and group A Streptococcus, and a slow increase from September to December for gastroenteritis.
Conclusions

The PARI network, not time-consuming for participants, based on automated data extraction from the computers of primary-care-pediatricians specially trained in infectious diseases and equipped with rapid diagnosis tests, provides real-time data. The impact of this surveillance on the pediatricians’ practice is a major step forward in public health.
RSV causes an important number of hospitalizations every year, especially in very young children.

Methods

The Valencia Hospital Network for the Study of Influenza and other respiratory viruses (VAHNSI) conducts annually a prospective, active-surveillance study. This analysis was performed using data from 2011/2012 to 2016/2017 influenza seasons and was restricted to children under 3 years old (y.o.).

All consenting admissions of non-institutionalized children, resident in a participating hospital catchment area, not discharged from a hospital within 30 days and having been hospitalized within 7 days of the onset of symptoms were included in the study.

Demographic and clinical information was collected by interviewing legal tutors and/or by clinical records review. Swabs were tested by real-time reverse transcription polymerase chain reaction (RT-PCR).

Hospitalization incidence rates were calculated by age group (<1, 1-<2 and 2-<3 y.o.) and season. RSV positivity rates and reasons for hospitalization were provided by age group (0, 1, 2, 3, 4, 5, 6 to <12, 12 to<24 and 24 to <36 months).

Results

The highest hospitalization rate was found in infants less than 1 y.o., taking its highest value in the 2016/2017 season (1475.89 per 100,000) and its lowest value in the 2013/2014 season (393.95 per 100,000).

The highest percentages of RSV positivity occurred at 2, 3 and 4 months of age (42%, 38% and 40%). The percentage decreased as age increased from 4 months onwards.
Main reasons for admission among RSV cases were ARI, cough, dyspnoea and fever, with differences across age groups.

Conclusions

RSV mostly affects very young children, especially babies less than 6 months of age, entailing an important social and economic repercussion.

Clinical Trial Registration (Please input N/A if not registered)

N/A
DIRECT IMPACT OF PNEUMOCOCCAL VACCINES IN ADULTS: A SYSTEMATIC REVIEW

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²GSK, Global Medical Affairs, Panama, Panama
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Background and Objective

A 23-valent pneumococcal polysaccharide vaccine (PPV23) has been used in many countries for decades to prevent pneumococcal diseases in older adults and at-risk populations. However, its effectiveness could not always be demonstrated. Introduction of pneumococcal conjugate vaccines (PCVs) in children led to substantial reductions in adult disease through herd protection. Some countries are now recommending vaccination of at-risk and elderly adult with PCV. Our review aimed to evaluate the direct impact of adult vaccination.

Methods

A literature search was conducted in MEDLINE between Jan 1st 1970 and Dec 31st 2017, evaluating the efficacy, effectiveness or impact of pneumococcal vaccines. All publications reporting clinical outcomes focused on pneumonia and/or invasive pneumococcal disease (IPD) in adults ≥50 years who had received at least one dose of either PPV23 or 13-Valent Pneumococcal Conjugate Vaccine (PCV13) were included. Reviews, systematic reviews and meta-analyses were excluded.

Learning Points Discussion

317 citations were identified (Figure), 21 publications met the inclusion criteria. The impact of adult vaccination with PPV23 was heterogeneous between the studies with different study designs and populations, from no effect on pneumonia, to substantial decreases in invasive and non-invasive pneumococcal infections, mostly in adults ≥ 65 years. Effects were potentially masked by herd immunity provided by PCV introduction into pediatric immunization programmes. Only one randomized controlled trial involved PCV reporting efficacy on IPD and pneumococcal pneumonia.

While PPV23 impact on adult disease is well documented showing heterogeneous results, there is currently limited data evaluating the direct impact of PCV in adults. Further studies are needed to better understand the potential added benefit of direct protection over herd immunity conferred by pediatric PCV vaccination.

Funding: GlaxoSmithKline Biologicals SA
GROUP B STREPTOCOCCUS BACTEREMIA IN NEONATES AND INFANTS - PRESENTATION OF TWO CASES IN OUR PEDIATRIC CLINIC, GENERAL HOSPITAL, IN CENTRAL GREECE


"Achilopouleio" General Hospital of Volos, Pediatric Clinic, Volos, Greece

"Achilopouleio" General Hospital of Volos, Pediatric Clinic, Volos, Greece

Title of Case(s)

GROUP B STREPTOCOCCUS BACTEREMIA IN NEONATES AND INFANTS - PRESENTATION OF TWO CASES IN OUR PEDIATRIC CLINIC, GENERAL HOSPITAL, IN CENTRAL GREECE.

Background

Group B streptococci (GBS) are a major cause of systemic and focal infections in neonates and young infants. Invasive disease in infants is categorized on the basis of chronologic age at onset. Early-onset disease occurs in newborns younger than 7 days, late-onset disease occurs in infants between the ages of 7 days and 4 months and late, late-onset disease occurs in infants older than 3 months of age.

Case Presentation Summary

Two young infants had been hospitalized in our Pediatric Clinic during October 2017 due to late-onset and late, late-onset GBS disease. 1st case: 23-day-old female infant presented with fever, irritability, poor feeding for 4 hours. Blood culture was positive for GBS, CSF culture was sterile. She received IV ampicillin for 14 days and cefotaxime for 10 days. Vaginal-rectal screening for GBS was incorrect. 2nd case: 3-month-old male infant presented with fever, vomiting and poor feeding for 20 hours. CSF specimen was only enough for culture and PCR, both of which were negative for GBS. Blood culture was sterile, but blood PCR came out positive for GBS. The infant received 14 days of IV ampicillin and cefotaxime. No vaginal-rectal screening for GBS had been performed.

Learning Points/Discussion

Universal antenatal screening of pregnant women for GBS colonization at 35 to 37 weeks' gestation is essential, because it lead to a decline in early-onset GBS disease. Unfortunately, though, it has not changed the rate of late-onset GBS disease. The more frequent presentation of late-onset disease is bacteremia, which should immediately be treated appropriately in order to prevent worse manifestations of the disease.
PEDIATRIC EBV-ASSOCIATED ENCEPHALITIS - A CASE REPORT
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Title of Case(s)
Pediatric EBV-associated encephalitis – a case report

Background
Epstein-Barr Virus (EBV) infections may present as mononucleosis alone or may be associated with central nervous system complications, like encephalitis, meningitis, cerebellitis, acute disseminated encephalomyelitis, transverse myelitis or radiculopathy.

Case Presentation Summary
A 2 years-old child was admitted in the emergency department with fever, cervical adenopathies and an episode of a probable epileptic seizure. Neurological exam was normal and blood workup revealed leucocytosis and a C-reactive protein 40.7mg/L. The boy was discharged with diagnosis of a simple febrile seizure due to a respiratory viral infection. One day later, the boy was admitted due to fever and two new episodes of seizures. The brain CT was normal and the cerebrospinal fluid (CSF) examination showed pleocytosis (74 leukocytes/mm³) and normal proteins and glucose. Abdominal ultrasound showed hepatosplenomegaly. Ceftriaxone and acyclovir were initiated empirically, based on the preliminary diagnosis of encephalitis. Later cultural CSF and polymerase chain reaction (PCR) analysis for HSV, enterovirus and EBV were negative. Cerebral MRI showed edematous lesions in lenticular, caudate nucleus and thalamus, small lesions in frontal white matter. EBV serum serology showed positive IgM and negative IgG and blood EBV PCR was also positive. The EEG revealed occasional frontal epileptiform activity. Encephalitis by EBV was assumed, he completed 14 days of acyclovir 60 mg/kg/day, with clinical improvement. EBV serology 1 month later showed seroconversion. Four months later, he maintains a normal development and neurological exam.

Learning Points/Discussion
The clinical findings adding to the inflammatory CSF, PCR detection of EBV DNA in the blood, and EBV serology consistent with acute infection, favored the diagnosis of an EBV encephalitis. However, EBV PCR in CSF was negative and brain MRI was nonspecific illustrating the challenges of this diagnosis.
HOSPITALIZATIONS RELATED TO RESPIRATORY VIRAL INFECTIONS IN CHILDREN UNDER 5 YEARS OLD IN THE VAHNSI FRAMEWORK DURING 6 CONSECUTIVE SEASONS (2011/2012 TO 2016/2017, VALENCIA, SPAIN)

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Background

Acute respiratory infection (ARI) is the main cause of morbidity and mortality worldwide. Influenza and respiratory syncytial virus (RSV), among other viruses, play a significant role in respiratory pathology, especially among young children.

Methods

The Valencia Hospital Network for the Study of Influenza and other respiratory viruses (VAHNSI) conducts annually a prospective, active-surveillance study. The current analysis was performed using data from 2011/2012 to 2016/2017 seasons (November to March-April) and was restricted to children under 5 years old (y.o.).

All consenting admissions of non-institutionalized children, resident in a participating hospital catchment area, not discharged from a hospital within 30 days and having been hospitalized within 7 days of the onset of symptoms were included in the study.

Demographic and clinical information was collected by interviewing the legal tutors and/or by clinical records review. Swabs were analyzed by real-time reverse transcription polymerase chain reaction (RT-PCR) and were tested for influenza, RSV, metapneumovirus, parainfluenza, rhinovirus/enterovirus, adenovirus, coronavirus and bocavirus.

Hospitalization incidence rates were calculated by virus, age group and season.

Results

Hospitalization incidence rates associated to respiratory viral infections were not constant across seasons, being higher in the last 3 seasons.

Differences across seasons were detected regarding the commonest virus as age increased. In infants under 1 y.o. the highest hospitalization rate was detected for RSV in all the study seasons.
children 1 y.o. or over the highest rate was detected for different viruses (RSV, influenza or rhinovirus/enterovirus), depending on the season.

Lowest rates were detected for metapneumovirus, adenovirus and parainfluenza.

Conclusions

Children are a vulnerable population for admission due to respiratory viral infection. Preventive measures must be taken into account.

Clinical Trial Registration (Please input N/A if not registered)

N/A
THE DIVERSITY OF FUNGAL COLONIZATION OVER ORAL CAVITY IN IMMUNOCOMPROMISED CHILDREN IS DIAGNOSED BY THE METHOD OF NEXT GENERATION SEQUENCING.

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Background

The oral cavity is a primary target for opportunistic fungal infection in immunocompromised individuals such as patients with hematological cancer. The traditional culturing methods for the diagnosis of fungal infection are time-consuming and laborious. Instead, molecular genetic analysis of next generation sequencing (NGS) provides a simple and rapid way.

Methods

The oral rinse solution from 30 children with hematological cancer under neutropenic status and 25 healthy controls were collected in this study. DNA extraction from oral rinse was performed. We quantified the fungal populations using real-time PCR of the fungal internal transcribed spacer region in these DNA samples. Sequences obtained from samples were analyzed together. For each sequence, nearest-neighbor species with more than 98% identity were selected as candidates.

Results

The total number of 9 samples (5 patients and 4 healthy controls) was analyzed by NGS to find out the diversity and abundance of fungal species in these samples. There are 19 different fungal species identified from these specimens including 4 candida species (C. albicans, C. glabrata, C. parapsilosis and C. tropicalis), in the study. These candida species are the predominant fungus in four patients (80%, 4/5) but none of healthy control. The NGS results demonstrated that the abundance of Candida species in patients is significantly higher than controls, at least one species among C. albicans, C. glabrata, C. parapsilosis and C. tropicalis.

Conclusions

These results suggest that high candida biodiversity might be involved in the pathogenesis of oral candidiasis and NGS may be a useful technique for investigating oral fungal infections.
13A. SCIENCE: PUBLIC HEALTH | EPIDEMIOLOGY

RETROSPECTIVE STUDY OF EXTERNAL OTITIS IN CHILDREN FOR THE YEARS 2016, 2017. IS THE OVERGROWTH OF MEDUSA THE CULPRIT OF THEIR AUGMENTATION?
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Background

Gram-negative bacilli, mainly Pseudomonas aeruginosa are the main causes of external otitis. The aim of the present study was to compare retrospectively the otitis cases among children who attended the Emergency Department of our hospital from January to March and from July to September for the years 2016 and 2017 respectively.

Methods

All patients from the Department of Pediatrics with positive ear sample cultures from January to March and from July to September for the years 2016 and 2017 were retrospectively investigated (Table 1).

Results

During July-September 2017, ear sample cultures positive for P. aeruginosa increased by 3.6 times comparatively with the respective months of 2016. Comparison of the years 2016 and 2017 showed significant difference between them concerning P. aeruginosa infections (p< 0.001). Among the 22 P. aeruginosa infection cases, five children had swum in a pool prior to symptoms’ manifestation, five had swum both in a pool and the sea, and two had swum in the sea only, whereas we could not contact the families of the remaining 10 children.

Conclusions

There was an augmentation in ear infections due to P. aeruginosa in 2017 in comparison to 2016. As there was a major problem of overgrowth of jellyfish in the Corinthian Gulf during the summer of 2017, which made swimming in the sea forbidden in many places, we made the hypothesis that perhaps swimming in a pool was the cause of the augmentation of P. aeruginosa ear infections among children.
Syphilis and pregnancy in Denmark, 2010-2017
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Background

The pregnancy-screening program in Denmark offers all pregnant women a serologic test for syphilis, HIV and hepatitis B as part of early prenatal care. Due to increasing incidence in cases in the general population, syphilis testing was reintroduced into the pregnancy screening in 2010, after being discontinued in 1998. Because of this rise in syphilis, the purpose of this study was to investigate the rising number of syphilis cases among pregnant women in Denmark.

Methods

All pregnant and non-pregnant women found in the National Pregnancy Screening Database and National Surveillance System for Infectious Diseases (NSSID) January 2010 - December 2017 were included. Information on date of diagnosis, ethnicity, mode and place of transmission and other demographic data were extracted from the NSSID. Syphilis test results were retrieved from the national Microbiology database.

Results

The study included 84 pregnant and 243 non-pregnant women, diagnosed with syphilis. Median age was 29 years and 35 years, respectively. Figure 1 shows the number of pregnant and non-pregnant, Danish and non-Danish women, diagnosed with syphilis in Denmark 2010-2017. Only 11 % of the pregnant women lived in one of the three largest cities in Denmark, in contrast to 42 % of the non-pregnant women. The risk of being diagnosed with syphilis was significantly higher for pregnant than
Conclusions

The importance of the pregnancy screening remains clear as it detects cases of syphilis in pregnant women, thus contributing to the prevention of congenital syphilis. The higher risk of being diagnosed with syphilis during pregnancy, compared to non-pregnancy, is interpreted as a sign of increased attention on syphilis in pregnant women and indicates an undiagnosed fraction of cases among non-pregnant women in Denmark.
CHARACTERIZATION OF ACUTE OTITIS MEDIA OTOPATHOGENS BEFORE THE INTRODUCTION OF THE PNEUMOCOCCAL CONJUGATED VACCINE INTO THE NATIONAL IMMUNIZATION PROGRAM IN POLAND

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Background

Bacterial etiologic data for acute otitis media (AOM) otopathogens in Poland are scarce. The aim of this study was to determine the bacterial etiology and antibiotic susceptibility patterns of otopathogens in children prior to the introduction of the pneumococcal conjugated vaccine (PCV) into the national immunization program (NIP) in Poland.

Methods

Demographic and laboratory data of children < 5 years old who underwent tympanocentesis due to AOM in Nieklanska Hospital Warsaw between 2010 and 2016, were collected. All middle ear fluids (MEF) cultures were processed at the hospital according to conventional culture methods.

Results

Out of 940 MEF cultures, 407 (43.3%) were positive for 419 isolates. The distribution of the pathogens and the proportion of Streptococcus pneumoniae (SP) and Haemophilus influenzae (Hi) that were antibiotic-resistant are presented in the Figure. No statistically significant differences in distribution of pathogens were observed over time or by age group (<12mo; 12-23mo; 24-59mo). Prevalence of penicillin-resistant SP significantly declined with time (11.3% - 2010-2012; 2.1% - 2012-2014; 0% - 2014-2016), but no significant differences in proportion of resistance to other antibiotics were found. Amoxicillin-clavulanate resistant Hi declined over the 3 time periods (7.7%, 4.2% and 2.0%, respectively), but resistance to other antibiotics did not vary significantly.

Conclusions

This is the largest dataset of MEF isolates from AOM patients in Poland during the pre-PCV period. The most prevalent otopathogen was SP, with high rates of resistance to macrolides,
clindamycin and oral cephalosporins. Penicillin-resistant and amoxicillin-clavulanate resistant Hi declined during the study period. These data can help to determine the appropriate treatment for AOM and can serve as the baseline before the introduction of PCV to the NIP in Poland.
Meningococcal infection, invasive bacterial diseases caused by *N. meningitidis* in particular, are still actual not only among children infections. Despite the fact that *Neisseria* spp. are generally sensitive to penicillins, nowadays we have a rise of antimicrobial resistance. Since 2017 even *N. gonorrhoeae* is under control in antimicrobial resistance surveillance. That's why it is important to study antimicrobial sensitivity rates of *N. meningitidis*.

Methods

28 *N. meningitidis* isolates were collected from blood (n=9) and CSF (n=19) of children with invasive bacterial diseases under 5 years from Minsk (n=10), Brest region (n=9), Vitebsk region (n=4), Mogilev region (n=3), Grodno and Minsk regions (n=1 each) during the period since 2011-2017 years.

Isolates were tested on Muller-Hinton agar with 20% horse blood serum by E-tests strips with benzylpenicillin concentration 0.016-256. Results interpreted according EUCAST guideline v.7.0.

Results

21 isolates of *N. meningitidis* were sensitive to penzylenicillin (MIC ≥0.06). MICs of sensitive isolates: <0.016 (n=2), 0.016 (n=6), 0.023 (n=7), 0.032 (n=2) and 0.047 (n=4). The serotype of sensitive *N. meningitidis* was B (n=18, all MICs), C (n=1, MIC=0.032), W135 (n=1, MIC=0.047) and one nontype isolate with MIC <0.016.

7 isolates had intermediate sensitivity with next MICs: 0.064 (n=2), 0.094 (n=2), 0.125 (n=2), 0.25 (n=1, which is also had intermediate sensitivity to ampicillin and amoxicillin). One isolate was *N. meningitidis* C with MIC = 0.094. Other - *N. meningitidis* B.

Conclusions

Thus, despite of the fact that there are no strongly resistant isolates to benzylpenicillin, isolates with intermediate sensitivity exists quite often. While antibiotics of the penicillin series are still widely used in clinical practice for the treatment of meningococcal infections, antimicrobial resistance surveillance to penicillin series in general and benzylpenicillin in particular is necessary to *N. meningitidis*, especially invasive isolates obtained from patients.
To study the clinical and epidemiological manifestations of intrauterine and septic infections (SI) among infants and postpartum women and to assess role of group B streptococci (GBS).

Methods

A retrospective analysis of the incidence of fetal and septic infections among newborns and puerperae in Moscow for the period from 2009 to 2016. Seven hundred and fifty clinical samples (vaginal secrets, urine, faeces, swabs from ears, eyes, and umbilical wound) were microbiologically studied. Sampling and primary seeding were performed by conventional methods.

Results

There was tendency of increasing incidence of intrauterine infections in newborns during the studied period. The incidence significantly increased from 10.2 to 67.3 per 1000 infants (t=2.1; p<0.05). The incidence of SI in postpartum women during the same period showed a significant downward trend (t =2.1; p< 0.05) with a mean annual rate of 1.6 per 1000 infants. SI in postpartum women was manifested most frequently as endometritis (85%), as well as suppuration of postoperative wound and dehiscence of postoperative sutures (15%). Seventy nine cases of perinatal infection caused by GBS were registered in Moscow from 2010 to 2016 with mean annual rate 0.07 per 1000 infants. Majority of cases of GBS infection in newborns was presented as intrauterine pneumonia (57.5%), infection syndrome (48.8%), meningitis (31.6%), meningitis with sepsis (11.5 %) as well as omphalitis (5.7%) and omphalitis in combination with intrauterine pneumonia (2.9 %). Fatal outcome was registered in 6 cases of GBS infection(10.2%).

Conclusions

During the studied period statistically significant increase of incidence of intrauterine infections in newborns in Moscow was observed while reducing incidence of SI in postpartum women was noted. Case-fatality ratio of intrauterine GBS infection of newborns amounted to 10.2%.
FACTORS AFFECTING THE SEROCONVERSION RATE OF 12-MONTH-OLD BABIES AFTER THE FIRST INJECTION OF MEASLES VACCINE IN THE SOUTHEAST OF IRAN

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³School of Public Health- Tehran University of Medical Sciences, National Reference Laboratory for Measles and Rubella, Tehran, Iran

Background

Within the past few years, several measles outbreaks have occurred in the southeast of Iran. In Iran, all routine immunization services provided by the public sector are free of charge. To learn about the effectiveness of the immunization services for producing a serologic response against measles, this follow-up study was designed and implemented in the southeast of Iran.

Methods

The follow-up study was designed and implemented in 5 Urban Health Centers located in 3 districts of Sistan-va-Baluchestan Province, Iran. In the pre-vaccination phase, 270 12-month-old babies were blood sampled; and in the post-vaccination phase, 4 to 7 weeks after Measles, Mumps, Rubella (MMR) vaccination, 236 of them were blood sampled (34 dropouts), and their sera were tested for IgG anti-measles antibodies, using indirect ELISA, in the National Reference Measles Laboratory.

Results

Out of the 236 participants, who had been blood sampled in the post-vaccination phase, 10 (3.7%) were excluded from the calculations of seroconversion rate, because they had protective levels of antibody before the vaccination. The seroconversion rate for the remaining 226 participants was 91.2% (95% confidence interval: 86.7 to 94.5). Among the variables studied, stunting (height-for-age z-score < -2) showed a strong relationship with the remaining seronegative after the vaccination (odds ratio = 5.6; 95% confidence interval: 1.7–18.2). The chance of seroconversion was inversely related to the mothers’ levels of education (up to 9 y of education vs. above nine years) (odds ratio = 0.2; 95% confidence interval: 0.06–0.4).

Conclusions

In the study population, the seroconversion rates for anti-measles antibodies after MMR vaccination are acceptable, even though in order to achieve the elimination goal, higher standards need to be achieved.
PREVENTION OF INVASIVE PNEUMOCOCCAL DISEASE CAUSED BY SEROTYPE 3: ACKNOWLEDGING THE DATA, RECOGNISING THE CHALLENGES

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Background and Objective

Serotype 3 (ST3) is one of the major serotypes causing invasive pneumococcal disease (IPD) among adults while the current burden is relatively low among children. Historically, prevention of ST3 infection by antibody mediated approaches has been inconclusive. This analysis aimed to evaluate the body of evidence for prevention of ST3 IPD by pneumococcal vaccines (PCVs).

Methods

Immunogenicity, efficacy, effectiveness and impact data of pneumococcal vaccines with respect to ST3 were reviewed. Epidemiological datasets were limited to those from countries with robust surveillance (n=13 <5yrs old, n=7 >65yrs old). Incidence changes vs pre-PHiD-CV/PCV13 baselines in each country were collated and standardized according to the year of PHiD-CV/PCV13 introduction.

Learning Points Discussion

Our review indicates:

- Immunogenicity data reveals no or limited boosting effect on ST3 irrespective of PCV. At licensure, PCV13 did not meet primary endpoints based on IgG for ST3 while a recent publication on mixed schedules reported a trend of decreased immune response for ST3 with a higher number of doses among children primed with PCV13.
- Significantly positive vaccine efficacy against ST3 in RCTs for various valency PCVs has not been demonstrated.
- Epidemiology data from countries after PCV introduction into national immunization programs is inconclusive but suggests a lack of vaccine effectiveness against ST3 in children with no herd impact visible in older adults (Figure).

Understanding these observations is essential to know why ST3 has been poorly controlled by PCVs. Immunological hypo-responsiveness may contribute to poor effectiveness against this serotype. ST3 has different features from other serotypes and the impact of the current approach using anti-capsular antibody to prevent disease has been inconclusive. This may suggest that different strategies will be required to prevent ST3 more effectively.
**Funding:** GlaxoSmithKline Biologicals SA

**Average % change in ST3 incidence (+/- S.E.)**

- **<5 Years**
- **>65 Years**

% Change from Baseline

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04B. SCIENCE: COMMUNITY ACQUIRED INFECTIONS: RESPIRATORY TRACT INFECTIONS

VIRAL PATHOGENS CAUSING ACUTE LOWER RESPIRATORY TRACT INFECTIONS IN CHILDREN UNDER 5 YEARS OLD IN BULGARIA

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Title of Case(s)

VIRAL PATHOGENS CAUSING ACUTE LOWER RESPIRATORY TRACT INFECTIONS IN CHILDREN UNDER 5 YEARS OLD IN BULGARIA

Background

Acute lower respiratory tract infections (LRTI) are a leading cause of morbidity and hospital admissions in children. This study aimed to determine the viral aetiology of these infections in children younger than 5 years of age during two successive epidemic seasons in Bulgaria.

Methods: Clinical, epidemiological data and nasopharyngeal swabs were prospectively collected from children under 5 years old presenting with acute LRTI during the 2016/2017 and 2017/2018 seasons. Viral etiology was determined by Singleplex Real Time PCR against 11 respiratory viruses.

Case Presentation Summary

Of the 387 children examined, 288 (74%) were positive for at least one respiratory virus. Co-infections with two and three viruses were found in 57 and 6 of infected children, respectively (22%). Overall, RSV was the most commonly detected virus (131/387, 33.9%), followed by rhinoviruses (15.8%), bocaviruses (10.9%), adenoviruses (8.8%); influenza A(H3N2) (7%); human metapneumovirus (5.2%); parainfluenza viruses 1/2/3 (4.4%); influenza type B (3.4%) and A(H1N1)pdm09 (1.3%). During the 2016/2017 season, detection rate of RSV was higher compared to 2017/2018 season (47% vs 15%). RSV subgroup B outnumbered those of the subgroup A in both seasons. At least one respiratory virus was identified in 73%, 55%, 87% and 65% of children with laryngitis/laryngotracheitis, bronchitis, bronchiolitis and pneumonia, respectively.

Learning Points/Discussion

Respiratory viruses, especially RSV, are principal pathogens of LRTI in children younger than 5 years of age. Diagnostic testing for respiratory viruses using molecular methods may lead to the reduced use of antibiotics and may assist in measures to control infection.
HIV POSITIVE CHILDREN AT AIDS DISSIDENTS FAMILIES – HOW TO HELP
N. Moisieieva

Title of Case(s)

HIV positive Children at AIDS dissidents families – how to help

Background

In Ukraine HIV – positive children have free access for ART, but among barriers to pediatric HIV care one of the most common is nonadherence to treatment of parents. Last year National Children AIDS Clinic faces postponed diagnostic and ARV treatment on 6 children because of parents were AIDS dissidents. All children have had 3rd or 4th clinical stages of HIV disease with severe cognitive problems, different opportunistic infections and risk of death. Generally, in Ukraine there were 11 cases of children’s deaths connected with parents non-adherence for ART in 2017.

Case Presentation Summary

All this children were infected with mother – to – child transmission. During pregnancy all mothers received HIV counselling, 3 of them refused HIV testing, and 5 of them refused prevention treatment ART. Parents refused Co-trimoxazole prophylaxis, ART, TB treatment and prevention. Clinical case. Child, male, 2,5 years all, was born to mother, who have not received prevention ART during pregnancy. During delivery, lower denied to provide HIV test of umbilical blood, and ART for children was nor prescribed. Mother was died 3 month ago with TB. Clinical examination: child has 20% weight deficit, during last 3 months he lost skills (walking,speaking), CD = 64 cell/ml; VL = 250000 copies/ml. Child father denies ART and TB treatment. Healthcare workers have no instruments to provide treatment for child.

Learning Points/Discussion

Ukrainian Health care providers need legal support to defend children health and life at families of AID- dissidents in cases when children are under risk of death and harm for health. Social workers, lawyers have to support children and replace them into foster families to save childrens life.
Background

Breast milk provides nutrition for infants but also delivers bioactive factors that have key protective and developmental benefits. In particular, cytokines are thought to play a role in immunomodulation although little is known about their impact on other health outcomes in early life. We evaluated the relationship between breast milk cytokines and infant growth in a low-income setting.

Methods

100 mother-infant pairs were followed up to 90 days postpartum as part of a prospective longitudinal cohort study in urban Gambia, West Africa. Cytokines were measured in colostrum within 12 hours of birth and breast milk at day 60-89 of life. Infant anthropometric data were recorded and converted to weight-for-age (WAZ), length-for-age (LAZ) and weight-for-length (WLZ) Z-scores. The change in Z-scores between birth and day 60-89 was used to define growth trajectories. Linear regression models were used to measure association between variables.

Results

Gambian infants demonstrated growth faltering by day 90 postpartum, with lower WAZ scores in female infants. There was no significant relationship between cytokines in colostrum and subsequent growth trajectories. On univariate analysis, cytokines in mature breast milk, including TNFα, IFNγ, IL1β, IL2, IL4 and IL6, were negative predictors of WAZ scores at day 60-89 (p<0.05). On multivariate analysis, the combination of maternal Hb and breast milk IL10, IL12, IL2, IL6, TGFβ2 concentrations contributed to lower final WAZ scores in female infants (p<0.05, r²=0.878).

Conclusions

Early growth in Gambian infants cannot be explained by the effects of cytokines in colostrum. The potential interrelationship of other factors, such as micronutrients, hormones or human milk oligosaccharides, must be elucidated. Growth outcomes later in infancy, however, are predicted by...
mature breast milk cytokine profile, which may be sensitive to maternal nutrition and disease. This warrants further investigation.

Clinical Trial Registration (Please input N/A if not registered)

N/A
Background and Objective

Influenza vaccines effectiveness is dependent of the circulating strains. As the trivalent influenza vaccines are composed of only one B lineage, the main circulating strain has to match to the one included in the vaccines. This study reviews the circulation of influenza B strains in Brazil from 2010 to 2016.

Methods

Brazilian published data on influenza B strains were reviewed. When different studies were assessing B strains of the same season, the samples were summed (2013 e 2014), except when samples were collected in the same region: the most recent data with the higher number of samples assessed was used in order to avoid double counting (2010 e 2011). If the number of samples included in Brazilian studies was very low, samples of the tropical South America region were reviewed (2012).

Learning Points Discussion

Our analysis of a total of 541 samples demonstrates that:

- Available information about influenza B circulation in Brazil is very limited;

- Vaccine mismatches have been high for the 2010, 2012, and 2013 seasons with an opposite circulating strain of 95%, 95%, and 94%, respectively.

- The recommended lineage in the vaccines was fully adequate just in one season (2011)

- Even though the mismatch was low in the last 3 seasons, it continues existing: 8%, 10%, 18% for seasons 2014, 2015, and 2016, respectively;

The Victoria and Yamagata lineages have often been circulating over the same season that can lead to significant mismatch of the influenza vaccine, up to 95%. Levels of mismatch directly impact the trivalent vaccines effectiveness with public health and economic impacts. The use of influenza quadrivalent vaccines should be more effective in reducing the burden of the disease.
CLOSTRIDIUM DIFFICILE TESTING IN THE PAEDIATRIC POPULATION IN NHSGG&C: A RETROSPECTIVE AUDIT
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Background

European and Health Protection Scotland guidelines recommend testing for Clostridium difficile infection (CDI) in all diarrhoeal stool specimens in children aged three or above. Since February 2017 Greater Glasgow and Clyde Health Board have been routinely testing for CDI in all stool specimens in this patient group. We performed a retrospective analysis on risk factors for CDI.

Methods

Data was extracted from our laboratory TELEPATH system searching for reported confirmed GDH and toxin positive CDI in paediatric patients under 16 years old. Data was then analysed using clinical information from electronic records as well as microbiology/infection consults recorded on our Clinical Portal system.

Results

16 patients tested positive: three were from the community and 13 from the hospital setting. For the hospital-associated patients three were considered colonisers and not treated. All other hospital cases were considered significant with some patients experiencing recurrences or relapses. Patients had one or more of the following risk factors: solid organ transplant, haematological or other malignancy, gastroenterology patient, recent antibiotics, other high risk medications such as proton pump inhibitors. Patients were treated as per our clinical guidelines: non severe cases received parenteral metronidazole and severe cases received parenteral vancomycin.

Conclusions

Although our dataset is small, our hospital is Scotland’s largest paediatric tertiary referral centre with many cases having significant risk factors for CDI. Our analysis suggests that risk factors such as malignancy, haematological or solid organ transplantation, and gastrointestinal surgery may predispose patients to significant dysbiosis and therefore CDI. Biochemical and haematological parameters alone, even though some of these form part of the CDI severity score, cannot replace careful clinical review. Underlying conditions, in particular immunocompromising conditions, are significant risk factors that may lower the threshold for treatment.
Background

The UK Royal College of Ophthalmologists issued guidance in October 2017 recommending that 'regular screening of adults or children taking ethambutol is not considered necessary' despite the potential for optic neuropathy. The NICE TB Guidelines recommend treatment with ethambutol (2HRZE/4HR) but make no statement on vision testing. Other guidance such as the British Thoracic Society's TB Drug Monographs recommend regular testing of selected groups. In the absence of clear UK guidance we report a survey of UK TB units assessing whether vision is routinely tested in patients treated with ethambutol.

Methods

The survey was produced for UK TB units using an online survey tool and circulated via the British Association for Paediatric Tuberculosis (BAPT) mailing list.

Results

The survey reports the clinician's profession and size of clinic; the unit's standard practice in routine and targeted assessment at baseline, 1 month, 2 months and/or further time points of visual acuity, colour vision discrimination and/or visual fields; specific indications for assessment (e.g. symptom screening, history of visual disturbance, renal dysfunction, >15 mg/kg/day ethambutol); and referral to ophthalmology for certain age groups, if unable to assess in clinic or other indications. We report if ethambutol is used at all or stopped if TB fully sensitive or unable to assess vision.

Conclusions

Vision screening practice in the UK is varied and not based on any national guidance. This survey highlights the need for clear guidelines on the testing of vision for patients taking ethambutol at recommended doses, before and during treatment.
Acute kidney injury and seizure associated with influenza A (H1N1) infection: A case report

Background

Neurological complications of influenza infection have been reported but renal complications are uncommon. We present a case of acute kidney injury and seizure associated with influenza infection.

Case Presentation Summary

A 15-year old boy presented with a four day history of fever, throat pain, cough, and gross macroscopic hematuria. On physical examination body temperature was 38°C. Chest examination revealed bilateral crepitations. Laboratory evaluation revealed hemoglobin 14.4 g/dL, white blood cells 7,470/mm³, platelet count 197,000/mm³, serum sodium 133 mmol/L, potassium 4.1 mmol/L, blood urea nitrogen 49 mg/dL, creatinine 3.29 mg/dL, albumin 3.2 g/dL, and creatinine kinase 559 IU/L. Urinalysis showed proteinuria and hematuria. The following immunological tests were negative or within normal range; anti-nuclear antibody, anti-streptolysin-O, complement 3 and 4. A renal ultrasound showed increased parenchymal echogenicity. Management involved adequate intravenous hydration, forced diuresis and intravenous ceftriaxone until the results of cultures. Throat swab was negative for group A beta haemolytic streptococci and Real-time nasopharyngeal PCR was positive for influenza A. After 48 hour the macroscopic hematuria disappeared but he had generalized tonic clonic seizure lasting one minute on the second day of admission. Laboratory evaluations revealed white blood cells:2800/mm³ (absolute neutrophil 1200/mm³), platelet:76000/mm³, blood urea nitrogen 23 mg/dL, creatinine 1.69 mg/dL, albumin 3.2 g/dL, and creatinine kinase 84 IU/L. Electroencephalogram and magnetic resonance imaging of brain were normal. No medications needed for convulsion. Five days later his serum creatinine level had decreased 1 mg/dL, his leukocyte and platelets had increased. He was discharged 6 days later.

Learning Points/Discussion

Influenza infection should be considered in differential diagnosis of unexplained gross hematuria, acute kidney injury with fever and cough in children.
EMERGING DRUG RESISTANCE SALMONELLA STRAINS IN CHILDREN
M. Kadry

Background

This work was carried out to study the occurrence of salmonella infections in chicken and children suffering from gastroenteritis in Egypt.

Methods

A total of 349 chicken meat and 40 stool specimens of children were collected, samples were subjected to bacteriological examination and identified biochemically as salmonella then subjected to serological identification, also were tested for their antibiotic susceptibility by disc diffusion method. Also, genotyping by PCR to detect salmonella enterotoxine gene (str) and their expression by infant mouse assay.

Results

The study revealed that 14 (4.01%) and 2 (5%) were positive for Salmonella species in chicken meat and children respectively and serological identification were (Salmonella Infantis, Salmonella Typhi, Salmonella Kentucky, Salmonella Rubislaw, Salmonella Poona, Salmonella Typhimurium, Salmonella Virginia, Salmonella Enteritidis and Salmonella Montevideo) and (Salmonella Typhimurium and Salmonella Enteritidis) in chicken meat and children isolates respectively. Disc diffusion method showed that 3 (21.4%) in chicken meat isolates and 2 (100%) in children isolates were multidrug resistant in which S. Kentucky have resistance to ciprofloxacin, the drug of choice for treating salmonellosis in children. Also, genotyping showed that 9 (64.28%) and 2 (100%) isolates confirmed to be enterotoxigenic strains in chicken meat and children respectively and this (str) gene have been expressed (100%) by infant mouse assay.

Conclusions

Special attention must be paid to antibiotics that are used exclusively in poultry farms, appropriate measures must be taken to control the spread of resistant bacteria to human and Molecular techniques remain the most sensitive method in detecting salmonella enterotoxin.
BACTERIAL INFECTIONS IN NEONATES WITH CONGENITAL HEART DISEASE

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**Background**

Despite marked success of antenatal and postnatal screening, bacterial pathogens continue to be an emerging etiology of invasive infections, and thus remains a significant issue especially for neonates with congenital heart disease. The objective of present survey was to determine the frequency of bacterial infections in neonates with congenital heart disease and to evaluate the implication on treatment and outcome.

**Methods**

This prospectively data analysis included term and preterm infants with congenital heart disease requiring maintenance of ductus arteriosus (PDA). We studied 66 cases of infants with congenital heart disease receiving PGE1 infusion, hospitalized in one public hospital with tertiary level of Neonatal Intensive Care Unit, during 3 years period January 2014 to December 2016. A complete blood count, C-reactive protein level and blood culture were obtained within first 24 hours and after 72 hours of life from all infants included in the study.

**Results**

Active surveillance has identified in our group 21 (31.8%) infected neonates of which 6 (9.1%) have had positive blood culture within first 24 hours age, 7 (10.6%) infants with positive blood culture after 72 hours, and 8 (12.1%) have had negative blood culture but abnormal blood cell count and elevated C-reactive protein level. A total of 43 (65.2%) infants were treated with prolonged antibiotics of which 30 (70%) were treated based on abnormal laboratory data. For those infants with positive blood culture, PEG1 infusion doses were higher compare to those with blood culture negative (0.048 versus 0.032 micro grams, p=0.01), and also for those infants who received antibiotics (0.049 versus 0.047 micro grams, p=0.02).

**Conclusions**

Bacterial pathogens impact the management of the neonates with congenital cardiac disease. A large number of infants received antibiotics solely based on abnormally laboratory data.
DIFFERENTIATING CEREBRAL MALARIA FROM BACTERIAL MENINGITIS IN RESOURCE-LIMITED COUNTRIES: A LITERARY REVIEW

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Background and Objective

Due to the similarity of their clinical presentation, differentiating cerebral malaria (CM) from bacterial meningitis (BM) is challenging, particularly in malaria-endemic regions. The aim of this study was to review the literature in order to identify potential symptoms, signs and routine biological features that could guide caretakers in discriminating CM from BM in rural settings of developing countries, thus reducing the burden of both diseases.

Methods

A title and abstract search was conducted using multiple Internet databases, reviewing the available literature on diagnostic approaches for CM and/or BM in developing countries.

Learning Points Discussion

23 articles were selected. In malaria-endemic countries, coinfections with severe malaria and invasive bacterial infections are not uncommon (6.4 %). Impaired consciousness, prolonged seizures, prostration and meningeal irritation signs were not useful in differentiating CM from BM. Malarial retinopathy was the only distinctive sign that could potentially discriminate between CM and BM, although not systematically present in CM. A leukocyte count of > 100 /µL in cerebrospinal fluid (CSF) was highly suggestive of BM. In the two studies where CSF leukocyte counts of > 10 /µL were found in CM children without evidence of BM, neither specified if all patients had undergone bacterial cultures or antigen testing, nor if antibiotherapy was used before lumbar puncture was performed.

Conclusion: Retinal examination by trained caretakers may be useful in differentiating CM from BM in malaria-endemic regions. An elevated leukocyte count in CSF is the most useful laboratory testing to discriminate between both diseases particularly when the leukocyte count is > 100 /µL in the presence of negative malarial tests. If the leukocyte count is low, repeating the lumbar puncture after 24 hours while continuing empirical therapy for both diseases may be useful.
Pneumococcal pneumonia resembling acute myocardial infarction in an adolescent male

Background

Group A Streptococcus pharyngitis or bacteraemia is associated with acute non-rheumatic streptococcal myocarditis that can mimic acute ST-elevation myocardial infarction (STEMI) in young males. We present a teenager with pneumococcal pneumonia and bacteraemia complicated by myocarditis and rhabdomyolysis, presenting with features of acute STEMI and cardiogenic shock.

Case Presentation Summary

A 16 year old boy with G6PD deficiency presented with 2 days of fever, sore throat, cough and diarrhoea. He had generalised myalgia and tea-coloured urine. On arrival, he had acute chest pain with hypotensive shock requiring inotropic support. ECG showed classical posterior-inferior STEMI. Cardiac enzymes were markedly elevated; CKMB 120.7µg/L, CK 1063U/L, NT-proBNP 3457pg/ml, troponin I 26857ng/L. Echo showed septal dyskinesia and globally impaired left ventricular function with ejection fraction of 35%. Emergency coronary angiography showed normal coronary arteries. Chest X-ray done later showed left lower zone pneumonia. Blood cultures grew Streptococcus pneumoniae the next day and he received 10 days of ceftriaxone with uneventful recovery. ECG and echo were normal within 1 and 5 days respectively. Cardiac enzymes improved over 3 days.

Learning Points/Discussion

Pneumococcal pneumonia is associated with true acute cardiac events causing higher mortality in adults, while acute non-rheumatic streptococcal myocarditis only mimics STEMI. This is seen in young males with no risk factors for coronary artery disease and have normal coronary arteries. Cardiac MRI shows late gadolinium enhancement and complete recovery occurs within weeks to months. To our knowledge this is the first reported case of pneumococcal infection mimicking acute STEMI in a similar fashion. Bacterial myocarditis is uncommon. Focus on the acute cardiac event may delay diagnosis and treatment of the infection.
A general recommendation for the pneumococcal conjugate vaccine (PCV) was issued for children ≤2 years in Germany in 2006. In 2009, two higher-valent PCVs (PCV10, PCV13) were licensed. Here, we present data on invasive pneumococcal disease (IPD) cases following PCV program onset.

Methods

Pneumococcal isolates from children with IPD were serotyped at the GNRCS using the Neufeld-Quellung reaction.

Results

From July 2016 to June 2017, the GNRCS received 116 IPD isolates from children <2 years, of which 16 had PCV13 serotypes. Ten of these were from unvaccinated children.

The 116 isolates represent a reduction of 25% (n=154) compared to 2005/2006 (before vaccination), but an increase since 2011-2012 (n=75). The total amount of cases has increased, but the PCV13 proportion has decreased from 88% before vaccine introduction to 69% at the introduction of higher-valent vaccines to 14% in 2016/2017.

Among PCV13-non-PCV7 serotypes, reductions were observed for children ≤2 years in serotypes 1 (-100%), 6A (-100%), 7F (-100%) and 19A (-90%). Serotype 3 showed no reduction, and serotype 5 remains rare in Germany. Compared to 2009/2010, reductions in children 2-4 years and 5-16 years were observed for serotype 1 (-89% and -100%) and serotype 7F (-100%, -90%), whereas cases of serotypes 5, 6A and 19A were rare. Serotype 3 decreased among 2-4 year old children from 2 cases to 1 and from 7 cases to 2 in 5-15 year olds.

In non-vaccine serotypes, 15A/B/C, 10A, 23B, 22F, 24F and 12F were most prevalent.

Conclusions

More than eight years after the introduction of higher-valent vaccines, PCV13 serotypes have almost disappeared among children. Serotypes 3, 10A, 15A/B/C, 22F and 24F are the most prevalent serotypes among children <16 years in Germany.
EPISODES OF SEIZURES AFTER VACCINATION AGAINST MEASLES-MUMPS-RUBELLA (MMR), DURING OCTOBER – NOVEMBER, 2017. DESCRIPTION OF THREE CASES, OF OUR CLINIC

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Title of Case(s)

EPISODES OF SEIZURES AFTER VACCINATION AGAINST MEASLES-MUMPS-RUBELLA (MMR), DURING OCTOBER – NOVEMBER, 2017. DESCRIPTION OF THREE CASES, OF OUR CLINIC

Background

Background: MMR vaccine (live attenuated viruses) provides immunity against their respective diseases. After introduction of the vaccine, the incidence of the three diseases has been significantly reduced. Some side effects are expected including febrile convulsion.

Case Presentation Summary

Case Presentation Summary: These are cases of preschool children who were hospitalized in our clinic: 1st incident: Toddler male, 27 months, presented two episodes of seizures. Vaccination with 2nd dose of MMR preceded 7 days before the episodes. The child had viral infection and presented two more episodes during hospitalization. 2nd incident: Toddler male, 2 years old, which presented two episodes of febrile-seizures. The child presented fever as 39.7° C, by 16 hours. Vaccination with 2nd dose of MMR took place 11 days before the episode. 3rd incident: Toddler female, 18 months, who presented sloth, acrocyanosis and perioral cyanosis during the rise of fever (38.6° C). Vaccination with MMR had preceded 14 days before the episode.

Learning Points/Discussion

Learning Points/Discussion: Vaccination with MMR has some focal and general complications. Despite the fact that the occurrence of seizures is a rare complication following vaccination with MMR (1/3000 children) in accordance with the bibliographic data, however in our clinic we observed an increased frequency (3 incidents only during two months). The possibility that this might be due to a specific batch of the vaccine, or to the increased frequency of preventive vaccination (because of this year's measles epidemic) is investigated.
The management of pulmonary hydatid cysts in children: a case report

Background

Echinococcosis is a serious public health problem that often affects lungs rather than the liver. Mostly, small pulmonary hydatid cysts are asymptomatic but if large, they can cause mass effects or rupture leading to lung complications. Both medical and surgical therapy are recommended for pulmonary echinococcosis while there are few reports on the management of pulmonary hydatid cysts rupture. Surgical treatment is effective in children with complicated cysts as well as uncomplicated ones, with low mortality rate.

Case Presentation Summary

A 5 year old boy was admitted to the Pediatric Department due to fever and cough. He had a positive history for echinococcosis with referred negative previous serology. The chest X-ray revealed a big area of radiopacity in the left lobe (figure 1); CT showed a large cyst (68x55x48 mm) with polycyclic configuration and hyperdense wall in the lingular pulmonary parenchyma. The echinococcus IHA titre was 1:256 and pulmonary hydatid disease was diagnosed. He was discharged with Albendazolo therapy, waiting surgery. After 20 days he was admitted to the Emergency Department due to respiratory distress. A chest X-Ray and TC documented pulmonary cyst rupture and he was admitted in pediatric intensive care for respiratory support. After clinical stabilisation the patient was discharged program made up of three cycles of 28 days therapy with Albendazolo with 15 days of stop between them.

Learning Points/Discussion

The echinococcus IHA titre was 1:2048 at the end of the first cycle and 1:4096 at the end of the second one. A TC was repeated before the third cycle of therapy and showed a reduction of the known polycyclic cyst. At the moment, the boy is waiting surgery.
A paediatric nurse working on a 43-bed inpatient ward was diagnosed with smear-positive pulmonary TB after 5 months of chronic cough. 173 high risk patients (<2 years old, immunocompromised, or >40 hours of contact) under her care were identified for contact tracing. We analysed patient uptake of recommended window prophylaxis (WP) and latent tuberculosis infection (LTBI) treatment.

Methods

Children received a clinical review, chest X-ray, and a tuberculin skin test (TST) (<5 years old) and/or an interferon gamma release assay (TB Quantiferon) (>5 years old). Infants <6 months old and children screened at <2 months from time of exposure were recommended isoniazid WP until a repeat TST at 6 months old or 8-10 weeks later respectively. Empiric LTBI treatment of 9 months isoniazid was considered for immunocompromised patients on an individual basis. Patient information leaflets and counselling were provided.

Results

126 immunocompetent and 36 immunocompromised children were screened. 2 were uncontactable, 7 refused screening. 2 immunocompromised children were excluded; 1 for delayed screening and 1 already on LTBI treatment.

8 immunocompetent children were diagnosed with LTBI; 7 (88%) agreed to receive LTBI treatment. 15 (47%) of 32 immunocompetent children accepted recommended WP; 1 child was non-compliant after 1 month.

7 immunocompromised children were recommended empiric LTBI treatment due to severe immunosuppression (n=5) or initial indeterminate TB Quantiferon result (n=2); 6 children (86%) agreed. 5 (33%) of 15 immunocompromised children accepted recommended WP; 1 child developed rash and discontinued WP after 2 weeks.

Conclusions

There was low uptake of isoniazid WP in high risk children exposed to pulmonary TB. This may be due to parental perception of a low risk of exposure and reluctance to take medication with potential adverse effects.
CLARIFICATION OF IMMUNISATION STATUS DURING PNEUMOCOCCAL CONJUGATE VACCINE SWITCHES IN NEW ZEALAND

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Background and Objective

New Zealand (NZ) introduced a pneumococcal conjugate vaccine (PCV) into the National Immunisation Programme in 2008 using PCV7 in a 3+1 schedule. Switches occurred in late 2011 (PHiD-CV), late 2014 (PCV13), and late 2017 (PHiD-CV). Transition periods complicate the comparisons of PCVs’ impact. We aimed to clarify the immunisation status of children during PCV transitions in NZ.

Methods

Descriptive analysis of immunisation status was performed using data from the National Immunisation Register for the 2011 and 2014 switches. Estimations of PCV use were calculated for 2014 and 2015.

Learning Points Discussion

- By mid-November 2011 and 2014, >70% of PCVs given to children were PHiD-CV and PCV13, respectively. The first infant to receive a complete primary series with PCV13 occurred in mid-January 2015.
- In 2014, 77.1% of children <2 years of age (YoA) were vaccinated with PHiD-CV according to a 3-dose priming schedule; 39.6% completed the 3+1 schedule. No child in 2014 received 3 doses of PCV13, while 4.9% received a mixed schedule of both vaccines.
- In 2015, 39.6% and 27.1% of children <2 YoA received a 3-dose primary course of PHiD-CV and PCV13, respectively. 34.4% received a booster dose of PCV13, but only 1% completed the 3+1 schedule of PCV13. 12.5% received a mixed primary schedule. In children 2-4 YoA, 63.9% received a 3+1 schedule of PHiD-CV, 8.3% a mixed PCV7/PHiD-CV primary series, while 3.5% received a PCV13 booster dose.
- In the first year post-switch in NZ (e.g. 2015), about 1/4 of children <2 YoA received the new vaccine (primary series) and 3.5% of children 2-4 YoA received it as a booster. Therefore, it is...
difficult to attribute changes in invasive pneumococcal disease rates solely to one vaccine.

**Figure. Timing of transition from PCV7 to PHiD-CV (in 2011) and from PHiD-CV to PCV13 (in 2014)**

PCV7, 7-valent pneumococcal conjugate vaccine; PHiD-CV, pneumococcal non-typeable *Haemophilus influenzae* protein D conjugate vaccine; PCV13, 13-valent pneumococcal conjugate vaccine.

**Funding:** GlaxoSmithKline Biologicals SA
SEROPREVALENCE OF HBV AND HIV CO-INFECTION IN CHILDREN AND OUTCOMES FOLLOWING HIGHLY ACTIVE ANTIRETROVIRAL THERAPY (HAART) IN UYO, SOUTH-SOUTH NIGERIA

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Background

Human immunodeficiency virus (HIV)/Hepatitis B virus (HBV) co-infection in Nigerian children has emerged as a major concern with the advent of Highly Active Anti-Retroviral Therapy (HAART). Its impact on the immune system and the liver has not been extensively studied in children. We set out to determine the prevalence of HBV seropositivity among HIV positive children on HAART and its effect on the immune response and liver enzymes.

Methods

This prospective longitudinal study was conducted at the Paediatric Infectious Diseases Unit of University of Uyo Teaching Hospital (UUTH) in Nigeria. The hospital is one of the sites of care for HIV patients under President’s Emergency Plan Funds for AIDS Relief (PEPFAR). With research ethical approval, all consecutive HIV positive children aged 2 months to 17 years on HAART were recruited. Age and gender; CD4+, serum alanine aminotransferase (ALT), creatinine and HBsAg were tested and documented at enrollment and 12 months later.

Results

One hundred and seventy one eligible patients were recruited for the study of which 72 (4.34%) were males and 94 (56.6%) were females. Male:female ratio was: 1:3 in favour of females. The mean age of the patients was 63+/-43.4 months. The prevalence of HIV/HBV co-infection was 6.02% (95% CL 2.4-9.7).

There was no significant effect of HBV status on the elevation of serum alanine amino transference levels with 12 months of HAART. Co-infected patients had an odds ratio of achieving immune response of 0.14(95% CL 0.79)

Conclusions

HIV/HBV co-infection rates in the study population are comparable to that of other localities. Serum alanine aminotransferase levels were not worsened with HAART and immune response of the co-infected children on HAART was lower.
MILD ENCEPHALOPATHY WITH A REVERSIBLE SPLENIAL LESION, A DIFFERENZIAL DIAGNOSIS TO CONSIDER IN CHILDREN

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Title of Case(s)

Mild Encephalopathy with a Reversible Splenial lesion, a differential diagnosis to consider in children

Background

Mild Encephalopathy with a Reversible Splenial lesion (MERS) is an uncommon clinical-radiological entity characterized by magnetic resonance imaging (MRI) findings of a reversible lesion in the splenium of corpus callosum associated with significant neurological manifestation of encephalopathy. We report three cases of children with different clinical and radiological presentation, associated to an infection.

Case Presentation Summary

The first case is a 14 years old girl admitted for malaise, fever, headache and later a worsening of neurological aspect with confusion, psychomotor crisis, urinary and fecal retention. Laboratory tests showed hyponatremia and HHV6 infection. Anomalies were evident to electroencephalogram (EEG) and somatosensory evoked potentials (SEEP). The brain MRI showed lesions in the corpus callosum at the splenium level.

The second patient is a 3 years old boy admitted for fever, hyponatremia and hypoglicemia. Neurological examination showed poor mental status, lethargy with absence of lower limb tendon reflexes. Cranial MRI showed a focal lesion in the splenium of the corpus callosum. The electroencephalogram (EEG) revealed diffuse slow waves. Pharyngeal swab PCR was positive for Influenza B.

The third case is a 11 years old female admitted to our department because of fever, strabismus of the left eye and diplopia. Neuro-ophtalmologic evaluation was normal. Cranial MRI revealed the presence of high signal lesion in the splenium of corpus callosum. The laboratory tests showed HHV6 infections.

Learning Points/Discussion

MERS is an important differential diagnosis to consider in children presenting with acute encephalopathy/encephalitis. In our experience, patient's symptoms recovered quickly and the splenial lesion disappeared, as described in literature. MERS in clinical practice is very low, but knowledges about its existence are essential to suspect and manage it.
Scrub typhus is a reemerging pediatric infection becoming prevalent in hitherto nonendemic regions. Literature is scant regarding clinical phenotype and genotype correlation which could be useful in the development of future diagnostics and vaccines.

Methods

We prospectively enrolled all febrile children 2 months to 14 years presenting to Pediatric emergency at our hospital in 2 time epochs: from June 2013 to December 2014 and June 2016-December 2017 (three years). Demographic profile and treatment history of all the children was noted. Our primary outcome was positive scrub typhus IgM assay by ELISA (InBios International Inc., USA). Of all the samples positive for scrub typhus ELISA, serum samples were randomly selected for indirect immunofluorescence assay (IFA) for *O. tsutsugamushi* (Fuller Laboratories, California, USA). IFA was done to confirm the diagnosis as well as to determine the genotype of the *O. tsutsugamushi* prevalent in our region. The test kit simultaneously detected and semi quantitatively determined IgM antibodies against *O. tsutsugamushi* using four strains namely Boryong, Gilliam, Karp and Kato.

Results

Out of 71 samples positive for scrub typhus ELISA, 15 samples were tested for IFA and of these maximum prevalence seen was of Karp genotype (8) followed by Kato (3), Boryong (1) and Gilliam (1). Two patients were mixed genotype having both Karp and Kato (1) and Karp and Boryong (1). IgM titres in most of the cases were 1:128. Six of the 8 children with Karp genotype had multisystem involvement in the form of acute undifferentiated fever, encephalopathy, hepatitis, shock, serositis and thrombocytopenia.
Conclusions

Karp was the most prevalent prototype of *O. tsutsugamushi* isolated which correlated with severe systemic manifestations in children.

Funding: Department of Science and Technology, Chandigarh Administration, Chandigarh, India
Background

Objective: to determine the incidence of influenza in hospitalisations in children and patients characteristics in Valencia Region, Spain.

Methods

Prospective active surveillance in 4-10 hospitals, during 6 seasons (November-April). Subjects under 18 years not institutionalised, with symptoms compatible with influenza were approached, and included after informed consent signature.

Non eligibility: hospitalised in previous 30 days, symptoms appearance 8+ days before.

Nasopharyngeal and pharyngeal or nasal swabs were collected, tested for influenza by real-time reverse transcription-polymerase chain reaction (RT-PCR).

Results

Of the 6332 screened patients, 4803 were eligible. 265 did not sign the consent. Therefore, 4538 patients were included, 4517 tested for influenza.

357 patients (7.90%) were influenza positives, 123 of them (34.45%) in patients less than one year, 174 (48.74%) in 1-4 years and 60 (16.81%) in 5-17 years. Percentages of influenza were similar in patients with asthma or bronchitis (7.66%) or without them (7.98%).

Among positives, 102 had influenza A(H1N1)pdm09, 169 A(H3N2), 62 influenza B and 24 influenza A not subtyped. Influenza A was found in 89% of the cases in patients under 5 years, however, in older subjects, influenza B represented 50% of the cases.

Among the 4538 patients included, 204 (4.50%) were vaccinated. Vaccination coverage was 9.40% (50/532) in children with asthma or bronchitis.
Length of hospitalisations was similar among influenza positives and negatives, with a mean of 5.03 (95%CI (4.88,5.18)) in less than one year and 4.14 (95%CI (3.97,4.30)) in 1-4 years.

Conclusions

Influenza had a moderate impact on hospitalisations in children. Influenza B represented 17.37% of the influenza cases in these 6 seasons. Influenza A was predominant in patients under 5 years. There was low vaccination coverage in children, even in risk groups.

Clinical Trial Registration (Please input N/A if not registered)

N/A
Background and Objective

It is widely assumed that all pneumococcal vaccine serotypes (VTs) as a cause of invasive pneumococcal disease (IPD) have reduced markedly following the introduction of pneumococcal conjugate vaccines (PCVs) in pediatric immunization programs. We assessed VT IPD trends in <5-year-old children in countries/regions following PCV introduction to determine if reductions in IPD were consistent for all VTs.

Methods

IPD datasets for <5-year-old children were identified by literature search and from publicly available surveillance reports in January 2018. Datasets were limited to those from countries/regions with robust epidemiologic surveillance before and after PHiD-CV/PCV13 introduction (n=8). Annual case numbers before and up to 5 years after PHiD-CV/PCV13 introduction were converted to % change relative to the PHiD-CV/PCV13 introduction year for each country/region. The average % change over all countries/regions was calculated per year pre/post-introduction.

Learning Points Discussion

Our analysis revealed:

- In PCV7-using countries, PCV7 serotypes and vaccine-related serotype 6A experienced dramatic decreases before PHiD-CV/PCV13 introduction and have continued to decrease in recent years.
- Serotypes 1, 7F, and 19A all increased during PCV7 use and have all decreased substantially following PHiD-CV/PCV13 introduction, although reductions in 19A have been more variable.
- Too few serotype 5 cases were available to provide any meaningful analysis.
- While serotype 3 also increased during PCV7 use, in contrast to all other VTs, serotype 3 IPD has fluctuated considerably in many countries since PHiD-CV/PCV13 introduction, with no net decrease when datasets were combined.
Eleven of twelve VTs with sufficient data available for analysis have demonstrated robust reductions in IPD in <5-year-olds following PHiD-CV/PCV13 introduction. Serotype 3 does not appear to be impacted by vaccination to the same extent as other VTs.

**Funding:** GlaxoSmithKline Biologicals SA
INVASIVE PNEUMOCOCCAL DISEASE IN REFUGEE CHILDREN RESIDING IN GERMANY: A POSSIBLE NICHE FOR VACCINE-TYPE AND ANTIBIOTIC-RESISTANT INFECTIONS

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Background

Refugee children arriving in Germany following political upheaval in the Middle East and Northern Africa were not routinely given a pneumococcal conjugate vaccine. The German National Reference Center for Streptococci collects invasive pneumococcal disease (IPD) isolates from all over Germany. We investigated refugee status as a potential risk factor for the development of childhood vaccine-type (VT) IPD.

Methods

Cases of IPD occurring from July 1, 2014 to June 30, 2017 in refugee children were compared to cases of IPD in German children over the same time period. The serotype and the presence of resistance to multiple (≥ 3) classes of antibiotics were compared for these groups and adjusted for age and season of infection.

Results

Refugee children had significantly higher odds of contracting VT IPD (OR 6.60, 95% CI 2.73 to 16.84) as well as significantly higher odds of contracting multiple-antibiotic-resistant IPD (OR 23.84, 95%CI 7.98 to 72.72) than German children.

Conclusions

To prevent a niche for VT IPD, not to mention non-invasive pneumococcal disease, the provision of catch-up pneumococcal conjugate vaccines should be considered for refugee children residing in Germany.
COMPARING INTERFERON-GAMMA RELEASE ASSAY WITH TUBERCULIN SKIN TEST FOR IDENTIFYING LATENT TUBERCULOSIS INFECTION BETWEEN CHILDREN < 5 YEARS AND ≥ 5 YEARS OLD

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⁶Pusan National University Children's Hospital, Department of Pediatrics, Yangsan, Republic of Korea

Background

The use of the interferon-gamma release assay (IGRA) for the diagnosis of latent tuberculosis infection in children under 5 years old is limited due to the low sensitivity. We compared the results of tuberculin skin test (TST) and IGRA in children under 5 years and over 5 years old who had vaccinated BCG.

Methods

We included the cases who were agreed to perform an IGRA in addition to TST by parent in tuberculosis contact tracing. TST was performed with PPD RT-23 2 TU (AJ Vaccines, Denmark) and IGRA was used with the QuantiFERON-TB Gold In-Tube (QTF) (Qiagen, Germany).

Results

A total of 80 subjects were recruited and a total of 110 tests were conducted. Forty-two (52.5%) were male, median age was 4 years of age. The positive rate of TST was 43.8% (35/80), but the positive rate of QTF was only 5% (4/80). All 4 QTF positive subjects were positive for TST. The positive rate of QTF in < 2 years old, 2 to 4 years old and ≥ 5 years old was 0%, 9.4%, and 3.8%. Otherwise, the positive rate of TST in < 2 years old, 2 to 4 years old and ≥ 5 years old was 46.2%, 25% and 28.8%, respectively. Of the 35 TST positive cases from 110 tests, 4 (11.4%) had TST+/QTF+, and 31 (88.6%) had TST-/QTF-. Of the 75 TST negative cases, 1 (1.3%) had TST-/QTF+, and 74 (98.7%) had TST-/QTF-. The concordance of both tests was very low (Cohen's kappa value=0.1309).

Conclusions

It was concluded that the use of QTF alone in children, especially under 5 years old in tuberculosis contact tracing could not still acceptable due to the much lower sensitivity than TST.

Clinical Trial Registration (Please input N/A if not registered)
N/A
Background

Healthcare-associated infections (HAI) are associated with increased morbidity and mortality and excess costs. Central line-associated bloodstream infections (CLABSI) are the most common HAI in neonates and children. The aim of this study was to develop a CLABSI collaborative network in neonatal and pediatric intensive care units and pediatric oncology units. Secondary objectives were to collect national benchmark data for CLABSI rates, isolated pathogens and antimicrobial susceptibility rates.

Methods

Active surveillance for CLABSI was conducted from June 2016 to February 2017. A collaborative network of 14 NICUs, 5 PICUs and 6 Pediatric Oncology Units (ONCs) participated in the program. Surveillance definitions of central line (CL), central line utilization (CLU) ratio, CLABSI event and CLABSI rate were based on 2014 Centers for Disease Control and Preventions' National Healthcare Safety Network criteria. Medical records were assessed daily for calculating CL days, patient days and susceptibility of isolated organisms.

Results
A total of 111 CLABSI episodes were recorded. The overall mean CLABSI rate was 4.41 infections per 1000 CL days and CLU ratio was 0.31. CLABSI rates were 6.02 in NICUs, 6.09 in PICUs and 2.78 per 1000 CL days in ONCs (Table). A total of 123 pathogens were isolated. The most common pathogens were Enterobacteriaceae (36%) followed by Gram-positive cocci (30%), non-fermenting Gram-negative bacteria (17%) and fungi (16%). Overall 38.5% and 37% of Gram-negative pathogens

Table. Pooled means and key percentiles of the distribution of CLABSI rates and CLU ratios by type of location

<table>
<thead>
<tr>
<th>Type of acute care facility</th>
<th>CLABSI RATE</th>
<th></th>
<th></th>
<th>CLU RATIO</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pooled</td>
<td>25%</td>
<td>Median</td>
<td>75%</td>
<td>Pooled</td>
<td>25%</td>
</tr>
<tr>
<td>NICUs</td>
<td>6.02</td>
<td>3.83</td>
<td>6.96</td>
<td>9.9</td>
<td>0.15</td>
<td>0.06</td>
</tr>
<tr>
<td>PICUs</td>
<td>6.09</td>
<td>3.58</td>
<td>5.96</td>
<td>6.52</td>
<td>0.68</td>
<td>0.43</td>
</tr>
<tr>
<td>ONCs</td>
<td>2.78</td>
<td>1.65</td>
<td>2.48</td>
<td>3.65</td>
<td>0.84</td>
<td>0.79</td>
</tr>
</tbody>
</table>

Conclusions

Nation-wide CLABSI rates were determined for pediatric patients. A worrying finding was the identification of high rates of carbapenem-resistant organisms. These data could be used to benchmark and serve as baseline data for the design and evaluation of infection control and antimicrobial stewardship interventions.
THE IMPACT OF POINT-OF-CARE-TESTING FOR INFLAMMATORY BIOMARKERS ON ANTIBIOTIC PRESCRIBING IN CHILDREN: A SYSTEMATIC REVIEW

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Background

One of the major causes of antimicrobial resistance is the over prescription of antibiotics. Point-of-care tests (POCTs) are rapid diagnostic tests that can be performed at the patient’s bedside by non-laboratory staff allowing for rapid results to support clinical decisions. At present POCTs can identify three host inflammatory biomarkers: C-reactive protein (CRP), Procalcitonin (PCT) and WCC (white cell count). The aim of this review was to assess what effect using POCTs measuring inflammatory biomarkers have on antibiotic prescription in children.

Methods

Embase, Medline, Web of Science, Scopus and Global Health databases were searched from database inception to November 2017. Included studies had to include children, had to use POCTs, and had to look at antibiotic prescribing as an outcome. Given the wide clinical heterogeneity among the papers a narrative summary of the results was performed.

Results

Five studies were found. Four of the studies were RCTs and one was a cross sectional study. The four RCTs included 1706 children and the cross sectional study included 4049 children. One study was conducted in Vietnam, while the others were from Europe. The intervention of all the studies was CRP POCTs; no studies looked at WCC or PCT.

Looking at the effects of POCTs, Do et al. based in Vietnam showed a statistical reduction in antibiotic prescribing with POCTs resulting in 44.5% of children being prescribed antibiotics compared with 64.3% of children in the control group (OR 0.39, 95% CI: 0.30-0.52, p<0.0001). The other 4 studies did not show a statistically significant result.

Conclusions

There is evidence to suggest that CRP POCTs could help to reduce antibiotic prescriptions in children. Unfortunately the lack of research on this topic makes it difficult to assess the true extent.

Systematic Review Registration (Please input N/A if not registered)

CRD42017073670
Background

Because tympanocentesis is not performed routinely in France for first line acute otitis media (AOM) and to follow the bacterial changes induced by PCV13, we set-up two epidemiological studies: the first, follows the otopathogens from nasopharyngeal flora of children with AOM, and the second investigates the otopathogens recovered from children with AOM complicated by spontaneous otorrhea. We present the results of this first study.

Methods

We conducted a quasi-experimental, population-based interrupted time series analysis based on a multicenter prospective cohort over 10 years in France, recruiting 138 pediatricians. Nasopharyngeal swabs were obtained from <2 years children with acute otitis media (AOM), from November 2006 to March 2017. Changes in bacterial nasopharyngeal carriage rate over time were analyzed using the segmented regression model with autoregressive error, adjusted on day care center attendance and antibiotic consumption trends.

Results

During the study period, 9,957 children with AOM were enrolled. Streptococcus pneumoniae (Sp), Haemophilus influenzae (Hi) and Moraxella catarrhalis (Mc) were identified by culture in 5,566, 5,116 and 5,539 children respectively (56%, 51% and 56%). PCV13 implementation was followed by sustained significant decrease in Sp carriage rate (-0.1% per month, p=0.005). Hi carriage rate non significantly increased after PCV13 (+0.5% per month, p=0.08), and became the most frequent
Conclusions

Most probably due to the change of AOM clinical profiles, 6 years after PCV13 introduction, we observed a significant carriage shift in otopathogens from nasopharyngeal flora.
INTRODUCTION OF THE HEXAVALENT VACCINES TO THE NATIONAL IMMUNIZATION SCHEDULE IN KAZAKHSTAN

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Background

National immunization schedule in Kazakhstan improved significantly in the last few years. In accordance with the recommendations of the World Health Organization, was included a hexavalent vaccines against pertussis, diphtheria, tetanus, viral hepatitis B, poliomyelitis and Haemophilus influenza type b. Using of these vaccines could help to achieve by reducing the number of injections, increased the vaccination coverage and ensured safe practice of immunization.

Methods

The main objective is assessment of the immunization coverage with hexavalent vaccines DTaP-HBV-Hib-IPV vaccination. Statistical forms No. 3 "Report on vaccines and other immunobiological products movement", No. 4 "Report on preventive vaccination coverage" used for the analysis of immunization coverage in the country. There are 5604 medical organizations in Kazakhstan. Data’s for vaccinated children are sent to 211 district-level organizations with adverse events monitoring.

Results

Combined vaccines used in Kazakhstan since 2013. Within the period, the immunization coverage of target group’s children with hexavalent vaccines increased each year and demonstrated the next data’s: in 2011y - 98,9%, 2012y - 98,9%, 2017y - 100%. Adverse events after hexavalent vaccine immunization not registered. No cases of pertussis, diphtheria, tetanus, viral hepatitis B, poliomyelitis and Haemophilus influenza type b from vaccinated children reported during the period.

Conclusions

Immunization of the target groups in Kazakhstan with hexavalent vaccine DTaP-HBV-Hib-IPV demonstrated a high protection level among the vaccinated children. The form in the fully liquid suspension in the syringe allowed minimizing the manipulation time during vaccination and reducing the frequency of adverse events after immunization.

Systematic Review Registration (Please input N/A if not registered)
Disclosure of HIV diagnosis to infected children receiving care in University of Uyo Teaching Hospital, Uyo, Nigeria

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Background

Disclosure of human immunodeficiency virus (HIV) diagnosis to infected children is still a challenge despite proven evidences that it has numerous social and medical benefits for the child and family. The aim of this study was to document the disclosure rate of HIV diagnosis to children in Uyo, Nigeria and determine the factors influencing disclosure or non-disclosure to these children.

Methods

This was a descriptive cross-sectional study. A pre-tested and validated semi-structured questionnaire was administered to consenting parents/caregivers of Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome (HIV/AIDS) infected children aged 6 to 17 years in care at the Paediatric Infectious Diseases Unit of the University of Uyo Teaching Hospital, Uyo (UUTH) from January to June, 2015.

Results

One hundred and twenty-two caregivers (26 males and 96 females), giving a male to female ratio of 1:3.7, aged 20 to 60 years, were interviewed. Sixty-eight (55.8%) of them had post secondary education. Twenty (16.4%) of the children aged 9 to 17 years (13.3±2.4 years) had been disclosed to. Age of the children, gender, orphan status, their level of schooling and their socio-economic class positively affected disclosure. Also, caregivers between ages 30 and 49 years who were more educated were more likely to disclose the HIV status of their children. Commonest reason for non-disclosure was child being sad (29.5%). Others were blaming the parents (18.0%), not understanding the import of the diagnosis (9.8%) and 6.6% feared child disclosing to others. Forty-four (37.7%) did not give reasons for non-disclosure. Sixty-seven (54.9%) of the caregivers who did not disclose said they would do so after 10 years of age.

Conclusions

A national protocol for paediatric HIV disclosure is desirable to aid increase in paediatric HIV disclosure to children.
Hand hygiene (HH) is the most important measure to prevent healthcare associated infections and avoid transmission of pathogens. The aim of this study was to determine HH compliance rates in pediatric units and identify barriers to compliance among health-care workers (HCWs).

Methods

Observational study for HH rates was carried out in 15 NICUs, 4 PICUs and 6 oncology units (June 2016-February 2017) in 14 Greek hospitals. Using a data collection tool based on WHO guidelines, observations were collected during all shifts by trained observers. Compliance and appropriateness rates were defined as follows: [(number of performed actions/number of opportunities) x 100] and [(number of appropriate performed actions/number of performed actions) x 100] respectively. At the end of this period, a questionnaire was given in paper form to HCWs to identify the barriers of HH compliance.

Results

A total of 6472 HH opportunities were observed. The total HH compliance rate was 71% and did not differ by unit type. The rate of appropriate HH was 52% (Table 1). The response rate among 749 HCWs from all units was 48%. Since the actual number of HCWs receiving the questionnaire was not available, response rate is underestimated. Emergency situations (73%), distraction from other responsibilities necessary for patient care (47%), heavy workload (34%), skin irritation from hand
products (24%) were the most frequent answers. Almost half of the responders did not participate in any HH educational activity during the previous year.

**Table 1: HH compliance rate (%) stratified by type of unit for the period Jun16-Feb17**

<table>
<thead>
<tr>
<th>Unit</th>
<th>Compliance Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>TOTAL</td>
<td>71</td>
</tr>
<tr>
<td>NICUs</td>
<td>72</td>
</tr>
<tr>
<td>PICUs</td>
<td>68</td>
</tr>
<tr>
<td>Oncs</td>
<td>72</td>
</tr>
</tbody>
</table>

**Conclusions**

HH compliance rates among pediatric departments are high. However, opportunities for improvement exist. Educational interventions can be designed according to HCWs barriers for increasing HH compliance rate.
01C. SCIENCE: ANTIBIOTIC STEWARDSHIP AND INFECTION CONTROL

PRE-EMPTIVE COHORT ISOLATION OF PAEDIATRIC RESPIRATORY VIRAL ILLNESS ON A MULTI-DISCIPLINARY GENERAL PAEDIATRIC WARD

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²National University of Singapore, Department of Paediatrics- Yong Loo Lin School of Medicine, Singapore, Singapore

Background

Children admitted with acute respiratory viral illness (RVI) require pre-emptive isolation for droplet transmission precautions. Cohorting of children infected with the same pathogen may occur if single beds are unavailable. In January-February 2016, a seasonal increase in RVI admissions on a background of overall increasing bed demands resulted in inappropriate patient isolation and possible exposures causing nosocomial infection. To improve appropriateness of droplet isolation/cohort precautions for RVI admissions on a multi-disciplinary medical and surgical paediatric ward in a tertiary university hospital.

Methods

Multiple interventions were implemented in March 2016. A self-contained 8-bed area was utilised for pre-emptive cohorting. Nurses allocated these beds to patients admitted with defined clinical diagnoses indicating acute RVI. Guidelines that recommended viral pathogen testing and an isolation/deisolation prioritisation workflow were introduced. Children with a confirmed viral pathogen identified were moved to a single bed on an isolation ward, or placed with other children with the same infection. Stricter infection control measures were reinforced. Retrospective data from January to July 2016 on bed allocation of children with acute RVI, and proportion of children with respiratory viral swab/aspirate testing, was collected.

Results

Pre-intervention (1 January to 17 March), 304 patients were admitted with acute RVI; 154 (50.7%) were appropriately cohorting. Post-intervention (18 March to 31 July), 607 patients were admitted with acute RVI; 440 (72.5%) were appropriately cohorting. Patients who received respiratory swab viral testing increased from 34.5% (n=105) to 62.3% (n=378) during the same respective periods.

Conclusions

A streamlined workflow based on pre-emptive cohorting of patients with clinically diagnosed RVI and increased testing for viral pathogens, led to more appropriate patient isolation and cohort droplet precautions. This may reduce risk of viral nosocomial infection.
Title of Case(s)

ACUTE ABDOMEN IN A CHILD WITH SALMONELLOSIS AND A KNOWN HISTORY OF TYPE I DIABETE MELLITUS

Background

Salmonella infections are mainly manifested as acute gastroenteritis with diarrhea, fever, abdominal pain, myalgia, headache, nausea and vomiting. Rarely this can lead to urgent surgery due to gastrointestinal perforation, salpingitis and peritonitis mainly in patients that belong to high risk groups. Also, it can not only mimic acute appendicitis through mesenteric lymphadenitis but has actually led to it. The purpose of this study is to describe an interesting case of acute abdomen in an immunocompromised patient as a complication of gastrointestinal salmonella infection.

Case Presentation Summary

A 6-year-old girl with a known history of type I diabetes mellitus presented to the emergency department of our hospital due to abdominal pain along with vomiting, loose stool and fever. Two days prior, her pediatrician prescribed amoxicillin plus clavulanic acid for suspected acute otitis media. On physical examination the patient’s tonsils were mildly swollen, red with whitish spots and an otoscopic examination revealed turbidity of the left tympanic membrane. Her abdomen was tender in all four quadrants especially in the right lower one (RLQ) and bowel sounds were present. Her laboratory tests revealed increased inflammatory markers. An abdominal ultrasound was performed followed by surgical evaluation. After a recommendation for further imaging, a computed tomography of the abdomen and pelvis was performed that revealed acute appendicitis. The girl successfully underwent surgery while salmonella was found from stool cultures that had been sent.

Learning Points/Discussion

Salmonella infection is a rare cause of acute appendicitis, so the general pediatrician should be cautious especially when managing high-risk patients and raise awareness about the complications of salmonellosis in immunocompromised patients. Salmonella infections can rarely lead to surgery.
Cranial osteomyelitis associated with Group A strep meningitis

Background

The incidence of group A streptococcal (GAS) meningitis is 1-3% out of all invasive GAS infections; it is a rare manifestation in children. It is described as a fulminant type of meningitis.

Case Presentation Summary

A 16-year-old female presented to the emergency department with severe headache, speech disturbance and recent otitis media with discharge, for which she had been given a 10-day course of oral penicillin. GAS was isolated from blood cultures, while MRI showed brain changes with left subdural collection, left meningeal enhancement and restricted diffusion of left cerebral cortex. Lumbar puncture was deferred because of the low platelet count. She was started on iv ceftriaxone and dexamethasone. After two weeks of intravenous ceftriaxone, due to a miscommunication, the antibiotic treatment stopped. Two days after stopping, symptoms of headache, fever, and rising CRP occurred. MRI revealed meningeal enhancement, and iv ceftriaxone was recommenced. Two weeks later, she developed frontal swelling. CT revealed osteomyelitis. IV antibiotics were continued with no change but follow up MRI 6 weeks later revealed extension of the osteomyelitis. At surgery, extensive bone destruction was found so craniectomy was performed with iv treatment continued; despite this, the patient remains well. Her right sided weakness and expressive speech problems have significantly improved.

Learning Points/Discussion

From surveillance of all invasive GAS over the past 2 years, there were 4 cases of paediatric GAS meningitis in Bristol. Two of them were fatal and while the other two recovered with minor impairment, the road to recovery was long with complications. Despite the initial appearance of recovery, the disease can follow a protracted course.
RITUXIMAB AS A SECOND LINE TREATMENT IN TWO CASES OF AUTOIMMUNE ANTI-NMDAR POST-HERPES SIMPLEX ENCEPHALITIS

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² Gregorio Marañon University Hospital, Division of Paediatric Infectious Diseases, Madrid, Spain

Title of Case(s)

Rituximab as a second line treatment in two cases of autoimmune anti-NMDAr Post-Herpes Simplex Encephalitis

Background

Incidence of encephalitis in childhood is 5-10/100000. Herpes Simplex Virus (HSV) is the first cause of severe encephalitis in children. Anti-NMDAR Encephalitis is a rare complication of this condition.

Case Presentation Summary

We present 2 boys, 12 (patient-1) and 3 months old (patient-2) respectively, that presented to A&E with fever, decreased consciousness and complex partial seizures. In both cases MRI (figure1) showed temporal lobe injuries compatible with herpetic meningoencephalitis and HSV-1 PCR in CSF was positive. They had an initial satisfactory evolution on acyclovir and antiepileptic drugs.

After 14 days of treatment, in patient-2 and 25 days in patient-1, both presented sudden deterioration, with new seizures, loss of developmental milestones and appearance of choreoathetotic movements. Repeat MRI showed progression of previous injuries with necrohaemorrhagic encephalitis (figure1). Autoimmune encephalitis was suspected, and then confirmed by presence of antibodies against brain glutamate NMDA receptor in CSF and blood serum.

Both patients received methylprednisolone (30mg/kg/day) during 5 days, 2 doses of Immunoglobulins (1gr/kg/day), and 5 cycles of plasmapheresis. No clinical improvement was observed, so Rituximab was started with 4 weekly doses, showing neurological improvement and decrease in chorea after the second dose. 7 months after treatment, patient-1 showed increasing aggressiveness and sleep disturbances as IgG anti-NMDAr rose in blood serum. Suspecting a relapse, a new cycle of Rituximab was administered with subsequent improvement and negativity of antibodies.

Learning Points/Discussion
Autoimmune encephalitis should be suspected if clinical worsening is observed during evolution of herpetic encephalitis and anti-NMDAr antibodies in CSF and blood serum performed. Treatment with Rituximab may improve significantly the course of the disease and should be considered early as second line treatment.
17F. SCIENCE: VACCINE EFFECTIVENESS AND EFFICACY

EFFECTIVENESS OF 13-VALENT PNEUMOCOCCAL CONJUGATE VACCINE ON INVASIVE PNEUMOCOCCAL DISEASE IN THE EUROPEAN UNION: RESULTS OF SPIDNET MULTICENTRE STUDY


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Background

The SpIDnet network conducts active population-based surveillance for invasive pneumococcal disease (IPD) in the European Union. Using surveillance data from 10 sites, we measured the effectiveness of 13-valent pneumococcal conjugate vaccine (PCV13) against IPD in children under five years old.

Methods

We included children 12-59-month-olds with IPD reported from January 2012 to December 2016 using a common protocol. We compared the odds of being fully vaccinated among IPD cases caused by
PCV13 serotypes (cases) to that among IPD caused by nonPCV13 serotypes (controls). We computed the effectiveness as \((1 - \text{pooled vaccination odds ratio}) \times 100\), adjusted for age, sex, underlying conditions, notification year and surveillance site (aVE). We reported aVE for serotype categories and specific serotypes with the corresponding 95% confidence intervals (CI).

**Results**

We included 273 PCV13 cases and 612 controls (range by site: 1-158 cases and 9-314 controls). The PCV13 aVE was 86% (95%CI: 77; 92) against PCV13 IPD, 95% (95%CI: 89; 98) against PCV7 IPD (number of cases/controls \((n)=79/543\)) and 81% (95%CI: 67; 89) against PCV13nonPCV7 IPD \((n=194/612)\). The PCV13 aVE was 92% (95%CI: 82; 97) against serotype 19A \((n=61/526)\), 55% (95%CI: 8; 78) against serotype 3 \((n=67/529)\), 84% (95%CI: 54; 94) against serotype 1 \((n=46/488)\), 98% (95%CI: 93; 99) against serotype 14 \((n=51/308)\), and 92% (95%CI: 59; 98) against serotype 19F IPD \((n=11/451)\).

**Conclusions**

SpIDnet results suggest a good PCV13 effectiveness against IPD caused by most specific serotypes analysed and a moderate effectiveness against serotype 3 IPD. The low number of cases by site, and the possible heterogeneity due to serotype circulation may limit the interpretation of these results. To better evaluate the direct effect of PCV13 vaccination programme, SpIDnet will complete the analysis by time since PCV13 vaccination.

**Clinical Trial Registration (Please input N/A if not registered)**

N/A
Background

According to the Korean Guidelines for Tuberculosis, a 9 month course of isoniazid (9H) or a 3 month course of isoniazid plus rifampin (3HR) is recommended for the patients of latent tuberculosis infection (LTBI). However, for childhood patients, it is hard to maintain medication for those period. We aimed this study to find what are the obstacles to good treatment compliance.

Methods

We reviewed the medical records of all confirmed pediatric latent tuberculosis cases in Chonbuk National University Children's Hospital, from January 2014 through December 2017. Visit dates, symptoms and signs possibly related to medication, and prescription details were mainly investigated.

Results

A total of 232 medical records of childhood LTBI cases were reviewed. Most children (N = 225) were on 9H. Seven adolescents completed 3HR and 3 of them mentioned orange colored urine. Sixteen children (6.9%), mostly infants and on 9H, showed refusal of medication in the early period of treatment but completed the course. Two infants had a few days of diarrhea but they could continue the medication. No cases in this study showed skin rash related to the medication. Twelve (5.2%) cases completed the medication behind the schedule due to delayed clinic visits. All pediatric LTBI cases in this study completed a course of either 9H or 3HR.

Conclusions

Adverse effects of childhood LTBI treatment were rare and tolerable. To complete the LTBI treatment course properly in children, reminding the visit schedules to caregivers are important. Providing reassurance to caregivers and easily administrable drug formula could improve the compliance for the LTBI treatment in children.
Background

Acute bacterial meningitis is an important cause of morbidity and mortality in pediatric patients. Early diagnosis and appropriate treatment are the most important factors for patient prognosis. But cerebrospinal fluid culture is not always resulted as positive. Multiplex PCR (Biofire FilmArray®), ensures important advantages at diagnosis and treatment by resulting within first 1 hour of CSF examination and resulting positive despite of negative CSF culture.

Methods

In this study, the effects of multiplex PCR on diagnosis and treatment, in patients between 0-18 years of age with the presumed diagnosis of meningitis in Marmara University Pendik Training and Research Hospital, were evaluated. Biofire Filmarray Multiplex PCR was tested in 59 patients’ CSF and compared with CSF culture.

Lumbar puncture was performed in patients with clinical signs or symptoms of meningitis such as fever, seizure, vomiting, rash, head ache, meningeal irritation findings, pulsatile fontanel, changes in consciousness. Glucose and protein levels, bacterial culture results, leucocyte count and multiplex PCR results were recorded.

Results

Multiplex PCR resulted as positive in 12 of 59 patients, while CSF bacterial culture resulted as positive in 4 of them.

Neisseria Meningitidis was detected in 2 patients with multiplex PCR in first hour of admission. The antibiotic treatment, isolation precautions and postexposure prophylaxis for contacts organised rapidly.

Streptococcus Pneumoniae was detected in 2 patients multiplex PCR test while their bacterial culture were sterile.

Viral pathogens were detected 8 patients and antibiotic treatment was stopped early in management.

Conclusions
Acute bacterial meningitis is an important cause of morbidity and mortality in pediatric patients. Multiplex PCR (Biofire FilmArray®), ensures important advantages at diagnosis and treatment by resulting rapidly.
FEVER IN THE CHILD COMING FROM THE TROPICS. 15 YEARS EXPERIENCE

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Background

International travelers have grown significantly over last years, as well as imported diseases from
tropical areas. Information about paediatric age is scarce. Our objective is to describe the
demographic and clinical characteristics of febrile children coming from the tropics.

Methods

Retrospective review of patients under 18 years old presenting at a tertiary hospital and surrounding
primary health care centers with stay in a tropical region during the last year between July 2002 and
July 2017. Patients were selected from microbiological charts of thick smears for malaria and dengue
serologies.

Results

162 patients were studied: 49.4% were born in Spain with a mean age of 3.5 years old (p25 1.4- p75
8.0). Main regions of origin were sub-Saharan Africa (58.6%) and Latin America (25.3%), mostly from
visiting their friends and relatives (52.4%). Only 18% attended to a pre-travel consultation and 7.4%
received complete chemoprophylaxis. The next main group was immigrants of recent arrival (35.8%).
The most frequent diagnosis were febrile syndrome, respiratory condition, and acute diarrhea. Most of
them were not severe cosmopolite diseases with no significant differences between regions. 51.9%
were managed as outpatients, but 40% were hospitalised, and 6.8% were admitted to Intensive Care
Unit. No specific diagnosis was achieved in 23% of the cases. However, 37 patients (22.8%) were
diagnosed of malaria.

Conclusions

In our study, 7% of the febrile children coming from the topics were admitted to Intensive Care Unit,
and nearly a quarter were diagnosed of malaria. The first consulted place was the Emergency Room
for more than 80% of the patients, while the rest went to Primary Care Health Centre. Furthermore,
less than one out of five patients attended to a pre-travel consultation.
04A. EDUCATION: SEVERE PNEUMONIA IN CHILDREN

COMPLICATED PNEUMONIA CAUSED BY STREPTOCOCCUS ANGINOSUS IN A CHILD

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Title of Case(s)

COMPLICATED PNEUMONIA CAUSED BY STREPTOCOCCUS ANGINOSUS IN A CHILD

Background

Streptococcus anginosus is a commensal bacteria but recent evidence shows that it can be also pathogenic, capable of causing abscesses or systemic infections. Importantly, studies reporting its identification in the pediatric population are rare.

Case Presentation Summary

A 6-year male with early infantile encephalopathy, global developmental delay, and recurrent respiratory infections since the first year of life, presented at the emergency room with low-grade fever, irritability and grunting, on day 1 of disease. The physical examination, laboratory findings and chest radiograph were in favor of a bacterial pneumonia. He was admitted with amoxicillin plus clavulanic acid. On day 2, a multiloculated pleural effusion was detected and the child underwent a left thoracic drainage; the pleural fluid was macroscopically purulent and the laboratory analysis were consistent with exudate. Antibiotic therapy was changed to ceftriaxone and the patient had clinical improvement. The bacteriologic exam of the pleuritic fluid identified Streptococcus anginosus. On day 11, the child restarted fever and the left pulmonary sounds were abolished, the blood exam revealed leukocytosis with neutrophilia, thrombocytosis and elevated C-reactive protein. Thoracic CT scan showed left empyema, atelectasis and consolidation with necrosis on the inferior pulmonary left lobe. The patient underwent a left decortication via video-assisted thoracic surgery. There was significant clinical improvement in the first 24 hours after surgery. The pulmonary sounds gradually improved and there was full recovery after a four-week course of ceftriaxone and a two-week course of clindamycin. In re-evaluations, the child was well with normal chest radiography.

Learning Points/Discussion

Pediatricians should be aware of these emerging agents. S. anginosus can cause serious infections that require rapid recognition and appropriate treatment to diminish the associated mobility and mortality.
13A. SCIENCE: PUBLIC HEALTH | AMP| EPIDEMIOLOGY

CIRCULATING NON-VACCINE SEROTYPES IN CHILDREN WORLDWIDE IN THE POST-PCV ERA: POTENTIAL FOCUS OF NEXT GENERATION PNEUMOCOCCAL VACCINES

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Background and Objective

Following the introduction of higher-valent pneumococcal conjugate vaccines (HV-PCVs), public health authorities recommend continuous monitoring of pneumococcal serotype prevalence. Our analysis aims to describe the most prevalent non-vaccine serotypes (NVTs) causing invasive pneumococcal disease (IPD) in children after the introduction of HV-PCVs in different countries/regions.

Methods

We used available laboratory-confirmed IPD surveillance data (from 2011 to 2016) reported for children ≤5 years of age in different countries/regions using HV-PCVs, to conduct a descriptive analysis of vaccine type (VT) and NVT IPD prevalence based on absolute case counts and relative frequencies.

Learning Points Discussion

- In our analysis, 22F, 33F, 15C, 12F, and 15B were among the most prevalent NVTs in children <5 years of age (Figure). Our analysis suggests there is no evidence of replacement by emergence of a single serotype across countries/regions.

- Despite several years of HV-PCV use, some VTs are still prevalent in these countries/regions, the 3 most common VTs being: 19A, 14, 6B (Finland, Latin America); 19A, 3, 7F (US, Canada, New Zealand, England and Wales); 19A, 3, 19F (Australia).

- This result highlights the importance of the assessment of PCV programs based on the impact on overall IPD rather than serotype-specific IPD. Limitations of this analysis include heterogeneity in surveillance activities and PCV schedules across countries/regions.

- Continuous monitoring will help determine requirements for next generation pneumococcal vaccines.
Figure. Distribution of NVTs (i.e. serotypes not included in PCV13) in IPD isolates from children <5 years of age in the HV-PCV period in different countries/regions. Only the 5 most common NVTs for the US were available. N, total number of NYT cases (except for the US: sum of the 5 most common NVTs).
WHAT CAN WE DO TO PREVENT NEONATE FROM INFECTION DURING PERINATAL PERIOD:
AN OVERVIEW TO TURKEY
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Background and Objective

The aim of this review is to discuss about things to do for prevent neonate from infections during perinatal period and the status of Turkey about mentioned topic.

Methods

Pregnancy follow-up and prenatal health care services becomes firstly for prevent neonatal infections. Women aged 20-34 and under 20 and over 35 had prenatal care in their first pregnancies (97%, 96%; respectively) though that rate decreased in the next pregnancies (92%) according to the data of Turkey Demographic and Health Survey (TDHS) 2013 conducted by considering fertility age.

All staff and visitors should wash their hands and use alcohol-based disinfectants. Respiratory equipment must be cleaned and moisturizing sterile water should be changed frequently, there must be a stethoscope of every baby, aseptic surgical techniques should be used in applications.

It is recommended to start breastfeeding early in the postnatal period. Breast milk and colostrum are protected from diseases such as diaper rash, diarrhea and respiratory tract infections. According to TDHS 2013 data, breastfeeding on the first hour and first day after birth increased (50% and 70%; respectively) compared to TDHS 2008 data (39%, 73%; respectively). At the same time the order of child deaths has changed over the years as a result of studies in Diarrheal Disease Control aimed at oral fluid treatment, Control of Acute Respiratory Tract Infections to Prevent Pneumonia and Neonatal Resuscitation Programs and Expanded Programme on Immunization implemented in our country.

Learning Points Discussion

In the perinatal period, to prevent newborns from infections, precautions have been taken since prenatal period, health personnel being educated on that issue, early detection of risks, health screening and implementation of health promotion programs are very important.
02A. SCIENCE: ANTIMICROBIALS: RESISTANCE AND PHARMACOLOGY

SENSITIVITY TO ANTIBIOTICS OF PLANKTONE AND BIOFILM FORMS CLINICAL ISOLATES EXTRACTED FROM CHILDREN WITH URINARY TRACT INFECTION

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Background

The aim of work is determine the antibiotic resistance of planktonic and biofilm (BF) forms clinical isolates from children with different types of urinary tract infection.

Methods

Number of clinical isolates-60: first group - infection of lower urinary tract 23 strains; second, acute pyelonephritis - 19; and third, chronic pyelonephritis - 18. Strains was presented by E. Coli (53%), S. Epidermidis (20%), E. Faecalis (12%) and other (15%). BF was determined using 96-well plate assay. BF parameters were estimated using optical density values (OD) of the samples (no BF<0.4 OD; small<0.46 OD; medium<0.52 OD; large>0.52 OD). Susceptibility to antibiotics was determined by the method of standard serial dilutions. Analysis of the results was performed using the SPSS program version 12. The results were considered statistically significant at p<0.05.

Results

Level of biofilm formation in third group (0.51 ± 0.07 OD) was higher than first (0.41 ± 0.06 OD)(p<0.01). Also was statistical difference in the ability to form biofilm between second (0.46 OD) and first group (p<0.05). Through the use of serial dilutions method we established antibiotic susceptibility to antibiotics planktonic strains and after biofilm formation to ceftriaxone (first group - 83 to 30%; second – 47 to 5%; third – 79 to 11%), cefixime (first group – 43 to 13%; second – 32 to 16%; third – 67 to 6%), gentamicin (first group – 87 to 52%; second – 89 to 21%; third – 72 to 28%), furagin (first group–96 to 83%; second – 89 to 84%; third – 89to72%).

Conclusions

The clinical isolates have different ability of biofilm formation depending on different types of UTI. After biofilm formation the number of strains resistant to antibiotics increased with statistical credibility (except furagin).

Clinical Trial Registration (Please input N/A if not registered)
STREPTOCOCCUS MINOR BACTERAEMIA AFTER DOG BITE

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Title of Case(s)

Streptococcus minor bacteraemia after dog bite

Background

The predominant organisms in animal bite wounds are the oral flora of the biting animal (notable pathogens include Pasteurella, Capnocytophaga, and anaerobes) as well as human skin flora (such as staphylococci and streptococci). Streptococcus minor is α-hemolytic, first described in 2004 as a new species isolated from the tonsils of dogs, cats and cattle. One case of human infection due to Streptococcus minor (grown from a wound swab) is reported in literature, but no known case of Streptococcus minor bacteraemia has ever been reported.

Case Presentation Summary

A 10 year old girl with previously identified global developmental delay, presented to our hospital after being mauled by a Pitbull dog. She had extensive injuries to abdomen, pelvis and upper leg, mainly focused on right hand side. Underlying fractures of the pelvic brim and right iliac crest were noted. Blood cultures grew Streptococcus minor, identified by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF) with CRP rising to 295. The wounds were surgically debrided several times and she was started on co-amoxiclav and teicoplanin (as she had previously been MRSA +ve). As there was evidence of bone involvement/osteomyelitis the planned duration of treatment was 6 weeks.

Learning Points/Discussion

This is the first report of Streptococcus minor isolated from human blood culture. It has previously been described in the oral and faecal flora as a known bacterium of dog flora. Although the pathogenicity of this organism is still unknown, this case suggests that S. minor can lead to serious infections.
Evidence suggest that high per-capita antibiotic consumption is correlated with higher rates of antibiotic resistance. Given that India was one of the top consumers of antibiotics in 2010, the aim of the present study was to investigate systemic antibiotic (J01) prescription rate and pattern in India by analysing private sector’s antibiotic prescribing data.

Methods

We analysed IMS medical audit data to estimate systemic antibiotics consumption in the Indian private sector for the year 2014. We reported antibiotic use as annual prescription rate per 1,000 persons. Antibiotic utilization was plotted and reported by age group, antibiotic class and disease condition. We used statistical software STATA 14.0 to perform the analytics.

Results

In India, approximately 519 million antibiotic prescriptions were dispensed in the private sector, which translates into 412 prescriptions per 1,000 persons in the year 2014. The antibiotic prescription rates were highest in the age group 0-4 years (636 prescriptions per 1,000 persons) and lowest in the age group 10-19 years (280 prescriptions per 1,000 persons). The most commonly prescribed antibiotic class was cephalosporins (J01D) (38.2%) followed by penicillins (J01C) (22.8%), quinolones (J01M) (16.3%) and macrolides (J01F) (14.0%). The top five disease conditions that contribute approximately 50% of the prescriptions were acute upper respiratory infections (J06) (20.4%), unspecified acute lower respiratory infection (J22) (12.8%), other disorders of urinary system (N39) (6.0%), cough (R05) (4.7%) and acute nasopharyngitis (J00) (4.6%).

Conclusions

We found a high antibiotic prescription rate for the 0-4 year age group, majority of those prescription were dispensed for acute upper respiratory infections and unspecified acute lower respiratory infections. Our figures also indicate an overuse of cephalosporins over other antibiotic classes.
01C. SCIENCE: ANTIBIOTIC STEWARDSHIP AND INFECTION CONTROL

ANTIBIOTIC SENSITIVITY PATTERN OF STAPHYLOCOCCUS AUREUS CLINICAL ISOLATES IN CHILDREN FROM KYIV PEDIATRIC INFECTIOUS DISEASES HOSPITAL IN PERIOD 2012 -2016

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Background

We aimed to perform statistical analysis of antibiotic sensitivity for the most frequent etiological agent of bacterial infectious diseases – S.aureus - in the children in the Kyiv Pediatric Infectious Diseases Hospital, the clinical base of the Department of Pediatric Infectious Diseases of the A.A. Bogomolets National Medical University between years 2012-2016.

Methods

Information was received from laboratory journal carried out according to the The Law of Ukraine of 5 April 2007 №167 "On approval of guidelines" Determination of the sensitivity of microorganisms to antibiotics " in order to implement the main provisions of the "WHO Global Strategy for Containment of Antimicrobial Resistance". The method of serial dilutions had been used for years to determine the sensitivity of microorganisms to antibiotics (based on the direct determination of minimum inhibitory concentration (MIC) of antibacterial drugs).

Results

The number of patients and clinical isolates – 498. Antibiotic susceptibility of bacterial was analyzed that was more frequency above other – S.aureus – 66%, Str.pyogenes - 15%, Kl.pneumoniae – 5%; and antibiotics that are often applied to specific pathogens. The sensitivity pattern of S.aureus to the following antibiotics: cloranfenicol - 39%, benzylpenicillin - 30%, ampicillin - 20%, oxacillin - 6%, cefotaxime - 61%, ceftriaxone 58%, cefoperazone - 72%, ceftazidime - 43%, cefuroxime - 67 % of vancomycin - 60% azithromycin - 28%, rifampicin - 51%, amikacin - 56% ciprofloxacin - 61%, ofloxacin - 32%, imipenem - 79% meropenem - 70%

Conclusions

In determining the sensitivity of clinical isolates of S.aureus in the children with different infectious diseases found high sensitivity to antibacterial agents of cephalosporin group (72-43%), fluoroquinolones (61-32%), carbapenems (79-70%), low sensitivity semi-synthetic penicillins (6-20%), azithromycin (28%), benzylpenicillin (30%).
**SYSTEMIC ANTIBIOTIC UTILIZATION IN INDIA AND ITS COMPARISON VIS-À-VIS EUROPEAN COUNTRIES: EVIDENCE FROM PHARMACEUTICAL SALES DATA (2008-2012)**

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**Background**

India was the largest consumer of antibiotics in 2010 in the world. High per-capita antibiotic consumption in countries are usually associated with higher rates of antibiotic resistance. The key objective of this research was to investigate the trends in consumption of major antibiotic classes in India and compare them with European Surveillance of Antimicrobial Consumption Network (ESAC-Net) countries.

**Methods**

For our study we used national level data on total antibiotic sales (2008-2012) in the private sector from the IMS Health’s Medicine Sales Audit data. We used ATC classification system and the defined daily dose (DDD) measurement unit to standardize dosage trends and assigned DDVs (2015 index) to all formulations based on the ATC/DDD index. We expressed our data in standardized matrices of DDD per 1000 inhabitants’ daily (DID) to compare antibiotic use of India with ESAC-Net countries, which was publicly available at the ATC third and fourth level. The antibiotic use was plotted and reported by year and antibiotic class.

**Results**

Our analysis suggests that in India per capita antibiotic consumption has increased from 13.1 DID in 2008 to 16.0 DID in 2012 - an increase of ~22%; antibiotic consumption rates are still low as compared to ESAC-Net countries (16.0 DID vs. 21.54 DID); use of newer class of antibiotics like carbapenems (J01DH) glycopeptides (J01XA), 3rd generation cephalosporins (J01DD) and Penicillin’s with beta-lactamase inhibitors has risen during 2008 to 2012; the antibiotic consumption pattern is seasonal in nature with peaks in July, August and September every year.

**Conclusions**

Our study has provided first reliable estimates of antibiotic use in India vis-à-vis ESAC-Net countries. In addition, our study could provide a reference point to measure the impact of interventions directed towards reducing antibiotic use.
Title of Case(s)
Neurosurgical resection of cranial nervous system Tuberculoma.

Background

Tuberculomas are conglomerate granulomatous foci within the brain parenchyma developing from coalescing tubercles acquired during an earlier period of haematogenous bacillaemia. Clinically silent nodular enhancing lesions are commonly seen in the setting of meningitis; occasionally, they are seen in miliary tuberculosis and no meningitis. These lesions generally resolve with therapy but may heal leave calcification. Unless the location of the lesion threatens obstructive hydrocephalus or brainstem herniation is life threatening, surgical intervention should be avoided as it may precipitate severe meningitis.

Case Presentation Summary

A 4-year-old from Ethiopia presented with acute right sided weakness and limp starting after a focal seizure. In the previous 9 months, he had experienced 6 episodes of seizures, diagnosed in Ethiopia as febrile convulsions. MRI showed an intra-axial lesion in the left frontal lobe with central calcification and surrounding oedema. The imaging was suspicious for tuberculoma. We recommended anti-tuberculous therapy without surgery, but due to concern regarding possible malignancy, the neurosurgeons performed fronto-parietal craniotomy and excision of the lesion with subsequent quadruple tuberculosis (TB) treatment. Quantiferon and Mantoux test were positive, HIV negative. Histology was typical of TB with caseous necrosis. Mycobacterium tuberculosis grew from the excision sample and urine with no resistance identified. CXR showed mild perihilar lymphadenopathy. Ultra sound showed no features to suggest abdominal tuberculosis.

Learning Points/Discussion

Although surgery is not generally recommended due to the risk of causing TB meningitis, there were no complications in this case. It was reassuring to have the confirmation of MTB with no resistance identified. The rarity of CNS tuberculoma, compared with brain tumours, in our population resulted in the reluctance of neurosurgery to believe that effective diagnosis and treatment could be accomplished without surgery.
ROLE OF IMMUNOGLOBULIN A IN MYCOPLASMA PNEUMONIAE UPPER RESPIRATORY TRACT CARRIAGE

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Background

*Mycoplasma pneumoniae* (Mp) is one of the most common bacterial causes of community-acquired pneumonia in children. Infection in the lower respiratory tract (LRT) may be preceded by asymptomatic carriage in the upper respiratory tract (URT). Recently, we showed that the presence of B cells is important for clearance of *Mp* from the LRT in a *Mp* infection mouse model. Interestingly, humoral immunity had limited effect on *Mp* load in the URT. Therefore we compared the humoral response to *Mp* in the URT with the LRT.

Methods

*Mp* or medium was installed intranasally in C57BL/6 or B cell-deficient μMT mice. Healthy children and children with selective IgA deficiency (sIgAD) from our outpatient clinic were recruited. Nasopharyngeal swabs and lavage fluids were isolated to determine *Mp* copy number by qPCR and *Mp*-specific IgM, IgA and IgG titers using an in-house ELISA.

Results

In *Mp* infected mice, *Mp*-specific IgG was markedly elevated in the bronchoalveolar lavage fluid. In contrast, the nasal lavage fluid contained high levels of *Mp*-specific IgA and very low IgG. Serum transfer of infected wild-type mice to μMT mice rescued clearance of *Mp* and increased *Mp*-specific IgG levels in the LRT. Interestingly, the serum transfer had no effect on *Mp* load and *Mp*-specific IgA levels in URT. To translate our findings to patients, we included 33 children with sIgAD and 477 healthy controls including 16 siblings of sIgAD patients to further examine the role of IgA in *Mp* carriage.

Conclusions

*Mp*-specific IgG responses dominated in the LRT, whereas *Mp*-specific IgA was increased in the URT, where it seemed to lower *Mp* load. Insights into the humoral response to *Mp* can benefit vaccine development and immunoglobulin treatment of patients with primary antibody deficiency.

Clinical Trial Registration (Please input N/A if not registered)
RHEUMATIC HEART DISEASE: STILL A CAUSE OF PEDIATRIC STROKE

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Title of Case(s)

Rheumatic heart disease: still a cause of pediatric stroke

Background

Rheumatic heart disease (RHD) has declined in the developed countries but remains a major cause of cardiovascular disease. Progressive valvular disease develops in the years following one or more episodes of acute rheumatic fever (ARF), most of the cases being asymptomatic. Some possible complications of RHD are atrial fibrillation, pulmonary hypertension, heart failure and less commonly stroke.

Case Presentation Summary

A 10 year-old boy was admitted to the emergency department due to sudden headache, blurred vision and gait imbalance. Neurological exam showed a limited supraversion of the right eye, diplopia, head tilt to the right, and gait ataxia. Initial brain CT was normal but 2 days later brain MRI showed left thalamic and mesencephalic ischemic lesions. 9 months earlier, a de novo murmur had led to a mitral valve (MV) regurgitation diagnosis. Transesophageal echocardiography confirmed a myxomatous MV with regurgitation. Immunologic, hematologic, infectious and vascular investigation were unremarkable, and a prothrombin G20210A gene mutation was detected. We discovered that 2 years before he had an untreated pharyngeal infection followed by migratory arthralgia, high CPR and ASO of 2968 U/ml. In the present context, this is highly suggestive of ARF with valvular involvement. The boy was discharged two weeks later with a normal neurological examination treated with monthly benzathine benzylpenicillin and warfarin for stroke secondary prevention.

Learning Points/Discussion

This patient probably had cardioembolic stroke due to RHD. A history of an untreated pharyngitis, arthritis and elevated ASO raised the high suspicion of a missed ARF. The prothrombin gene mutation likely increased the risk for a thrombus. This case reminds us to remain alert to complications of untreated streptococcal pharyngitis in an era of judicious antibiotic use campaign.
EFFICACY AND SAFETY OF THE ROTAVIRUS INFECTION VACCINE PROPHYLAXIS IN KHANTY-MANSIYSK AUTONOMOUS REGION-UGRA

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Background

46.5% of all acute gastrointestinal infections (AGI) were diagnosed as rotavirus infections (RVI) in 2016. RVI incidence rate among children 0-17 years old increased from 374.7 to 983.9 per 100 000 during 2006-2016 (+162.9%) in the region with the highest observed for children 0-2 years old. We aimed to assess the safety and efficacy of the vaccine prophylaxis of RVI with rotavirus pentavalent vaccine (Merck, Sharp&DohmeCorp., USA) conducted in the region in 2015-2016.

Methods

Vaccine prophylaxis programs were conducted in Khanty-Mansiysk (n=700), Surgut (n=200), Nizhnevartovsk (n=200), Nyagan (n=200). The proportion of vaccinated children among all of the first year of age was 4.9% in Nizhnevartovsk, 5.8% in Surgut, 21.7% in Nyagan and 43.7% in Khanty-Mansiysk. The safety was evaluated assessing post-vaccination reactions and complications. The immunization effect was evaluated by the assessment of RVI incidence rate among children 0-2 years old (2015-2016) and of the rate of all AGI among vaccinated children.

Results

No post-vaccination complications were observed, common post-vaccination reactions were observed among 11.9% of vaccinated children. The RVI incidence rate decline was observed in 2015-2016 among children 1 and 2 years old in Khanty-Mansiysk by 82.95% and 73.4%, in Nyagan - fivefold and 93%, in Nizhnevartovsk – 12.8% and 9%, respectively. Within a year after vaccination 18 children were diagnosed with AGI (1.7%) including 2 with RVI (0.19%) and 16 (1.5%) with other AGI etiology: 6 - bacterial AGI, 1 - norovirus AGI, 9 - non-identified AGI etiology. Among vaccinated children no cases of severe or moderate AGI were observed.

Conclusions

Our study confirmed the safety and efficacy of rotavirus vaccine prophylaxis among children as one of the best ways to control the AGI and RVI incidence rate.
AUDIT OF ANTIBIOTIC STEWARDSHIP IN THE PAEDIATRIC INTENSIVE CARE UNIT

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Background

Within the Paediatric Intensive Care Unit (PICU) of a tertiary paediatric hospital, a multi-disciplinary initiative to improve antibiotic stewardship was undertaken. An audit cycle was completed to monitor for change.

Methods

In October 2016 and October 2017, data was collected weekly, for four weeks, by two trained personnel. The data was collected using the Hospital Antibiotic Prudent Prescribing Indicator (HAPPI) tool, which assesses quality indicators of antibiotics stewardship. All PICU patients were eligible. Patients were excluded if they were not receiving antibiotics or if they were previously audited. After the first audit cycle, the PICU staff were educated through daily reminders, information leaflets and departmental educational posters.

Results

In the initial pre-education audit 22 of 36 patients were eligible. In the subsequent post education audit 19 of 33 patients were eligible. In comparison of the pre-education to post education groups, there was an improvement in:

1. the documentation of indication/diagnosis in notes (47.8% to 94.7%)
2. the documentation of indication/diagnosis in medication chart (26.0% to 89.4%)
3. the documented review of antibiotics (47.3% to 92.8%)
4. the plans at > 72hrs for on-going therapy and review (61.1% to 100%)
5. collection of appropriate cultures (82.6% to 100%)
6. the guideline use of indicated antibiotics (56.5% to 89.4%)
7. the de-escalation of IV antibiotics at 48 hrs or according to guidelines (68.8% to 100%)
8. the duration of antibiotic to < 7 days or guidelines (77.7% to 85.7%)

Conclusions

This audit cycle demonstrated that an interventional education programme can improve documentation, reviewing and planning of antibiotic administration, appropriate culture investigations, use of indicated antibiotics, and de-escalation and duration of antibiotics.
EVIDENCE OF FUNGAL CO-COLONIZATION IN CYSTIC FIBROSIS CHILDREN CHRONICALLY COLONIZED WITH ASPERGILLUS FUMIGATUS

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Background

Cystic fibrosis (CF) is an inherited multisystem disorder characterized mainly by chronic obstructive lung disease. Although bacteria are considered the primary pathogens, fungi, such as A. fumigatus, have recently gained the attention for their possible negative effect on lung function. Evidence suggests that mixed colonization indicate a poorer prognosis. The aim of our study was to investigate the microbiota of patients chronically colonized with A. fumigatus in our CF center.

Methods

A case-control study of CF children was performed. Chronic colonization was defined as two or more positive sputum cultures in a given year. Each patient chronically colonized with A. fumigatus (AC) was matched with three control CF patients never colonized with A. fumigatus for age, sex and year of birth (±3 years). All sputum cultures from regular visits were collected.

Results

Twenty AC patients were detected and were matched with 60 controls. Among AC patients’ sputum samples, 10 different types of microorganisms were detected, while only 6 among control patients. The presence of C. albicans in sputum samples was significantly higher among AC than control patients (65.0% vs 23.3%; P=0.001), but an independent association was not confirmed from the logistic regression analysis after adjustment for confounders. No significant differences were detected regarding S. aureus and P. aeruginosa (70.0% vs 66.7%; P=0.783 and 70.0% vs 50.0%; P=0.119, respectively).

Conclusions

In our CF center, AC children seem to be co-colonized with C. albicans in high frequency even if this observation, which is in line with our clinical experience, was not confirmed from the statistical analysis. The lung microbiota of AC patients merits further study as mixed colonization may alter the levels or spectrum of virulence factors produced by bacteria or fungi.
Background

The availability of new vaccines can complicate the definition of immunization programs. This complexity can be managed using combined vaccines and co-administration. Co-administration should be considered when combined vaccines are not available and/or there is a need to expand the administration of vaccines. Here, we present an evaluation on the co-administration of MMRV (V Oka/Merck strain) and meningococcal vaccines.

Methods

The terms including “co-administration of MMRV and meningococcal vaccine(s)” were used for a Pubmed search. National and International guidelines and recommendations including the Calendario per la vita 2016 (subscribed by several Italian Scientific Societies), the Advisory Committee on Immunization Practices (ACIP), the WHO and CDC were also consulted on this topic.

Results

Several articles addressed the immunogenicity and safety profile of co-administration of the MMRV (V Oka/Merck) and meningococcal conjugate vaccines. Co-administration as also stated by the International Health Authorities is possible when there are specific indications in the data sheet (SCP) of the vaccines or because there are no specific contraindications and/or there are scientific publications to support it. In Italy, National recommendations also support co-administration of all MMRV vaccines with monovalent MenC conjugate vaccines.

Conclusions

Co-administration is indeed a powerful strategy for several preventive approaches in order to obtain a greater compliance, a reduction of costs, a simplification of operational procedures and the possibility of adopting new vaccines. Co-administration of the MMRV (V Oka/Merck) vaccine with the MenC conjugate vaccines is supported by extensive literature data on immunogenicity and safety and by indications of authoritative international institutions in the field of vaccinations (e.g. WHO, CDC).
Background

Invasive candidemia is the third cause of healthcare associated infections. The use of central venous catheters (CVC) is a major risk factor, and mortality seems to increase without removal.

Methods

This is a ten year retrospective study in a single center. Catheter-Related bloodstream infection (CRBSI) was defined according to Infectious Diseases Society of America (IDSA) guidelines. “Conservative treatment” was defined by CVC removal after more than 72 hours of infection.

Results

Thirty six children under 18 years old were included. The four most common species responsible for CRBSI were C. albicans (39%), C. parapsilosis (22.2%), C. tropicalis et C. lusitaniae (11%). Three strains were resistant to fluconazole (two strains of C. krusei and one strain of C. glabrata). Only one patient had non-effective empiric antifungal therapy by fluconazole with a strain of C. glabrata resistant. Treatment was conservative in 26 patients (72.2%), whereas catheter was removed for 10 cases (27.8%). Specific mortality was 19.4% (n= 17) but without significant difference between the two groups concerning mortality or transfer to intensive care unit. Persistence of candidemia after 72 hours was observed in 20% of the non conservative-group and in 73% in the conservative-group (p=0.01), but was not associated with any increase of disseminated candidiasis.

Conclusions

Infection control was better in the non-conservative treatment group whereas there was no significant difference on mortality, which could be explained by an earlier removal of CVCs for most severe patients. CVC removal within the first 72 hours after invasive candidiasis diagnostic is not always performed but remains the rule in critical patients. Conservative treatment is associated with prolonged candidemia.
Pyomyositis in Dengue fever-a rare presentation

Background

We hereby report an interesting case of pyomyositis in a child diagnosed with dengue fever.

Case Presentation Summary

A 9 year girl presented to us with fever, pain abdomen, vomiting and decreased urine output since 4 days. On admission, child had an episode of hypotension and required resuscitation with intravenous fluids. Her abdominal pain was localised to right iliac fossa region with guarding and rigidity. An ultrasound abdomen was done which was normal. Fever workup revealed Dengue IgM serology to be positive and child was managed symptomatically. Two days later, abdominal pain worsened and repeat ultrasound showed large collection (5 x 1.3 cm) in right iliac fossa region. Computed Tomography of abdomen showed a well defined peripherally enhancing collection measuring 2.4X6.2X16.9 cm in anterior abdominal wall muscle in right lumbar region without intraperitoneal extension (Fig.1). Surgical drainage of pus was done and negative suction drain was put in situ. Pus culture showed growth of Methicillin Resistant Staphylococcus Aureus sensitive to Vancomycin which was given for 14 days. Repeat ultrasound done on day 12 of admission showed minimal residual collection (7.1mm in maximum thickness) and thereby drain was removed. Child’s symptoms resolved, thereby she was discharged on oral antibiotics for one more week. Her immunodeficiency workup was
normal.
Learning Points/Discussion

Dengue infection is a major vector-borne disease in tropical and subtropical regions. Myositis associated with viral infection maybe seen due to direct viral invasion of the muscle fibres and toxin generation. Predisposing factors to superadded bacterial infections can be immunodeficiency, trauma, malnutrition or concurrent infection. A high index of suspicion for bacteremia and development of septic foci among critically ill patients with dengue is thus warranted.
THYMOMEGALY AND RECURRENT DISEASE EPISODES IN CHILDREN

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Background

Children with recurrent episodes of different conditions, such as rash, dermatitis, upper and lower respiratory tract infections, sinusitis, chronic cough, adenoidal and tonsil hypertrophy, diarrhea are frequently referred to allergist/Immunologist.

Methods

Under observation were 17 children from age 14 months to 9 years of old. During investigation period acute infectious processes were excluded. Among patients’ chronic conditions of sinusitis, adenoidal and tonsil hypertrophy predominated – 55% of cases. In 1 patient – 9 years of old boy – obesity was markedly apparent.

Results

Imbalanced gut microbial flora: increased population of Hemolytic Escherichia coli, Escherichia coli with lower fermentation ability were detected in 75% of patients. Decreased quantities of Bifid bacteria and Lactobacilli were observed in all patients. As for nasal-pharyngeal flora, pathogenic micro flora with Streptococcus pyogenes and Staphylococcus aureus were in significant quantities in 63% of cases. Elevated total IgE was observed in 98% of cases: from mild (3%), moderate (48%) to significant (49%) level. The hallmark of whole study group was ultrasound changes of thymus. In 1 case CT scan of thorax was made. Thymus tissue was assessed according to measurements of weight, shape and ultrasound density. Thymomegaly revealed in all 17 children. In 1 case thymomegaly detected at 3months of age, was urgently operated due to remarkable increase in size of thymus at 6 months of age. Low risk (benign) thymoma was the case. In 7 cases tissue density was increased in addition to mild thymomegaly.

Conclusions

1. During treatment children with recurrent chronic conditions in different diseases changes in thymus tissue should be considered

2. Specific immunological investigation is necessary to carry out along with ultrasound thymus monitoring

Systematic Review Registration (Please input N/A if not registered)

N/A
01C. SCIENCE: ANTIBIOTIC STEWARDSHIP AND INFECTION CONTROL

TEN YEAR TRENDS AND RESISTANCE PATTERNS OF BLOOD AND CSF CULTURES IN CHILDREN UNDER 3 YEARS OLD

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Background

Bacterial infections in children are a major cause of hospitalisation in the UK, and resistance patterns to common antibiotics can have significant regional variation. This is a retrospective analysis describing a 10-year temporal trend and resistance patterns of blood and CSF cultures of children aged under 3 years in Oxford between January 2005 to December 2014.

Methods

Of 38913 blood and CSF cultures taken in children aged under 3 years old in 2005-2014, 35325 were analysed after excluding samples from post-mortems and unknown locations, unprocessed samples and duplicates. Results were classified as positive if a single organism was isolated and negative if there was no or mixed growth. We further characterised antimicrobial resistance patterns for selected gram-negative bacilli (GNB).

Results

Overall, 6% of blood cultures and 2% of CSF cultures were positive, of which 57% were coagulase-negative staphylococcus (CONS). Numbers of cultures per year increased, while positivity rates declined from 10% to 4% (blood cultures) and 5% to 2% (CSF cultures). Vaccine-preventable organisms were negligible in neonatal units and declined over time elsewhere, and no positive cultures for *Listeria monocytogenes* were seen in 10 years. Resistance was present to ceftriaxone (local first-line treatment) in 13% of *E.coli* and in 18% of *Klebsiella*, while no resistance was seen to meropenem.

Conclusions

Despite increasing investigations in the form of cultures, the number of culture-confirmed infections declined over time, driven by a marked decline in the number of CONS especially in neonates. This may reflect a lowering threshold to culture, but the decline in CONS may also reflect recent efforts to reduce contamination rates on the neonatal unit, demonstrating the potential impact of improved infection control.
EPIDEMIOLOGY AND PREVENTION OF HIV IN ALBANIAN CHILDREN

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Background

Albania is a country with low-level HIV epidemic. The first pediatric HIV/AIDS case was reported in 1996 post mortem. The annual number of cases reported remained low, 2-3 cases.

The aims of the study was: to assess the impact of programmatic efforts and other factors on HIV epidemic. To identify areas for development in HIV surveillance Methods

Retrospective cohort observational study, Information collected was from our clinic from 1996-2017, includes dates of 42 cases with HIV diagnosis (15 females, 25 males). Demographic information, HIV testing information, clinical and laboratory dates AIDS diagnoses and infection stage, route of transmission. Clinical information (CD4 counts, viral loads and ART information, psycho-motor development of the patients before and after treatment, the frequency of the different infections that we had seen in the patient).

Results

The most common risk factors for the cases were MTCT (78%) blood transfusion (16%), surgery (3%) and unknown (3%). In the city were 79 % and 21% in the rural places. Overall, 30% of all HIV diagnoses were from Tirana, followed by other major cities including Durres and Vlore. 14% of patients being diagnosed with a CD4 count <350 cells/mm3 and 13% CD4 counts <200 cells/mm3 (representing severe immunosuppression). Of the 42 patients death was reported in 8 cases. This is equivalent to a crude death rate of 19%. (8/42).

Conclusions

Albania has several strengths in its response to the HIV epidemic. The availability of free health care, HIV testing and HIV treatment is both beneficial for the individual patients living with HIV and reduces barriers for testing among those populations most at risks.
10A. SCIENCE: FUNGAL INFECTIONS


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Background

*Candida* species are a common cause of invasive infection in neonates and children. The aim was to study the epidemiology and microbiology of invasive candidiasis in the largest tertiary Greek pediatric hospital.

Methods

A retrospective cohort study was performed from January 2008 to December 2017. Every first *Candida* isolation from each episode of invasive candidiasis was included. Identification and susceptibility testing were performed according to local procedures, while antifungal susceptibility testing was performed according to CLSI methodology.

Results

During a 10-year period, 178 incidences of invasive candidiasis were recorded. Seventy-seven isolates (43.3%) were detected in neonatal intensive care units (NICU), 46 (25.8%) in pediatric clinics, 27 (15.2%) in hematology/oncology units (HOU) and 28 (15.7%) in pediatric ICU (PICU). The tissue distribution included blood (87.1%), cerebrospinal (7.9%), peritoneal (3.9%) and pleural fluids (1.1%). Ten different *Candida* species were detected. *Candida albicans* was the most frequently isolated species (47.8%) followed by *Candida parapsilosis* (28.7%), *Candida lusitaniae* (6.2%), *Candida glabrata* (4.5%) and *Candida tropicalis* (4.5%). The resistance in fluconazole was 0.0% among *C. albicans* isolates and 9.6% among *C. parapsilosis* isolates. Interestingly, a high number of anidulafungin-resistant *C. parapsilosis* was noted (41.4%).

Conclusions

In our hospital, fluconazole sensitive *C. albicans* was the most frequently identified species compared with *C. non-albicans*. High-level anidulafungin resistance among *C. parapsilosis* detected in our study raises serious concerns about its empirical use. Local epidemiology monitoring is always necessary to understand its burden in pediatric populations.
CHALLENGING MANAGEMENT OF PROSTHETIC VALVE INFECTIVE ENDOCARDITIS: USEFULNESS OF 18F-FDG PET/CT IN DIAGNOSIS AND FOLLOW UP

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Title of Case(s)

Two challenging diagnosis of PVE where 18F-FDG PET/CT was essential to define the diagnosis.

Background

The use of foreign material to correct Congenital Heart Diseases (CHD) have contributed to increase the incidence of prosthetic valve infective endocarditis (PVE). The diagnosis of PVE is challenging, symptoms can be atypical and blood cultures are often negative. Modified Duke Criteria and echocardiography are mainly used for the diagnosis of PVE. 18F-FDG PET/CT might be a supplementary diagnostic technique.

Case Presentation Summary

A 14-year-old girl with surgically corrected transposition of great arteries was admitted to our hospital for fever of unknown origin (FUO) and elevated inflammatory markers. She had received a prosthetic aortic valve and pulmonary homograft replacement eight months before. Echocardiography resulted negative, as well as blood cultures. Considering the high clinical suspicion of PVE, an 18F-FDG PET/CT was performed showing aortic uptake and evidence of splenic embolism. The 18F-FDG PET/CT performed after 6 weeks of antibiotic therapy showed a signal reduction on the prosthetic valve.

A 19-year-old boy, with a biological aortic valve implanted 5 years before, was admitted to our hospital for persistent fever. Blood tests showed normal WBC count and slightly elevated CRP, with negative blood culture. Serology for Coxiella burnetii resulted diagnostic for chronic infection. Echocardiography resulted negative; 18F-FDG PET/CT was performed showing aortic PVE then specific antibiotic therapy was started.

Learning Points/Discussion

Early diagnosis is critical since delay in therapy has been associated with a poor outcome. Our cases support the usefulness of 18F-FDG PET/CT in the suspicion of endocarditis with negative echocardiography. Further studies are necessary to determine if the repetition of the 18F-FDG PET/CT during follow up is useful to monitor the response to antibiotic therapy and the correct timing.
SEVERE INFECTION WITH CAMPYLOBACTER JEUNI IN A 8 YEAR OLD CHILD

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Title of Case(s)

Severe infection with Campylobacter jejuni in a 8 year old child

Background

Campylobacter jejuni is a frequently detected bacteria in diarrheal disease in children, causing usually autolimitant enteritis in immunocompetent patients.

Case Presentation Summary

A 8 years old female, known with minor thalassemia, was admitted to our hospital with a 24 hours history of fever, diffuse abdominal pain, watery diarrhea and vomiting. Blood tests showed leukocytosis (30,000/mm³) with neutrophilia, anemia (Hb 10,8 g/dl) and systemic inflammatory response (CRP = 183 mg/l).

She was started on antibiotic treatment with Ceftriaxone, later changed due to allergic reaction to Ertapenem and symptomatic treatment. The stool culture detected Campylobacter jejuni. The evolution under treatment was favorable until day 10 of treatment when she suddenly developed upper abdominal pain and vomiting, with no fever. Surgical consult and abdominal ultrasound (US) showed no abnormalities but blood tests showed high pancreatic enzymes (lipase - 6356 U/l, amylase - 717 U/l), dues suggesting the diagnostic of acute pancreatitis. Abdominal US showed a heavily distended gallbladder. CT- scan without contrast showed no modifications of the pancreas. After gastroenterology consult she was started on Octeotride for 5-7 days and alimentary diet with dynamic CT-scan evaluation, echography and blood tests that showed pancreatic enzyme variations but with a slow favorable evolution.

Learning Points/Discussion

Pancreatitis caused by Campylobacter enteritis is rare, but when the patient develops upper abdominal pain or increased levels of pancreatic enzymes not consistent with the course of gastroenteritis then concomitant pancreatitis needs to be considered. The particularity of the case is in the rare complication (pancreatitis) of an enteritis with Campylobacter jejuni in a immunocompetent 8 year old child.
03A. SCIENCE: SEVERE BACTERIAL INFECTIONS

BRAIN, SUBDURAL AND EPIDURAL ABSCESSSES IN CHILDREN – 11 YEAR RETROSPECTIVE REVIEW

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Background

Brain, subdural and epidural abscesses, although rare in the paediatric population, have significant morbidity and mortality. This study aimed to characterise children and adolescents with these diagnoses and their medical-surgical approach over a period of 11 years.

Methods

Retrospective descriptive study of the medical records of children and adolescents diagnosed with brain, subdural or epidural abscesses at a paediatric hospital from July 2006 to June 2017.

Results

Sixteen children were included, 11 male, with a median age of 8.8 years. The presence of predisposing factors was found in 81.3%, with the most frequent being trauma (37.5%) and sinusitis (25%). Nonspecific symptoms predominated and 37.5% children presented with the classic triad of fever, headache and focal neurological deficit. The most frequent initial imaging study was CT (68.8%), with half needing subsequent MRI for diagnosis. The median time from initial symptoms to diagnosis was 10 days (0-55). Eight had brain, 5 subdural and 3 epidural abscesses. The most frequent aetiological agents identified in brain abscesses were strictly anaerobic bacteria (38.5%), in subdural abscesses were the Streptococcus anginosus group (40%) and in epidural abscesses was Staphylococcus aureus (100%). There were 9 different empiric antibiotic treatment combinations, with the most frequent (43.8%) being ceftriaxone, vancomycin and metronidazole. 56.3% received steroids and 93.8% were submitted to surgery. Treatment duration was on average 58 ± 22.5 days. There were no deaths but 2 cases of subdural abscesses, that were complications of other primary diagnoses, have sequelae.

Conclusions

The frequent nonspecific clinical features at presentation might delay diagnosis and the lack of clear and consensual current guidelines contribute to diverse therapeutic choices and treatment duration. MRI should be the imaging of choice.
Obesity and Coinfection: Relating Severity Factors in Respiratory Infection in Children

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Background

Viral acute respiratory infection (ARI) are the main cause of hospitalization in children. Obesity has emerged as a new risk factor in severity of viral infection. The aim of this study was to evaluate if obesity and overweight, coinfection and RSV viral load (VL) are associated with severity in ARI in children.

Methods

We studied 125 children <2 years hospitalized for viral ARI between June-August 2017, without chronic diseases or underweight. Nutritional status (NE) was estimated (normal weight, obese and overweight). RSV, HMPV, HCoV, PIV, FLUA-B, HBoV, Rhinovirus/Enterovirus and ADV were detected by multiplex PCR in nasopharyngeal aspirate. Coinfections and NE was analyzed by $X^2$. RSV VL was quantified by real-time PCR. Severity was evaluated by hospitalization and oxygen therapy days. The association between NE, coinfection and severity were analyzed using OLS regression, VL and severity through Spearman’s correlation and VL and coinfection with Mann-Whitney U-test.

Results

11 (8.8%) patients were obese and 30 (24%) overweight; 60 (48%) was female and 76 (56.8%) presented pneumonia. RSV was the most frequently virus detected (89, 71.2%) followed by Rhinovirus/Enterovirus 33 (26.4%) and HBoV 26 (20.8%) principally; monoinfection was presented in 65 (52%) cases. RSV monoinfections presented higher VL than coinfections with other viruses. VL was not associated with severity. Coinfection was more frequent in obese patient <6 months ($p<0.01$). Obese children, but not overweight, <6 months with coinfection have a more severity than normal weight children without coinfection (Table 1). RSV viral load is associated with monoinfection ($p<0.05$) but not with severity ($p > 0.05$; $r=-0.07$).
Conclusions

Obesity and coinfection are associated to severity in children <6 months.

Acknowledgements: We thank Hospital Dr. Exequiel González Cortés and Servicio Materno-Infantil Clínica Dávila, Conicyt-Fondecyt-11150599. Clinical Trial Registration (Please input N/A if not registered)
THE EPIDEMIOLOGICAL CHARACTERISTIC OF AN ACUTE RESPIRATORY VIRAL INFECTIONS AND INFLUENZA AT CHILDREN IN MOSCOW.

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Background

Acute respiratory viral infections (ARVI) is one of the frequent reasons of hospitalization, and causes up to 7% of all causes of death of children in a hospital. We have analyzed epidemiological features of a ARVI and flu at children up to 17 years in Moscow.

Methods

We used the retrospective epidemiological analysis for the description of incidence. And also the analysis results of laboratory PCR researches behind 2014-2017.

Results

The incidence of a ARVI among children was higher than that in the territory of the Russian Federation, and was fluctuate from 83550,2‰ (2015) to 117242‰ (2009). The highest incidence of ARVI was registered in age group 1-2 years and 3-6 years. During the post-pandemic period increased incidence of ARVI in group of children till 1 year old was noted, in 2011 the maximum incidence in this group was 200714‰. Involvement of children of 1-2 years and 3-6 years is characteristic of epidemic process of flu, as well as of an ARVI. The smallest indicators of incidence of flu were noted in group of children till 1 year old. In 2009, 2011 and 2012 the incidence of flu in Moscow was higher that across the Russian Federation. In the last several years it has been established that paraflu viruses, adenoviruses and virus of flu A(H3N2) were more often diagnosed for children of 7-14 years, the RS-virus and a virus of flu A(H1N1)pdm09 at children of 3-6 years, a flu B virus in group of 3-6 years and 7-14 years.

Conclusions

Involvement of children of 1-2 and 3-6 years is characteristic of an epidemic process of a ARVI and flu.
Background

In 2012, HHV-6A and HHV-6B were classified as separate viruses. But in Russia there are limited and contradictory data about the prevalent type of HHV-6.

Methods

We conducted a pilot study of the prevalence of HHV-6A and HHV-6B in children with acute respiratory infection (ARI) and in healthy control group in Moscow, Russia. The study included 207 children from 1 to 10 years old with fever and pathology of the upper respiratory tract and 100 healthy children. Healthy controls were matched to cases on age and sex. The DNA of HHV-6 in blood plasma samples was detected by qualitative PCR and quantitative real-time PCR (using commercially available diagnostic kits AmpliSens Russia). We used real-time PCR with TaqMan method for the detection of HHV-6A, and HHV-6B genotypes in blood serum.

Results

A total of 58 cases were positive for HHV-6 viral DNA. Of which 44 cases met the criteria for ARI, and 14 controls were included in the study. There were 33 boys (56.9%) and 25 girls (43.1%). HHV-6A were detected in 46% of the children (n=27) and HHV-6B – in 53% (n=31). Patients with ARI had more HHV-6 – 56.8% (n=25) than HHV-6B – 43.2% (n=19), p>0.05. Healthy children had prevail HHV-6B (12 from 14). Among children with ARI under 3 years, 73.7% had HHV-6A (n=14), and 26.3% - HHV-6B (n=5), p<0.05. Among children with ARI 3 years and above, 33% had HHV-6A (n=13), and 67% - HHV-6B (n=26), p<0.05.

Conclusions

On the basis of our data we found out that the children with ARI have HHV-6A and HHV-6B with the similar frequency. Healthy children have prevail HHV-6B. Further studies of the HHV-6 types prevalence in Russian population are needed.

Clinical Trial Registration (Please input N/A if not registered)
VALIDATION OF THE 10 MG/KG ISONIAZID DAILY DOSE IN YOUNG INFANTS. NON-COMPARTMENTAL PHARMACOKINETIC ANALYSIS OF EXPERIMENTAL DATA


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Background

In 2010, increased daily doses of first-line anti-tuberculosis medicines in children were recommended by WHO. Pharmacokinetic data on the new doses in young infants are scarce. We aimed to characterize the pharmacokinetics of the once-daily isoniazid dose at 10 mg/kg of body weight in children aged less than 6 months.

Methods

National multicenter prospective pharmacokinetic study in Spain. Blood samples for isoniazid concentrations were drawn at 2, 4 and 6 hours post-dose, or at 1, 3 and 6 hours post-dose (randomly assigned). The N-acetyltransferase 2 (NAT2) gene was analyzed to determine the acetylation status. Data were analyzed using the non-compartmental pharmacokinetic software Winonlin®.

Results

Twenty-three pharmacokinetic profiles were performed in 20 infants (8 females) at a median (IQR) age of 19.0 (12.6-23.3) weeks, treated because of primary chemoprophylaxis (n=14) or tuberculosis (n=6). According to NAT2 genotypes, the acetylator status were homozygous fast (n=1), heterozygous intermediate (n=13) and homozygous slow (n=7). Non-compartmental pharmacokinetic analysis showed a median (IQR) isoniazid Cmax of 4.80 (3.72-6.67) mg/L and in 4 cases (17.4%) the Cmax >3 mg/L target recommended in adults was not reached. Median (IQR) isoniazid area under the concentration-time curve and half-life were 23.50 (13.36-36.65) mg*h/L and 2.92 (2.01-3.17) hours, respectively. Age at assessment or acetylator status had no impact on Cmax values, but a trend
towards larger isoniazid AUC (p=0.053) and longer half-life (p=0.057) was observed in homozygous slow acetylators. Treatment was well tolerated in all patients and mildly elevated levels of alanine aminotransferase (range, 61-76 UI/L) were observed in 3 out of 22 cases (13.6%).

Conclusions

In our series of young infants receiving isoniazid, no major safety concerns were raised but the target adult levels were not reached in 17% of cases.

Clinical Trial Registration (Please input N/A if not registered)
A RARE CASE OF SEPTIC ARTHRITIS DUE TO CLOSTRIDIUM NOVYI IN A 4-YEAR OLD GIRL
AND REVIEW OF THE LITERATURE
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Title of Case(s)
A RARE CASE OF SEPTIC ARTHRITIS DUE TO CLOSTRIDIUM NOVYI IN A 4-YEAR OLD GIRL
AND LITERATURE REVIEW

Background

Clostridium species are anaerobic bacilli, rarely reported as SA-causative agents in children without
predisposing factors. Thus, more information regarding the optimum management of clostridial-SA is
required. Here, we present a case of a 4-year old, previously healthy, girl with Clostridium novyi-SA, in
a Greek tertiary Children’s Hospital.

Case Presentation Summary

On admission, a week after sustaining an injury, our patient presented with an inflamed right knee with
significant limitation of motion and low-grade temperature. Blood tests revealed elevated inflammatory
markers. Ultrasound showed anechoic effusion over the patella; X-ray was normal. The synovial fluid
obtained through drainage on Day 1, revealed marked neutrophil predominance. Empiric initial
treatment included a combination of IV-clindamycin/cefotaxime. Fluid cultures yielded C. novyi, and
the treatment was switched to IV-penicillin according to antibiogram. On Day 15, due to a newly-
presented patella pain, an MRI was performed which excluded a co-existing osteomyelitis. She
progressively recovered and was discharged after a 21-day course of IV antimicrobials and
transitioned to oral penicillin for a total of 8 weeks antimicrobial treatment. On follow-up, the child had
an uneventful recovery.

Learning Points/Discussion

To our knowledge, literature review revealed 10 clostridium-SA cases (mainly C.perfringens and
C.welchii) in children, commonly associated with a history of injury, although hematogenous route has
been described. Clinical presentation was identical in the majority of cases. As treatment duration has
not been established (from 6 to 12 weeks), we opted for prolonged antimicrobial treatment which
appeared to be associated with a favourable outcome. Since targeted treatment is essential and
possibly protracted, arthrocentesis prior to antimicrobial administration remains the diagnostic and
therapeutic mainstay of suspected SA in children.
02A. SCIENCE: ANTIMICROBIALS: RESISTANCE AND PHARMACOLOGY

TRANSCRIPTIONAL ANALYSIS OF EXTENDED SPECTRUM BETA-LACTAMASE GENES UNDER ANTIBIOTIC STRESS

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Background

Infection caused by resistant organisms is a major public health problem in the developing countries. Extended-spectrum beta-lactamases, are remarkably diversified due to their continuous mutation. The present study was undertaken to study the molecular mechanisms of ESBL resistance, possibly their role in diarrheal infections in children and to analyze comprehensively the changing paradigm of antibiotic resistance.

Methods

In the present study, transcription analysis of ESBL genes (TEM, SHV, CTX-M, and OXA) was carried out in resistant and sensitive isolates in compared to healthy controls (n=15). Total RNA was isolated from 2 ml fresh overnight LB broth culture from stool samples of children under five and converted into c-DNA. m-RNA expression of TEM, SHV, CTX-M and OXA in resistant (cefotaxime) (n=15) and sensitive isolates (n=15) in compared to healthy controls (n=15) was seen by Real-Time PCR (Tm=60°C). 16SrRNA was used as internal control. Relative quantification or the fold change in expression of the beta-lactamase genes was calculated as N-fold= 2−ΔΔCt for all isolates versus the control group. P < 0.05 was considered statistically significant.

Results

We found a high variance in the gene expression in resistant and sensitive isolates with lots of heterogeneity among the isolates. The level of expression of TEM gene showed a range of 0.87–20.73-fold expression levels when compared to the control group, for SHV (1.43-18.03), CTX-M (1.42-14.99) and OXA (1.41-14.99). This study revealed the direct relation between the m-RNA expression and presence of antibiotic resistance.

Conclusions

High expression levels were observed for resistant isolates found which makes this drug resistance gene an important molecular marker. Relative transcript levels of these genes would help us gain a better understanding of the role these functional genes.

Clinical Trial Registration (Please input N/A if not registered)

N/A
03B. SCIENCE: COMM.AQC. INVASIVE BACTERIAL INFECTIONS (NON-RESPIRATORY)

MANAGEMENT OF URINARY TRACT INFECTIONS BY ESBL-PRODUCING MICROORGANISMS IN THE PAEDIATRIC PATIENT: CAN WE IMPROVE?

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Title of Case(s)

Management of urinary tract infections by ESBL-producing microorganisms in the paediatric patient: Can we improve?

Background

There is an increasing incidence in urinary tract infections (UTI) caused by extended-spectrum beta-lactamases (ESBL) producing bacteria. Carbapenems are the treatment of choice, which means hospital admission. In adults, alternative antibiotics are used in some cases, but evidence in paediatrics is limited and treatment guidelines not available. We describe the management of UTI by ESBL in our centre and study the differences between healthy patients and those with underlying pathology. Demographic, clinical and microbiological data from a tertiary maternity and child University Hospital between April 2016 and January 2018.

Case Presentation Summary

Fifty cases were collected (60% girls, median age: 2.1 [IQR 0.8-6.4] years). The majority (58%) had underlying pathology (34% nephro-urological, 24% immunosuppression). About 68% presented with fever and only one patient had bacteraemia. The isolated pathogens were E. coli (76%), K. pneumoniae (22%) and P. mirabilis (2%). The most common targeted treatment were carbapenems (48%), with a total duration of 9.3 days (SD ± 2.4). Eight patients (16%) relapsed after an interval of 1.6 months (IQR 0.8-2.0), without identifying significant differences between those who received carbapenems and those who did not. No significant differences were observed between the two groups regarding presentation or clinical evolution (Table 1).

Learning Points/Discussion

In our study, UTI by ESBL occurred more frequently in patients with underlying disease, although we did not observe differences in the clinical evolution between groups. During the acute phase, we did not identify differences between patients who received carbapenems from those who did not. We observe a great heterogeneity in the management of these infections. Limitations: observational study, absence of long-term follow-up and complementary studies to detect sequelae.
THE PITFALL OF ORAL MUCOCUTANEUS CANDIDA PARAPSILOSIS IN A CHILD WITH HIV INFECTION

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THE PITFALL OF ORAL MUCOCUTANEUS CANDIDA PARAPSILOSIS IN A CHILD WITH HIV INFECTION

Background

Candida parapsilosis is an emerging and leading cause of invasive candida infection. Children with immunodeficiency including HIV infection have the highest risk for this infection. Mucocutaneous candidiasis is frequent manifestation in HIV children that often met difficult in diagnostic and management. A multidisciplinary approach like surgical debridement, pathological anatomy, clinical microbiology, and medical treatment is needed to have a good outcome. The purpose of this case is to report the first case of oral mucocutaneous Candida parapsilosis in pediatric patient with HIV infection focusing on its diagnosis approach and management.

Case Presentation Summary

A 3 years old HIV boy under antiretroviral treatment came with chronic wound perioral with black crust that occur after felt down from his bike. He treated with many antibiotics (ampicillin, gentamisin, meropenem) based on Klebsiella pneumonia and Acinetobacter baumanii sensitivity from wound swab culture without significant improvement. Suspicious of squamous cell carcinoma from skin biopsy resulted a doubt because the clinical presentation did not match. He then underwent wide excision debridement and open biopsy culture revealed candida parapsilosis. Antibiotics treatment then was stopped. Fluconazole based on sensitivity isolate and switching to 2nd line ARV have been administered and led to a good outcome.

Learning Points/Discussion

Candida infection has to be considered in chronic wound in immunocompromised condition such as HIV patients. Surgical debridement, microbiological examination, antifungal and review of previous treatment to consider the resistance of 1st line ARV led a good outcome, highlighting the need for multidiscipline approach.
ANEMIA IN AN INFANT: WHEN THE ORIGIN MATTERS

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Title of Case(s)

The third case of CM ensued in a HIV-infected mother in a non-endemic country.

Background

Congenital malaria (CM) is defined as the detection of asexual forms of Plasmodium spp. in a blood sample of a neonate during the first week of life or later if there is no possibility of postpartum infection by a mosquito bite. CM seems to occur in less than 5% of infected pregnant women. HIV infection increases susceptibility to malaria during pregnancy.

Case Presentation Summary

A 2-month-old male child was admitted to our hospital due to anaemia and exposure to HIV. He was born in Italy prematurely by caesarean section after a bicorial, biamniotic pregnancy. The mother resulted affected by HIV when she arrived in Italy from Nigeria during pregnancy. On initial evaluation, the child was in good general condition; he had hepatosplenomegaly and haemoglobin level was 9.1 g/dl. A myelosuppression effect due to the Zidovudin was initially hypothesized. Due to Hb level decrease (Hb 6.8 g/dl), the child required two blood transfusions in two weeks. Autoimmune and congenital causes of anaemia were excluded. Because of persistent anaemia and spleen enlargement, Plasmodium spp was researched on peripheral blood resulting positive and the PCR confirmed the Plasmodium falciparum infection. The same form of Plasmodium was researched on mother’s peripheral blood resulting positive, then the diagnosis of CM was confirmed.

Learning Points/Discussion

As an increasing number of people travel to and emigrate from malaria endemic countries, CM should be always suspected in infants born to women from these areas and with unexplained anaemia, fever and hepatosplenomegaly. A complete anamnesis of infant’s mother and the inclusion of Plasmodium spp research into the TORCH screening should be performed avoiding delay in diagnosis and treatment.
06C. SCIENCE: DIAGNOSTIC TOOLS

DETERMINATION AND IN SILICO STUDY OF NEW PHYLOGENETIC GROUPS IN ENTEROPATHOGENIC E.COLI IN CHILDREN UNDER FIVE YEARS OF AGE.

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Background

Enteropathogenic Escherichia coli (EPEC) are a leading cause of infantile diarrhea. At present, E.coli populations are structured in seven major phylogenetic groups. Strains responsible for extraintestinal infection belong to phylogroups B2 or D than A or B1. Phylogroups E and F contain strains, of which O157:H7 is the best known member, and form a sister group to phylo-group B2 respectively. The phylogroup C is closely related but distinct from phylo-group B1. The aim of this study was to gain insight on the distribution of phylotypes in enteropathogenic Escherichia coli virulence genes and their association with clinical characteristics in children under five years of age suffering from diarrhea in Delhi, India.

Methods

80 diarrheagenic E.coli strains were isolated from children with diarrhea and examined for the presence of enteropathogenic E.coli by real time PCR after performing antibiotic susceptibility testing. A quadruplex PCR was performed to distribute isolates among seven phylogroups. Statistical analysis was used for the comparison of the categorical data.

Results

64 (80%) were found to be EPEC. There was predominance of phylogenetic group A (38) followed by phylogenetic groups B1 (14), D (4), F (3), B2 (2), C (2) and E (1). One isolate remain unclassified. In silico studies was performed to understand their relationships.

Conclusions

Phylogenetic studies are important to improve the understanding of E.coli population and the relationship of strains and their hosts and disease and it established a link between phylogenetic group and virulence.

Clinical Trial Registration (Please input N/A if not registered)

N/A
Background

Increased nitric oxide production is one of the proposed mechanisms for vasodilation in septic shock. There is limited literature evaluating nitric oxide levels in neonatal septic shock. We designed this study to evaluate inducible nitric oxide synthase (iNOS) levels in neonatal septic shock.

Methods

Neonates developing shock within 44 weeks post-menstrual age, were included. Blood sample for iNOS measurement was taken within 30 min of shock onset. The iNOS levels were evaluated by double-antibody sandwich enzyme-linked immunosorbent assay (ELISA). Enrolled neonates were prospectively followed till 28 days of life. We compared iNOS levels between neonates with septic shock vs shock due to non-septic etiologies as well as between survivors and non-survivors. We performed multiple logistic regression analysis to investigate whether baseline iNOS levels independently predicted mortality.

Results

Forty four neonates were enrolled, 22 each with septic and non-septic shock. Two groups had comparable iNOS levels [55 (50, 59) versus 52 (47, 56) IU/mL, p-value= 0.07. Ten neonates survived and 33 died. Nonsurvivors and survivors had comparable demographic variables, obstetrical complications, similar perinatal transition, and clinical variables (except neonates in septic shock group had lower BP, urine output, higher score of neonatal acute physiology-II scores, and higher oxygen requirement as compared to non-septic shock group). The two groups had comparable iNOS levels. We included gestational age, mean BP, illness severity scores, type of shock and iNOS levels in multivariable logistic regression model. Mean BP and type of shock independently predicted mortality.

Conclusions

There was no difference in iNOS levels between neonates with septic shock versus non-septic shock as well as between survivors and non-survivors. Inducible NOS levels did not predict mortality among shocked neonates within first 28 days of life.

Clinical Trial Registration (Please input N/A if not registered)

N/A
Background and Objective

Congenital malaria (CM) is among the less common features of the disease, and neonatal infection remains extremely rare both in endemic and non-endemic areas. P.falciparum is the main responsible of CM in endemic countries in contrast to non-endemic area where P.vivax and P.malariae are reported more frequently. In non endemic countries diagnosis may be challenging. We report a review of the literature about CM in Europe.

Methods

Case reports and reviews published in the last 30 years were used as sources to identify all the cases of CM in Europe and to summarize clinical features, diagnostic tool and treatment. We use standard search strategy using as key words on PUBMED “congenital malaria”, “congenital malaria case reports” and “malaria in non-endemic countries”. We excluded all the case reports about CM in endemic countries.

Learning Points Discussion

In the last 30 years, 35 cases of CM were reported in Europe. Among reported cases, 21 (58%) were caused by P.vivax. Maternal history of malaria may not occur and it is not a criteria for the diagnosis of CM. In most cases of CM, the diagnosis is made at 10-28 days of age and among the reported cases it was diagnosed after 21 days in 15 of 36 cases (42%). The symptoms are rarely at birth possibly because of the presence of IgG transferred from mother during the pregnancy and protective effect of HbF.

The clinical manifestations of CM do not differ significantly from bacterial or viral sepsis.

Considering the migratory flow from endemic area to non-endemic area, CM should be included in the differential diagnosis of neonatal sepsis in neonates born to women from malaria endemic countries in order to avoid a delayed diagnosis.
POSTEXPOSURE PROPHYLAXIS IN PEDIATRICS: EXPERIENCE IN A TERTIARY HOSPITAL IN SPAIN


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Background

The use of postexposure prophylaxis is increasing worldwide, but experience is still scarce in pediatrics and most protocols are based on adult data. We analyze indication, adherence and tolerance and transmission risk in children and adolescents, before and after the introduction of integrase inhibitors (INSTI) as antiretroviral prophylaxis in youths.

Methods

Retrospective descriptive study including all children and adolescents <18 years with previous HIV exposure, attended in a tertiary hospital between 2013 and 2017. Risk was categorized according to guidelines to evaluate the indication of postexposure prophylaxis. Regimens, adherence, tolerance and follow-up data were analyzed in two study periods.

Results

A total of 57 patients were included, 12 (21%) in the INSTI period. 47 were sexual exposures, and 10 accidental needlestick. Mean age was 9.2±4 years, 60% female. Four patients with needlestick and 24 with sexual exposure were categorized as high risk. One needlestick and 14 sexual contacts started prophylaxis. The main reason for not starting prophylaxis was >72h from exposure. Most patients received ZDV+3TC+LPV/r (49%), FTC+TDF+LPV/r (27%), RAL+ FTC+TDF (33%). Two cases stopped treatment for GI intolerance (both on LPV/r), one changed regimen because of rash and one adolescent stopped treatment on her own. In 21%, the protocol was not fulfilled, mainly because of lost to follow-up. In two cases pediatric formulation was unavailable at the emergency department, and in another 3 cases the treatment was started at the outpatient clinic one day later. No case of HIV transmission was diagnosed.

Conclusions

The use of INSTI improves tolerance and adherence. Delay in consultation remains the main obstacle for postexposure prophylaxis in children. Protocols for risk stratification are mandatory, as treatment must be started immediately, and experienced professionals are required for follow-up.
NEONATAL CITROBACTER KOSERI MENINGITIS: CLINICAL CHARACTERISTICS AND OUTCOMES

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Background

Citrobacter koseri is an uncommon cause of meningitis associated with brain abscesses in neonates that cause high morbidity and mortality. We report the clinical-biological characteristics and outcomes of neonatal meningitis due to C. koseri over a 14-year period in France.

Methods

We identified paediatric patients with C. koseri meningitis prospectively reported to a national paediatric surveillance network between 2001 and 2014.

Results

Among 5,446 cases of paediatric bacterial meningitis recorded in 233 paediatric wards and 168 microbiology departments, 16 (0.3%) were due to C. koseri. Two cases were excluded because patients were not neonates. Median age at disease onset was 9 days (5-19 days). Early- and late onset disease were respectively 14.3% and 85.7%. Blood cultures were positive in 58.3% of cases (n=7/12). Seven patients (50%) were hospitalized in paediatric intensive care unit and five (35.7%) required assisted ventilation. Seizures occurred in 42.9% (n=6/14) followed in half of the cases by status epilepticus (3/14; 21.4%). The mortality rate was 21.4% (n=3/14). The most common complications in survival patients were cerebral abscesses (n=7/11; 63.6%), intracerebral haemorrhagic or ischemic infarction (n=3/11; 27.3%), ventriculitis (n=2/11; 18.2%) and cerebral oedema (n=1/11; 9.1%). The most frequently prescribed treatment was the association of cefotaxim and ciprofloxacin or meropenem. Surgical drainage was necessary in three patients.

Conclusions

C. koseri is a rare cause of neonatal bacterial meningitis with high mortality rate. Brain abscesses were extremely frequent and tended to compromise patients’ survival.
CRYPTOCOCCAL INFECTIONS IN CHILDREN: DO NOT LOSE SIGHT OF THE FOREST FOR THE TREES

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Title of Case(s)

Cryptococcal infections in Children: Do not lose sight of the forest for the trees

Background

Cryptococcal infections have been described in children with HIV infection. These infections are associated with difficulties in diagnosis, treatment and significant morbidities. We describe 5 cases of cryptococcal infections, evaluated for primary immunodeficiency after ruling out HIV infection and revealed myriads of primary immune defects.

Case Presentation Summary

Case-1: 3-year-old boy developed fever, pain abdomen and jaundice. Examination revealed generalized lymphadenopathy, and hepatomegaly. Investigations showed anemia, conjugated hyperbilirubinemia and elevated alkaline phosphatase. Lymph node biopsy revealed multiple necrotizing granulomas and numerous refractile fungal yeasts in giant cells, confirming Cryptococcus. Immune deficiency work-up revealed elevated immunoglobulin E, reduced Th17 cells and p-STAT3.

Case-2: 3-year-old girl had recurrent pneumonia, oral thrush and otitis media. Examination revealed wasting, oral thrush, clubbing and bilateral crepitation. CT guided FNAC revealed Cryptococcus. Further evaluation revealed idiopathic CD4 lymphopenia (absolute CD4 count 274 cells/mm3).

Case-3: 4-year-old boy had fever, rash and pain abdomen. Examination showed generalized lymphadenopathy, hepatosplenomegaly and umblicated lesions over trunk. Cervical lymph node FNAC showed granulomatous inflammation and Cryptococcus.

Case-4: 16-year-old boy presented with fever, jaundice and protuberant skin lesions for 2 months. The skin, axillary lymph node biopsy and blood culture showed Cryptococcus neoformans. He had reduced expression of IL12Rβ2β1 on lymphocytes.

Case-5: 4-year-old presented with fever, headache and altered sensorium. investigation showed multiple hypo-dense lesions in spleen. CSF and blood culture revealed Cryptococcus neoformans. Evaluation showed decreased IL12Rβ2β1 expression.

All patient were treated with injection amphotericin B and flucytosine followed by fluconazole.

Learning Points/Discussion
Cryptococcal infections in children can present with myriad of manifestation. Early diagnosis and timely management is critical. A diligent search for underlying immune defect in children with these infections may uncover rare immune defects.
THE USE OF DAPTOMYCIN IN THE TREATMENT OF BACTERAEMIA, BONE & SOFT TISSUE INFECTIONS IN A TERTIARY PAEDIATRIC CENTRE, A CASE SERIES

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Title of Case(s)
The use of Daptoycin in the treatment of bacteraemia, bone & soft tissue infections in a tertiary paediatric centre, a case series

Background

Daptoycin, a once daily antibiotic, with excellent activity against resistant and sensitive staphylococci and streptococci, expands therapeutic options, facilitates outpatient parenteral therapy (OPAT), can enable hospital discharge, save bed days and enhance patient experience. We report our experience with daptoycin in the paediatric setting.

Methods

Retrospective data review of children and adolescents in whom daptoycin was initiated by the infectious diseases service, November 2016 to December 2017, inclusive.

Case Presentation Summary

Results

12 infected patients, 6/12 bacteraemic, median age 15 (range 8-17) yrs, median weight 47 (range 23.5 – 90) kg. [spinal rod /implant (7), osteoarticular (4) ) bacteraemia with no focus (1)] received daptoycin. Infection was polymicrobial in 4. Gram positive organisms included MSSA (5), MRSA (2), CoNS (4) E. faecalis (3), Strep. dysgalactiae (1). Reasons for Daptoycin use included: OPAT facilitation (10) antibiograms (5), antibiotic intolerance (3). All received 6mg/kg/day for median 23(range 6 – 62) days. Diarrhoea and hypernatraemia, likely unrelated, prompted readmission for one PEG fed patient. CK levels remained normal in 9/9 tested patients. One patient succumbed to underlying malignancy. One required rod removal for concomitant GNB infection. 10 recovered clinically with normalisation of inflammatory markers; 3/10 remain on prolonged oral therapy for chronic bone/spinal implant infection. No treatment failures have been identified over a median 6 (range 2-11) months since initiation. 10/12 patients managed with OPAT represented a saving of 282 bed days.

Learning Points/Discussion
This cohort includes those with complicated and chronic infection. Daptomycin, well tolerated, is potentially a very useful addition and can be used to facilitate early hospital discharge when patients require continuing parenteral therapy.
Background

4MO Boy with one day vomiting and diarrhea associated with 1 wk cough and snuffles in contact with older sister with flu like illness 1wk ago brough to the ED at 10:15am while examination followed by IV cannulation attempt developed sudden cardiac arrest and pronounced dead at 12:32pm

Case Presentation Summary

4MO Boy with one day vomiting and diarrhea associated with 1 wk cough and snuffles in contact with older sister with flu like illness 1wk ago brough to the ED, at 10:15am, pale looking, HR 160- 17/-min, O2 sats 96 in RA, no fever, active, alert crying, few crepetations at base of chest, other osystemic exam normal, difficult IV access, while trying IV access child bacame extremely pale HR dropped to 60/min and stopped braething at 11:17am, CPR commenced intubated and IO inserted normalx saline bolus, adrenaline, Ceftrioxone, NaHCO3, atropin for asystole, Insulin + Dextrose for Hyperkalaemia, continued to have severe metabalic acidosis, asystole after 1hr of resuscitation was stopped with parental consent, baby was declared RIP at 12:32pm

Postmortem pathology reported sudden unexpected infant death due to Enterovirus infection causing Acute Myocardial cell necrosis and heart failure, Entero virus detected in large Bowel and spleen, Norovirus detected in small Bowel.

Learning Points/Discussion

Most children and Infants infected with Enterovirus group and sub groups like Echovirus, Coxsackie Type B4 have mild symptoms and get well quickly, but clinicians should never forget that it can cause a devastating unexpected , sudden death.
Title of Case(s)

Pneumonia by *Kingella kingae* and bone-marrow suppression, what has HHV-6 has to do with it?

Background

*Kingella kingae* is a microorganism that can be part of the oropharynx's flora in children under 2 years of age. *K. kingae* can cause osteoarticular and endocarditis infections, but in less than 5% of the patients cause pneumonia.

Case Presentation Summary

A 22-month-old boy who was referred to our hospital because of a viral gingivo-stomatitis with malaise, laryngeal stridor and cyanosis. The blood test showed leukopenia (2.200/mcL) with no neutrophils, moderate lymphopenia (1.800/mcL), CRP 15.70 mg/dL and Procalcitonin 23.22 ng/mL.

The X-ray chest showed a lobar pneumonia in the middle and lower right lobe that was the cause of hypoxemia. Non-invasive ventilation was instaured with supplemental oxygen therapy and broad-spectrum antibiotics, antifungals, acyclovir and gammaglobulins. After 24 hours of admission, an anemia and thrombocytopenia appeared, requiring blood transfusion, but recovered the number of leukocytes. Within 48 hours of admission, the blood culture was positive to *Kingella kingae*. Positive polymerase chain reaction (PCR) to Herpes virus 6 in blood was also detected.

He had a good evolution, with gradually resolution of the oral lesions and pneumonia in a week. The infant was discharged home after completing 2 weeks of intravenous treatment with ampicillin.

Learning Points/Discussion

An extension study with serologies, immunoglobulins and lymphocyte populations were normal. The unique find was a positivity of the PCR for HHV-6 in blood. Otherwise, is pending a larger immunitary study, to confirm the normal function of the immune system.

It has been described in the literature that a viral infection can facilitate the transfer of *Kingella* from the oropharynx to the blood, but it has not been found bone-marrow supression caused by herpes virus 6 in healthy children.
WHEN BILATERAL SPASTIC PARALYSIS IS THE PRESENTING FEATURE OF HIV INFECTION

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Title of Case(s)

WHEN BILATERAL SPASTIC PARALYSIS IS THE PRESENTING FEATURE OF HIV INFECTION

Background

HIV encephalopathy is the most common neurologic manifestation of HIV infection in children and can be its presenting feature, namely as spastic tetraplegia. Neurodevelopment impairment in HIV-infected children is still common, especially in non-treated children.

Case Presentation Summary

A previously healthy 8-year-old boy was referred to our institution with a 2-year history of motor and cognitive regression. He first presented dysarthria and subsequently a gait disturbance and bladder and bowel incontinence. He had weight loss and numerous molluscum contagiosum lesions. Neurologic examination was remarkable for dysarthria, muscular atrophy and spastic paraparesis with brisk and spreading stretch reflexes, especially on the right side, bilateral extension plantar responses and extinguishable clonus. MRI revealed cortico-subcortical, cerebellar and brainstem atrophy, with prominent ventricles and sulci, and multifocal white matter lesions which, together with the clinical picture, were suggestive of HIV infection, which was confirmed by serologic testing, viral load was 174456 copies/mL with 148 CD4/mL, CSF viral load was 193258 copies/mL. Antiretroviral therapy (ART) was started and eighteen months later, with an undetectable viral load and 836 CD4/mL, the patient had a better school performance and recovered some motor skills. MRI was repeated at this time and showed a notorious improvement.

Learning Points/Discussion

This presentation of both spastic paraparesis and pseudobulbar palsy was common in the pre-highly active ART era, and is probably associated with the late diagnosis in this child. ART seems to have a good impact on this disease. Contrary to what happens in adults with HIV encephalopathy, ART seems to have a good impact on the disease with radiological regression and good prognosis.
Atypical meningitis and strabismus in a healthy boy by Listeria monocytogenes.

Background

Bacterial meningitis is an acute life-threatening disease. The more frequent bacteria are Neisseria meningitidis and Streptococcus pneumoniae. Listeria monocytogenes is a very uncommon pathogen at pediatric age except for newborns and immunosuppressed patients.

Case Presentation Summary

2-year-old boy who consulted at the emergency room because of 4 days of fever (40°C) and headache. Blood analysis was performed: leucocytes 16,880/mcL and CRP 10,37mg/dl. The lumbar puncture had 165 leucocytes/mcL, glucose 46mg/dL and proteins 56.5mg/dL.

Ceftriaxone was started empirically. After 24 hours, a new convergent strabismus appeared. Local complications of the CNS were ruled out with an MRI. The culture of the cerebrospinal fluid was positive to Listeria monocytogenes. At that point, the antibiotics were replaced with ampicillin and gentamicin, adding the first days rifampicin because of the persistence of the fever. The funduscoppy showed papillae edema. After antibiotic therapy, the infant recovered at all from the acute meningitis, but persisting the strabismus that resolved after a few weeks, without any other neurological sequelae.

After discharge, primary and secondary immunodeficiencies were ruled out. Learning Points/Discussion

We report a case of an acute meningitis caused by an atypical microorganism in a 2-year-old healthy boy. The father could be the source of the infection because he worked as a butcher and it has been described L.monocytogenes infections in these communities.
UNEXPECTED DIAGNOSIS: MANDIBULAR MASS AND CUTANEOUS LESIONS
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Title of Case(s)
UNEXPECTED DIAGNOSIS: MANDIBULAR MASS AND CUTANEOUS LESIONS

Background

Mandibular mass with inflammatory signs presents a clinical conundrum: osteomyelitis, parotiditis, chronic recurrent multifocal osteomyelitis and tumoral masses must be considered. Timely and accurate diagnosis is mandatory to avoid unnecessary exams and to start appropriate therapy, thus improving prognosis.

Case Presentation Summary

Ten-month-old boy with a 2-month history of painful progressive enlarging unilateral mandibular mass, with inflammatory signs, oral mucosae purulent discharge, and intermittent fever, with no improvement after two antibiotic cycles in the last month (amoxicillin clavulanic acid, and flucloxacinil and clindamycin). The appearance of redish-violet papulovesicular lesions, some with central erosion, were noted in the face, trunk and limbs in the previous month. Laboratory testing revealed: 9.8 g/dL hemoglobin, 19000 WBC (56% neutrophils), CRP 2 mg/dL, SR 26mm/h and lactate dehydrogenase 601 UI/L. Facial CT showed an expansive lesion on the right masseter muscle and hemimandible, with bone marrow invasion and cortical disruption (with signs of bacterial superinfection). Antibiotherapy was changed to cefuroxime and clindamycin, with fever resolution. Bone biopsy revealed lymphohistiocytic infiltrate (S100+, CD1a+, CD68+ and CD163+) and the mass was surgically excised; skin biopsy showed neoplastic cells S100+ and CD1a+, consistent with multisystem Langerhans cell histiocytosis (LCH). Bone scintigraphy revealed hypercaptation focus on the eighth left rib, right frontal and temporal bones. Brain MRI and abdominal ultrasound were normal. The child is now under a prednison, vincristine and cytarabine protocol with good clinical evolution.

Learning Points/Discussion

Although rare, LCH must be excluded when a child presents with a facial bone mass. The prognosis is worse in multisystem involvement and when diagnosis is made at an early age. Timely diagnosis is crucial for prompt therapy institution. Inflammatory/superinfection signs may be misleading and delay diagnosis.
Invasive meningococcal disease (IMD) is one of the most feared infections in pediatric care due to the mortality and high risk of neurological sequelae.

Methods

We conducted a retrospective observational study of IMD in the pediatric population under 14-year-old admitted in our hospital from 2007-2018. We divided in subgroups of survivors or not survivors. The objective of our study is to analyze the cases of IMD in our hospital and if there were changes after the meningococcal B vaccine was introduced in 2016.

Results

45 confirmed cases of IMD were collected. All cases were sepsis and 71% added an acute meningitis. Median age was 3.4 years-old (40 months for the survivors versus 16 months). Median hospital stage was 7 days, 2 days in PICU. The mean treatment was cefotaxime or ceftriaxone, adding in some cases vancomycin. The serogroup B was found in (44/45) and one case of serogroup W135. Inotropic drugs were used in 40% of all patients and 20% needed mechanical ventilation (100% of deceased). The median CRP was 12.6 mg/L (no differences between the two groups) and Procalcitonin 35.2 ng/mL (26ng/mL versus 83ng/mL). The median WBC was 18.400/mcL versus 3.000/mcL in not survivors. PT was 54% in the survivors versus 22%. In 2 cases we found IMD despite the meningococcal B vaccination (serotypes not in the vaccine). Mortality was 8.9% and was higher in young patients with leukopenia and coagulopathy.

Conclusions

In our country, the estimation of the meningococcal B vaccination coverage is low. After 2015, 71% of the cases did not have the meningococcal B vaccine. It is paramount to continue improving the vaccination coverage to reduce new cases of IMD in the future, despite we know some serotypes are not included.
PANTON-VALENTINE LEUKOCIDIN ASSOCIATED STAPHYLOCOCCUS AUREUS MUSCULOSKELETAL INFECTION IN CHILDREN - A REFLECTIVE CASE SERIES OF LONG TERM COMPLICATIONS

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Title of Case(s)


Background

Panton-valentine Leukocidin (PVL) associated Staphylococcus aureus infections (SA-PVL) cause severe invasive disease. The endotoxin is expressed in both methicillin sensitive (MSSA) and methicillin resistant (MRSA) strains. Though rare, it is more commonly detected in cases with necrotising infection. In children, SA-PVL is most associated with septic shock, extensive and/or multiple soft tissue, bone and/or joint infections and pneumonia. This case series of SA-PVL infections with musculoskeletal involvement in a paediatric population illustrate presentation, management and destructive sequelae.

Case Presentation Summary

Case 1: 2 month old with septic shock, acute respiratory distress syndrome and leg swelling. Subsequently she had distal femoral growth arrest secondary to acute osteomyelitis. She also had myositis. Case 2: 20 month old with septic shock, acute respiratory distress syndrome and acute shoulder septic arthritis. There was subsequent chronic osteomyelitis of the humerus with a pathological fracture and non-union treated with vascularised fibula graft. Case 3: 15 year old with acute ankle septic arthritis, subsequent chronic osteomyelitis of the distal tibia with chondrolysis and clinical arthrodesis. Case 4: 10 year old with right distal femoral osteomyelitis, pathological fracture and bone loss treated with external fixator and bone transport. He also had infective endocarditis and thromboemboli.

Learning Points/Discussion

Suspicion of SA-PVL should be considered in patients presenting with severe sepsis. PCR is essential for diagnosis. Additional antibiotics to the empirical management may be necessary. For musculoskeletal infections, multiple surgical debridements are necessary and devastating long term complications of joint destruction and bone loss can develop. Increased awareness of the rapid onset and severe consequences of SA-PVL infections with early joint microbiology/infectious disease and surgical input are essential.
HUMAN HERPESVIRUS 6 PRIMARY INFECTION - IS THAT SIMPLE?

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Title of Case(s)

HHV-6 PRIMARY INFECTION - IS THAT SIMPLE?

Background

Primary infection with human herpesvirus 6 (HHV-6) may result in a spectrum of clinical disease, ranging from asymptomatic infection to acute febrile illnesses with roseola. Rarely HHV-6 primary infection can manifest as encephalopathy/encephalitis.

Case Presentation Summary

A 7-month-old male presented with an arrest of ongoing activity with altered awareness, a blank empty stare and eye deviation. The child’s temperature was normal, his physical exam was unremarkable. Cerebrospinal fluid (CSF) examination revealed 1 white blood cell (WBC)/mmc, glucose 62 mg/dl and protein 58 mg/dl. The patient was started on empiric acyclovir, as acute encephalitis was suspected. Next day febrile fever, repetitive myoclonic seizures and maculopapular rash on his face and trunk appeared. In few days left-sided hemiparesis developed. Magnetic resonance imaging (MRI) on the 7th day of the disease was normal. Ceftriaxone and antiepileptic therapy was prescribed.

All results, including immunological and virological tests by polymerase chain reaction (PCR) in blood and CSF, were negative. In CSF on the 8th day of disease HHV-6 DNA by qualitative PCR was negative whereas the blood sample examined for PCR HHV-6 was positive. The electroencephalogram (EEG) on the 13th day of the disease revealed interhemispheric asymmetry.

The patient received immunoglobulin (2g/kg) and intravenous ganciclovir (5mg/kg twice daily for 14 days), resulting in a slight improvement of the clinical condition. Nevertheless, 7 months later, he still had left-sided hemiparesis and partial seizures.

Learning Points/Discussion

Children with suspected viral encephalitis should be investigated for HHV-6. Occasionally, HHV-6 is not detected in the CSF. The lack or low level of viral DNA in the CSF samples suggests that direct invasion of the central nervous system by HHV-6 probably is not the main cause of encephalopathy/encephalitis.
SEVERE FEBRILE NEUTROPENIA IN A TEENAGER UNDER ISOTRETINOIC TREATMENT

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Title of Case(s)
SEVERE FEBRILE NEUTROPENIA IN A TEENAGER UNDER ISOTRETINOIC TREATMENT

Background

Acne is one of the most common diseases in adolescents. In serious cases of nodular acne or resistant to regular treatment, isotretinoin has excellent outcome. Nevertheless, its clinical use has been associated with severe adverse effects such as psychosis, rhabdomyolysis, seizures and disorders in blood cells.

Case Presentation Summary

A 15yrs old male teenager presented with severe hyperpyrexia, abdominal pain, vomiting and lower back pain over the last 48hrs. On clinical examination he was in poor general condition with tachycardia, diffuse abdominal pain, pharyngitis, painful cervical lymphadenopathy, spleen and liver enlargement and oliguria. Severe cystic acne lesions were noted on chest, back and face. He was on isotretinoin treatment for the last 10 days, which he was discontinued 4 months ago due to side effects. Initial blood tests showed lymphocytosis, leucopenia, neutropenia, thrombocytopenia and elevated CRP. On admission he was treated as infectious mononucleosis but over the next 12 hours he was rapidly deteriorated with anuria, increase of serum urea, creatinine and severe neutropenia (table 1).

Thus, he was treated with broad spectrum antibiotics (ceftriaxone and clindamycin) as for severe febrile neutropenia-toxinemia like reaction. He impressively improved within the next 4 hours and laboratory tests returned to normal within 12 hours.

Learning Points/Discussion

We present a case of a healthy otherwise teenager with severe febrile neutropenia with two possible infectious sites: pharyngitis and nodular acne, whose bone marrow was impressively suppressed. We supposed that this could be related to isotretinoin use, although there is no clear evidence for neutropenia in relation to isotretinoin and we suggest physians to inform patients in isotretinoin treatment for acne for seeking prompt medical advice in case of febrile disease.
03A. SCIENCE: SEVERE BACTERIAL INFECTIONS

A COMPREHENSIVE STUDY OF PAEDIATRIC SEPSIS INCIDENCE
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Background

Although sepsis is recognized as a major contributor to the burden of diseases in children, data on sepsis incidence are incomplete. Epidemiological studies are based on either administrative data, which have shown poor agreement with clinical data, or are restricted to paediatric intensive care units, whereas sepsis might be treated in wards. Sepsis definitions in adults have been revised due to increased insight in pathobiology, but does not include paediatric sepsis. The aim of this study was to estimate the incidence of severe sepsis in all paediatric clinics in a region and to calculate incidences based on different sepsis definitions.

Methods

A retrospective review of medical records of children, treated with intravenous antibiotics in all paediatric clinics in the region of Skåne, Sweden on 24 dates from July 2016 to July 2017. The incidences were calculated based on the population <18 years at the year-end 2016, which was 278773.

Results

164 patients were included in the study of whom 142 were regarded with an infection, 7 with severe sepsis according to the paediatric sepsis definitions, and 15 with an infection and one organ dysfunction.

This is equivalent to a severe sepsis incidence of 38/100 000 person-years (95% CI 10-66/100 000). When the SIRS was not required and when only one organ dysfunction was required, the incidence rose to 82/100 000 person-years (95% CI 40-123/100 000).

Conclusions

We estimated the paediatric incidence of severe sepsis, even though based on small number of patients, the study design is comprehensive. When defining sepsis as an organ dysfunction and infection, which is more in accordance with the sepsis-3 definitions for adults, the number were doubled suggesting the present paediatric definitions might gain of revision

Clinical Trial Registration (Please input N/A if not registered)

N/A
TIMELINESS OF VACCINATION IS A NECESSARY COMPONENT OF THE EFFICACY OF IMMUNIZATION

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Background

Today there is an increasing trend in the incidence of vaccine-preventable infections both in Russia and in many European countries. This growth is determined by many reasons, including the loss of healthcare workers’ alertness of the need to adhere to the quality of immunization. At the same time, the efficacy of immunization is directly dependent on coverage and timeliness of vaccination.

Methods

We analyzed the coverage and timeliness of pediatric population vaccination in Russia, Moscow, and three pediatric out-patient clinics.

Results

While coverage against all infections is 95% or higher, there is a lack of the timeliness of vaccination. In Russia in 2016 only 47.4% of children aged from 3 to 6 months were timely vaccinated against diphtheria and tetanus and in Moscow only 49.2%. Moreover, in three out-patient clinics percentage of timely vaccinated children has decreased from 21.8% in 2012 to 1.7% in 2017. In Russia in 2016 48% of children at the age of 18 months have had booster immunization, in Moscow 54.9% and in out-patient clinics from 49% to 55%. In Russia in 2016 97% of children aged 7 and 14 years have gotten booster immunization. Vaccination of children against hepatitis B is also being performed with delay, only 47.7% of children in Russia and 49.6% in Moscow have gotten complete vaccination course by the age of 6 months. More than 90% coverage is achieved only at the age of 1 year. However, immunization coverage against measles of children aged 1 and 6 years is above 95%.

Conclusions

Therefore, it’s necessary to optimize the work on the timeliness of vaccination because a decrease in its quality leads to an increase in the incidence of vaccine-preventable infections.
CONGENITAL RUBELLA SYNDROME: A SINGLE CENTRE EXPERIENCE FROM CHANDIGARH, NORTH INDIA

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Background

Rubella is a common cause of acute viral exanthem during childhood. However, major public health importance of this disease relates to the teratogenic effects of primary rubella infection occurring in pregnant women. True data about burden of congenital rubella syndrome (CRS) in India is not available widely. To describe the profile of CRS in children at tertiary care centre Postgraduate Institute of Medical Education and Research, Chandigarh, North India.

Methods

This was a review of records of children diagnosed to have CRS from our hospital during the period 2005-2015.

Results

There were 28 clinically diagnosed cases of CRS during this period. A total of 17 (61%) had laboratory evidence of IgM Rubella positivity in baby. There were 24 males and 4 females (M:F=4:1), having mean age of 2.8 ± 3.5 months. None of the mothers received rubella vaccination in past. All these babies were low birth weight at birth while 21(75%) had microcephaly. Structural heart defects (21/28) were the most prominent manifestation in these babies; out of them PDA (15/28) was most common. Other manifestations included cataract (18/28), hearing impairment (8/28), purpuric rash (6/28), developmental delay (8/28) and hepatosplenomegaly (26/28). Out of 18 cataract cases, it was bilateral in 12 and unilateral in 6.

Conclusions

To conclude CRS can present with a diverse form of clinical patterns. Because the burden of chronic disability due to congenital fetal infection causes serious multisystemic malformations resulting in severe morbidity and mortality, there is a need to mount effective CRS surveillance and preventive measures including appropriate vaccination against rubella.
AN AUDIT OF MANAGEMENT OF NEUTROPENIC AND NON-NEUTROPENIC FEVER IN HAEMATOLOGY-ONCOLOGY PATIENTS BY A UK TERTIARY PAEDIATRIC HOSPITAL

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Background

Febrile neutropenia is a common complication and results in significant morbidity and mortality in children receiving chemotherapy for malignancy. In our tertiary centre, management guidelines for use within the hospital and for our shared care centres are based on the National Institute of Clinical Excellence guidelines published in 2012. We performed a prospective audit of haematology-oncology patients with neutropenic and non-neutropenic fever admitted to or discussed with our centre to assess adherence to current management guideline, determine outcomes and identify areas of our guideline requiring modification.

Methods

In August 2017, haematology-oncology patients with neutropenic or non-neutropenic fever were prospectively identified using electronic prescribing records and documentation on electronic referral systems. Information was collected on age, diagnosis, level of neutropenia, clinical presentation, antimicrobials used, investigations performed and microbiology results.

Results

Fifty-one patients were identified (25 inpatients, 26 telephone advice). Mortality was 5.9% with one death due to gram-negative sepsis. Symptoms were documented in 53% and only 10% had clear evidence of risk stratification. As first-line treatment, 57% received the recommended piperacillin-tazobactam and aminoglycoside or ciprofloxacin. Six patients received meropenem first line, with no clear indication in one case. Positive blood cultures were identified in 12%, most commonly coagulase negative staphylococcus. Overall, 67% of patients were managed as per guideline. Common reasons for guideline deviation were prolonged aminoglycoside use and early addition of antifungals or teicoplanin/vancomycin.

Conclusions

Existing guidelines are not always followed in our centre. Reasons for this could include a lack of clarity in the guidance or individual patient complexity, resulting in treatment plans which deviate from the guideline.

Education is required on improving clinical assessment and risk stratification documentation. Work is currently on-going to update the guideline to make it more user-friendly.
SEQUELAE AFTER MEASLES VACCINATION IN PEDIATRIC PATIENTS WITH SIGNIFICANT NEUROLOGIC DISEASE

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Background

Measles outbreaks constitute considerable healthcare burden in the pediatric population and pose significant risk for unvaccinated children due to underlying medical conditions. Measles vaccination is recommended for outbreak control. Our aim is to present a small case series of previously unvaccinated children with severe neurologic disease who were vaccinated during the measles outbreak in Greece (2017-2018) and describe their vaccination side effects.

Case Presentation Summary

Recommendation for trivalent measles-mumps-rubella (MMR) vaccine administration was made to 3 distinct groups of neurologic patients, whose severe underlying condition had prohibited measles vaccination. Vaccination side effects (seizures, fever, neurodevelopmental regression) were retrieved 30 days following vaccination, for both dosages. Overall, 22 children were included (14 with intractable epilepsy, 7 with neurometabolic disease, 1 with severe pervasive developmental disorder). Three children denied vaccination. Side effects included afebrile seizures (3/19), fever (3/19) and seizures with fever (2/19). No child exhibited developmental regression. Afebrile seizures appeared 5-10 days post vaccination and had benign characteristics. No child needed adjustment of its antiepileptic treatment. A patient with Dravet syndrome, received both MMR doses with no sequelae. Fever appeared one week post vaccination, lasted 1-2 days, and was mild. In two children, seizures were in conjunction with fever, resembled typical febrile seizures, with no encephalopathy. Of note, these children received the quadrivalent (MMRV) vaccine.

Learning Points/Discussion

The main side effects of measles vaccination were vaccine-associated seizures, on the grounds of known epilepsy. No aggravation of epilepsy was observed. The seizures had a benign course. MMRV administration was related to increased likelihood for febrile convulsions. No long-term neurologic or neurodevelopmental sequelae were observed.
CLINICAL OBSERVATION OF THE FAMILY CASE OF GENERALIZED MENINGOCOCCAL INFECTION CAUSED BY GROUP W STRAIN (MEN W).

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Title of Case(s)

CLINICAL OBSERVATION OF THE FAMILY CASE OF GENERALIZED MENINGOCOCCAL INFECTION CAUSED BY GROUP W STRAIN (MEN W).

Background

Serogroup landscape of Invasive Meningococcal Disease (IMD) is heterogenic and varies from one territory to another. Also, the prevalence of a certain strain on the territory may change in the course of time. Recent worldwide epidemiology data report the increase in number of severe IMD cases referred to MenW strain.

Case Presentation Summary

In 2017 in St Petersburg we observed the family case of generalized IMD caused by Men W strain. The 7-years-old twins were infected by their Mom who had nasopharyngeal symptoms, sore throat and sub febrile fever two days prior to the incidence. IMD in both boys manifested with severe headache, repeated vomiting and slackness that has been rapidly passing into lethargy and sopor. Patients were admitted to the hospital within 24 hours from the onset. In admission, their condition was assessed as extremal. Clinical symptoms of purulent meningitis, cerebral edema, pre-coma and multiple organ failure were observed. Single elements if hemorrhagic rash were observed on legs. Both kids were immediately put on mechanical lung ventilation and stayed with it fir 4 days. Massive antibacterial, anti-shock and anti-edematous treatment started. Clinical blood tests verified moderate leukocytosis (10x10⁹/L) with a leycocyte shift to young forms. Cerebrospinal fluid analysis confirmed high neutrophilic pleocytosis (42000/3 and 28000/3) with protein increase up to 2.3 g/L.

Learning Points/Discussion

We achieved stabilization of patient’s condition by the 5th day from the therapy start. Sanitation of cerebrospinal fluid was confirmed on the 16th day. ST11 sequence-type of MenW strain was isolated from the blood and liquor of patients and from the nasopharyngeal swab of their Mom that confirmed MenW circulation in the family.
ESP18-0592
E-POSTER VIEWING - MAY 28-JUNE 2 - EXHIBITION HOURS

04B. SCIENCE: COMMUNITY ACQUIRED INFECTIONS: RESPIRATORY TRACT INFECTIONS

PARTICULARITIES OF INFLUENZA IN PEDIATRIC PATIENTS IN THE 2016-2017 INFLUENZA SEASON IN A TERTIARY CARE HOSPITAL IN ROMANIA


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Background

Despite vaccine availability, influenza continues to evolve in seasonal epidemics and to determine significant morbidity, particularly in children.

Methods

Romania is part of the GIHSN network. We are now reporting data for all hospitalized patients diagnosed with influenza in the GIHSN-study in the 2016-2017 influenza season, highlighting particularities in infants/toddlers/preschoolers/school children/teenagers, compared to adults.

Results

We identified 172 cases of influenza: 8 infants (attack-rate 25.8% in patients with influenza-like illness, 5 A/H3 and 3 B/Victoria), 24 toddlers (attack-rate 25.3%, 13 A/H3 and 11 B/Victoria), 26 preschool children (attack-rate 53.1%, 11 A/H3 and 15 B/Victoria), 94 school children (81.7%, 6 A/H3 and 88 B/Victoria), no teenagers (n=4 screened in this age group), and 20 adults (attack-rate 20.2%, 12 A/H3 and 8 B/Victoria). Only two cases (1.2%) had been vaccinated.

Infants had influenza-A more frequently than B (HR=1.9, 95%CI:0.8-4.9, non-statistically-significant – NSS) and so did toddlers (HR=1.7, 95%CI:1.1-2.6, statistically-significant). Preschoolers displayed a NSS tendency towards B-viruses (HR=1.3, 95%CI:0.9-1.8), a trend significant in school children (HR=8.2, 95%CI:3.7-18.4). Adults had significantly more influenza-A (HR=1.9, 95%CI:1.1-3.3).

In terms of associated risk-factors, no patients had COPD or asthma. None of the pediatric patients had cardiovascular-diseases, diabetes, chronic-kidney-disease, rheumatologic-diseases, autoimmune-diseases, cirrhosis, or neoplasms compared to 12.2%/10%/12.2%/12.3%/5%/10%/5% of adults. Evolution was generally favorable under antiviral-treatment; however one toddler (4.2%) died,
one preschooler (3.8%) and one school child (1.1%) required intensive-care and subsequently recovered. No deaths occurred in adults.

Conclusions

The pediatric population in our study was generally healthier that the adult population. However, more children required intensive-care, reinforcing the knowledge that children may have a higher risk for developing severe influenza, compared to adults.

Acknowledgement

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All-authors contributed equally.
IMMUNOLOGICAL RECONSTITUTION INFLAMMATORY SYNDROME AND THROMBOTIC MICROANGIOPATHY - SEVERE COMPLICATIONS IN A CHILD WITH AIDS

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Title of Case(s)

IMMUNOLOGICAL RECONSTITUTION INFLAMMATORY SYNDROME AND THROMBOTIC MICROANGIOPATHY - SEVERE COMPLICATIONS IN A CHILD WITH AIDS

Background

Although rare in developed countries, immunological reconstitution inflammatory syndrome (IRIS) is still a severe problem in advanced immunosuppression caused by HIV infection. It is associated with many complications, including secondary thrombotic microangiopathy (TMA).

Case Presentation Summary

Ten-month-old boy diagnosed with HIV/AIDS in the context of a Pneumocystis jiroveci pneumonia, with an initial viral load (VL) of 1460000 copies/mL and CD4 9/uL. Highly active antiretroviral therapy (HAART) was started (lamivudine, zidovudine, lopinavir/ritonavir). Two weeks after starting HAART, he developed fever and mucous and bloody diarrhea. At the time he had a VL of 3280 copies/mL and 109 CD4/uL (1100% increase). He had anemia (8.6x10⁹/L), thrombocytopenia (68x10⁹/L), hepatic tests elevation (AST 141U/L, ALT 218U/L), hypertriglyceridemia (190mg/dL), hypofibrinogenemia (0.8g/L), hyperferritinemia (1194ng/mL) and low sedimentation rate (4mm/h). Soluble CD25 was 22167 pg/mL. Macrophagic activation syndrome in the context of IRIS was assumed and he started metilprednisolone (2mg/Kg/day) and iv immunoglobulin with temporary clinical and analytical improvement, although with persistent diarrhea. Despite extensive investigation, including colonoscopy with biopsy for opportunistic infectious agents, none was identified. Clinical deterioration occurred after one month with thrombocytopenia (minimum 8x10⁹/L), anemia (minimum 4.2x10⁹/L), schizocytes on the blood smear, LDH elevation (1748U/L), low haptoglobin (<0.07g/L) and low ADAMTS activity (0.17). Assuming TMA secondary to HIV and with no improvement after plasma infusion, plasmapheresis was initiated with sparse response, and the patient died in disseminated intravascular coagulation with massive intestinal blood loss.

Learning Points/Discussion
This child had a very severe course after HAART initiation, with development of IRIS and TMA, which is in agreement to the dismal outcome. Severe persistent diarrhea may have been caused by HIV intestinal lymphatic tissue infection or intestinal microangiopathy.
OCCURRENCE RATE AND TYPE OF COMPLICATIONS IN PATIENTS HOSPITALIZED WITH MEASLES IN THE CURRENT OUTBREAK, IN THE NATIONAL INSTITUTE FOR INFECTIOUS DISEASES, ROMANIA

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Background

Measles is a highly transmissible disease, which can be effectively prevented through vaccination. However, we are currently experiencing a lengthy measles outbreak in Romania, which started in February 2016.

Methods

We are presenting data regarding the complications of measles in patients hospitalized in the National Institute for Infectious Diseases "Prof. Dr. Matei Balş", from December 2016 to January 2018.

Results

In the studied period, 487 patients were admitted with measles in our hospital. Of these, 85.4% had ages below 18 years old, with the highest incidence in the 1-3 years age group (30.2% of all patients). Most cases had not been vaccinated.

In terms of comorbidities, 2.9% of patients presented HIV infection, 1.4% congenital malformations, 1.2% malnutrition, 1% HBV infection, 0.8% genetic disorders, and 0.2% diabetes mellitus.

Only 12 cases (2.5%) presented no complications. The most frequent complication was acute viral pneumonia (69.6%), 13.1% presented acute respiratory distress, while bacterial pulmonary superinfections were identified in 8.4% of cases. Hematologic complications were also frequent, with 25.1% anemia and 19.1% thrombocytopenia. Overall, 17% of patients presented ophthalmological complications, and 16.2% otorhinolaryngological complications. We also identified 4 cases (0.8%) of secondary nephritis, and 16.6% cytolysis. Neurological complications were relatively rare (0.6%), but severe, and included meningoencephalitis.

The evolution was generally favorable, but 0.4% of patients developed sepsis with subsequent recovery following treatment, and 0.4% died due to respiratory failure.
Conclusions

The rate of complications in the current measles outbreak is very high, in both immune-competent and immune-depressed patients.

Acknowledgement

All authors had equal contributions.
01C. SCIENCE: ANTIBIOTIC STEWARDSHIP AND INFECTION CONTROL

ONE THIRD OF NEONATES ARE EXPOSED TO ANTIBIOTICS DUE TO MATERNAL INTRAPARTUM ANTIBIOTICS – VALIDATION OF A POINT-PREVALENCE SURVEY METHODOLOGY AT A LONDON TERTIARY CENTRE

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Background

Perinatal exposure to antibiotics may impact on the maternal and newborn microbiome and may have direct and indirect effects on the immune maturation of infants. Various prophylactic and therapeutic indications result in women receiving antibiotics in labour or during C-section, but the prevalence of exposure has not been systematically studied.

Methods

Weekly repeated point-prevalence surveys (PPS) capturing all births in a 24h interval at a London tertiary hospital over a 3-month period. Data validation was carried out by medical note review. Antibiotics given after the onset of labour or during C-section were considered intrapartum.

Results

Women received intrapartum antibiotics in 59 of 160 (37%, 95%-CI 29 – 45%) deliveries captured in the weekly repeated PPS over 13 weeks. The weekly proportions ranged between 20% and 60%. 10/59 (17%) of the women receiving antibiotics gave birth by vaginal delivery. In 89% the indication for antibiotic use was prophylaxis (mainly for C-section), in 11% an infection was treated. The median interval between last antibiotic and delivery was 30mins (IQR 15mins, 1hr 15mins). 37 women (63%) received Cefuroxime, 10 (17%) Benzylpenicillin. 8 of the 10 women giving birth by vaginal delivery and receiving antibiotics received Benzylpenicillin.

Comparison of the findings with patient records of all deliveries showed that 10% of women were misclassified, with mainly missed antibiotic use in vaginal deliveries. Therefore, the true proportion of women receiving intrapartum antibiotics is likely higher than reported here.

Conclusions

At least 1/3 of women at our centre receive an antibiotic in labour or during C-section. Our study has demonstrated the feasibility and acceptable accuracy of the PPS method. Data collection at other centres is necessary and currently in process.
THE HHV-6 AND HHV-7 IN NEWBORNS IN ST. PETERSBURG, RUSSIA
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Title of Case(s)
THE HHV-6 AND HHV-7 IN NEWBORNS

Background

The exanthem subitum (ES) is the common childhood illness for the children of 6-18 months of life. Approximately 90% cases of ES are caused by the HHV-6 and 10% - by HHV-7, which typically occurs later than HHV-6. After birth children have protective maternal antibodies to HHV-6 and HHV-7, which decreased to 6 months of age, but titer of maternal anti-HHV-7 can decrease later. However rare cases of HHV-6 in newborns were observed. Nevertheless, we didn’t find any published references about the cases of HHV-7 infection in newborn.

Case Presentation Summary

Objective. We aimed to find the cases of HHV-6 and HHV-7 ES in newborn children in St. Petersburg, Russia.

Methods. Forty-three newborn infants with fever and/or rash were included at St.Petersburg Filatov’s Children Hospital (Russia) from 2015 to 2016. The DNA of HHV-6 and HHV-7 in blood plasma samples were detected by qualitative PCR and quantitative real-time PCR. HHV-6A- and HHV-6B genotypes in blood serum were detected with newly developed real-time PCR kit.

Results. Totally 11 patients (25%) were positive for HHV-6 viral DNA. All of them were infected with HHV-6 of genotype B. There were 6 boys (54%) and 5 girls (46%). The age of patients varied from 14 days to 28 days. HHV-7 was found in 2 patients of 27 and 33 days of life. The most frequent diagnosis was ES. Four patients had rash without fever.

Learning Points/Discussion

It is considered that ES is a rare disease in newborn infants. However in our small sample 25% of infants with fever and/or rash were infected with HHV-6. The clinical manifestations in these patients were milder than classic ES after six months of age.
ADVERSE EVENT FOLLOWING IMMUNIZATION DURING MEASLES RUBELLA VACCINE CAMPAIGN IN EAST JAVA PROVINCE INDONESIA

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Background

Indonesia introduces measles rubella (MR) vaccine as the replacement for measles vaccine in 2017. The introduction was started with a mass campaign in Java Island. In East Java, the second most populated province in the island, there were more than 8 millions 9 months – 15 years old children. This study reported the adverse event following immunization (AEFI) episodes during the campaign.

Methods

The data were collected from all district health offices in the East Java Province from 1 August until 1 December 2017. The source of primary data were the community health centers, hospitals, private clinics, the medical doctors, and the family of the patients. For each case, the district health officers filled the AEFI forms, interviewed the involved health personnel, checked the vaccine and the procedures, and visited the home of the patients. Later, the data were also analyzed by the East Java Provincial AEFI Committee.

Results

During the campaign period, 8,944,291 children were immunized. Serious and non serious AEFI reports came from only 20 among 38 districts. There were 602 non serious (incidence rate 0.0067\%) and 86 serious (incidence rate 0.00096\%) events. Six children died (3 because of encephalitis, 1 case with cyanotic spell – congenital heart disease, 1 children with sepsis, and 1 because of intracranial bleeding), but the final analysis on all death cases did not find any relation with the vaccine. Among 80 other hospitalized cases, only one diagnosis, thrombocytopenia, showed consistent causal to immunization.

Conclusions

The incidence rate of AEFI during this MR vaccine campaign in East Java Province were below the international standard. More studies are needed, especially at the non reporting districts, to reveal the underdiagnosed cases. In general, MR vaccine is safe.
Masks of the Infectious Diseases

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Background

It is a common practice for an allergist to conduct differentiated diagnosis of allergic rash and that caused by an infectious disease. Diagnostic value of rash during infectious diseases is not straightforward. It is particularly difficult to conduct differentiated diagnosis of allergic and infection-induced rash in a situation of ambiguous clinical evidence of a virus infection.

Methods

This study analyses 149 clinical cases of children admitted into the department of allergies of The City Children Clinical Hospital No 4 of the city of Minsk with acute urticaria in 2015 year. To confirm the diagnosis we used the following methods - polymerase chain reaction (PCR), enzyme-linked immunosorbent assay (ELISA) and general blood analysis.

Results

According to the clinical and laboratory tests, 12% of patients were found to have infectious diseases accompanied by rash. The following have been revealed: enterovirus (7 children), parvovirus (6 children), human herpesvirus 6 (3 children), yersinia (2 children). Infectious exanthema are characterized by lack of allergies in the anamnesis, symptoms of “infection” before (1-7 days prior) or during the rash (cough, running nose, sore throat, fever, stomach aches, diarrhea, nausea), lack of itching, gradual pattern of breakouts (top-bottom being the most common) and their symmetry.

Conclusions

Most allergic rashes are masks of infectious diseases.
Pneumonia with parapneumonic effusion or pleural empyema in children resolves with pleural tap-guided antimicrobial treatment

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Background

For children with pneumonia and parapneumonic effusion or pleural empyema (PPE/PE) different management approaches and antimicrobial treatment regimens have been described. Six months outcome following empirical treatment with amoxicillin with/without clavulanic acid for a total of two weeks or a pleural tap-guided regimen was evaluated.

Methods

Children ≤16 years of age with radiologically diagnosed PPE and initial diagnostic pleural tap hospitalized at the University Children’s Hospital of Zurich were included over a 15-year period (2001-2015). Empirical antibiotic treatment was given for 14 days and rationalized according to microbiological findings and susceptibility testing of culture results from initial pleural tap. Clinical and radiological follow-up was scheduled up to 6 months or until full recovery.

Results

In 113 of 146 children (77%) with PPE/PE and initial pleural tap a pathogen was identified by culture, PCR and/or antigen testing. *Streptococcus pneumoniae* was detected in 90 (80%), *Streptococcus pyogenes* in 13 (12%) and *Staphylococcus aureus* in 7 cases (6%), all but two cultures were sensitive to amoxicillin/clavulanic acid. 70% of all patients received treatment with amoxicillin with/without clavulanic acid for 14 days. Of 138 children with follow-up, 51% and 78% fully recovered after 4 and 6 months respectively, 96% had no sequelae at the end of follow-up.

Conclusions

Overall prognosis in children with PPE/PE was good. Empirical treatment with amoxicillin with/without clavulanic acid was sensitive in most cases and was performed for 14 days in 70% of all children. Tap-guided treatment resulted in full recovery in over 95% of children with PPE/PE.
Background

Cystic Fibrosis (CF) and primary ciliary dyskinesia (PCD) are the most famous autosomal recessive disorder associated with impaired mucociliary clearance, which promotes upper and lower airway infection. Comparison of CF and PCD airways microbiota is traditional approach in the analysis. In contrast we had possibility to compare PCD with other diseases in the group of congenital pulmonary airway malformation (CPAM). The present study aimed to reveal characteristics of the Proteobacteria airway infection in different CPAM diseases.

Methods

Tracheal aspirate and sputum of 18 children with PCD and 24 children with other CPAM diseases were analyzed by molecular-genetic methods on the base of amplification and sequencing of microbial ribosomal and housekeeping genes. The children of 1-18 years old were hospitalized in the department of pulmonology and allergology of National Medical Research Center of Children's Health.

Results

Only two PCD patients (11%) were infected by Gammaproteobacteria (Haemophilus influenzae and Pseudomonas aeruginosa), and one patient was infected by Burkholderia cenocepacia ST878 (Betaproteobacteria). These three patients of 9-15 year old had pulmonary disorder complicated by otitis and rhinosinusitis. 83% of PCD children (1-18 years old) were infected by Lautropia mirabilis (Burkholderiaceae). In the group of other CPAM diseases there were 42% of children (1-16 years old) infected by Gammaproteobacteria in association with Fungi, and 38% of patients were infected by L. mirabilis.

Conclusions

Important differences in airway microbiology between PCD and other CPAM were revealed. L. mirabilis could be considered the early marker of chronic lung disorder.
FACTORS ASSOCIATED WITH THE RISK OF RECURRENT PNEUMOCOCCAL MENINGITIS IN CHILDREN

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Background

Pneumococcal meningitis (PM) is a severe life-threatening disease, which in rare cases can be recurrent in children. We analyzed the anamnestic, clinical, microbiological characteristics and outcome of pediatric patients with recurrent pneumococcal meningitis (RPM), and sought to identify risk factors associated with recurrences.

Methods

This multicenter nationwide retrospective case-control study was based on data from the French Surveillance Network of Bacterial Meningitis, collected between 2001 and 2015. RPM were defined as cases. They were matched with 2 controls that were born the same year and had suffered unique pneumococcal meningitis (UPM) the same year as the first episode of PM for cases.

Results

Out of the 1634 PM collected in children throughout France, 62 recurrences occurred in 24 patients (1.5%). RPM were significantly less frequent during winter than UPM (27% vs. 48%, p=0.03). Concomitant ENT infections were more frequently found in UPM, when compared to the first PM episode in cases (56% vs. 30%, p=0.04) or to all episodes of cases (56% vs. 28%, p<0.01). Neutrophil count in cerebrospinal fluid (CSF) was higher in patients with RPM (p<0.01). A CSF leak was the only underlying condition found for RPM (83% of cases vs. 10% of controls, p< 0.01). No immunodeficiency was reported in RPM patients, while 13% of UPM patients had preliminary immune deficiency (non-significant difference). Deaths (17%) were not different between the 2 groups. Neurological deficiency was more frequent in children with RPM (p=0.03).

Conclusions

RPM in children is a very rare condition with potentially severe consequences. When occurring, an underlying CSF leak should systematically be searched.
Background

The pleural effusion is defined by the presence of pus in the pleural cavity. It is always a news topic, given the increase in its incidence and high morbidity. Our study had as objectives to analyze the epidemiology, clinical,evolutionary characteristics and discuss the treatment modalities.

Case Presentation Summary

Materials and Method

We realised a retrospective study over four consecutive years, 2014-2017, 65 children were hospitalized in our service for pleural effusion .Data were collected from Medical records of patients.

Results

We collected 65 patients whose average age was 6 years.60 of our patients were properly vaccinated according to the national immunization program (Haemophilus influenzae b,not pneumococcus). The clinical symptomatology was dominated by dyspnea in 80% of cases .Initial chest radiography objectified free effusion in 75% of cases, encysted in 25% of cases The causative organisms were identified in 15 patients, isolated in pleural fluid (Streptococcus pneumoniae 6 cases, 5 cases Staphylococcus aureus, Serratia sp 2 cases, 1 case aeruginosae Pseudomonas,Citrobacter 1 case).The evolution was satisfactory in 93% of cases.

Learning Points/Discussion

Conclusion

The pleural effusion is a therapeutic emergency whose prognosis is related to early diagnosis and treatment.
SUPPURATIVE OTITIS MEDIA IN CHILDREN IN ANGOLA

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Background

Chronic suppurative otitis media (CSOM) is an important cause of hearing loss in children and constitutes a serious health problem globally. We studied a cohort of children with otorrhoea in five provinces of Angola, a Sub-Saharan country.

Methods

Children attending services of oto-rhino-laryngology due to otorrhoea were submitted to full clinical examination and interview. Ear secretion and nasopharyngeal samples were collected, transported frozen, and cultured in Sweden using standard techniques.

Results

Of 203 children, 91 (45%) were female. Their median age was 5 years (range 0-15). Unilateral disease was detected in 76% (153/201), bilateral in 24% (48/201) of children. Otorrhoea had lasted <15 days in 24% (48/201), and ≥1 year in 39% (78/201). Clinical hearing loss presented in 49% of children (96/196), and correlated with the duration of otorrhoea (p = 0.003). Of the children’s homes, 47% (94/202) lacked running water, and 12% (25/203) electricity. Of parents, 8% (24/307) had never attended school and 19% (59/307) only some classes of primary school. When comparing with the capital province Luanda, in poorer Lunda sul province, otorrhoea had lasted longer and hearing loss was more common (p=0.02). 133 ear discharge and 108 nasopharyngeal swabs yielded 376 and 212 individual isolates, respectively. Proteus spp. (n=50, 13%), Pseudomonas aeruginosa (n=39, 10%) and Enterococcus spp. (n=39, 10%) were dominating in ear discharge. Pneumococci and Staphylococcus aureus were detected in 15% (n=32) and 7% (n=15) of nasopharyngeal samples, respectively.

Conclusions

In Angola, otorrhoea is long-lasting, causes hearing loss, and associates with resource-limited living conditions. Ear discharge cultures reveal difficult-to-treat Gram-negative bacteria. Ear infections should be treated early to avoid severe sequelae. More studies are needed.
PARVOVIRUS ASSOCIATED WITH NEUROLOGIC SYMPTOMS

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Title of Case(s)

PARVOVIRUS ASSOCIATED WITH NEUROLOGIC SYMPTOMS

Background

Recently, an increasingly number of reports in pediatric patients with parvovirus B19 associated with neurologic symptoms has been reported. Immunologic mechanisms can be related with this type of illness presentation.

Case Presentation Summary

A previously healthy 16 year-old presented to the emergency department with high fever, arthralgia, headache and an erythematous rash in the superior limbs for two days, vomiting and photophobia since that day. On admission, he had ill-appearance and stiffness of neck. Laboratory work-up revealed 1114/ul leucocytes, 81.9% neutrophils and 185000/ul platelets, C protein reactive 128.2mg/L; cerebrospinal fluid (CSF) was clear, with 87 cells (61.6% polymorphonuclear lymphocytes), protein and glycose were normal. Ceftriaxone, vancomycin and acyclovir were initiated empirically, based on the preliminary diagnosis of meningitis. On 3th day of admission, the patient maintained the fever, headache and intense photophobia, with the rash progression to the trunk. Fundoscopy revealed papilledema and cerebral magnetic resonance showed signs of intracranial hypertension (IH). To cover possible zoonosis, it was added doxiciclin and anti-edematous measures which resulted in progressive clinic al improvement. From etiologic study, we highlight positive serum DNA parvovirus (<215UI/ml), negative CSF DNA parvovirus, serum IgM-/IgG+ (21.91 RU/ml), no available CSF antibodies. Assuming the patient had a parvovirus meningitis complicated with IH, immunoglobulin was administered for 5 days with progressive clinical improvement, no neurologic sequels, allowing the suspension of anti-edematous therapy.

Learning Points/Discussion

In conclusion, parvovirus seems the cause of meningitis complicated with IH with clinical evolution which is in agreement with other reports. The definitive diagnose is difficult to make so the clinical and laboratorial surveillance is necessary to better understand the etiology.
LONG-TERM PERSISTENCE OF RUBELLA AND MEASLES ANTIBODIES IN CHILDREN WITH JUVENILE SCLERODERMA ON IMMUNOSUPPRESSIVE TREATMENT - A CASE CONTROL STUDY.

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Background

Juvenile localized scleroderma (jLScle), a limited autoimmune disease, renders patients susceptible to infections due to their defective immune system and the immunosuppressive treatment. However we lack data regarding response and long-term immunity conveyed by specific vaccines. In this study we determined the immune status against measles and rubella in previously vaccinated jScle patients, prior to commencement of treatment and at one and three years, and compared this to healthy controls.

Methods

This was a prospective controlled study including 28 newly diagnosed jLScle patients and 56 healthy controls. All participants had two doses of the live attenuated MMR vaccine in early childhood. Demographic, clinical laboratory and treatment data were collected. Seroprotection rates and rubella-measles-IgG titers (expressed as GMC’s) were measured at enrollment and at 12 and 36 months. The Hospital’s Research and Ethics’ Committee approved the study; written informed consent was obtained.

Results

The two groups had similar demographic characteristics, vaccination history and immunization status. Seroprotection rates were adequate for both groups. Nonetheless, the jLScle group had lower seroprotection rates at one and three years. Measles-GMC’s were similar between the patient and control group at all time points. Rubella-GMC’s were significantly lower in the jLScle compared to the control group (p<0.01) at one and three years’ follow up but not at diagnosis. The use of methotrexate did not seem to exceed any effect seroprotection rates but had a negative impact on GMC’s, which was more pronounced for rubella.

Conclusions

In conclusion, although seroprotection rates were similar between the two groups, rubella GMC’s were significantly lower in the jLScle group. Further studies are required to address the question of long-term immunity conveyed by immunizations given at an early stage in children with rheumatic diseases.

Clinical Trial Registration (Please input N/A if not registered)
Background
Mosquitos of *Aedes* type spread in southern European countries. It may increase the risk of transmission of dengue. Paediatric population is a high-risk group to develop severe cases: plasma leakage, hemorrhagic syndrome, shock. OMS revised in 2009 the dengue forms classification and suggested in 2013 a tool book to support the management of patients. Our purpose was to describe clinical and therapeutic features of severe pediatric dengue forms in the French Polynesian Hospital Center. We compared our practices to OMS recommendations.

Methods
From June 2013 to April 2017, we conducted a retrospective study. Children under 15 year-old, hospitalized in Continuing or Intensive Care Unit of the French Polynesian hospital center, for severe dengue, were included. Their clinical, biological, therapeutic characteristics, and evolutive data were analyzed. Our practices were compared to OMS recommendations.

Results
Children under 5 year-old are significantly exposed to severe dengue forms. Plasma leakage, causing shock for 51% of cases, is the most common gravity sign (84.3%), ahead of organ damage (21.6%), and hemorrhagic risk (15.7%). The occurrence of a prolonged shock worsens coagulopathy and organ failure. Mortality is low (3.6%), on condition of a rigorous initial assessment and a close surveillance of patients during the critical illness.

Conclusions
In the absence of specific antiviral treatment, and of vaccination policy in high-risk areas of French territory, management of the disease is based on the early detection and takeover of warning signs and severe forms. Especially in children, reducing morbi-mortality is based on the formation of care workers to children hemodynamic assessment. Development of tools as OMS dengue management guide book, diffusion of vital parameters depending on age and patient's bedside ultrasonography are to promote.
INTRODUCTION

The incidence of rare IFD in children after allo-HSCT was 1.5% (n=7/461), auto-HSCT – 0.4% (n=1/232). Rare IFDs developed more often in patients with acute leukemia (45.4%). The etiological structure of confirmed rare IFD in children were Mucorales at six patients (54.5%), two cases of IFD caused by Fusarium spp. (18.2%), one – Trichosporon asahii (9.1%), one – Scedosporium apiosperum (9.1%), and combination of Fusarium spp. and Paecilomyces spp. were diagnosed in one patient (9.1%). Antifungals were prescribed in 100% and all pediatric patients with mucormycosis had combination therapy.

CONCLUSIONS

The median day of onset of IFD was 92 days after allo-HSCT and 138 after auto-HSCT, 134 days after start of CT. Combination antifungal therapy improves 1 year survival in children and adult with mucormycosis (n=30) (40% vs 10%, p=0.05). Overall survival at 12 weeks and 1 year from the diagnosis of IFD was 46.2% and 36.4% and was not differ in age groups.
LABORATORY AND MOLECULAR SURVEILLANCE OF PAEDIATRIC ENTERIC FEVER IN BENGALURU, INDIA REVEALS A DOMINANCE OF FLUOROQUINOLONE RESISTANT H58 LINEAGE II WITHOUT MULTI DRUG RESISTANCE (MDR)

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Background

India is endemic for enteric fever, caused by Salmonella serovars Typhi and Paratyphi A, and affects children disproportionally. Multi-drug resistant strains are those resistant to first-line antimicrobials namely, chloramphenicol, ampicillin and cotrimoxazole and were a major public health problem a decade ago. This study aims to characterize the antibiogram and molecular structure of circulating S. Typhi strains among children in South India.

Methods

Isolates were obtained from children attending the St. John’s Medical College Hospital between June 2016 and June 2017 and were subject to antibiotic sensitivity testing using Kirby-Bauer disk diffusion tests. CLSI criteria were used to gauge sensitivity patterns to chloramphenicol, amoxicillin, trimethoprim-sulfamethoxazole, ceftriaxone, nalidixic acid and ciprofloxacin. Isolates obtained were also subjected to whole genome sequencing to identify the mechanisms implicated in drug resistance.

Results

All 36 isolates tested, were resistant to pefloxacin and ciprofloxacin. There was no phenotypic resistance to first-line antimicrobials or to cephalosporins. Twenty-five belonged to H58 lineage II, 9 to lineage I and 2 to non-H58 groups. SNPs in gyrA, conferring resistance to fluoroquinolones were seen in all 36 isolates with 9 S. Typhi isolates containing SNPs in 3 quinolone resistance determining (QRDR) sites namely gyrA S83F, gyrA D87N, and parC S80I simultaneously.

Conclusions

Fluoroquinolones have little role to play in the treatment of enteric fever in this region owing to widespread resistance mediated by the H58 lineage II strains. This lineage is dominant and is rapidly replacing H58 lineage I strains which were formerly associated with MDR typhoid. The re-emergence of strains sensitive to chloramphenicol and cotrimoxazole could be exploited during treatment regimes to conserve cephalosporins from the emergence of resistance.
COMPARATIVE ASSESSMENT OF THE SENSITIVITY AND ACCURACY OF RAPID TEST KITS FOR EARLY INFANT DIAGNOSIS OF HIV

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Background

Pediatric Human Immunodeficiency Virus (HIV) infection remains a significant public health problem in resource-limited countries, particularly in sub-Saharan Africa. Therefore the importance of early infant diagnosis (EID) of HIV cannot be over emphasized and it is critical to improving neonatal survival and reducing the risk of neonatal death and future HIV transmission. Majority of these deaths occur in resource-limited areas due to inability to diagnose the infection/disease due to lack of equipment necessary to make diagnosis.

Methods

In this study, the sensitivity and accuracy of the Rapid test kits (RTK) Determine and Unigold on infants aged 6 months to less than 18 months is determined using DNA Polymerase Chain Reaction (DNA PCR) as the gold standard. A total of 236 samples were tested with the RTKs and DNA PCR.

Results

Out of 236 samples, 204 (86%) had matching results with the DNA PCR while 32 (14%) did not match. The non-corresponding results were observed to have occurred at age range of 6 months to 12 months, however, children aged 13 months to 17 months all had corresponding results between rapid test kits and DNA PCR. The 14% non-corresponding results were false positives without any false negatives indicating that RTKs were 100% sensitive to the detection of HIV infection among infants when compared to DNA-PCR. The specificity of the RTKs was also found to be 82.3%.

Conclusions

This study shows that the RTKs, Determine and Unigold fared well p<0.05 against the DNA PCR and therefore can be used in resource limited areas as screening tests for infants before a confirmatory test can be conducted. This will greatly reduce the cost of EID of HIV in infants and make it easily accessible in poor communities.
Invasive meningococcal disease (IMD) is a severe and life-threatening disease with a relatively high case fatality, especially among infants and young children. Lithuania is one of the largest burden areas of IMD in Europe. More than half of IMD cases are registered in Vilnius region and Men-B is the dominating serotype. Our aim was to analyse clinical manifestations of IMD in children before introduction of universal meningococcal B vaccination in the country.

Methods

All children diagnosed with IMD at Children’s Hospital*, from 2007 to 2017 were included into this retrospective study. Age distribution, seasonality, clinical manifestation and laboratory data were analysed.

Results

A total of 346 children were diagnosed with IMD. Infants and young children were diagnosed with IMD more frequently (<1 yr. – 30.3%, 1-3 yrs. – 34.4%, ≥ 4 yrs. – 35.3%). IMD was more common during winter and spring months (28.0% and 33.2%, respectively). The most common clinical manifestation were acute meningococcemia (60.9%) and meningococcal meningitis (19.7%). Meningococcemia combined with meningitis was diagnosed in 4.9% of cases. Waterhouse-Friderichsen syndrome was rare (3.7% of all cases). In total 28 patients died (8.1%). One third of cases (33.4%) were confirmed by blood or CSF culture. Serogroup B was dominating (94.0%) and just few cases were caused by Men-C. Sensitivity of N.meningitidis to penicillin was high (100%) in 2007-2011, later there was an increase of intermediately susceptible strains (57-93%).

Conclusions

Infants and young children are at greatest risk to acquire IMD.

The most common clinical manifestation was acute meningococcemia.

Decreasing sensitivity to penicillin is the reason of change of initial treatment from penicillin to third generation cephalosporins.
Relatively high mortality confirms the necessity of introduction of universal Men-B vaccination in Lithuania.
AN OPPORTUNISTIC MUCO-CUTANEOUS INFECTION WITH NONTUBERCULOUS MYCOBACTERIA DURING ADALIMUMAB TREATMENT
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Title of Case(s)
AN OPPORTUNISTIC MUCO-CUTANEOUS INFECTION WITH NONTUBERCULOUS MYCOBACTERIA DURING ADALIMUMAB TREATMENT

Background
Adalimumab is a tumor necrosis factor-alpha (TNF-α) used for refractory non-infectious uveitis in children. Anti-TNF therapy has been be associated with opportunistic infections, such as atypical mycobacteriosis.

Case Presentation Summary
A 12-year-old girl with idiopathic anterior and intermediate uveitis, under treatment with adalimumab and cyclosporine, presented with a 4-months nodular, erythematous vegetative lesions of the nasal septum, palate, tonsil and right foot. She denied fever, weight loss or cough and had no response to antibiotics. She had a domestic aquarium and dealt with horses, but did not recall preceding trauma. Blood tests showed leukocytosis, an erythrocyte sedimentation rate of 53mm/h and a C-reactive protein level of 0,9mg/L. The interferon-gamma release assay test and the thorax x-ray was negative. The nasal septum, palate and tonsil biopsy revealed giant cells non-necrotic granuloma, with DNA amplification for HSV-1 and the foot skin biopsy shown wart-like epithelium. All lesions amplified for atypical mycobacteria DNA. Anti-TNF-α was discontinued and intravenous acyclovir together with clarithromycin, rifampicin and levofloxacin. The culture turned positive for Mycobacterium marinum and she is currently on clarithromycin and rifampicin for six months, with slow but complete regression of muco-cutaneous lesions.

Learning Points/Discussion
Although rare, atypical mycobacteria infections in patients taking TNF-α inhibitors have been reported in the literature. The diagnosis of Mycobacterium marinum infection is difficult and requires a high degree of suspicion. Treatment is challenging and usually includes clarithromycin combined with rifampicin or ethambutol for at least 2 months after disease regression. The multifocal mucous involvement is to our knowledge not previously reported and the authors wonder whether treatment or prophylaxis should be maintained longer to prevent relapses.
IS IN VITRO SUSCEPTIBILITY TO COLISTIN RELIABLE: BREAKTHROUGH GRAM-NEGATIVE BACTERIAL INFECTIONS DURING THE COLISTIN TREATMENT

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Background

The rising incidence of colistin-resistant pathogens and bacterial resistance has emerged in many parts of the world. Breakthrough infections during colistin treatment were described in few case reports recently.

Methods

This study was conducted retrospectively in patients who were admitted to two reference pediatric critical care unit and received colistin between January 2011 and December 2016.

Results

Table 2: Demographic and clinical characteristics of the patients with colistin breakthrough bacteremia

<table>
<thead>
<tr>
<th>Age (months) (gender)</th>
<th>Underlying disease</th>
<th>Reason for ICU admission</th>
<th>Pathogen for colistin treatment</th>
<th>Breakthrough Infection/pathogen</th>
<th>Day of colistin treatment</th>
<th>Treatment regimen</th>
<th>Treatment after breakthrough infection</th>
<th>Day of mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>19/F</td>
<td>Chronic lung disease</td>
<td>VAP</td>
<td>Pseudomonasa eruginosa</td>
<td>CLABSI/Acinetobacter baumanii</td>
<td>7</td>
<td>Colistin+ ciprofloxasin</td>
<td>Colistin+ Ciprofloxasin + Tygecycline</td>
<td>8/AM</td>
</tr>
<tr>
<td>6/M</td>
<td>Congenital heart disease</td>
<td>VAP</td>
<td>Acinetobacter baumanii</td>
<td>CLABSI/Rhizobium radiobacter</td>
<td>5</td>
<td>Colistin+ meropenem</td>
<td>Colistin+ amikacin</td>
<td>-</td>
</tr>
<tr>
<td>Patient</td>
<td>Diagnosis</td>
<td>Infection Type</td>
<td>Pathogens</td>
<td>Treatment</td>
<td>Mortality Rate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>---------</td>
<td>-----------</td>
<td>----------------</td>
<td>-----------</td>
<td>-----------</td>
<td>----------------</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8/F</td>
<td>Congenital heart disease</td>
<td>VAP</td>
<td>Acinetobacter baumanii, Pseudomonas aeruginosa</td>
<td>Colistin+ Piperacillin-tazobactam</td>
<td>6/10 (9.6%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9/F</td>
<td>Chronic lung disease</td>
<td>CLABSI</td>
<td>Acinetobacter baumanii</td>
<td>Colistin</td>
<td>9/10 (9.6%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>180/F</td>
<td>Leukemia</td>
<td>CLABSI</td>
<td>Acinetobacter baumanii, Klebsiella pneumoniae</td>
<td>Colistin+a-minocycline</td>
<td>5/7 (71.4%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6/F</td>
<td>Chronic neurologic disease</td>
<td>VAP</td>
<td>Acinetobacter baumanii</td>
<td>Colistin</td>
<td>5/7 (71.4%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10/F</td>
<td>Neurometabolic disorder</td>
<td>VAP</td>
<td>Acinetobacter baumanii</td>
<td>Colistin+a-minocycline</td>
<td>9/11 (81.8%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12/M</td>
<td>Chronic neurologic disease</td>
<td>CLABSI</td>
<td>Acinetobacter baumanii</td>
<td>Colistin+ Trimethoprim-sulfamethoxazole</td>
<td>11/11 (100%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>36/M</td>
<td>Genetic syndrome</td>
<td>CLABSI</td>
<td>Acinetobacter baumanii, VAP/Pseudomonas aeruginosa</td>
<td>Colistin+a-minocycline</td>
<td>5/7 (71.4%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>189/F</td>
<td>Trauma</td>
<td>UTI</td>
<td>Klebsiella pneumoniae, Acinetobacter baumanii</td>
<td>Colistin+a-minocycline</td>
<td>7/7 (100%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

AM: Attributable mortality; CM: Crude Mortality; CLABSI: Central line associated bloodstream infection; UTI: Urinary tract infection

Conclusions

In the present study, we evaluated 104 colistin treatment episodes and determined 10 (9.6%) breakthrough infection with another gram-negative pathogen during colistin treatment with a mortality rate of 20%.
Title of Case(s)

A child with severe combined immunodeficiency presented with aspergilloma and effectively treated with voriconazole and micafungin due to amphotericin B anaphylaxis.

Background

Invasive aspergillosis (IA) is a serious life-threatening complication in immunocompromised children. Herein we describe a boy with severe combined immunodeficiency presented with aspergilloma and effectively treated with voriconazole and micafungin due to amphotericin B anaphylaxis.

Case Presentation Summary

A 3-month-old boy admitted due to fever persisting for more than 1 month and leukopenia. Tachypnea, fever, hepatomegaly were noted on physical examination. Total blood count revealed anemia (leukopenia (0.3 X10³/µL), neutropenia (ANS:0), lymphopenia (0.3X10³/µL)). Bone marrow aspiration was incompatible with malignancy. Total immunoglobulin levels, CD3, CD8, CD16+56, CD19 were all low for age compatible with severe combined immunodeficiency. Meropenem and vancomycin was started. Retrocardiac consolidation was noted on chest radiography. A soft tissue mass of 28x26x30 mm with central hypodense necrosis was seen on thoracic computed tomography compatible with angioinvasive aspergillosis. Blood galactomannan was found high 1.4 (n:0-0.5). Liposomal amphotericin B was started, but hypotension, cyanosis and desaturation were noted at the time of infusion. Due to anaphylaxis, amphotericin B was stopped and micafungin and voriconazole were started. Aspergillus fumigatus was cultured on biopsy taken from thoracic mass. Allogenic bone marrow transplantation was done at the 62 th day of hospitalisation. Blood galactomannan level decreased and he was not neutropenic at the 26 th day of bone marrow transplantation. At the 87th day of micafungin and voriconazole treatment, soft tissue mass disappeared at control thorax tomography. At the 129th day of hospitalisation patient was
Learning Points/Discussion

Aspergilloma must be kept in mind at the first presentation of patients with immunodeficiency. Bone marrow transplantation and prompt antifungal therapy are lifesaving.
Prevalence of Rotavirus, and Enteric Pathogens Among Pediatric in Patients from Katutura Central Hospital in Namibia

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Background

Diarrheal disease ranks third in the global estimates for mortality in children < 5 years. In Namibia diarrhea disease contributes 3% of these deaths. Data on the pathogens associated with diarrhea disease in the country is currently unavailable.

Methods

From February 2015 through June 2015, stool samples were collected with flocked swabs from a total of one hundred and forty two patients who attended the Katutura State Hospital, Windhoek, Namibia for acute diarrhea. We used the Seeplex Ace diarrhea panels for detection of viruses and bacteria in the samples by PCR.

Results

Out of the 142 samples, viral pathogens accounted for 37 (26.0%) while bacterial pathogens accounted for 77 (54.2%). Of the 37 cases of viral diarrhea the following were obtained for each pathogen: Norovirus GI, 1 (2.7%), Astrovirus, 4 (10.8%), Rota, 8 (21.6%), Adenovirus, 11 (29.7%), Norovirus GII, 13 (35.1%). The prevalent bacterial pathogens were E coli H7, 17 (22.0%), Salmonella, 16 (20.8%), VTECH, 12 (15.6%), Y enterocolitica, 9 (11.7%), Aeromonas, 8 (10.4%) and C perfringens, 8 (10.4%). Multiple infections were present in 27 out of the 142 children (19.0%). The overall median age of the children was 12 months while those with multiple infections had a median age of 10 months.

Conclusions

The study identified Noro virus GII, Adenovirus and Rota virus as the prevalent viral pathogens seen at the Katutura State Hospital in Windhoek Namibia.
FIRST REPORTED USE OF ZIDOVUDINE FOR PREVENTION OF PERINATAL HIV TRANSMISSION IN A PREMATURE CHILD ON ECMO

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Title of Case(s)

FIRST REPORTED USE OF ZIDOVUDINE FOR PREVENTION OF PERINATAL HIV TRANSMISSION IN A PREMATURE CHILD ON ECMO

Background

The effects of extra corporal membrane oxygenation (ECMO) on pharmacokinetics (PK) of drugs is difficult to predict. Generally, an increased volume of distribution, decreased drug elimination, and sequestration of the drug to the ECMO circuit are factors influencing the PK of drugs during ECMO. Zidovudine is the only antiretroviral agent suitable for intravenous use in newborns for the prevention of perinatal HIV transmission. No reported cases of the influence of ECMO on the PK of zidovudine in prematures were found.

Case Presentation Summary

A premature child (32 weeks) born from a virologically suppressed HIV infected mother required ECMO to undergo the resection of an intrathoracic lesion compromising the lungs. IV zidovudine was administered for the prevention of HIV transmission. To cope with the increased volume of distribution ($V_d$) and avoid the risks caused by undertreatment, IV zidovudine was dosed 9mg/kg/day (150% of the dose normally used in premature infants) for the duration of ECMO. Plasma samples were taken before, during and after ECMO. Samples were analyzed using liquid chromatography. Therapeutic drug monitoring (TDM) was used to observe treatment and PK parameters were calculated using non-compartmental analysis in WinNonlin.

With clearance 0.62 L/h, $V_d$ 3.3 L, and $t_{1/2}$ of 3.6 h, zidovudine concentrations remained above 0.8mg/L during ECMO. This exposure was higher than normally seen in prematures and has been correlated to increased safety risks in earlier studies. No adverse events were reported in this case and zidovudine levels returned to normal on standard doses after ECMO cessation.

Learning Points/Discussion

In future occasions, standard IV dosing of zidovudine in premature children on ECMO is recommended under the guidance of TDM.
WHAT IS THE VALUE OF BUDGET IMPACT MODELS IN VACCINE DECISION MAKING? THE CASE OF PEDIATRIC HEXAVALENT VACCINES IN EUROPE

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Background and Objective

Starting with the Expanded Programme on Immunization in the 1970's, vaccinations against diphtheria, tetanus, pertussis, and poliomyelitis have been recommended globally. More recently, vaccination against Haemophilus Influenzae type B (Hib) and Hepatitis B (HepB) have become universally recommended. Because these vaccines are part of the standard childhood immunization calendar – typically administered in the first year of life on three-dose schedules with either short (2/3/4 or 2/4/6 month) or long (2/3/11 or 2/4/11 month) intervals, there is clear utility in the use of combination hexavalent vaccines. Currently, there are three hexavalent vaccines licensed for use in most European countries.

National Immunization Technical Advisory Groups (NITAGs) and Health Technology Assessment (HTAs) agencies frequently use economic considerations, including budget impact, in deciding both on overall immunization calendars, and reimbursement. The objective of this study was to evaluate what information is publicly available on the use of budget impact models in vaccine decision making in Europe; and to evaluate what role budget impact models might have on consideration of a newly available hexavalent vaccine when other combination vaccines are already available.

Methods

We reviewed the literature concerning budget impact models for vaccines in European countries, and developed a model to compare budget impact across the three hexavalent vaccines.

Learning Points Discussion

• Budget impact models have greatest utility when the product is a new formulation (ie, a single combination vaccine replacing two vaccines) rather than second to market.
• Quantifying the health impact of incremental changes in vaccine formulation when disease levels are very low after nearly 50 years of vaccination is very challenging.
• Seemingly small differences in presentation and ease of use characteristics can have significant budget impact.
17D. EDUCATION: PERTUSSIS IN 2018

MACROLIDE RESISTANT PERTUSSIS IN AN INFANT WHOSE MOTHER WAS NOT VACCINATED AGAINST PERTUSSIS
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Title of Case(s)
Macrolide resistant pertussis in an infant whose mother was not vaccinated against pertussis

Background
Pertussis infection has been recognized as a global cause of morbidity and mortality, especially amongst infants in the first months of life. The most severe course of infection is seen in unvaccinated infants, who can develop life-threatening complications.

Case Presentation Summary
A 6 week-old boy was admitted to PICU from a local hospital due to respiratory collapse. The diagnosis of pertussis was made 1 week after initial symptoms including coughing, and he started a 10-day course of erythromycin, 4 days after which he was admitted to our PICU. Despite treatment with azithromycin and cefotaxime, he deteriorated clinically, developing pronounced leukocytosis. While in extremis he obtained two blood exchange transfusions and intravenous immunoglobulin with good clinical effect. The pertussis strain identified showed resistance to erythromycin, clarithromycin and azithromycin. The bacteria had good sensitivity to trimethoprim-sulfamethoxazole and he was therefore given this treatment for 19 days. The total length of antibiotic treatment was 23 days. The patient required invasive mechanical ventilation and high-flow nasal therapy (Optiflow®) for 16 days and 11 days respectively. On day 25 he could be transferred to the standard paediatric department. His mother had not been vaccinated in childhood, and developed similar symptoms few weeks before him.

Learning Points/Discussion
The vaccination of pregnant women, which is well described, can significantly decrease the severe courses of pertussis infection in neonates and infants. Usual treatment of pertussis with antibiotics can fail due to bacterial resistance. Blood exchange transfusion is an important therapy to consider in severe cases of pertussis infection with significant leukocytosis.
Background

The profile of adopted children in Spain has changed in the last few years. The Spanish families received more children with special needs and pathologies, that require an urgent adoption. Objective: To analyze these children’s characteristics and their health status once they arrive to Spain.

Methods

A descriptive retrospective study of 32 adopted children (47% girls) with special needs, who arrived to Spain during 2016-2017 from China 16, from Vietnam 15 and 1 from Bulgary, and were followed up in the International Adoption and Tropical Pathology reference unit.

Results

81% were adopted by two-parent families, 28% have another child. Average age on arrival: 18 months. 50% of them came previously to our adoption consultation and the most frequent diagnosis during these consultation are shown in table 1.1.

93% provide previous serology tests (HIV/Hepatitis/Syphilis): negative except a positive one for syphilis, one for HVB.

87% presented a vaccination calendar, only completed in 4 cases (12.5%).

17 children showed BCG scar (53%); 4 with positive Mantoux test, all with negative IGRA tests.

At arrival in Spain, children’s diseases are shown in table 1.2. Three patients who were diagnosed with hematological diseases, one of syphilis and one of Hepatitis B were ruled out. New diagnosis were found: HVB chronic hepatitis: 1 patient, HVC infection 1 child, and parasitosis 3 patients.
Conclusions

The most frequent pathology found in adopted children with special needs were weight/size delay, microcephaly and anemia. Parasitosis is also frequently found.

We found a high prevalence of chronic HBV/HCV hepatitis. 87.5% of the children need to complete vaccination.

It is recommended that before and after arrival these adopted children with special needs must be seen in a medical consultation specialized in International adoption because of their complex pathology.
Background

The gut has a large gram-negative bacterial load, which has a highly immunogenic cell wall (endotoxin). Endotoxin exposure produces strong innate immune responses in monocytes, which can alter their responses to subsequent stimuli. Local gut inflammation and systemic inflammation in circulation can increase intestinal permeability (IP), allowing further translocation of endotoxin into the body, exposing it to circulating immune cells.

This study investigates whether children with non-gastrointestinal infections have increased IP and corresponding plasma endotoxin, and whether this corresponds to any innate immune system changes.

Methods

Children requiring hospital admission with non-gastrointestinal infections and no diarrhoea/vomiting (‘cases’; n=11), and healthy controls (n=19), aged 0.5-5 years were given a lactulose-mannitol test. Blood was taken for circulating endotoxin, monocyte activation markers, and innate immune responses following 24h culture-stimulation with fungal-cell-wall component zymosan.

Results

Cases had higher IP (Lactulose:Mannitol ratio 0.09 v 0.03; p=0.025) and circulating endotoxin (0.24EU/mL v 0.025 EU/mL; p=0.04), with a modest non-significant correlation between the two (r=0.38, p=0.08). In cases, the monocyte HLA-DR+ percentage was lower (p=0.001), and FcγRI-receptor CD64+ percentage was higher (p=0.04). Cells from cases produced significantly less IL-1β (p=0.04) and TNF-α (p=0.03) in response to zymosan. Subjects with higher endotoxin (>0.1 EU/mL) had lower monocyte expression of T-cell co-stimulator CD86 (p=0.03), and following 24h zymosan-stimulation, monocytes had reduced percentage expression of CD64 (p=0.02).

Conclusions

Children with non-gastrointestinal infections had increased IP, and their increased circulating endotoxin level likely represents increased translocation across the leakier gut wall. These cases showed both anticipated monocyte changes with infection, and additionally a less-marked cytokine response on subsequent stimulation. Changes seen in children with high endotoxin represent a reduced ability to respond to further stimulation, which could affect their innate defences against new infections.

Clinical Trial Registration (Please input N/A if not registered)
IMMUNITY TO HAEMOPHILUS INFLUENZAE TYPE B AND PERTUSSIS IN HIV-INFECTED CHILDREN

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Background

Children living with HIV are at increased risk of disease from bacterial infections as Haemophilus influenzae type b (Hib) and pertussis. Data are limited on immunity to these vaccine-preventable diseases in HIV-infected children. The objectives of the study were to evaluate immunity to Hib and pertussis in perinatally HIV-infected children followed up at Kiev City AIDS Center.

Methods

We conducted a retrospective single-center cohort study of 142 HIV-infected children and analyzed the vaccine coverage and level of vaccine antibodies against pertussis toxin and anti-Hib PRP IgG antibodies. The seropositivity rate and geometric mean titers (GMT) of antibodies of group of HIV-infected children (n = 51) were compared with the data of 22 immunocompetent HIV-uninfected children.

Results

Immunization coverage of HIV-infected children was lower than in general population. Coverage was 63.6% for pertussis and 16.8% for Hib. The median age of HIV-infected children at time of study was similar to uninfected children: 12.5 and 12.1 years. There was no difference in GMT of serum anti-PRP antibody in HIV-infected (4.5±0.37) and uninfected children (4.9±0.58). Most HIV-infected children had anti-Hib antibodies ≥ 1 μg/ml (84.3%), 23/51 (45.1%) ≥ 5 μg/ml. The median PT IgG concentration was 115 IU/ml in HIV-infected children and 84 IU/ml in uninfected children (p 0.005), 62.7% of HIV-infected children has level serum PT IgG > 100 IU/ml.

Conclusions

This study demonstrates a significant proportion of HIV-infected children with lack of protective immunity to pertussis, considering the needs for booster dose. Most of these children have immunity to H. influenzae type b acquired after infection. They are to be protected by supplementary strategies for booster doses of Hib vaccine.

Clinical Trial Registration (Please input N/A if not registered)

N/A
SURFERS: BEWARE NOT ONLY OF SHARKS

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Title of Case(s)

SURFERS: BEWARE NOT ONLY OF SHARKS

Background

Shewanella spp. are saprophytic bacteria that are part of the marine microflora in warm climates and are rarely pathogenic. However, Shewanella spp. infections are being increasingly reported and being implicated as an important and developing cause of maritime-associated disease.

Case Presentation Summary

A previously healthy, fully immunized 9-year-old boy with fever and a swollen right thigh came to the ER. He had injured his right leg 4 days earlier when he was surfing. He came to a local hospital ER where the wound was cleaned and sutured. The patient was discharged home with a diagnosis of minor wound. Dressing changes were performed the next two days but local heat and swelling over his right thigh soon developed, followed by fever and malaise. He received cefuroxime for the next 2 days but finally he came again to a tertiary hospital.

Upon arrival, he was acutely ill. His body temperature was 39. Physical examination showed an extremely swollen right thigh with edematous, dark red to purple-colored skin, with hemorrhagic bullae. Under the suspicion of necroziting fasciitis and septic shock, IV cefepime and amikacine were given after blood cultures were drawn. An urgent surgical procedure was performed, including fasciotomy and extensive debridement of the devitalized tissue. A vacuum system was placed. The patient had a favorable clinical response. Blood cultures and tissue samples both yielded Gram-negative rods, which were eventually typed as putrefaciens by ID 32 GN (bioMerieux, Vitek, Inc-Hazelwood, MO, USA)

Learning Points/Discussion

Shewanella species are frequently present in sea water and affect mostly the immunocompromised or elderly with altered skin. Given the possible catastrophic consequences, without early intervention, a review about the management of soft tissue infections caused hypothetically by shewanella may be of importance.
Health care associated infections (HCAI) in pediatric age represent an important cause of morbidity and are associated with long-term hospitalization and increased use of broad-spectrum antibiotics.

Objective: analysis of HCAI on a general pediatric ward of a Pediatric Hospital.

Methods

Prospective observational study of patients between the ages of 1 month and 18 yo, registered in the system of epidemiological surveillance of nosocomial infections (SESNI), hospitalized in the general pediatric from 1st January 2015 to 31st December 2017.

Results

The SESNI registered 117 patients, of which 61 were confirmed HCAI. The median age was 19 months (1 month-18 years), 54% female. Median days of hospitalization were 14 (4-407 days), 39 (61%) patients with an underlying disease. There were 89 episodes of HCAI (12 patients with >1 episode), corresponding to 1.5 episodes/patient with a prevalence of 0.74%. 30 (34%) were respiratory infections and 20 (22%) gastrointestinal infections. Bacterial infections corresponded to 49 (55%) episodes, viral infections to 38 (43%) episodes and 2 were fungal infections. An agent was isolated in 67 (75%) episodes, being rotavirus the most frequent viral agent (11 episodes), followed by respiratory syncytial virus (RSV) in 10 episodes; the most frequent bacterial agent was Klebsiella pneumoniae, 6 episodes (2 ESBL), followed by P. aeruginosa in 5. Of all the episodes, 54 (61%) required antibiotherapy and vancomycin were the most used (16 episodes).

Conclusions

In this study, the prevalence of HCAI were 0.74%, and the most prevalent were respiratory and gastrointestinal infections. Rotavirus and RSV are important nosocomial agents in pediatric wards. Bacterial infections caused the majority of HCAI, with predominance of Enterobacteriacea, 2 ESBL strains, leading to the use of large spectrum antibiotherapy. A considerable number of chronic patients with long admissions had >1 episode, which shows that these patients need special care and additional prevention measures.
03A. SCIENCE: SEVERE BACTERIAL INFECTIONS

SEROGROUP Z INVASIVE MENINGOCOCCAL DISEASE – FIRST CASE REPORT IN PORTUGAL

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Title of Case(s)

SEROGROUP Z INVASIVE MENINGOCOCCAL DISEASE – FIRST CASE REPORT IN PORTUGAL

Background

First described in 1961, Neisseria meningitidis serogroup Z disease reports in the literature are scarce being mostly associated with carriage.

Case Presentation Summary

A nine-year-old boy with a history of type 1 diabetes and hypothyroidism presented to the pediatric emergency room with fever and a rash. Physical examination revealed slurred speech, neck stiffness and a purpuric rash. Blood tests and lumbar puncture were performed and prompt empirical treatment with ceftriaxone was initiated in the first hour. Cerebrospinal fluid was clear with 820 white cells and the gram stain showed gram-negative diplococci bacteria. Approximately six hours after admission the patient evolved with hypotension resistant to fluid resuscitation that improved with dopamine administration. The patient presented a very favorable clinical evolution without perfusion deficits and shock reversion 12 hours after. Despite moderate unilateral knee arthritis and mild headaches, he was discharged 7 days later without any sequels. Serogroup Z and clonal complex sequence type ST-cc865 were achieved by whole-genome sequencing including in silico determination of serogroup and MLST.

Learning Points/Discussion

The authors describe the first case of Neisseria meningitidis serogroup Z in Portugal and one of the few reports of invasive disease in the literature. Adequate surveillance is of major importance and should be warranted as the emergence of new virulent pathogenic strains raises concerns about rare meningococcal serogroups becoming epidemic.
Background

Fever is one of the most common reasons why parents seek medical attention for their children. Only in 5-15% of cases the reason of fever is serious bacterial infection. The term “fever phobia” was first used in 1980 [Schmitt, 1980] to describe what parents feel if their child has fever. “Fever phobia” leads to inappropriate fever management practices and immediate seeking for medical attention. International recommendations for parents advise to evaluate the child’s overall condition and use antipyretic agents only if the child appears distressed.

Methods

The parents of children who had presented to the Emergency Department (ED) of Children’s Clinical University Hospital with fever were recruited on voluntary basis in 2017. The data were collected via multiple choice survey and qualitative semi-structured interviews.

Results

76 patients were recruited in this study. 94.5% of parents believed there is a dangerous level of temperature. 60.3% thought that temperature is a sign of serious illness. 54.2% were seeking medical attention within the first 24 hours. 50% use antipyretic agents at a temperature of 38°C. During qualitative interviews the following issues were identified:

- Overwhelming sense of duty to decrease the temperature
- Fear that their child might die or be permanently harmed because of fever
- Inappropriate fever management practices
- Expecting emotional support from medical staff aside from medical advice.

Conclusions

There is still “fever phobia” in Latvia among the parents. The main criterion for using antipyretic agents is the measured value of temperature, not the child’s overall condition. Parents tend to seek medical attention at a very early stage of illness. Additional educational work from doctors is needed to reduce the parental fear of fever and to enhance ability to notice additional symptoms aside from fever.
PECULIARITIES OF MENINGOCOCCAL MENINGITIS IN EARLY DIAGNOSIS OF DISEASE IN EARLY AGE CHILDREN

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Title of Case(s)

Peculiarities of meningococcal meningitis in early diagnosis of disease in early age children

Background

Bacterial meningitis continues to be an important cause of mortality and morbidity in neonates and children throughout the world. Bacterial meningitis is one of the top ten causes of death associated with infectious diseases in children. Identifying which children are most likely to have bacterial meningitis is the main task of early diagnosis of disease. Increase the effectiveness of early diagnosis of meningitis in children can prevent severe serious complications and long-term consequences.

Case Presentation Summary

We analyzed 54 cases of meningococcal meningitis in children treated in the Regional Pediatric Hospital (Chernivtsi, Ukraine). The average age of the patients was 2.9±0.7 years, boys (63%), children from organized groups (80%) and patients living with siblings (60%) were prevailed. The most frequent complaints before hospitalization were febrile hyperthermia (89%), decreased appetite (85%), vomiting (78%) and weakness (78%). Most of the children were hospitalized in severe (63%) and extremely severe condition (18%), which led to primary hospitalization in the PICU in 70% cases. Incomplete meningeal symptoms were described, in particular, stiffness of neck was verified in 78% cases, other meningeal symptoms were observed only in 23% patients. Half of the children had signs of one of the types of hyperesthesia, 33% of the patients had signs of microcirculation disturbance. Among these symptoms, fever (3.1±0.3 days) and meningeal symptoms (2.3±0.3 days) were observed the longest. Changes in the clinical blood counts reflected an inflammatory reaction (leukocytosis) in 88% children and anemia in 52% patients.

Learning Points/Discussion

An incomplete meningeal symptom complex with signs of hyperesthesia and cerebrospinal hypertension, leukocytosis and anemia were informative for early diagnose of the meningococcal meningitis in early age children.
INFECTIONOUS COMPLICATIONS OF NON-SURGICAL MANIPULATION OF BILE DUCT AND ADHERENCE TO PROPHYLACTIC PROTOCOL

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Title of Case(s)

INFECTIONOUS COMPLICATIONS OF NON-SURGICAL MANIPULATION OF BILE DUCT AND ADHERENCE TO PROPHYLACTIC PROTOCOL

Background

For bile duct non-surgical manipulation, our local protocol indicates peri-operative antibiotic prophylaxis (PAP) with 24 hours of endovenous piperacillin-tazobactam. Our purpose is to describe the incidence and characteristics of its infectious complications, to evaluate their association with specific risk factors (common bile duct absence, liver transplantation) and the adherence to the PAP protocol; as a part of our Paediatric Antibiotic Stewardship Program.

Case Presentation Summary

Epidemiological, clinical and microbiological data were collected from all consecutive episodes of bile duct non-surgical manipulation in paediatric patients (≤ 18 years) performed in our center in a 9-years period (from 2009 to 2017). We analyzed 74 episodes in 23 patients.

Median age was 4 years (ICR 1,3-7), 56% female. Biliary atresia was the commonest disease (36.5%). Regarding to risk factors, 53 episodes (61%) occurred in liver-transplanted patients and 54 (73%) in common bile duct absence. There were 19 infectious complications (25.6%), mainly in the first 24 hours: 4 fever without source, 8 sepsis and 7 cholangitis. Blood cultures were positive in 6/18 and bile cultures in 12/13 (mainly Gram-negative bacilli). Thirty episodes were performed under antibiotic treatment due to a previous infection. PAP was correct in 21/44 episodes (48%).

Learning Points/Discussion

Adherence to PAP protocol needs to be optimized in order to evaluate its usefulness in non-surgical manipulation of bile duct, since there is a significant number of infectious complications after these procedures, mainly in the first 24 hours. Neither prophylaxis nor previous antibiotic treatment seem to be effective in preventing them, so bile duct manipulation should be limited to accurate indications. Liver transplantation and common bile duct absence seem to increase this risk.
AN UNUSUAL TROPICAL BORRELIOsis DIAGNOSIS IN A TEENAGER COMING BACK FROM SENEGAL

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Title of Case(s)

An unusual tropical borreliosis diagnosis in a teenager coming back from Senegal

Background

Tick-borne relapsing fever (TBRF) is a bacterial disease due to different species of Borrelia, transmitted by a tick. One of them Borrelia crocidurae is endemic in West Africa. Limited cases of TBRF were reported in Europe, all of them were imported disease. We report a case of B. crocidurae infection with malaria-like symptoms in a teenager coming back from Senegal.

Case Presentation Summary

A 15-year-old child was referred to our Paediatric Emergency Unit four days after he return from Senegal. His symptoms were fever (40 °C), recurrent headaches and vomiting, the rest of the examination was normal. Biological investigations showed a mild thrombocytopenia of 101 G/l, low prothrombin time 56%, CRP was 40 mg/l and PCT 17 mg/l. Cerebrospinal fluid analyses were normal. Quantitative Buffy Coat (QBC) excluded the diagnosis of malaria, however blood smear showed few forms of spirochaetae. The presence of Borrelia crocidurae was identified after amplification and sequencing of 16S rRNA gene from blood sample and confirmed by the National reference centre of Borreliosis. The patient was given doxycycline 100mg b.i.d for 10 days, resulting in apyrexia 24 hours later and successful treatment without neurologic complication.

Learning Points/Discussion

Foreigners visiting endemic African countries are concerned by TBRF which is often misdiagnosed as malaria. Direct microscopic visualization of borreliae in blood sample obtained from a febrile patient was unusual, as the number of circulating spirochaeta decreased rapidly during the episodes of fever. Amplification of the 16S rRNA gene using PCR is the most sensitive method and provides a rapid diagnosis. Early introduction of treatment helps to prevent neurological complications. Relapsing borrelioses should be incorporated to all tropical fever syndromic laboratory kits.
WHEN PULMONARY TUBERCULOSIS REQUIRES RIFAMPICIN THERAPEUTIC DRUG MONITORING: A CASE REPORT

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Title of Case(s)

WHEN PULMONARY TUBERCULOSIS REQUIRES RIFAMPICIN THERAPEUTIC DRUG MONITORING: A CASE REPORT

Background

Tuberculosis remains a major public health issue with 6.3 million new cases reported in 2016, 7% of these in children. Although treatment for fully sensitive tuberculosis is well established, treatment failures are recognised, and optimisation of therapy needs to be considered on an individual basis. We report a case of a treatment failure in a teenager.

Case Presentation Summary

A 14 years-old Somalian girl presented with a six week history of fever, productive cough, night sweats and vomiting, not responding to amoxicillin-clavulanate and clarithromycin. A chest radiography showed an opacity in the left lingual and upper lobe. The sputum smear resulted positive for acid fast bacilli and grew fully sensitive Mycobacterium tuberculosis (TB). She was started on quadruple TB therapy at standard doses. After initial improvement, at six weeks of therapy she represented with hematemesis and hand sweats. Her chest radiography showed disease progression. Directly-observed therapy (DOT) was initiated but the urine colour did not turn orange. Therapeutic drug monitoring for rifampicin was requested and resulted very low.

Learning Points/Discussion

A patient not responding to anti-TB treatment should be evaluated for poor adherence, drug-resistance, complication of pulmonary TB and lung disease from other causes. Rifampicin is one of the key drugs in the treatment of tuberculosis and optimising the dose is essential for successful treatment.
01C. SCIENCE: ANTIBIOTIC STEWARDSHIP AND INFECTION CONTROL

REAL WORLD DATA SHOWS INADEQUATE USE OF ANTIBIOTICS AND LACK OF IMPACT OF PNEUMOCOCCAL CONJUGATE VACCINE IN ACUTE OTITIS MEDIA IN SPAIN

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Background

To describe Acute Otitis Media (AOM) in children aged 4 years or less and antibiotic prescription for AOM in vaccinated and not vaccinated with Pneumococcal Conjugate Vaccine (PCV).

Methods

Retrospective cohort of children 2 months to 5 years of age, born between 2008 and 2013 in Valencia. Data was obtained from the Valencian health electronic databases (covering over 95% of the population). All databases were linked through a unique personal identification number. AOM diagnoses (CIE-9 381 and 382) and antibiotic prescriptions were retrieved from the primary care databases. A child was considered vaccinated when at least one dose of the vaccine was registered prior to diagnosis, and completely vaccinated if received two doses at age 6 months and a booster after 12 months of age.

Results

From a cohort of 480,558 children, 382,853 cases of OMA were diagnosed in 217,063 children (45.17% of the study cohort). 60.2% of the children received at least one dose of PVC vaccine (44.7% completed vaccination). 53.33% of the completely vaccinated were diagnosed of AOM and 36.23% in non-vaccinated. Antibiotic was prescribed in 74.33% of the AOM episodes, with no difference between vaccinated and non-vaccinated. Amoxicillin-clavulanate was the most prescribed antibiotic (31.02%) with no difference between vaccination groups. No change in the antibiotic prescription occurred by calendar year.

Conclusions

There are both a high incidence of AOM diagnosis in children aged 4 years or less in Valencia and a clear inappropriate antibiotic prescription for AOM. These drive toward a lack of impact of PCV vaccination in antibiotic prescriptions.
Influenza-related myocarditis and importance of prompt antiviral treatment

Background

Severe influenza infection represents a leading cause of global morbidity and mortality. Although influenza is primarily considered a viral infection that results in pathology limited to the respiratory system, clinical reports suggest that influenza infection is frequently associated with a number of clinical syndromes that involve organ systems outside the respiratory tract. Herein we describe a girl presented with myocarditis and pericardial effusion due to influenza infection.

Case Presentation Summary

A 13-year-old girl with no underlying disease admitted to hospital with complaints of rhinorrhea, fever, myalgia for 3 days and syncope. Tachypnea, dispnea, tachycardia and hypotension, rales on auscultation were noticed. Chest radiography showed cardiomegaly and bilateral paracardiac infiltration. Echocardiomegaly revealed cardiomegaly, pericardial effusion, ejection fraction of 45%. Blood cardiac enzymes were increased. Pericardiocentesis was done and 150 ml exudative fluid was cleared. PCR for viral agents were sent from pericardial fluid. Due to pneumonia, myocarditis and pericardial effusion, sulbactam ampicillin, vancomycin, oseltamivir were started after blood cultures and nasopharyngeal respiratory viral panel were taken. She had no vaccination against influenza. Influenza A (H1N1)pdm09 was isolated from both nasopharyngeal and pericardial fluid specimens. She was discharged at the 10th day of hospitalization after full-recovery of cardiac functions.
Clinically diagnosed myocarditis, based on a combination of symptoms, elevated cardiac enzymes, and echocardiographic findings, has been reported in approximately 0.4%-13% of hospitalized adult patients with documented influenza. Additionally, studies from vaccine and antiviral therapeutic trials also highlight an important association and suggest that specific pharmacologic strategies may prevent or reduce the risk of many of the cardiovascular complications of influenza. Influenza must be kept in mind in the differential diagnosis of especially unvaccinated patients presented with myocarditis in the influenza season.
RESPIRATORY VIRUS DETECTIONS USING MULTIPLEX MOLECULAR TESTING IN A TERTIARY-CARE HOSPITAL IN SPAIN: EPIDEMIOLOGY AND CLINICAL DATA IN A YEAR COHORT

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Background

Respiratory infections are the main cause of hospitalisation in paediatric hospitals. Different viruses lead to similar clinical pictures. This study analyse the epidemiology and clinical data of respiratory infections in the molecular era, using multiplex real-time reverse-transcription polymerase chain reaction (RT-PCR).

Methods

Descriptive retrospective cohort study of respiratory-related admissions in <14-year-old children tested for respiratory viruses by multiplex RT-PCR in a tertiary-care hospital in 2016-2017 epidemic season. The test was performed in nasopharyngeal swab/aspirate, bronchoalveolar lavage or tracheal aspirate. Hospitalisation-related infections were excluded. Epidemiologic, diagnostic and therapeutic characteristics were collected. Statistical analysis by subgroups was performed.

Results

Over the study period, 144 patients were included. Median age of the patients was 20 months (IQR 14-43.5). Lower respiratory tract infections were present in 108. Median length of hospital stay in survivals was 9 days (IQR 6-15). The positivity rate of virus detection was 84.72%. 52 samples had co-detections. The more frequently detected virus was Rhinovirus (51.4%) followed by RSV (23.6%) with a seasonal distribution (Figure 1). Oxygen therapy was applied in 75% of children -along median 7 days (IQR 4-11.75). Overall, 53.5% received short-acting β2-adrenergic agonists as bronchodilator, 22.2% epinephrine and 24.3% hypertonic saline. Intensive care was required in 34 cases -median length of stay 9 days (IQR 4-11). In subgroup analysis, Rhinovirus detection cases were significantly milder, while Metapneumovirus and RSV cases had longer stay and oxygen. Four deceases (3.6%) were registered (two patients had previous conditions).
Conclusions

In our study, human Rhinovirus was the most frequently detected, with a less severe course. This result could support the bystander hypothesis. RSV and Metapneumovirus related-cases were more severe, suggesting bigger efforts over these infections. Multiplex identification of viruses could identify future strategies of prevention.
The burden of paediatric sepsis in Gipuzkoa

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Background

Sepsis is the leading cause of death in children worldwide. Until recently no universal vaccine existed against meningococcal B serogroup, one of the leading bacteria involved in children sepsis. The aim of this study is to analyse the clinical course, epidemiological characteristics and sequela of children with sepsis in Gipuzkoa, Spain.

Methods

Retrospective review of all children aged under 14 years admitted to our paediatric intensive care unit at Donostia University Hospital with confirmed or probable diagnosis of sepsis, severe sepsis and septic shock between January 2003-December 2017

Results

A total of 214 cases were identified most of them occurring in previously healthy children (82.8% (n=177)). The incidence ranges throughout the years studied between 20 and 9-10 the past two years. The average age was 23 months (Range 0.35-204) with 27% (n=58) of the cases occurring in infants below 1 year. 69% (n=149) were laboratory confirmed cases The most frequently isolated pathogen was Neisseria meningitidis n=87 (58%) (B-serogroup 74, C-serogroup 7, non-serogrouped 6 cases) The most prevalent trigger of sepsis were bloodstream infection (44%) Central nervous infections 27 (18%) abdominal infections 15 (10.1%) pneumonia 15 (10.1%) Kidney infection 6 (4%). The diagnosis was sepsis in 85.1% and sepsis+meningitis in 32 children 14.9%. Mean hospital length of stay was 3 day (1-126). 16 patients (7.4%) were exitus. Exitus occurred more frequently in children aged more than 1 year (5.4%12.3%;p<0.05). 7% of the survivors (n=15) were discharged with any kind of physical sequelae.
Conclusions

Despite the decreased incidence of sepsis over the past two years, sepsis remains a life threatening condition with substantial morbidity and mortality. Evidenced-based recommendations regarding the acute management of sepsis and septic shock are the first step toward improved outcomes for this important group of critically ill patients.
SEVERE PANTON VALENTINE LEUKOCIDIN METICILLIN-SENSITIVE STAPHYLOCOCCUS AUREUS INFECTION: A CASE REPORT

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Title of Case(s)
SEVERE PANTON VALENTINE LEUKOCIDIN METHICILLIN-SENSITIVE STAPHYLOCOCCUS AUREUS INFECTION: A CASE REPORT

Background

Panton Valentine Leukocidin S. aureus (PVL-SA) has repeatedly been associated with more severe disease than PVL negative S. aureus infections, although controversy exists as to whether PVL-toxin is the major virulence determinant. Surveillance studies in England found PVL-SA in less than 5% of S. aureus related disease, and less than 2% of S. aureus bacteraemias.

Case Presentation Summary

A previously well two-years-old girl presented in poor clinical conditions with a 5 days history of fever and swollen left eye. She was diagnosed with periocular cellulitis and was started on intravenous ceftriaxone and metronidazole. A brain MRI was also performed confirming the diagnosis. Her blood culture grew fully sensitive S. aureus. A cardiac ultrasound revealed no abnormalities. However, she developed sixth nerve palsy after five days of treatment and an urgent brain CT showed a small extra-axial collection in the posterior fossa, and septic emboli in both lungs. Repeated brain MRI reported a cavernous sinus thrombosis. Therapy was switched to flucloxacillin, and when PVL was reported, rifampicin was added. Once stable, using an elastomeric device for flucloxacillin delivery, the patient was discharged under the supervision of our paediatric outpatient parenteral antimicrobial therapy team (p-OPAT); she required a prolonged intravenous treatment course of three months and completed her antimicrobial treatment with a further month of oral amoxicillin-clavulanate. The patient made a full recovery.

Learning Points/Discussion

This case illustrates that PVL-MSSA can cause very severe invasive disease in children. Clinicians and laboratories should routinely submit isolates for PVL from children with invasive MSSA disease, because this would improve the knowledge of the epidemiology of the disease. Optimal antimicrobial combination and length of therapy is not well established.
PATHOGENIC ROLE OF RESPIRATORY VIRUSES IN CHILDREN WITH HUMORAL IMMUNODEFICIENCIES


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Background

Patients with Humoral Immunodeficiencies (H-ID) have recurrent respiratory infections resulting in significant morbidity and mortality, but the role of respiratory viruses is not well known.

The objective was to describe viral respiratory infections in H-ID children and their relationship with clinical symptoms and pulmonary function.

Methods

Prospective observational single-center study in H-ID children during 1 year. For each patient (and a family member as control) a nasopharyngeal aspirate for multiple respiratory virus detection by PCR was taken every 3-4 weeks. Symptoms questionnaires were filled biweekly for patients and controls. Spirometry, sputum culture, IgG levels, FBC, C-reactive protein and ESR were also performed in patients.

Results

Fifteen patients (4 females) with a median age of 12±5.1 years (2 with <5yo) with the following diagnoses were enrolled: X-linked(4) and Autosomic recessive(1) Agammaglobulinemia, B lymphopenia after HSCT(3)/Rituximab(1) and unknown cause(1), CVID(2), CTLA-4 haploinsufficiency(1), Hyper IgE syndrome(1), PI3K-δ syndrome(1).

Sixty-six episodes were analyzed, identifying viruses in 18 (27.3%): rhinovirus(12), adenovirus(3), influenza-A(1), RSV(1) and coinfection rhinovirus-adenovirus(1). In family members 57 samples were collected, and viruses were identified in 12 (21%).

In the 18 episodes with viral identification: bacteria were isolated in 3/5 of sputum cultures (H.influenzae[2], S.pneumoniae/P.aeruginosa[1]), 15.4% (2/13) had IgG levels <600mg/ml. During
viral infection, 89% (16/18) presented symptoms and 70% spirometry alterations, 44% (8/18) received antibiotic treatment, 22% (4/18) bronchodilators and 22% required hospital admission.

Age <5 years(p=0.001), absence of bacteria in sputum(p=0.036), spirometry alterations(p=0.007), antibiotic treatment (p=0.011) and hospital admission (p=0.001) were statistically significant in relation to viral isolation; whereas absence of symptoms(p=0.047) was associated with negative viral PCR.

Conclusions

Pediatric H-ID patients present, despite Ig replacement therapy, recurrent and significant respiratory viral infections that cause respiratory symptoms, altered pulmonary function, need for antibiotics and hospital admission.
EFFECTIVENESS OF A DEDICATED HEPATITIS B IMMUNISATION SERVICE IN THE PAEDIATRIC DEPARTMENT IN A DISTRICT GENERAL HOSPITAL IN SOUTHEND, UK - RE-AUDIT

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Background

Hepatitis B can be transmitted vertically to newborns and has a 90% chance of becoming a chronic disease. 95% of chronic carriage can be prevented by appropriate vaccination. Our paediatric department is exceptional in following up babies after hepatitis B vaccination. Eligible babies are seen in immunisation clinic till serology blood results confirm appropriate antibodies response. This re-audit’s aim was to measure performance in hepatitis B vaccination coverage against local guidelines for antenatal and postnatal care of babies who received vaccination. Results were compared with previous audit (04/2006-12/2008).

Methods

Retrospective cohort review of neonates born between 01/01/2014-01/03/2016 who received hepatitis B vaccination before discharge as per local policy. Data identified by review of positively screened mothers from antenatal screening and cross-checked with data from immunisation paediatric nurse specialist. Patients’ records were subsequently reviewed whether doses and serology blood tests were performed as per protocol.

Results

Total of 25 neonates received hepatitis B vaccination before discharge (01/01/2014-01/03/2016). 100% of all babies born to hepatitis B positive mothers received first dose of vaccination as inpatient. 93.75% of babies born to hepatitis B positive mothers received vaccination in 24 hours. 92% of all eligible babies received 2nd dose, 84% received 3rd dose and 40% received 4th dose. 81% of eligible patients had serology tested. 2 babies (8%) were missed from follow up.

Conclusions

Results showed that designated immunisation nurse increases likelihood of completion of the immunisation program. It is essential to use best efforts to reduce risk of chronic hepatitis B in paediatric population. From 2017 hepatitis B vaccination (Hexavalent DTaP/IPV/Hib/HepB) was introduced to childhood primary immunisation schedule in UK. This will improve coverage and reduce number of babies requiring additional follow up in immunisation clinics.
07A. EDUCATION: HIV MANAGEMENT DECISIONS

VISCERAL INVOLVEMENT AS INITIAL MANIFESTATION OF AIDS-RELATED KAPOSI’S SARCOMA

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Title of Case(s)

VISCERAL INVOLVEMENT AS INITIAL MANIFESTATION OF AIDS-RELATED KAPOSI’S SARCOMA

Background

Kaposi’s Sarcoma (KS), is more likely to be developed in HIV-infected patients, typically with low CD4 cell count and high HIV viral load. Oral cavity, gastrointestinal tract, and respiratory system are the most frequent sites of non-cutaneous disease. Although visceral involvement as initial manifestation of KS is relatively uncommon, pulmonary involvement can be its first manifestation occurring in the absence of mucocutaneous disease in 15%. Mainstay of treatment is antiretroviral therapy (ART). When chemotherapy is indicated, pegylated liposomal doxorubicin is recommended as first-line treatment.

Case Presentation Summary

17-year-old male, Guinea-Bissau native. Observed by weight loss >40%, cough, night sweating and fatigue, coincident with moving to Portugal 8 months earlier. On observation: caquetic, digital clubbing and decreased vesicular murmur on pulmonary auscultation. No dyspnea, hypoxemia or mucocutaneous lesions. Chest X-ray showed bilateral cottony infiltrate. Pursuant to investigation, the diagnosis were: HIV-1 infection (C3 stage CDC Atlanta) with CD4+ 24 cell/mm3 and viral load 136,000 copies/mL; chronic hepatitis B with normal liver function. Initiated ART with emtricitabine/tenofovir and dolutegravir. Hypothesis of pulmonary tuberculosis excluded due to negative IGRA and cultural examinations on bronchoalveolar samples. Chest CT-scan with bilateral nodal images raised fungal pneumonia concerns, thus initiating voriconazole, replaced by liposomal amphotericin B in the absence of improvement. Transbronchial lung biopsy was performed, demonstrating KS infiltration with herpesvirus 8 identification. Upper digestive endoscopy and colonoscopy were conducted, with multiple infiltrative lesions. Began chemotherapy with pegylated liposomal doxorubicin, which maintains.

Learning Points/Discussion

KS is an AIDS-defining disease and should be considered in HIV-infected patients, with severe immunosuppression and pulmonary findings even without mucocutaneous disease. Radiological findings are variable. ART changed the course and incidence of KS and its visceral involvement.
KINGELLA KINGAE BACTEREMIA IN ADOLESCENT WITH CONGENITAL HEART DISEASE – CASE REPORT
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Title of Case(s)
KINGELLA KINGAE BACTEREMIA

Background

Kingella kingae is being increasingly recognized as an important invasive pathogen in children, causing bacteremia, osteoarticular infections and endocarditis mainly in infants and younger children. However, if underlining chronic diseases are present, it may occur in older ages.

Case Presentation Summary

A 16-year-old adolescent with congenital heart disease (pulmonary atresia with ventricular sept defect and major aorto-pulmonary collateral arteries [MAPCA's], submitted to corrective surgery with implantation of biologic pulmonary valve 1 year earlier), was admitted with a 4-day history of intermittent headache, associated with epigastric pain, diarrhea, vomiting, tiredness and fever with shivering. On examination, she was febrile, presenting with systolic heart murmur, right hypochondrium and epigastric pain and dental cavity with inflammatory signs in a lower molar. Laboratory tests showed neutrophilic leukocytosis, thrombocytopenia, elevated C-reactive protein (28,46 mg/dL) and erythrocyte sedimentation rate (55 mm/h). Chest radiography and urinary test were normal. ECG showed the already known right bundle branch block. Stool and blood cultures were obtained and IV ceftriaxone 4g/day was started. Kingella kingae was isolated in the blood culture. Transthoracic echocardiogram evaluation was undertaken, not showing any signs of vegetation. The patient showed clinical and analytic improvement, being apyretic since the 8th day of antibiotics. Second blood culture obtained at that time was negative. She completed 14 days of systemic antibiotic therapy and was discharged clinically well.

Learning Points/Discussion

The authors would like to highlight the non-specific symptoms associated with Kingella kingae bacteremia and stress the need for echocardiographic evaluation to exclude endocarditis, once it has implications on the duration of therapy. The gold standard for this evaluation is transesophageic echocardiogram, however it is more invasive and with clinical improvement, transthoracic echocardiogram may be a valid alternative.
Background

Gaps in knowledge about the use of antimicrobials in hospital neonates must be addressed to inform the implementation and monitoring of effective stewardship programmes in neonatal intensive care units (NICU) in Brazil.

Aim: To describe antimicrobial use in NICUs.

Methods

The GARPEC project aims to implement standardized web-based surveillance methods for antimicrobial use in hospitalised children and neonates worldwide. This study was a part of the GARPEC project to measure antimicrobials use in neonatal units through successive one-day cross-sectional point prevalence surveys (PPS) in Brazil.

Results

We followed 70 neonates, totaling 142 prescriptions, in 2 NICUs of Rio de Janeiro state, Brazil. 58% (41/70) of patients were male and 24% (17/70) received invasive ventilation. Community acquired infections were the indication for antibiotic use in 39/59 (66%) patients. Sepsis was the most common diagnosis reported and present in 47% (33/70) of neonates. The most common antibiotics prescribed were gentamicin (40/142, 28.2%), ampicillin (21/142, 14.8%) and cefazolin (18/142, 12.7%). Prescribing levels were low for vancomycin (8/142, 6%), meropenem (9/142, 6%), and cefepime (3/142, 2%).

Conclusions

This study demonstrates that PPS can be implemented to monitor antimicrobial use in NICU. The use of broad-spectrum antibiotics was not common in our NICU.
HERPES ZOSTER ENCEPHALITIS IN AN IMMUNOCOMPETENT 8 YEAR-OLD GIRL WITH DOCUMENTED VARICELLA DURING INFANCY

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Title of Case(s)

Herpes Zoster Encephalitis in an Immunocompetent 8 year-old Girl

Background

Varicella Zoster virus (VZV) may be associated with neurologic complications in children, such as febrile convulsions, encephalitis, stroke or sinus thrombosis. Herpes Zoster (HZ) is a reactivation of VZV in a person with previous acute VZV infection or vaccinated with life attenuated vaccine. While in adults, HZ encephalitis is a recognised complication, it is rarely described in children.

Case Presentation Summary

We present a case of a VZV immune 8-year-old girl with a painful vesicular skin eruption in a C2-C4 distribution, progressive hemiplegia and hemi-sensory syndrome. CT showed an area of hypodensity in the contralateral thalamus. CSF analysis revealed a high lymphocyte count and MRI of brain and spine demonstrated multiple lesions of T2 hyperintensity. She was treated with high dose acyclovir, steroids and intravenous immunoglobulin. She received intense physio- and occupational therapy. Within 2 weeks of initial presentation, she has regained over 75% of her function.

In view of the rash with a typical dermatomal distribution, multifocal MRI findings and time relationship between the rash and onset of neurologic signs, she was diagnosed with HZ encephalitis. CSF PCR testing for zoster was negative.

Learning Points/Discussion

In jurisdictions with universal varicella vaccination, decrease in the incidence of acute CNS complications in children is reported. However, mass introduction of VZV vaccine remains controversial, because of feared increase of the age and severity of primary varicella and of the incidence of Herpes Zoster.

This is a rare presentation of HZ encephalitis in an immunocompetent child with a documented episode of primary varicella during infancy. We reviewed literature available on CNS complications of Herpes Zoster, their risk factors, diagnosis, management and outcomes in immunocompetent vaccinated and unvaccinated children.
Title of Case(s)

Haemorrhagic necrotic brain lesions and irreversible brain damage caused by Serratia Marcescens in a premature neonate.

Background

Serratia marcescens is a rare cause of sepsis in premature neonates and neurological spread can be ominous.

This case report relates to a very low birth weight neonate born at 28-weeks gestation who developed the rare condition. The report will discuss details of the cause, pathophysiology, diagnostic and therapeutic management.

Case Presentation Summary

A baby girl was born by planned caesarian section at 28 weeks gestation to allow her mother to proceed to high strength chemotherapy for an aggressive carcinoma of the breast. At the time of delivery, the baby girl was in a stable condition with initial respiratory distress requiring surfactant and intubation and subsequent Continuous Positive Airway Pressure. On day 6 of life there was a sudden deterioration in the health of the neonate and she was treated with antibiotics for suspected sepsis. There was subsequent deterioration over the following hours which resulted in severe respiratory acidosis requiring her to be intubated and ventilated.

A cranial ultrasound was used which identified bilateral widespread intracerebral bleeding. Repeat ultrasound after twenty four hours demonstrated widespread damage with liquefaction of the original blood.

Blood cultures were taken at the time of deterioration which were reported as positive for Serratia marcescens. Antibiotics were altered but the baby girl was noted to have a very poor prognosis and redirection of care was agreed upon.

Learning Points/Discussion

Clinical signs are often non-specific when patients are septic form Serratia Marcescens. It is important that high risk neonates have the correct diagnostic measures including the use of cranial ultrasound by the neonatal cot and aggressive antibiotic therapy.
Background and Objective

The administration of parenteral fluids is a key recommendation in paediatric sepsis management, although not supported by strong scientific evidence.

A large randomised controlled trial from Africa (FEAST trial) showed that rapid fluid resuscitation in children increased mortality by 3.3%, compared with no fluids. The reasons for these unexpected results are unclear and subject to debate.

We reviewed European paediatric sepsis guidelines to compare recommendations regarding use of fluids and examine the impact of the FEAST trial on these recommendations.

Methods

A literature review of Medline, Embase, and SIGN was performed, searching for European guidelines. We also included guidelines from the USA and the World Health Organization (WHO) to broaden the comparison. Websites of paediatric associations were also searched, and paediatricians from included countries contacted to obtain outstanding guidelines.

Guidelines’ quality was assessed using the AGREE-II criteria. The levels of evidence used to inform recommendations were converted to the Oxford Levels of Evidence for comparison.

Learning Points Discussion

• 13 guidelines were identified. 10 were published after the FEAST trial; of these 4/10 guidelines mentioned the FEAST trial
• 10 guidelines were from Europe, one from the USA, one from the WHO, and one from the Surviving Sepsis campaign
• The AGREE quality scores varied widely between guidelines, but the levels of evidence informing recommendations were similar
• All guidelines recommended immediate administration of fluids. 10/13 guidelines recommended a first bolus of 20 ml/kg, 3/13 guidelines considered restrictive fluids in specific circumstances, and 6/13 recommended the use of blood gas and lactate to guide management.
• The results of the FEAST trial have not led to changes in recommendations regarding fluids administration in guidelines published after the trial, except in one guideline.
Non-tuberculosis mycobacterium (NTM) is opportunistic infection with difficult eradication for the cystic fibrosis (CF) patients. NTM can be acquired at an early age and, also after lung transplantation. Accurate identification is a key point of successful treatment, and prevention of severe complications. The aim of the present study was to elaborate molecular-genetic approaches to culture-independent identification of NTM and to eradication control.

Methods

Four CF patients (13-36 years old) were under the long-term monitoring. Sputum of the patients was collected, and analyzed by hsp65 gene amplification and sequencing. Microbiome was identified by high-throughput sequencing of 16S rDNA amplicons.

Results

NTM species identification demonstrated that two patients were infected with *M. abscessus*, the third patient – with *M. avium*, and the fourth – with *M. chelonae*. One patient with *M. abscessus* has died at the age of 19. The second patient was successfully treated, however shortly thereafter he was infected with *Pseudomonas aeruginosa*. Two last patients received multi-component therapy resulted in NTM eradication, it was confirmed by high-throughput sequencing of microbiome. These two patients have *cfr* gene mutations subjected to Ivacaftor treatment, which improved lung function significantly. Several weeks late microbiome analysis revealed the increase in the proportion of different Proteobacteria, especially Sphingomonadaceae representatives, and the trace amount of Mycobacteria. It was the result of the improved lung drainage by Ivacaftor.

Conclusions

The use of the two genes (16S rDNA and hsp65) together improves the NTM species identification. High-throughput sequencing of 16S rDNA amplicons can be useful for monitoring patient’s microbiome and treatment outcomes.
Background

Osteomyelitis (OM) and septic arthritis (SA) are uncommon in children in Western populations\(^1\). Resistant and virulent organisms including MRSA and Panton-Valentine Leukocidin–producing (PVL) \textit{Staphylococcus aureus} make effective treatment challenging\(^2\). Current data suggest incidence of PVL-producing \textit{Staphylococcus aureus} is low in the UK and more commonly associated with meticillin sensitive \textit{Staphylococcus aureus} (MSSA) than in North America.

Methods

31 paediatric patients from Sandwell and West Birmingham Hospitals NHS Trust coded as OM or SA between 2010 and 2016 were identified retrospectively. Data were accessed from casenotes \((n=21)\) and electronically. Rates of OM or SA caused by PVL-producing \textit{Staphylococcus aureus} were compared to recent literature and patients’ treatment reviewed.

Results

There were 25 confirmed cases of OM, one SA. Age range was 2 weeks - 16 years. (Median age 8 years). Microbiological findings included positive blood cultures, with \textit{Staphylococcus aureus} identified in six patients’ blood (five MSSA, one MRSA). Five samples were PVL-producers, including the MRSA. \textit{Streptococci} were cultured in two. Intra-operative samples \((n=11)\) revealed MSSA as the most common organism \((n=10)\). One was MRSA. PVL-production wasn't identified in these. Patients with PVL-producing \textit{staphylococcus} infections all required operative management; longer antibiotic courses \((median 12 weeks versus 6 weeks for non-PVL)\) and had more complications. They also required broader-spectrum antibiotic treatment to achieve response. They did, though make a good recovery.

Conclusions

83% of \textit{staphylococci} in blood cultures were PVL-producers, a higher proportion than suggested by European data\(^3\). These patients provide a treatment challenge, often requiring broader-spectrum antibiotic treatment. Therefore, obtaining samples for culture and testing for PVL-production is essential to optimise therapy. Our patients had no long-term disability. Sample size was small, however, our results correlate with London regarding low UK incidence of PVL-positive MRSA.
NEW PAEDIATRIC DRUG CHART AS A MEANS OF QUALITY IMPROVEMENT FOR ANTIBIOTIC STEWARDSHIP

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Background

Audit performed to check for quality of antibiotic prescriptions to expected standards set by Department of Health Advisory Committee on Antimicrobial Resistance and Healthcare Associated Infections in UK. The audit standards included that all prescribed antibiotics should have
1. Indication and duration on drug chart.
2. Documented review at 48-72 hours and with appropriate plan.
3. Compliance to antibiotic guideline for choice of antibiotic.

Methods

Paediatric drug charts were reviewed for indication and duration of antibiotic, review of intravenous antibiotics at 48 hours with culture results and clinical status and compliance to local antibiotic guidelines for choice of antibiotic. Effects on patient care (prolonged course/ broader spectrum) were noted. One day per week during grand round the team was educated about need to mention indication, duration and review of antibiotics on drug charts. Subsequently new drug chart was designed and reaudited.

Results

Audit cycle completed.
Results old drug chart
62 % antibiotic prescriptions had no indications.
77 % antibiotic prescriptions had no duration mentioned.
53 % IV prescriptions had no clear documented review or plan at 48-72 hours.
27 % prescriptions were not compliant with antibiotic guidelines for choice of antibiotic.
Impact on patient care 42% had prolonged IV antibiotics and had no indication to justify this.
11% were on broader spectrum antibiotics.
New drug chart
92% antibiotics with indication
50 % had duration mentioned.

Conclusions

No prompt for indication, duration and review of antibiotics on old drug chart affected quality of prescriptions. New drug chart designed with separate area for antibiotics having mandatory fields for indication, duration & review. There was improvement seen with reaudit. Thus drug charts can be used as a quality improvement measure for antibiotic stewardship. Regular re-audits of antibiotic prescriptions can help maintain quality.
Background and Objective

Group B streptococcus (GBS) is a common cause of early-onset sepsis and meningitis in neonates, therefore prophylaxis is widely prescribed. However, there are concerns regarding over-treatment. Antibiotic resistance is increasing in GBS and the emerging threat of penicillin resistance has been reported.

Modern routine microbiology laboratories are beginning to use whole genome sequencing (WGS) to improve diagnosis, typing and antimicrobial treatment of bacterial infections as well as for outbreak management. This review seeks to inform clinicians how WGS could be used to improve GBS detection and treatment.

Methods

The literature since 2000 was reviewed. In Ovid, Embase, PubMed and Google Scholar, the key words used were “group B streptococcus”, “Streptococcus agalactiae”, “molecular”, “virulence gene”, “antibiotic resistance”, “whole genome sequencing” and “routine microbiology laboratory” and 54 relevant publications were identified.

Learning Points Discussion

- Whole genome sequencing (WGS) has successfully been used for the identification of GBS directly from clinical samples, but it is not a routine method.
- Serotyping with WGS is equivalent to established methods.
- Detection of virulence genes, e.g. for toxins, or their absence might lead to improved understanding of who will benefit from antibiotic prophylaxis.
- The presence of antibiotic-resistance genes could potentially improve the choice of antibiotics.
- WGS can improve outbreak management. Where specific genetic traits are identified, identification of symptomatic cases and improved screening of asymptomatic cases becomes possible.
- GBS colonises different hosts, e.g. humans, dogs, fish, cattle, which could be the source of outbreaks.
- Whole genome sequencing has a turn-around time of currently 3-4 days and costs are several times that of bacterial culture; this must improve for it to be used as standard in the modern routine microbiological laboratory.
Background

As the world moves towards sequential malaria elimination, there is a need to adequately measure the intensity of malaria transmission in an efficient manner that allows for systematic deployment of tools for effective malaria control. This study aimed to compare spleen rate determination and Plasmodium falciparum parasitaemia prevalence among children two to ten years of age (PfPR 2-10) in a period of low and high transmission.

Methods

The study was carried out in Sokoto, Northwestern Nigeria, which is characterised by a marked seasonality of malaria transmission. It has a high intensity of transmission in the rainy season and a low intensity in the dry season. Palpation of spleens was done using Hackett’s method and thick and thin films were prepared for children 2 to 10 years of age. The prevalence was calculated for both in respective seasons and compared. Correlation analysis was also done along with subgroup analysis.

Results

1017 children were recruited in a two-point study, 511 in the rainy season and 506 in the dry season. Overall, 354 had malaria parasitaemia (34.8%) while 372 of them had palpable splenomegaly (36.6%). However, while the parasite rate was higher than the spleen rate during the rainy season (49.3% vs 42.1%), the reverse was the case in the dry season (20.2% vs 31.0%). The age-specific rates for each were similar and there was a high correlation between the parasite and spleen rates.

Conclusions

It concluded that in terms of monitoring transition from high to low endemicity, it may be necessary to use both methods of estimation of endemicity, because one may not show the complete picture.

Clinical Trial Registration (Please input N/A if not registered)

N/A
Bronchiolitis is the leading cause of hospital admission among infants during winter months. The objective was to analyze the characteristics and course of children admitted for bronchiolitis and to identify factors related to Respiratory Syncytial Virus (RSV) etiology and a longer hospital stay. Additionally a comparison in demographics between years was performed.

Methods

Retrospective review of children admitted for bronchiolitis (January 2016-December 2017), with an analysis of the major clinical and epidemiological variables. A logistic regression analysis was performed on the factors associated with a longer hospital stay.

Bronchiolitis was defined as the first or second lower respiratory tract viral infection in infants < 2 years.

Results

209 bronchiolitis were admitted, 61% male, median age 3.8 (1.8-8.3) months.

RSV was identified in 63% and it was related with more fever (p=0.004), less intake (0,048), higher severity score (0.008), more bacterial infection (p=0.017), oxygen therapy (p<0.001), PICU admission (p=0.008) and relapse (p=0.001).

Prenatal smoking was correlated with more PICU admission (p=0.006).

Independent factors associated with a longer hospitalization stay (median 3 (1-4) days) were younger children (p=0.001), bacterial infection (p<0.001) and oxygen saturation < 92% (p<0.001).
Eleven patients were admitted to PICU, 9 relapsed, but globally 95% have good progress.

Children admitted in November-December-2017 were younger than 3 months (p<0.001), associated higher severity score (p=0.011) and more admission to PICU (p =0.041) vs. November-December-2016.

**Conclusions**

RSV was related with higher severity score, more bacterial infection, oxygen therapy, PICU admission and relapse.

Prenatal smoking was correlated with more PICU admission.

Independent factors associated with prolonged stay were younger children, bacterial infection and lower oxygen saturation.

Children admitted during November-December-2017 were younger and associated more admission to PICU vs. November-December-2016.

Most of the children had good progress.
VACCINATION DURING PREGNANCY: WOMEN IN GREECE ARE UNAWARE AND EXPRESS CONCERNS FOR SAFETY

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Background

Flu and pertussis vaccines are recommended in pregnancy as an important measure for preventing infection to mothers and newborns. Although there is good evidence on safety of both vaccines, uptake is very low in Greece.

We aimed to describe the knowledge and attitude of mothers in Greece on vaccination during pregnancy and identify barriers and facilitators that could be used to increase uptake.

Methods

This was a cross-sectional survey that was conducted with an anonymous questionnaire of 34 items on a person-to-person interview with mothers of children presented at the emergency department or hospitalized at a tertiary children’s hospital in Athens, Greece. Data collected included demographics, questions on knowledge and perceptions, and vaccination status during the last pregnancy.

Results

154 mothers of a median age of 33 years (IQR:28-37) responded to the questionnaire and 47.7% had a higher education.

125(81.2%) have given birth after 1/1/2013 and 14(11.2%) were vaccinated for flu and 1(0.08%) for pertussis.

Most frequent reasons given for non-vaccination for flu and pertussis respectively, were a)unawareness (54.4%,84.8%); b)safety(34.4%,8.8%) c)their gynecologist advised them not to (13.6%,8%)
Even though the majority (92.8%) believes that vaccines are beneficial, only 36.8% believe that flu vaccination is safe during pregnancy and 18.4% for pertussis with higher rates among mothers who gave birth after 2013 (Table 1).

Conclusions

We detected very low rates of vaccination for flu or pertussis during pregnancy in Greece with high percentages of mothers admitting unawareness and expressing concerns on safety. The majority would trust their gynecologist for information. Education and incorporating vaccination during routine pregnancy appointments are necessary actions to improve uptake.
EVALUATION OF THE 10-VALENT CONJUGATE VACCINE EFFECT IN ALL-CAUSE PNEUMONIA HOSPITALIZATION IN CHILDREN WITH SICKLE CELL DISEASE

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Background

Pneumonia is a leading cause of hospitalization in individuals with sickle cell disease (SCD), described as a high-risk group for pneumococcal infection. Data on hospitalization and outcomes in such patients are lacking in the Brazilian population. We describe the effect of the routine PCV10 immunization (introduced in 2010) in hospitalization due to pneumonia in children with sickle cell disease.

Methods

We’ve conducted a hospital-based retrospective observational study of children under 17 yrs. with SCD and hospitalized due to pneumonia. Hospitalization information in such group was extracted from medical records and analyzed according to the pre-vaccination period (2005-2009) and post-vaccination period (2010-2015).

Results

A total of 695 hospitalizations were identified in this population – 337 before (67.4/year) and 358 after PCV10 introduction (59.6/year). An infectious cause was responsible for 143 (42.4%) and 184 (51.3%) of them when comparing periods, of which 97 (28.7%) and 114 hospitalizations (31.8%) were due to pneumonia, respectively. When analyzing pneumonia-related hospitalization before and after the vaccine use, there were no changes in the average annual rates (19.4 vs 19), median hospitalization duration (7 days vs 7 days). The median age decreased from 113 months to 75 months in the post-vaccination era, and female distribution increased (37.7% vs 47.8%), respectively. Only one pneumonia-related death occurred during the study period.

Conclusions

Our data suggest no reduction in hospitalization and hospitalization length due to all-cause pneumonia in children with sickle cell disease after PCV10 vaccination. Younger children were more affected after vaccine introduction. Mortality was very low in both periods.
Background and Objective

We assessed the incidence and the estimated incidence of invasive pneumococcal disease (IPD) in children <5 year of age, following the introduction of pneumococcal conjugate vaccines (PCVs; PHiD-CV and PCV13) in pediatric immunization programs in countries with available data. We aimed to determine the relative contribution of vaccine serotypes (VTs) and non-vaccine serotypes (NVTs) to overall IPD.

Methods

IPD data sets following PHiD-CV/PCV13 introduction, for children <5 years of age, were identified by literature searches and from publicly available surveillance reports, in January 2018. Estimated incidences from Latin American countries were derived from SIREVA II reports and assessed separately. The most recent year of surveillance data was extracted. Case numbers were converted to rates/100,000 using 2015 population estimates from the United Nations, Department of Economic and Social Affairs, Population Division (available at: https://esa.un.org/unpd/wpp/).

Learning Points Discussion

Our review of the data indicates:

- Despite consistent PCV use in many countries, a limited number of VTs continue to circulate and cause disease, irrespective of which PCV is in use.
- VT rates of IPD vary from 0.5 to 7.2/100,000. In many countries, this represents a small proportion of the overall IPD, which ranged between 3.8 and 15.1/100,000 (Figure).
- The predominant VTs still circulating are serotypes 3 and 19A, with incidences varying up to a maximum of 5.3/100,000 and 5.2/100,000, respectively (Figure).
- A substantial proportion of the remaining IPD is due to NVTs in many countries.
Serotypes 3 and 19A are the major VTs still circulating post PHiD-CV/PCV13 introduction, but represent a small proportion of overall IPD in most countries. NVTs are playing an important role in IPD and should be the focus of the next generation PCVs.

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UPTAKE OF PERTUSSIS VACCINE AMONG PREGNANT WOMEN IN VICTORIA, AUSTRALIA: TEMPORAL, GEOGRAPHICAL AND SOCIOECONOMIC VARIATION

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Background

In June 2015, the State Government of Victoria (Australia) implemented a vaccination program, providing pregnant women – from 28 weeks’ gestation – with publicly-funded pertussis-containing vaccine. The rationale of the program was to protect infants most vulnerable to severe pertussis infection in the weeks immediately after birth and prior to receipt of scheduled infant immunisations. We examined uptake of pertussis vaccine among women giving birth in Victoria in the first two years of the program.

Methods

All births between July 2015 and June 2017 were extracted from the Victorian Perinatal Data Collection (VPDC). We explored temporal trends in uptake of pertussis vaccine, and a range of predictors of uptake including sociodemographic and geographical factors. Uptake by birth hospital was also examined. Hospitals were categorised into one of six capability levels relating to maternal and neonatal care complexity, and availability of infrastructure, workforce and services.

Results

Between July 2015 and June 2017, 154,597 births were captured on the VPDC. Consistent and increasing uptake of antenatal pertussis vaccine was observed: from 38% in July 2015 to 82% (interquartile range: 72%-92%) in June 2017. There was considerable variation in uptake by birth hospital, with exceptionally high uptake (≥90%) in 27 (41%) hospitals by June 2017. A range of sociodemographic and other factors were associated with uptake over the two-year period.

Conclusions

Our study demonstrated very high uptake of the pertussis vaccine among pregnant women in Victoria, Australia. To our knowledge, this is the highest reported globally. Substantial variation in uptake by birth hospital highlights the importance of understanding local system factors in delivering vaccination programs for pregnant women. Identifying sociodemographic and other factors associated with uptake can be used to guide targeted intervention and program enhancement.
Prenatal Ultrasound and MRI Brain Prediction of Congenital CMV Infection: A Case Series

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Title of Case(s)

Prenatal Ultrasound and MRI Brain Prediction of Congenital CMV Infection: A Case Series

Background

Cytomegalovirus (CMV) is the most common cause of congenital infection and the leading cause of neurological disability and sensorineural hearing loss, yet it is under recognised due to the challenges in its diagnosis both postnatally and prenatally, whereby the prenatal pathognomonic features of congenital CMV infection are not well established.

Case Presentation Summary

We report all confirmed cases of congenital CMV infection referred to a tertiary-level fetal medicine unit in London over a 15-year period. 32 cases were identified.

Ultrasound abnormalities were reported in 23/32 (72\%) cases. The most common extra-cranial abnormality was intrauterine growth retardation (10/18, 56\%), followed by echogenic bowel (9/18, 50\%). The most common cranial abnormality was ventriculomegaly (10/15, 67\%), followed by microcephaly (8/15, 53\%).

10/15 (67\%) cases with cranial ultrasound abnormalities had foetal MRI brain evaluation. MRI confirmed the ultrasound cranial findings in all cases and adds additional information to 9/10 (90\%) cases. Temporal lobe abnormalities (4/10, 40\%) were the most common additional information not detected via ultrasound, whereby 1 case on a background of normal cranial ultrasound that had a
brain MRI performed also reported a temporal lobe abnormality.

Learning Points/Discussion

Our ultrasound findings on the commonest cranial and extra-cranial abnormalities in congenital CMV infection are consistent with the literature. While these findings are suggestive of a congenital infection, they are not pathognomonic for congenital CMV infection.
Foetal MRI brain is likely to increase the positive predictive value for the diagnosis of brain abnormalities in congenital CMV infection. The findings of temporal lobe abnormalities could be pathognomonic for congenital CMV infection, supported by the literature which also found temporal lobe abnormalities to be predictive of symptomatic congenital CMV infection.
EQUAL VIRULENCE BUT DISTINCT CLINICAL FEATURES AND LABORATORY FINDINGS BETWEEN RHINOVIRUS AND RESPIRATORY SYNCYTIAL VIRUS BRONCHIOLITIS IN TAIWANESE CHILDREN

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Background

Acute bronchiolitis, one of the leading causes of hospitalization for young children, is actually a heterogeneous condition, depending on which virus infected. This study aimed to determine the frequency of viral pathogens causing acute bronchiolitis and to explore the association between different viral pathogens, clinical characters and laboratory findings in hospitalized children.

Methods

We enrolled consecutive children <2 years of age hospitalized with a diagnosis of bronchiolitis between October 2014 and June 2017. Nasopharyngeal aspirate specimens were collected and tested for respiratory viruses using the respiratory virus panel xTAG RVP FAST v2. Human rhinovirus(HRV) infection was confirmed by using HRV-specific polymerase chain reaction if the sample was positive for enterovirus/rhinovirus(RV-EV). HRV genotypes were also deduced from sequence analysis. The demographic data, clinical presentations, and laboratory findings of included children were obtained by medical chart review.

Results

A total of 184 cases were enrolled throughout the study period. At least one virus was detected in 163/184 (88.6%) of included children. Respiratory syncytial virus (RSV) in 25.5%, HRV in 17.4%, and RSV/HRV co-infection in 12.5% of cases. HRV infection was confirmed in 94.6% (53/56) of sufficient RV-EV positive specimens, which comprised HRV-A (20, 37.7%), HRV-B (1, 1.9%), and HRV-C (32, 60.4%). In comparison, the younger age, the presence of fever, and lower white blood cell count were associated with RSV infection (p<0.05). Instead, the elder age, eosinophilia, and presence of atopic feature were associated with RV infection (p<0.05).

Conclusions

Despite equal virulence, the clinical characters and laboratory findings were distinct from RSV and RV infection. Our data call attention to the heterogeneity of bronchiolitis and the demand for further research on both RSV and rhinovirus bronchiolitis.
Efficacy of Dolutegravir-Based Antiretroviral Regimens in Perinatally HIV-1-Infected Youth with Long-Term Virological Failure.

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Background

Dolutegravir (DTG) is a potent antiretroviral drug, however, access to it in Asia remains limited. This study aimed to assess the efficacy of a dolutegravir-based regimen in HIV-infected youth with persistent virological failure with boosted-PI regimens.

Methods

A cohort of perinatally HIV-infected youth aged between 15 and 24 years who were failing on second-line boosted protease inhibitors (PIs) for >2 years participated in the access program. Cases with no major PI resistance mutations (RAMs) were given tenofovir/emtricitabine plus DTG. Cases with major PI RAMs were given darunavir/r in addition to this. Endpoints assessed were the proportion of patients achieving HIV viral load suppression <200 copies/mL and CD4 change over time.

Results

Between January and October 2017, 15 youth with a median (range) age of 21 years (16-24), weighing a mean of 46 kg (37-65) were enrolled into this access program. The ongoing failing ARV regimens were atazanavir/r (53%), lopinavir/r (27%), darunavir/r (20%). Eleven youth used DTG-based regimens and 4 used DTG-darunavir regimens. The median duration of virological failure was 5.5 years (range 2-13). Median CD4 and plasma HIV RNA was 92 (7-367) cells/mm³ and 4.8 (3.8-5.7) log₁₀ copies/ml respectively. At their latest visit, a median of 16 weeks, 8 (53%) and 13 (87%) had HIV RNA <200 and <1000 copies/ml, respectively. Median (range) change in CD4 cell count from baseline was 36 (-1 to 458) cell/s/mm³.

Conclusions

Dolutegravir-based regimens can be utilized effectively as rescue regimens for youth failing on second-line PI-based regimens. Access to generic dolutegravir is urgently needed for HIV-infected youth with treatment failure in resource-limited settings.

Clinical Trial Registration (Please input N/A if not registered)

N/A
**DIFFERENCE IN SERUM IL 33 LEVEL OF CHILDREN WITH RESPIRATORY SYNCYTIAL VIRUS AND RHINOVIRUS BRONCHIOLITIS**

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**Background**

Interleukin 33 (IL33), a member of the interleukin 1 cytokine family, serves as an alarm signal of epithelial cells and interacts with both the innate and adaptive immune systems. In the present study, we are aimed to examine the relation of serum IL 33 levels to the severity of bronchiolitis and viral etiology.

**Methods**

The clinical data, nasopharyngeal aspirates, and serum of 184 enrolled infants hospitalized with bronchiolitis were collected during study period. We used Luminex RVP version 2 to test nasopharyngeal aspirates for 19 viruses and subtypes. We tested serum for IL33 and a panel of cytokines and chemokines by using MILLIPLEX® MAP Human Cytokine / Chemokine assay. The severity of bronchiolitis was assessed by respiratory severity score. Viral etiology was defined as a solitary respiratory syncytial virus (RSV) or rhinovirus (RV), RSV and RV co-infection, and infections with other viruses.

**Results**

Of all cases, at least one viral pathogen was identified in 88.6% of patients (RSV in 25.5%, RV in 17.4%, and RSV-RV co-infection in 12.5%). The median age of the 184 enrolled infants was 10 months. In comparison to RSV bronchiolitis group, a significantly higher severity score was found in RV bronchiolitis group (p= 0.033). Higher levels of Tumor necrosis factor-alfa (TNF-α); IL 4, and 10 were significantly associated with RSV bronchiolitis group. By contrast, there was higher serum level of IL 33 and IL 25 found in RV bronchiolitis group. (p=0.003, and p <0.001, respectively). For severity, the only TNF-α level was inversely associated with clinical severity. (p=0.007)

**Conclusions**

In the present study, the levels of serum IL 33 were significantly different between RSV and RV bronchiolitis. These findings highlight the role of IL33 in the pathogenesis of bronchiolitis.
A HEAD SCRATCHER
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A Head Scratcher

Background

Owing to its rarity, Tularemia is usually not considered in the differential diagnosis for cervical lymphadenopathy. However, when patients present with suppurative lymphadenitis, particularly after an insect bite, clinicians should maintain a high index of suspicion for this condition.

Case Presentation Summary

A previously healthy 4-year-old female presented with the acute onset of fever, headaches and right ear/neck pain. She was febrile to 39.4°C but non-toxic with red streaking from her right ear to her neck. She was diagnosed with AOM and prescribed amoxicillin but failed to respond. She had no reported exposure to animals, unpasteurized foods or recent travel. She had a tick removed from the scalp a day prior. Given unremitting symptoms, she was evaluated in the ED, where concern was raised for mastoiditis. CT was notable for soft tissue swelling and lymphadenopathy consistent with cellulitis. Clindamycin was started resulting in overall improvement, and she was discharged on amoxicillin-clavulanic acid to treat possible Lyme disease in addition to cellulitis. One day later, symptoms returned with fevers, worsening right ear/neck pain, as well as loose stool and emesis. She was readmitted. Neck CT identified two fluid collections along the right cervical chain for which she underwent I&D. She was discharged with a 7-day course of oral ciprofloxacin. Blood and I&D cultures finalized negative. Francisella tularensis Ab titers resulted positive, and she was subsequently treated with gentamicin with resolution of symptoms.

Learning Points/Discussion

- Tularemia is caused by Francisella tularensis and is transmitted by ticks, fly bite, mosquitos, small mammals, inhalation or ingestion
- First-line treatment is with aminoglycosides
- Diagnosis is made on the basis of clinical picture and/or serology (after the second week of illness) due to difficulty in culturing F. tularensis
ASEPTIC ABSCESSES IN AN IMMUNOCOMPROMISED HOST

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Aseptic Abscesses in an Immunocompromised Host

Background

Immunocompromised hosts represent a vulnerable group of patients at high risk of invasive bacterial and fungal infections. Steroids are typically contraindicated in the setting of disseminated infection, due to the risk of acute decompensation. We describe a challenging case of disseminated necrotic lesions that, when biopsied, resulted in a surprising diagnosis.

Case Presentation Summary

A 20-year-old female with ulcerative colitis on vedolizumab presented with a 2-week history of malaise, myalgia, and a 48-hour history of left-sided pleuritic chest and flank pain. Due to initial suspicion for pulmonary embolism, a CTA was performed revealing multiple splenic lesions concerning for abscesses. Exposure history included travel to Western and Eastern United States, and a recent camping trip. On examination, she was hemodynamically stable with left upper quadrant and flank tenderness. Abdominal CT revealed multiple enlarged, necrotic lymph nodes within the right upper quadrant and retroperitoneum in addition to splenic hypoattenuating lesions. Biopsy of these lesions was complicated by hemopneumothorax resulting in clinical deterioration. She then developed acute onset of fever with new nodular skin lesions on her shins. Broad-spectrum antibacterials and antifungals were initiated due to concern for a disseminated infection. Her skin lesions were biopsied and noted to be frankly purulent. Gram stain was negative, and tissue and blood cultures remained negative. Histology from skin lesions, however, showed a neutrophilic panniculitis. A case of aspecfic
abscesses was suspected and high-dose steroids were initiated with rapid clinical improvement.
Image 1A  Purulent material from nodule after biopsy
Image 1B  MRI with splenic abscesses noted
Learning Points/Discussion

- To consider the broad differential of disseminated necrotic lesions in an immunocompromised host
- To consider the unusual diagnosis of aseptic abscesses, particular in association with inflammatory bowel disease
- To understand the differences in treatment approaches of aseptic vs typical abscesses
09C. SCIENCE: INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS

INVASIVE PNEUMOCOCCAL DISEASE AT A BRAZILIAN PEDIATRIC ONCOLOGY CENTER

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Background

Pediatric oncology patients (POP) have high risk of infections caused by impaired immunity. Invasive pneumococcal disease (IPD) is an important cause of severe infection in these patients and it is associated with high mortality. There are few available studies that have evaluated the incidence of IPD in pediatric patients with cancer as well as the associated risk factors (RF). This study aims to evaluate the incidence and RF associated with IPD in POP at a Pediatric Oncology Center in Brazil.

Methods

This is a retrospective case-control study. All IPD cases in children with cancer from 2005 through 2015 were reviewed. Each case of IPD was matched with 2 controls from the cohort of patients on the basis of year of IPD, age and disease in order to assess risk factors. The density incidence was calculated as the number of IPD per 100,000 patients-year.

Results

We identified 51 patients with IPD. All pneumococcus were isolated from blood cultures. The median age was 5-year-old and 69% were male. The mortality rate was 7%. The IPD incidence density rate in POP was 423 per 100,000 patients-year, which is significantly higher when compared to the rate in the general pediatric population. All isolates were susceptible to penicillin and ceftriaxone. Heamatological malignancies and severe neutropenia were associated with a higher risk to IPD.

Conclusions

Although pneumococcal disease decreased after the introduction of 10-valent pneumococcal vaccine into the Brazilian national immunization program in 2010, there was not a trend toward decrease in the IPD incidence rate in our cohort. Knowledge on the incidence of IPD in pediatric patients with cancer is important to assist in the development and implementation of measures to reduce the burden of this disease.
MATERNAL AND INFANT SAFETY OUTCOMES AFTER ADMINISTRATION OF ACELLULAR PERTUSSIS VACCINE: A RETROSPECTIVE COHORT STUDY OF NEW ZEALAND MATERNITIES

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Background

We aimed to assess the safety of acellular pertussis vaccine in the New Zealand maternal immunisation programme using linkage of national administrative datasets.

Methods

Retrospective cohort study of all women in NZ pregnant in 2013. Outcomes were defined dichotomously by the presence of specified ICD-10-AM codes. Cox proportional hazards models were adjusted for birth status; ethnicity; NZ Deprivation Index; maternal age; history of antenatal care; BMI; history of chronic disease; parity; model of care; influenza vaccination; calendar year; infant immunisations; and gestational age at birth.

Results

Of 68,550 pregnant women eligible to receive funded vaccine during 2013, 8,178 (11.9%) received Tdap and 60,372 (88.1%) did not. We found no association between receipt of Tdap and gestational hypertension, pre-eclampsia, gestational diabetes mellitus, fetal growth restriction, placental abruption, chorioamnionitis, PROM, labour dysfunction, first or second-stage labour dysfunction, fetal distress, post-partum haemorrhage, maternal fever during labour, C-section delivery, maternal sepsis, maternal fever after labour, anaemia, neurologic disorders and hyperemesis gravidarum.

We found an increased risk for lactation disorders (AHR=1.63; 95% CI [1.2–2.3]) and perineal laceration during delivery (AHR=1.13; 95% CI [1.07–1.19]).

Among infant outcomes we found a protective effect against moderate to late preterm birth (OR 0.831; 95% CI [0.729, 0.947]), low birth-weight and small for gestational age (OR=0.721; 95% CI [0.57–0.91]); and no association between maternal Tdap and stillbirth, Apgar score at 5-minutes after birth, microcephaly, asphyxia, sepsis or infection, and hypoxic ischemic encephalopathy.

Infant exposure to Tdap during pregnancy was associated with a higher mean birth-weight, risk for ankyloglossia (OR=1.241; 95% CI [1.044, 1.474]), and neonatal erythema toxicum (OR=1.661; 95% CI [1.163, 2.372]).

Conclusions

We found no safety concerns associated with the administration of Tdap during pregnancy.
Clinical Trial Registration (Please input N/A if not registered)

N/A
LOW VITAMIN D STATUS IN NURSING PAKISTANI MOTHERS IN AN ENVIRONMENT OF AMPLE SUNSHINE: A CROSS-SECTIONAL STUDY.

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Background

Vitamin D deficiency is ubiquitous but the nursing mothers are relatively out of focus. To ascertain the vitamin D levels of the nursing mothers in south Punjab, Pakistan and its determinants we embarked on this study.

Methods

This cross sectional study recruited 67 mothers with convenience sampling, during August 2016 to June 2017 from the community. Their serum vitamin D levels & its determinants were ascertained. The SPSS 23.0 was used for analyses.

Results

The mean age of the mothers was 25.75± 4.4 years. The median age (and mode) was 25 years (range 18-37 years). The majority of mothers were less than 25 years of age (62.7%), uneducated (68.7%), from rural area (70.1%), lived in open houses with ample sun exposure (85.1%) and belonged to low socioeconomic strata (71.6%).

Serum 25(OH)D ranged from 7.2 to 43.8 nmol/L with mean 20.87± 7.69 nmol/L. The median and mode were 21.8 nmol/L & 24 nmol/L, respectively. The proportion of mothers with vitamin D < 20 nmol/L (severe deficiency) was 44.8%, <30 nmol/L (deficiency) 49.3% and <50 nmol/L (insufficiency) 5.9%. All were below 50 nmol/L i.e. the below optimal vitamin D levels.

The only significant determinant of vitamin D sufficiency was found to be oral supplementation with vitamin D.

Conclusions

The majority of Pakistani mothers in south Punjab are vitamin D deficient & universal vitamin D supplementation is the need of the hour.
Title of Case(s)

Shanghai Fever: a new presentation of Pseudomonas disease in Brazil

Background

*Pseudomonas aeruginosa* is an important agent of healthcare associated infections, especially in immunocompromised hosts. Shanghai fever is a community-acquired enteritis associated with sepsis and isolation of *Pseudomonas spp*. It is a rare severe condition that affects previously healthy infants. Most case reports are from East Asian countries. To our knowledge, we describe the first case of Shanghai Fever in Brazil.

Case Presentation Summary

A previously healthy seven month-old boy was admitted to the intensive care unit (ICU) due to septic shock with disseminated intravascular coagulation. He had three days of fever and bloody stools. Ceftriaxone was prescribed because of suspected *Salmonella* enteritis.

After three days, two necrotic skin lesions suggestive of ecthyma gangrenosum were observed on his right leg and perineum. Ceftriaxone was changed to piperacillin-tazobactam for empirical *Pseudomonas* coverage.

On the eleventh day he presented peritonism and abdominal distension. Laparotomy revealed three bowel perforations (sigmoid colon and rectum). Colostomy was performed. Antibiotics were changed empirically to vancomycin and meropenem. He was discharged after 28 days.

Cultures from skin biopsy and peritoneal fluid yield *P. aeruginosa*. Blood cultures were negative. Primary and acquired immunodeficiencies were ruled out.
Learning Points/Discussion

The presence of *Pseudomonas* in stool cultures is rare and with controversial significance. In ICU setting, colonization is a late event and can be related to diarrhea without systemic symptoms. Treatment does not change outcome.

Shanghai Fever is not associated to hospital-acquired colonization, but to more virulent community strains of *Pseudomonas*, demonstrating higher cytotoxic and invasive profiles.

It is important to have a high level of suspicion of *Pseudomonas* as an agent of sepsis related to diarrhea or ecthyma gangrenosum in healthy infants not responding to standard empirical treatment.
In the mid-1990s methicillin resistant *Staphylococcus aureus* strains emerged in a community. These strains have virulent and resistance specific features, as more toxins and methicillin and erythromycin resistance.

The aims of this study were to identify strains of *Staphylococcus aureus* isolated in hospitalized children in a hospital, to determine the molecular and microbiological characterization of these strains and to describe children’s clinical features.

Methods

From July 2009 to July 2015 *Staphylococcus aureus* isolated from blood of children hospitalized at Santa Casa São Paulo Hospital-Brazil were selected in Microbiology Laboratory. Standard microbiological tests were made for *Staphylococcus aureus* identification. Antimicrobial resistance pattern was performed by disc diffusion. Polymerase chain reaction was used to detect *mecA* and *LukS-PV/LukF-PV* genes in these isolates.

Clinical information were collected in patient records. This study was approved by Ethical Committee of our Institution.

Results

92 staphylococcal isolates from 75 children were selected in a period of study. 60 children had underlying disease. 37 isolates were methicillin resistant. 38 strains harboured *mecA* gene. 12 isolates, from 10 children, had PVL genes. 2 PVL+ isolates were methicillin resistant. 10 children PVL+: 7 acquired community infection (culture positive in the first 48 hours of hospital admission); 5 were previously healthy; 4 had joint infection, 3 sepsis, 2 had toxic shock and skin infection and 1 had sepsis, pneumonias and skin infection.

Conclusions
The rate of methicillin resistant *Staphylococcus aureus* in our hospital in the period of study was 40% (37/92). 43% (16/37) methicillin resistant *Staphylococcus aureus* isolates had hospital microbiological pattern. The PVL genes are in our environment. In according to the literature the PVL genes are not related to antimicrobial resistance, are identified in community strains and can lead to exuberant inflammation.
ENHANCED PASSIVE SURVEILLANCE OF ADVERSE EVENTS FOLLOWING IMPLEMENTATION OF A MENINGOCOCCAL B VACCINE HERD IMMUNITY STUDY "B-PART-OF-IT" IN SENIOR SCHOOL STUDENTS IN AUSTRALIA

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⁴Kids Research Institute, National Centre for Immunisation Research and Surveillance, Sydney, Australia
⁵Royal Children's Hospital, Paediatrics, Melbourne, Australia

Background

The meningococcal vaccine (4CMenB) is available in many countries but is not routinely used in adolescent vaccination programs in any country, despite a high disease incidence in this age group. This study aimed to determine the safety of 4CMenB in the largest vaccinated cohort of adolescents to date.

Methods

A cluster randomised controlled trial of senior school students was implemented in South Australia with participating schools randomised to intervention (4CMenB in 2017) or control (4CMenB in 2018). Vaccine safety was monitored by enhanced passive surveillance with reporting of any adverse events following immunisation (AEFI) by parents, students, teachers, and immunisation providers to a designated telephone line. All AEFI were followed to resolution. Any unexpected serious AEFI were referred to a Specialist Immunisation Service (SIS).

Results

A total of 34,500 students were enrolled in the study with 18,337 receiving vaccine from April–June 2017 and 96% receiving both doses (n=17,600). The median age was 16 years (age range 13-58 years). Of a total of 35,937 doses administered, 139 (0.39%) AEFI were reported in 138 students, with 38% (53/139) undergoing medical review including 6 serious AEFI and 8 being reviewed at the SIS. All those able to be contacted (87%) reported full recovery. 79% of reports were from parents. One case of anaphylaxis was assessed as probably related to vaccine. Most common AEFI reported were headache, injection site reaction and nausea. AEFI were reported less frequently following the second dose (n=53/17,600; 0.30%) compared to first dose (n=86/18,337; 0.47%; p=0.01).

Conclusions

Reporting of AEFI was low and consistent with the expected safety profile of 4CMenB in adolescents, including a lower AEFI rate following the second dose, in the largest post licensure use in this age group.
POST IMMUNISATION FEVER IN NEONATES: ASSESSMENT OF MOTHERS’ PRACTICES IN PART OF SOUTH WEST NIGERIA

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Background

Immunisation in Nigeria is fraught with controversies and misconceptions which raises apathy towards it leading to incomplete or total boycott of the immunisation process. Cultural consideration steeped in illiteracy and post-immunisation (P-I) challenges are some of the reasons for poor immunisation coverage. This study is a prospective survey.

Methods

150 mothers who visited the infant welfare clinic of the Comprehensive Health Centre in Ilara Mokin, Ondo State were monitored for 60 days from December to February, 2017. A self administered cross-sectional survey was conducted using a semi-structured questionnaire. The correlation between the respondent KAPs and their demographics characteristics was investigated.

Results

60% and 40% of mothers have good and poor knowledge of post-immunisation fever respectively. 50% will bring their children back to the health facility. Parity ($\chi^2 = 0.002$, At 95% confidence level using Chi-square with the level of significance at <0.05) was the characteristic that has a positive correlation with knowledge and practice of mothers in managing P-I fever. New mothers were more likely to have poor knowledge of how to handle P-I fever.

<table>
<thead>
<tr>
<th>Respondents' knowledge on Post-Immunisation Fever (n=150)</th>
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<tbody>
<tr>
<td>Statement</td>
</tr>
<tr>
<td>Immunisation can cause fever</td>
</tr>
<tr>
<td>Should be discontinued whenever P-I fever occurs</td>
</tr>
<tr>
<td>P-I fever should be treated at health facility</td>
</tr>
<tr>
<td>P-I fever means that the vaccine is not good</td>
</tr>
<tr>
<td>Immunisation schedule should be discontinued when P-I fever occurs</td>
</tr>
</tbody>
</table>

Conclusions
This study established that post-immunisation fever poses great challenge to mothers of neonates and this may affect the willingness of mothers to bring their children for the complete immunisation schedule. The need for a pre-immunisation information dissemination and follow up of immunised neonates by Community Health Extension Workers is recommended.
Brain Abscess secondary to *Staphylococcus intermedius* in a Previously Healthy Girl

Background

*Staphylococcus intermedius* is a coagulase-positive staphylococcus that is closely related to *S. aureus* and shares some virulence factors. *S. intermedius* can be found on the body surfaces and oral flora of animals like dogs, cats, horses. As this bacterium is a zoonotic pathogen, it has been identified very rarely as a cause of infection in humans. There are various reported cases range from dog bite wounds, bacteremia, pneumonia, skin and brain abscess. Herein, we report brain abscess caused by *S. intermedius* in a previously healthy girl.

Case Presentation Summary

A 4 year-old girl presented to our clinic with the complaints of fever and partial seizure. She had the history of headache, fever, nausea and vomiting for one month. She was lethargic and right hemiparetic. Laboratory investigation revealed white blood cell count 24 600/mm³, erythrocyte sedimentation rate 74/hour, C-reactive protein 2.93 mg/dl. The chest x-ray, echocardiography and abdominal ultrasonography findings were all normal. The immunoglobulin, peripheral blood lymphocyte subsets and *Nitro blue tetrazolium* were normal. Cranial computerized tomography (CT) demonstrated an abscess of 32x36 mm in left parietal lobe. Abscess drainage was done by neurosurgery, Gram staining of the pus revealed gram-positive cocci and *S. intermedius* was identified in culture. The patient had a good recovery without any residual hemiparesis with a 8 week course of intravenous treatment with vancomycin. The control imaging of brain was normal.

Learning Points/Discussion

Childhood brain abscesses are rare but serious infection of the brain parenchyma which need urgent diagnosis and treatment. Immunocompromised states and congenital heart disease are considered as predisposing factor but rarely can develop without any underlying process as in our patient.
CASE SERIES OF LIVER ABSCESSES IN CHILDREN

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A case series of Pediatric liver abscesses

Background

Liver abscesses in children pose both a diagnostic and therapeutic challenge in tropical countries. A case series of 4 liver abscesses managed between March 2017-18 is presented with retrospective analysis of clinical, microbiological, radiological characteristics and therapeutic methods with clinical outcome.

Case Presentation Summary

Of the 4 children diagnosed with liver abscess, all were males with mean age of 10.8 years. Fever was present in all, loose motions in two, one had right shoulder pain. All had tender right hypochondrium. Leucocytosis above 15000/cmm was present in 3 of 4 children. Deranged coagulopathy was noted in one. One child had micro abscess involving both lobe. Rest had right lobe involved with segment 6 being the commonest followed by segment 7. Pleural effusion was noted in two patients. Aspiration was required in two patients. Organism could be detected only in one. There was no bacteremia in any. One child with abscess was on antitubercular treatment for pulmonary Tb, amoebic abscess was diagnosed based on concomitant history of amoebic abscess in father but antibodies to E histolytica was negative. The abscess improved with Metronidazole and Dilorxand furoate. Another child was initially treated as amoebic abscess on radiological finding suggestive of amoebic abscess, no organism detected and positive E histolytica antibodies but had to be restarted on antibiotics due to poor clinical response. Mean defervescence of fever was 10.75 days, mean total antibiotic duration was 17.5 days. The commonest antibiotic combination used was Co-amoxiclav plus Metronidazole plus Amikacin.

Learning Points/Discussion

High degree of suspicion is required in to diagnose liver abscesses due to non-specific complaints. Despite microbiological and radiological facilities, it is challenging to differentiate pyogenic from amoebic liver abscesses.
Atypical Cutaneous Manifestations of Ataxia-Telangiectasia Infected By Fusarium

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Title of Case(s)

Atypical Cutaneous Manifestations of Ataxia-Telangiectasia Infected By Fusarium

Background

Ataxia-telangiectasia (A-T) is a rare immunodeficiency syndrome characterized by progressive neurologic impairment, cerebellar ataxia, ocular telangiectasia, defects in DNA repair. Dermatologic manifestations of A-T include cafe-au-lait macules, poikiloderma, seborrheic dermatitis, cutaneous granulomas. An abnormal angiogenic response of the endothelial cells or pericytes can be possible causes of skin findings. Herein, we report a patient with A-T having varied progressive skin lesions on bilateral arms and foot biopsy of which revealed vasculitic inflammatory lesions. Lesion on foot was complicated with Fusarium infections that proceeded to osteomyelitis.

Case Presentation Summary

A 13 year old boy diagnosed A-T, having the history of non-hodgkin lymphoma, bladder wall telangiectasia admitted with fever and purulant discharge from lesions on foot penetrating to bone. He had large, deep, multiple eroded skin lesions and telangiectasia in eyes, ears. He was immobile due to cerebellar involvement. He was on intravenous immunoglobulin treatment. Laboratory investigation revealed white blood cell count 3300/mm³ (neutrophil:3300, lymphocyte:1000), erythrocyte sedimentation rate 110/hour, C-reactive protein 12.6 mg/dl. The culture of the three discharge yielded Fusarium proliferatum. The blood cultures were sterile. Posaconazole was used to be started due to the history of allergic reaction to amphotericin B and voriconazole. The magnetic resonance of the foot demonstrated osteomyelitis. The lesions were successfully treated without development of invasive infections.

Learning Points/Discussion

Fusarium species cause a broad spectrum of infections in humans, including superficial infections as well as locally invasive and disseminated infections.

The skin may occasionally be a portal of entry, may predispose to the development of invasive fusariosis in immunocompromised patients. Although it is not the first choice and the clinical experience is limited, posaconazole can be used as salvage therapy.
SUBACUTE SCLEROSING PANENCEPHALITIS IN A ROMA ADOLESCENT

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Title of Case(s)

SUBACUTE SCLEROSING PANENCEPHALITIS IN A ROMA ADOLESCENT

Background

Subacute sclerosing panencephalitis (SSPE) is a rare and fatal complication of measles characterized by cognitive and motor deterioration, with death typically occurring within one to three years of symptom onset. Prior to measles vaccination programs, the incidence of SSPE in developed countries was estimated at 1 case per 100,000 population, but was 100 times higher in some developing nations suggesting that environmental or genetic factors, or specific measles genotypes might be risk factors. A consistent SSPE risk factor has been measles infection before the second birthday.

Case Presentation Summary

A 13-year-old boy presented with frequent myoclonus started a month ago that sometimes led to a fall on the ground. His clinical examination revealed dysarthria, gait disorder, personality changes and intellectual deterioration. From his medical history, the patient was totally unvaccinated and was infected with measles at the age of two years. Brain MRI was normal. However, EEG revealed periodic bursts of high-amplitude, slow-wave complexes every 6 seconds correlated with myoclonous which is a highly characteristic pattern of SSPE. CSF analysis revealed elevated measles IgM and IgG antibody titters, elevated IgG index and the presence of oligoclonal bands. The patient received valproic acid and was started on intrathecal interferon α. Since there were no serious side effects, intraventricular infusions continued through an ommaya reservoir. Unfortunately the patient developed serious complications including convulsions, high fever, progressive weakness and rigidity that led to treatment discontinuation.

Learning Points/Discussion

SSPE remains a devastating condition. Intraventricular Interferon α infusions were associated with serious side effects in our patient and led to treatment discontinuation. Prevention through vaccination is the only way to eradicate this fatal complication.
Distant BCG disease in a child with suspicion of Hyperimmunoglobulin E Syndrome

**Background**

The bacilli Calmette-Guérin (BCG) vaccine is included in the national childhood immunization program and administered to all newborns in countries where tuberculosis is endemic. The BCG vaccination is safe and severe adverse effects are extremely rare in immunocompetent children. However, immunocompromised hosts like primary immunodeficiencies (PID) are prone to complications of vaccine. BCG confirmed from one site beyond a local or regional ipsilateral process like pulmonary secretions (gastric or tracheal aspirate) is called distant BCG disease. Herein, we report a child with PID who had developed distant BCG disease. *Mycobacterium bovis* was isolated both in gastric aspirate and vaccine site.

**Case Presentation Summary**

A three year old girl admitted with lymphadenitis having purulent discharge. She had the history of failure to thrive, eczema, recurrent perianal abscess, recurrent pneumonia and pneumatocele. She was born from non-consanguineous couple, she was only vaccinated with BCG vaccine. On physical examination, she had colostomy bag, perianal fistula and a large lymphadenitis in 5x5 cm diameter on left arm at the localisation of BCG scar. *Mycobacterium bovis* was isolated in the lymphadenitis exudate and gastric aspirate. The microorganism had isoniazid and pyrazinamide resistance (pyrazinamide having native resistance). The chest radiography showed the previous pneumatocele with no sign of tuberculosis and osteomyelitis was excluded. The immunological evaluation revealed Ig 315 mg/dl, Ig A 15 mg/dl, IgM 40 mg/dl, IgE >5000 IU/ml and lymphocyte subset analysis was normal. Hyperimmunoglobulin E Syndrome scoring system was 40 and was considered as indeterminate HIES.

**Learning Points/Discussion**

BCG dissemination in a child with the recurrent infections may be the presenting clinical picture of a PID and may be associated with a disseminated disease.
A CASE OF NEONATAL CITROBACTER KOSERI MENINGITIS WITH GOOD CLINICAL OUTCOME

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Title of Case(s)

A CASE OF NEONATAL CITROBACTER KOSERI MENINGITIS WITH GOOD CLINICAL OUTCOME

Background

_Citrobacter koseri_ is a rare cause of bacterial meningitis commonly leading to severe outcomes with formation of intracerebral abscesses. Despite adequate treatment, death rate is high (approximately 30% worldwide), and neurological sequelae are common in the survivors. We describe a neonate with abnormal neuro-imaging but good clinical outcome.

Case Presentation Summary

A full-term neonate born from a normal delivery, with no risk factors for sepsis, presented with fever and refusal to feed at two days of age. After blood and cerebrospinal fluid cultures, she was started on cefotaxime and amoxicillin. Cerebrospinal fluid grew fully sensitive _Citrobacter koseri_. The initial brain ultrasound showed an avascular echogenic area in the left frontal region, the brain MRI showed frontal multi-loculated cyst, without mass effect. The treatment was switched to ceftriaxone as the baby improved and she was treated for a total of 35 days as an outpatient. After three months a repeat brain ultrasound showed resolution of the lesion. At 18 months follow up her neurodevelopment remains normal for her age.

Learning Points/Discussion

Around 76% of newborns with _C. koseri_ meningitis develop brain abscesses compared to other Gram-negative meningitis (10%), the reason for this difference is not known. In newborns with Citrobacter meningitis, brain imaging is mandatory. The length of therapy should be extended with prolonged courses if abscesses are present. Due to the high risk of long-term neurological sequelae we recommend follow-up for at least 24 months.
Invasive Meningococcal Disease by Neisseria meningitidis B in two unvaccinated patients

Background

The capsule of *Neisseria meningitidis* is a virulence determinant, based on capsular polysaccharides, meningococci are assigned to serogroups, six of which are associated with invasive disease. Infants younger than 1 year old and adolescents are particularly at increased risk of meningococcal disease. Meningitis and septicemia caused by serogroup B strains of *Neisseria meningitidis* continue to be an important health concern worldwide. But this serogroup is not common for Turkey, where W135 is the most prevalent serotype because of hajj and umre. Herein, we report two *Neisseria meningitidis* serogroup B in two risk groups, a 1 year old and an adolescent.

Case Presentation Summary

One year old girl admitted with high fever, malaise, and purpura. She had severe refractory septic shock, she was started on ventilatory support. Laboratory investigation revealed white blood cell count 4800/mm3 (neutrophil:3600, lymphocyte:1000), C-reactive protein 5 mg/dl. The cerebrospinal fluid (CSF) analysis was normal and culture was sterile. *Neisseria meningitidis* was isolated in blood culture. She recovered completely with fluid resuscitation, inotropic and vasopressor support. A 15 year old boy admitted with fever, headache and purpura. Meningeal irritation signs were positive. *Neisseria meningitidis* was isolated in CSF. Both of the patients were unvaccinated, the immunosystem evaluation was normal. The serogroup analysis of both were serogroup B.

Learning Points/Discussion

Invasive meningococcal disease has a fulminant course and high mortality. Effective vaccines are available for meningococcal serogroups A, C, Y and W135. Vaccine against serogroup B strains for global use has been challenge due to frequent antigenic variations among this serogroup. It is important to emphasize that invasive meningococcal disease will not be controlled until effective vaccines for all serogroups are available.
A RETROSPECTIVE CASE SERIES OF NEONATAL SEPTIC ARTHRITIS: EXPERIENCE IN A SINGAPORE TERTIARY CHILDREN'S HOSPITAL

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Background

Neonatal Septic Arthritis is an uncommon but devastating infection with a high rate of sequelae. This retrospective study aims to determine the clinical epidemiology and outcome of neonates admitted to our hospital with septic arthritis.

Methods

Neonates with bacteriologically and/or radiologically confirmed septic arthritis from January 1999 to December 2014 were identified from discharge and laboratory records and data collection was done by retrospective review of their case notes.

Results

Six neonates met the inclusion criteria. All are male with the gestational age (GA) ranging from 25 to 37 weeks (mean GA 33 weeks). The median age at presentation was 15 days (range 12 to 18 days). Joint swelling was the most common presenting complaint (66.7%). Fever was present in only two neonates and all patients had lower limb involvement. Bacterial cultures were positive in 83% of patients and the most common isolated pathogen was Methicillin-resistant Staphylococcus aureus (MRSA) which accounted for 67% of infections. Three neonates with MRSA septic arthritis had bacteremia and multiple joint involvement. Radiological abnormalities were noted in all patients. 67% underwent arthrotomy and all patients received 6 weeks of antibiotics. The average hospital stay was 48 days and sequelae of septic arthritis were observed in 50% of the patients during follow-up.

Conclusions

Disseminated infection with bacteremia and multiple joint involvement are characteristic clinical features of MRSA septic arthritis in neonates. Our study highlights the increasing prevalence of MRSA in neonatal septic arthritis. It is therefore of paramount importance that MRSA be considered as a possible pathogen for neonatal septic arthritis in countries with high incidence rate of MRSA.
EVALUATION OF MEAN PLATELET VOLUME AND RELATED PARAMETERS IN CHILDREN WITH MENINGITIS

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Background

Meningitis is a serious illness in the childhood. Because of high mortality and high morbidity, early definition and treatment of meningitis is very important. Mean platelet volume is one of the markers of inflammation.

Methods

In this retrospective study we planned to examine laboratory parameters of first day of admission, second to fourth day of treatment and before discharge from hospital in children with meningitis and compare first findings with control group consisting of healthy children.

Results

In both groups there were 22 girls (35.5%) and 40 boys (64.5%). The median age of case group was 35.5 months (3 days - 17.9 years) and the median age of control group was 75.5 months (1.5 months - 16.4 years). In case group first values of WBC, CRP, LDH, neutrophil/lymphocyte ratio were higher than case group (p=0.000) and albumin was lower than control group (p=0.000). There were no significant difference in MPV, RDW, platelet and PDW values in both groups. In case group, the seasonal distribution of admission time was 33.9% summer, 24.2% winter, 22.6% autumn, 19.4% spring. Median hospitalization time was 20 (5-220) days. The median hospitalization time was significantly higher in concomitant illness group (p=0.003). In 59 cerebrospinal fluid samples we found 49.2% culture positive, 50.8% culture negative. In CSF culture positive group first value MPV was lower than CSF culture negative group and also second (p=0.042) and third (p=0.025) value of CRP were higher than culture negative group. CSF glucose value was lower in culture positive group than culture negative group (p=0.009).

Conclusions

There is a need for more extensive prospective controlled studies in this area.

Clinical Trial Registration (Please input N/A if not registered)

N/A
HIGH SEROPREVALENCE OF TRICHINELLOSIS IN CHILDREN IN ISTANBUL, TURKEY

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Background

Trichinellosis is acquired by eating raw or undercooked meat of an infected animal. In Turkey, the infection is rare due to religious restrictions and hunting is not widespread. However, a large outbreak with the consumption of minced beef illegally mixed with pork developed in 2004. This study was conducted with the aim of determining the prevalence of Trichinella IgG antibodies and its distribution according to age groups, in Istanbul.

Methods

Blood samples were obtained from randomly selected subjects including children and sera were stored at -20°C until the test was performed. Specimens were analyzed for specific Trichinella IgG antibodies (IVD Research Kit, Carlsbad-USA) using EIA method. The seroprevalence of Trichinellosis was evaluated by classifying into four groups due to ages and genders. Chi-square Test and Fisher's Exact Test were used for statistical analysis.

Results

Out of 1079 samples, 157 (14.7%) were obtained from children aged between 0-12 years. Distribution due to gender was 75(47.8%) girls, 82(52.2%) boys. Trichinella specific IgG antibodies were seen in all age groups and overall seropositivity was found to be 3.5%. For children, seropositivity rate (9.5%) was higher than adults with statistical significance (p <0.001, $X^2 = 19.94$). There was no difference due to genders.

Conclusions

In our study, overall seropositivity was low, but we detected the higher Trichinella seropositivities in children, which may be related with more consumption of raw or undercooked meat products such as sausage, bacon, ham and salami. The possible risk of mixing beef with pork infected with Trichinella in these products may be the cause of high rates. Considering the seropositivities in our study, we recommend the usage of diagnostic tests for Trichinella infection for risk groups in routine practice, in Turkey.
SURVEILLANCE OF MRSA COLONIZATION DURING AN OUTBREAK IN THE NEONATAL INTENSIVE CARE UNIT

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Background and Objective

We report on an outbreak of MRSA in our Neonatal Intensive Care Unit in 2016. During two months, 11 neonates and 7 adults (n=4 parents, n=3 employees) were found to be colonized with MRSA after screening based on epidemiological risk factors (placement in same room and/or care provided by same member of nursing staff as index patient or follow-on cases). No systemic infections were observed. For affected adults, decolonization regimens according to our national guidelines were instituted. In addition, the evidence supporting decolonization attempts for neonates was discussed to guide management of colonized infants. Thus, in this study we aimed to summarize current guidance on MRSA decolonization in term and preterm neonates.

Methods

We are currently performing a systematic review of published decolonization approaches in neonates (in particular premature or small for gestational age infants). Items of interest are the exact decolonization regimen(s) used, the proportion of infants successfully decolonized with each regimen, and any reports of adverse events of decolonization. To identify relevant manuscripts, we searched Medline and Embase for articles published between 1997-2017 using the following search terms: 1) neonates, 2) MRSA, 3) decolonization. A total of 372 articles were identified for screening of which 199 have been excluded to date (n=88 duplicates, n=111 articles excluded based on title or abstract screen).

Learning Points Discussion

- An ongoing review of the grey literature and international guidance did not identify any evidence-based recommendations for decolonization regimens of term and preterm neonates.
- Decolonization of extremely preterm neonates can have serious clinical consequences, such as temperature instability and breathing problems during the required procedures.
- (Multiple) decolonisation runs in neonates have relevant socioeconomic impact, therefore effectiveness and costs must be weighed.
FIRST CASE REPORT OF INTRAVENTRICULAR TIGECYCLINE IN A NEONATE WITH XDR ACINETOBACTER BAUMANNII VENTRICULITIS

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Title of Case(s)

Intraventricular Tigecycline in a Neonate with XDR Acinetobacter baumannii ventriculitis

Background

Acinetobacter baumannii has a propensity to cause CNS infections and its difficult eradication remains a challenge in neonates. We describe an extensively drug resistant (XDR) Acinetobacter baumannii ventriculitis, which required intraventricular tigecycline after failure of intravenous and intraventricular colistin.

Case Presentation Summary
Baby of A (27 weeks, 1028 gram, female) acquired healthcare associated Acinetobacter baumannii infection on day 5 of life (sensitive to: colistin, sulbactam; intermediate sensitive: tetracycline and resistant: cephalosporins, carbapenems, fluoroquinolones & aminoglycosides). Her lumbar cerebrospinal fluid (CSF) showed 32000 cells/mm$^3$, protein-564 mg/dL, glucose 1mg/dL and culture grew Acinetobacter baumannii. She was treated with IV colistin (6 mg/kg/day). Magnetic resonance imaging (MRI) confirmed the diagnosis of ventriculitis on day 17 of life (Fig1.a). After 6 weeks of intravenous colistin, repeat ventricular CSF grew Acinetobacter baumannii sensitive to doxycycline, tigecycline, minocycline and the MIC to colistin was high (16 mcg/mL). Ultrasound head showed ventriculitis and septations (Fig 1b). She was started on intraventricular colistin (10 mg every 48 hours). After 2 weeks of intraventricular colistin (70 mg of cumulative dose), the ventricular CSF culture again grew Acinetobacter baumannii (same antibiogram). Hence daily intraventricular tigecycline (3mg/day) was added to intraventricular colistin (5 mg/day). Ventricular CSF became sterile after one week. Intraventricular tigecycline and colistin were stopped after 2 weeks after getting 2 sterile culture reports one week apart. Serial cranium ultrasound showed static hydrocephalus and she was discharged home on day 80 of life. At discharge, neurological exam showed axial hypotonia, grasp reflex present, good suck, complete moro reflex.

**Learning Points/Discussion**

Intraventricular tigecycline can be considered for management of XDR Acinetobacter baumannii ventriculitis resistant to intravenous and intraventricular colistin.
Background

Tuberculosis is a serious public health problem not only due to its magnitude of spread but also development of resistance to existing drugs. The pediatric tuberculosis is a special component in TB, as the diagnosis is difficult in these cases. This study focuses on the status of the pediatric tuberculosis in the district of Haryana.

Methods

It was a record based study. The data was collected from the Nikshay Project which is a routine monitoring tool for all TB cases registered with Government and private health care system. Data entered by using Microsoft excel and analyzed by using STATA-9.

Results

The data shows gradual increase in the pediatric tuberculosis cases in the district from the year 2012 to 2014. The mean age of the participants was around ten years and majority of cases belongs to female gender (60.8%). Mean age among males were found to be 9.4 years and among females was 10.6 years and this was found to be statistically significant. From 67% sputum results were not found and from rest 56% were sputum positive. 94% of the pediatric tuberculosis cases were in the category 1 and around 6% were receiving category 2. Around 50% of the pediatric cases were pulmonary and rest 50% is extra-pulmonary. Around 94% of the cases were new case. From all the cases only 11.7% had the HIV report.

Conclusions

Although there is increased programmatic response to pediatric tuberculosis the cases of pediatric TB are on rise. Majority of the cases sputum test results were not available. The TB HIV collaboration is not working properly as the figures from this study indicates. There exists a gender difference in the tuberculosis cases, which also need to be handled.
CLONAL DIVERSITY, SEROTYPES AND ANTIMICROBIAL RESISTANCE INFERENCE OF S. PNEUMONIAE CAUSED INVANSIVE DISEASE IN INDIAN CHILDREN BETWEEN 2009-2017

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Background

Although Streptococcus pneumoniae is a leading cause of childhood pneumonia in India, very few studies have explored pneumococcal epidemiology using multilocus sequence typing (MLST). We aimed to study the population structure characteristics of pediatric invasive pneumococci by MLST, its serotype and antimicrobial resistance pattern and relate to serotypes included in the current pneumococcal conjugate vaccine (PCV13) used in National immunization programme.

Methods

125 IPD isolates from several hospitals in the country collected during 2009-17 were analyzed. Serotypes were determined by PCRSeqTyping and/or Quellung reaction. Multi-locus sequence types were identified analyzing seven housekeeping genes (aroE, gdh, gki, recP, spi, xpt, ddl). Sequence Types were analyzed for clonality with eBURST algorithm. Antibiotic susceptible profile was generated by broth microdilution method.

Results

MLST analysis identified 59 known and 29 novel STs. eBURST analysis grouped the isolates into 5 clonal complexes and 67 singletons. The most frequent clonal types found were ST473 (n=6), ST289 (n=6) and ST320 (n=5). 18 (14%) isolates were related to seven of the 43 PMEN clones. The most common serotypes were serotype 19F (n=15), 1(n = 11) and 19A(n = 10). Antibiotic resistance for Erythromycin, Levofloxacin, Tetracycline and Cotrimoxazole was 31, 8, 40 and 60% respectively. Penicillin non-susceptible pneumococci accounted for 12%of isolates. 29% of the isolates had multidrug resistance. PCV13 covered 65% of the serotypes.

Conclusions

A high level of serotype and genetic diversity was observed in pediatric IPD strains. This study underscores the importance of a detailed population study to determine circulating pneumococcal serotypes and to monitor vaccine impact.
Background

Knowledge of trends in antimicrobial use in hospitalized pediatric patients is essential for implementing pediatric antimicrobial stewardship programs. The aim of this study was to assess the pattern of antimicrobial prescriptions in hospitalized pediatric patients in Greece.

Methods

One-day point-prevalence survey was conducted in three consecutive semesters in 2016-2017, as part of the Global Antibiotic Resistance, Prescribing and Efficacy in Neonates and Children (GARPEC) project. Five tertiary level hospitals in 4 Greek cities participated. Patients were included if they were on antimicrobial treatment at 08:00am on the day of the survey.

Results

A total of 176 antimicrobial courses (297 prescriptions, ranging from 11 to 176 among hospitals) were analyzed. Of the antimicrobial prescriptions, 80.1% were intravenous and 17.5% oral. Of all prescriptions 50% were administered for community-acquired infections (CAIs), 29% for hospital-acquired infections (HAIs) and 17.5% for medical/surgical prophylaxis. The most frequent antimicrobials were: 3rd generation cephalosporins (18.5%), penicillins (13.8%) and aminoglycosides (13.1%). In 53.4% of the courses, monotherapy was used for CAIs (60.6%) and medical/surgical prophylaxis (26.5%). The most common diagnosis was urinary tract infections (9 different antimicrobial regimens) and bacterial lower respiratory tract infections (LRTIs, 4 antimicrobial regimens). When combinations of two antimicrobials (31.2%) were prescribed, the most frequent diagnosis was bacterial LRTIs (8 CAIs/9 HAIs) followed by sepsis (4 CAIs/4 HAIs). There were 21 different antimicrobial regimens, where cephalosporins predominated. Co-administration of three antimicrobials was found in 17 courses (7 oncology patients) and was given mainly for bacterial LRTI or fever of unknown origin. Aminoglycosides, cephalosporins and glycopeptides were frequently prescribed (13 different antimicrobial regimens).

Conclusions
High rates of multiple antimicrobials and diverse combinations found in this survey constitute an appropriate target for antimicrobial stewardship programs.
VARICELLA VACCINATION IN A NON-FINANCED PROGRAM
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Background

Objective

To describe varicella vaccination status in children of the Valencia Region, Spain.

Methods

A retrospective population-based cohort study based on health databases. The study population was children of the Valencia Region born between 2006 and 2014 and followed during the study period 2009-2014. Data sources: population information system (SIP), vaccine information system (SIV) and outpatient information system (SIA) (incident cases of varicella, ICD-9: 052.X were obtained). Vaccination coverage was estimated by month and year, year of birth, age and health department. Children younger than one year with and without an episode of varicella in the first year of life have been considered to evaluate their vaccination status.

Results

The cohort included 411664 children. Of them, 36.6% were vaccinated with at least one dose and 14.3% with two doses. Coverage (at least one dose) per cohort ranged 42-51% in children born 2006-2011. Subjects born in 2012 and 2013 had lower coverage (32% and 6%, respectively). Coverage oscillated between 13% and 49% among health departments. Of 3600 children with a varicella diagnosis during first year of age, only 4.3% were vaccinated with the first dose during the second year of age, while 33% of children without varicella during the first year were vaccinated.

Conclusions

Coverage in the study period is moderate and variable among health departments. There is a temporal pattern marked by the shortage of the vaccine. Although clinical guidelines recommend varicella vaccination even after a varicella episode, we found a clear indication bias.
CHARACTERIZATION OF NON-VACCINE S. PNEUMONIAE CAUSING INVASIVE PNEUMOCOCCAL DISEASE (IPD) IN INDIAN CHILDREN: PRE-PCR ERA

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Background

Pneumococcal conjugate vaccine with 13 serotypes was recently (May, 2017) introduced into the primary infant immunization program of the nation. Although the use of PCVs are a remarkable public health success, their long-term utility is threatened by non-vaccine coverage, serotype replacement and switching. Knowledge of serotype prevalence, sequence types and their resistance patterns of non-vaccine types is of importance in the backdrop to estimate the impact of PCV.

Methods

124 S. pneumoniae IPD isolates from children <5yrs collected across India from 2009-2017 were included in the study. Isolates were serotyped with quellung and PCRSeqTyping. Analyzing seven housekeeping genes, MLST sequence types were identified. eBURST algorithm was used to identify the clonality. Antibiotic susceptible profile was generated by broth microdilution method.

Results

Of the 124 IPD isolates, 42(33%; blood–31, CSF-11) were non-PCV13 vaccine types. The most common serotypes were 15B (n=7), 20(n=3),10A(n=3), 16F(n=3) and 24A(n=3). The other NVTs were 8(n=2), 11A (n=2), 17F(n=2), 33F(n=2), 34, 28F, 13, 10F, 18A, 35A, 27, 7B, 45,9L,31,25F,36 and 2(n=1each). 11CSF isolates belonged to serotype 15B, 34,13,33F,20,35A,27,45,9L,17F and 8. MLST resolved the population into 39 known STs and 5 novel STs. All the 42 isolates were singletons. Tetracycline, cotrimoxazole and erythromycin showed 44, 44 and 30% resistance respectively. Resistance to Penicillin and levofloxacin was not observed.

Conclusions

The study reveals the importance of non-vaccine types causing invasive pneumococcal disease. With routine childhood vaccination using PCV13, potential for emergence and expansion of non-vaccine serotypes is of concern. To recognize the elevated NVTs in pneumococcal disease and/or carriage, surveillance studies are needed to document the dynamics.
CASE OF DIPHTHERIA INTOXICATION DUE TO IRREGULAR IMMUNIZATION

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Title of Case(s)

Case of diphtheria intoxication due to irregular immunization

Background

Diphtheria infections in R. Macedonia are not common in last two decades. This infection is associated with sepsis and severe general condition with lethal consequences. Cause of diphtheria infection is Corynebacterium species. Prompt diagnose should be done with appropriate treatment.

Case Presentation Summary

Patient was 1, 8 year girl brought in health care professional office in severe intoxicated condition. She was immediately transported on intensive care unit at Children's Clinic. Therapy with third generation cephalosporin, corticosteroid and inhalator therapy with anticholinergic and beta 2 antagonists was administered. Also diuretic therapy administered. Blood count: HBG 97, HCT 28.1, WBC 10.9, urine status, CRP 9.3 mg/l, ABS refers to acidosis and SO2 86.1%. Ion status normal, protein status normal, RTG pulmo shows inflammation, after 3 days pneumoslide IgM positive for adeno virus, tracheal aspirate: Candida albicans, blood culture diphtheria positive. After 4 weeks of hospitalization, extended antibiotic therapy was recommended.

Learning Points/Discussion

Irregular immunization can lead to severe infectious disease which could end up lethal.
DOSE-DEPENDENT EFFICACY OF ACELLULAR PERTUSSIS VACCINE IN INFANTS: A CASE-CONTROL STUDY

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Background

Pertussis is a vaccine-preventable disease with the highest morbidity and mortality in infants. Primary vaccination with 2 or 3 doses in the first 6 months of life followed by a reinforcing dose offers good protection against infection. Coverage data show that delayed vaccination is a major problem in many countries. Thus, the question of whether incomplete vaccination offers at least partial protection against complicated pertussis is important. The primary objective of this study is to estimate dose-dependent vaccine efficacy (VE), to reduce incidence of hospitalization of infants due to pertussis.

Methods

Using nationwide registers, we are currently performing a retrospective case-control study comparing immunization data of children hospitalized for pertussis with healthy controls from the same birth cohort. VE is defined as the percentage of hospitalizations avoided with a certain number of doses and will be calculated using a multivariable logistic regression. Data of cases come from the Swiss Pediatric Surveillance Unit (SPSU) pertussis project, and control data is obtained through the Swiss National Vaccination Coverage Survey (SNVCS). Both registers are ongoing continuously under the auspices of the Federal Office of Public Health.

Results

The study comprises around 90 reported severe pertussis infections in infants with a mean age of 161 days during 2007-2016. Cases will be matched with more than 300 healthy controls to fit a multivariable logistic regression and report percent VE.

Conclusions

Vaccination registers are valuable tools for assessing vaccine impact in populations, but reliable assessment is only possible if data quality can be reviewed and monitored continuously. We take advantage of two independent nationwide healthcare registers to estimate dose-dependent pertussis vaccine efficacy, aiming to inspire the set-up of vaccination registers in those countries which still do not have one.
EFFECTS OF MECONIUM ASPIRATION IN NEW BORN IN DEVELOPING COUNTRIES IN -- SUB SAHARAN AFRICAN PERSPECTIVE -- HOW MUCH HIV/AIDS CONTRIBUTES.

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Background

Sub-Saharan Africa still has the highest child Mortality rates in the world. Global child mortality has dropped by 53% - from 12.7 million in 1990 to 5.9 million in 2015. South Africa has reduced its child mortality rate from 60 deaths per every 1000 live births in 1990 to 41 in 2015. Though the MDG target is 20.

Methods

Our study were overserved & put on consideration of the following criteria –

Detection of Prematurity and Fetal gasping secondary to hypoxia, inadequate removal of meconium from the airway prior to the first breath, Use of positive pressure ventilation (PPV) prior to clearing the airway of meconium etc.

The inhaled meconium can cause a partial or complete blockage of the airways, causing difficulty breathing and poor gas exchange in the lungs. In addition, the substance is irritating and causes inflammation in the airways and potentially, causes chemical pneumonia.

Factors that promote the passage of meconium in utero includes-

Placental insufficiency, maternal hypertension, Preeclampsia, Oligohydramnios, maternal drug abuse, especially of tobacco and cocaine, maternal infection-corioaminitis, etc.

Results

The possibility of inhaling meconium occurs in and around 10% of all births. Out of this 1-3% causes MAS. Its generally happens after 34 to 42 weeks of gestation. 30% of them needs ventilation

In the industrialized world, meconium in the amniotic fluid can be detected in 8-25% of all births after 34 weeks' gestation. Of those newborns with meconium-stained amniotic fluid, approximately 10-15% develop meconium aspiration syndrome.

Conclusions
Our study concludes in HIV/AIDS and TB predominated developing countries with less availability of prenatal care and where home births are common, incidence of meconium aspiration syndrome is thought to be higher than, and is associated with a greater infant mortality rate.
SEASONAL INFLUENZA - 3 YEAR'S OBSERVATIONAL STUDY IN CHILDREN FROM BRASOV, CENTRAL ROMANIA

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²Childrens Clinic Hospital, Pediatrics, Brasov, Romania
³Faculty of Mathematics and Informatics-, Informatics, Brasov, Romania

Background

Seasonal influenza is an infectious disease of the respiratory tract caused by an influenza virus. Outbreaks of seasonal flu follow largely predictable seasonal patterns and occur annually. Romania has no published data regarding the seasonal influenza in children.

Methods

We conducted a retrospective study at the Clinical Children Hospital Brasov, Romania on 3 seasons of influenza, from 2015 throughout 2017. Main objective was to analyze flu incidence in our pediatric population.

All patients that presented at the Emergency Department with flu like symptoms received a rapid flu test. From the overall 5184 provided test, 437 were positive (9%)

Results

As a general trend, we observed that virus A was the most encountered positive test with 73% in 2015, 91 % in 2016 respectively 85% in 2017 while virus B peaked in at the end of each flu season. Average age was of 5 years old for virus A, while those affected by virus B were older than 8 years of age. We observed that the local trend is according to the predicted trend for this hemisphere with first cases in December that reached a maximum prevalence of 0.11% in January and reached a nadir at the end March of every year. Boys were slightly more affected 56%, the mean CRP value was 1.75 mg/dl, mean lymphocytes 2112/µl and average neutrophil 5357/µl. There was a slowly but constant increasing number of flu cases in the studied years, with significant statistical correlation between the number of lymphocyte and year (p=0.0131) and hemoglobin level and studied year (p=0.04989).

Conclusions

Vaccination of children for flu is mandatory during autumn and winter.
RSV BRONCHIOLITIS: VALIDATION OF THE DIAGNOSIS IN HOSPITALIZATIONS
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Background

Objective

To validate the reliability of the bronchiolitis cases due to Respiratory Syncytial Virus (RSV) recorded in the Minimum Basic Data Set (MBDS), by calculating the positive predictive value (PPV) using the Valencia Microbiological Network (RedMiVa) as the reference standard.

Methods

A retrospective population-based study with health databases of the Valencia Region was used. The study population was children under 2 years of age born between 2008 and 2012 which had an admission for RSV bronchiolitis (ICD-9 466.11), during the study period 2008-2012. According to the definition of Mc Connochie we only consider the first admission for bronchiolitis (466.11) in first diagnostic position. RedMiVa (results of the laboratory diagnostic tests of RSV) and MBDS (discharge diagnoses) were the data sources used.

A laboratory test result was associated with a hospitalization only if the test was done from 5 days before admission to the discharge date. Since the 20% of the hospitalizations do not have an associated test result, this missing information was estimated by multiple imputation techniques. The imputation and PPV were estimated using a Bayesian model which includes the age, the year of admission, and considering the hospital as a random effect. All values were calculated by simulation techniques using Markov chains (MCMC).

Results

Of the 3707 RSV bronchiolitis hospitalizations, 96.6% occurred in children under one year of age. Among them, 20.3% (n = 753) had no associated laboratory test, 4.3% (n = 160) had negative test result and 75.3% (n = 2790) had positive test result. According to the imputation model, the estimated PPV was 93.7% CI (95%) (92.7-94.7).

Conclusions

The PPV of bronchiolitis due to RSV was 94%. Only 6% of the diagnoses would be incorrect.
Knowledge of antimicrobial prescribing trends in hospitalized neonates is essential for implementing antimicrobial stewardship programs. The aim of this analysis was to assess the pattern of antimicrobial prescriptions in hospitalized neonates in Greece.

Methods

One-day point-prevalence survey was conducted in three consecutive semesters in 2016-2017, as part of Global Antibiotic Resistance, Prescribing and Efficacy in Neonates and Children (GARPEC) project. Five tertiary level hospitals in 4 Greek cities participated. Neonates were enrolled if they were on antimicrobial treatment at 08:00 am on the day of the survey.

Results

A total of 108 antimicrobial courses (207 prescriptions, ranging from 11 to 99 among the hospitals) were studied. Antimicrobials were given intravenously in all but one case. Combinations of two antimicrobials were given in 77.8%, whereas monotherapy in 17.6%. Sepsis was the predominant diagnosis (48.8%), followed by prophylaxis due to maternal risk factors (25.6%), gastrointestinal infections (6.8%), bacterial lower respiratory tract infections (6.3%) and probable or proven catheter-related bloodstream infections (3.9%). The most frequent antimicrobials used were ampicillin (34.6%), aminoglycosides (32.7%), glycopeptides (12.5%), 3rd/4th generation cephalosporins (7.7%), and carbapenems (6.3%). In 20 episodes of community-acquired sepsis, ampicillin and aminoglycoside were used in 90%. By contrast, in 21 cases of hospital-acquired sepsis, 10 different antimicrobial regimens were used. Combination of carbapenem/glycopeptide was used in 28.6% and cephalosporin/glycopeptide in 14.3%. For prophylaxis due to maternal risk factors combination of two antimicrobials was used in 65.6% (ampicillin plus aminoglycoside) and monotherapy in 34.4% (82% aminoglycoside, 18% ampicillin).

Conclusions
Ampicillin combined with aminoglycoside constitutes the most commonly used antimicrobial regimen in neonates. Relatively high glycopeptide and meropenem use is of concern. Existence of diverse combinations of antimicrobials constitutes an appropriate target for antimicrobial stewardship programs.
Cystic Leukoencephalopathy as a manifestation of Congenital Rubella Syndrome

Background

The neurological manifestations of Congenital Rubella Syndrome (CRS) include psychomotor retardation, chronic meningoencephalitis, parenchymal necrosis and vasculitis with calcifications. Cystic leukoencephalopathy has rarely been reported with CRS. We present a series of 3 cases with cystic leukoencephalopathy as a manifestation of CRS.

Case Presentation Summary

Case 1: 3-month-old boy, presented with abnormal involuntary posturing since 1½ months. Antenatally, the mother had polyhydramnios and rash in fifth month of pregnancy. The child had retrognathia, low set ears, upturned nose, long philtrum, narrow forehead with dystonic posturing and brisk muscle stretch reflexes. MRI showed diffuse white matter changes with cystic changes in bilateral Fronto-parieto-temporal areas. CT scan showed Bilateral cerebral calcifications. Echocardiography was normal.

Case 2: Presented for treatment of congenital cataract at 6 weeks of age. Additionally, had a 4 mm non-restrictive Patent Ductus Arteriosus (PDA) with severe pulmonary hypertension, hepatomegaly and microcephaly. Skull showed severe over-riding of sutures with large anterior fontanelle. Ultrasonography of head showed multiple echogenic foci in periventricular region and basal ganglia. MRI brain showed multiple periventricular white matter hyperintensities bilaterally along with cystic changes.

Case 3: The third child presented with severe microcephaly, PDA, developmental delay and sutural over-riding at age of 2 months. MRI showed periventricular white matter hyperintensities bilaterally, cystic changes and basal ganglia calcification.

All three children had positive serum anti-Rubella IgM antibodies. The mothers were positive for anti-Rubella IgG antibodies. Vaccination status of mothers was uncertain. Blood serology for toxoplasma, HSV, HIV, Syphilis and cytomegalovirus were negative.

Learning Points/Discussion
These three children highlight neurological findings uncommonly associated with CRS like refractory dystonia, cystic leukoencephalopathy with basal ganglia calcifications. These neuro-imaging features mimic Aicardi-Goutieres syndrome and congenital cytomegalovirus infection.
EFFECTIVENESS OF A NON-SYSTEMATIC VARICELLA VACCINE PROGRAM

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Background

To estimate the effectiveness of non-systematic vaccination against varicella in children of the Valencia Region, using real world data.

Methods

A cohort of all children born between 2006 and 2014 was followed during the study period 2009-2014 using the population based registries of Valencia Region, Spain. Data sources: population information system (SIP), vaccine information system (SIV) and outpatient information system (SIA) (diagnosis of varicella, ICD-9 codes 052.X). Vaccine effectiveness (VE) was estimated by a Bayesian Poisson regression model adjusted by sex, age, year and health department.

Results

The cohort included 408,491 children (37% vaccinated with at least one dose). The incidence rate of varicella per 1000 children-year was 25.1 (95% CI: 24.8-25.3), being 9.3 (95% CI: 9-9.6) for those one dose-vaccinated and 1.5 (95% CI: 1.3-1.7) for two doses-vaccinated. VE was 78.4 (95% CI: 77.3-79.5) for the first dose and 96.1 (95% CI: 95.5-96.7) for the second.

Conclusions

Varicella VE estimated with the databases in preventing primary care events is 96%, similar to previous publications.
04B. SCIENCE: COMMUNITY ACQUIRED INFECTIONS: RESPIRATORY TRACT INFECTIONS

RESPIRATORY TRACT INFECTION RELATED HEALTHCARE UTILISATION IN UK CHILDREN WITH DOWN'S SYNDROME

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Background

Children with respiratory tract infections (RTIs) often present to general practitioners (GPs) with a mild and short viral illness. In certain ‘at-risk’ children, such as those with Down’s Syndrome (DS), RTIs can become more serious and result in hospital admissions. This study aims to quantify RTI-related primary and secondary healthcare utilisation in children with DS and controls.

Methods

A total of 992 children with DS aged 0-18 years and 4,874 matched controls were included in this retrospective cohort study using the CALIBER data source. Individuals were followed up for occurrences of RTIs and antibiotic prescriptions to calculate rates of consultation, hospitalisation and prescription of antibiotics using Poisson regression. The Wilcoxon test allowed for comparison of hospitalisation length of stay.

Results

RTI-related healthcare utilisation was significantly higher in children with DS for both GP consultations (RR 1.73; 95%CI 1.62-1.84) and hospitalisations (RR 5.70; 95%CI 4.82-6.71). Antibiotic prescribing was also higher in children with DS (Adjusted RR 2.34; 95%CI 2.19-2.5).

RTI-related hospital stays were longer for children with DS (Mean 5.2; 95%CI 5.0-5.4 days) than controls (Mean 2.4; 95%CI 2.2-2.6). The risk of an RTI-related hospitalisation following an RTI-related GP consultation was higher in children with DS (RR 3.15; 95%CI 2.35 – 4.24). In those hospitalised, the time to hospitalisation was similar in children with DS (median of 8.0 days; 95%CI 3.0-19.0) and in controls (median of 8.0 days; 95%CI 2.0-18.0).

Conclusions

This is the first study of RTI-related healthcare utilisation in children with DS utilising linked primary and secondary care data. Children with DS have higher rates of consultations, antibiotic prescribing, hospitalisations, and longer hospital stays compared to controls. Children with DS are also more likely to be hospitalised following an RTI-related GP consultation.
SURVEILLANCE FOR CENTRAL LINE-ASSOCIATED BLOODSTREAM INFECTIONS (CLABSI)s: ACCURACY OF DIFFERENT SAMPLING STRATEGIES

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6University of Thessaly, Departments of Paediatrics & Neonatology-NICU, Larissa, Greece
7General Children's Hospital of Athens "Agia Sofia", Bone Marrow Transplant Unit, Athens, Greece
8General - Maternity District Hospital "Helena Venizelou", Neonatal Intensive Care Unit, Athens, Greece
9General Children's Hospital of Athens "Agia Sofia", A Neonatal Intensive Care Unit, Athens, Greece
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11General Children's Hospital of Athens "P. & A. Kyriakou", Neonatal Intensive Care Unit, Athens, Greece
12University General Hospital of Athens "Attikon", Third Department of Pediatrics-National and Kapodistrian University of Athens, Athens, Greece
13General Children's Hospital of Athens "Agia Sofia", Department of Paediatric Hematology-Oncology, Athens, Greece
14Venizelio General Hospital, Neonatal Intensive Care Unit, Heraklion, Greece

Background

Active daily surveillance of central line days (CLDs) in the assessment of CLABSI rates is time consuming and burdensome for healthcare workers. Sampling of denominator data is a method that could reduce the time necessary to conduct active surveillance. Our objective was to evaluate the accuracy of CLD estimates using various sampling strategies in neonatal and pediatric departments in Greece and to assess the impact on CLABSI rates.

Methods

Daily denominator data were collected in 22 units (4 PICUs, 12 NICUS and 6 ONCs) across Greece for 6 consecutive months. 32 sampling strategies were evaluated using the original data as following: 1 fixed day/week, 2 fixed days/week and 1 fixed week/month. CLDs for each month were estimated as follows: (number of CLDs in the sample/number of sampled days/month)*30. The estimated CLDs were used to calculate CLABSI rates. The accuracy of the estimated CLABSI rates was assessed by calculating the percentage error [(observed CLABSI rates-estimated CLABSI rates)/observed CLABSI rates].

Results
The sampling over 2 fixed days/week seems to provide the most accurate estimates of the monthly CLABSI rates for all the different types of units compared to other strategies (1 fixed day/week, and 1 fixed week/month). The percentage error was found to be ≤5% in ≥85% of months in which sampling was conducted, for several day-pair samples as presented in Table 1. Moreover, results showed that lower number of CLD per month (cut-off 75 days) lead to more accurate estimate of CLABSI.

Table 1: Number (%) of months with percentage error of estimated monthly CLABSI rates below or equal to 5% for each type of participating units

<table>
<thead>
<tr>
<th>NICUs (71 months)</th>
<th>PICUs (24 months)</th>
<th>ONCs (34 months)</th>
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<tr>
<td></td>
<td>Sample</td>
<td>Sample</td>
</tr>
<tr>
<td>Mon-Fri</td>
<td>61 (85.9%)</td>
<td>Mon-Tue</td>
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<tr>
<td>Tue-Wed</td>
<td>61 (85.9%)</td>
<td>Mon-Fri</td>
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<tr>
<td>Wed-Sat</td>
<td>61 (85.9%)</td>
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<td>Wed-Sun</td>
<td>63 (88.7%)</td>
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<td>Thu-Sun</td>
<td>63 (88.7%)</td>
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Conclusions

Sampling over 2 fixed days per week seems to provide a valid alternative to daily collection of CLABSI denominator data. These findings and similar strategies should be evaluated for the surveillance of other healthcare-associated infections.
HERPES ZOSTER IN CHILDREN FROM THE VALENCIA REGION, SPAIN

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Background

Objectives:

To estimate the incidence of herpes zoster (HZ) in children from the Valencia Region and to study the distribution of HZ by varicella history and vaccination status.

Methods

A cohort of all children born between 2006 and 2014 was followed during the study period 2009-2014 using the population based registries of Valencia Region, Spain. Data sources: population information system (SIP), vaccine information system (SIV) and outpatient information system (SIA) (diagnosis of varicella and HZ, ICD-9 codes 052.X and 053.X). The incidence rate (IR) of HZ was estimated and the distribution of cases was analyzed by varicella diagnosis and vaccination status.

Results

From the 411,969 children included, 1,143 presented an incident case of HZ. 28% (N = 320) of cases occurred in varicella vaccinated, 17% (N = 54) of which had previous diagnosis of varicella. Of the 72% (N = 823) of cases in non-vaccinated, 29% (N = 235) had no previous diagnosis of varicella, corresponding to 21% of the total cases. The HZ IR per 100,000 children-year was 17.97 (95% CI: 13.29-23.75) in <1 year; 58.77 (95% CI: 50.12-68.49) in 1 to <2 years; 66.3 (95% CI: 57.10-76.58) in 2 to <3 years; 80.92 (95% CI: 70.25-92.76) in 3 to <4 years and 96.01 (95% CI: 88.07-104.47) in ≥4 years. The IR was 67.90 (95% CI: 62.47-73.67) in boys and 71.02 (95% CI: 65.29-77.12) in girls.

Conclusions

The incidence rate of HZ increases with age. There is an under-codification of varicella given that 21% of cases of HZ have no varicella recorded.
Gastroenteritis caused by rotavirus accounts for considerable morbidity in young children. GSK’s oral live-attenuated human rotavirus vaccine was introduced in routine immunization in 2006. Our research aimed to assess the GSK’s rotavirus vaccine effectiveness (VE) as measured by laboratory-confirmed rotavirus infection after referral to hospital and/or emergency departments in children <5 years with gastroenteritis.

Methods

We performed a systematic search in the PubMed and Cochrane databases for peer-reviewed studies conducted in real-life settings, published between January 2006–July 2016 and reporting data on GSK’s rotavirus VE. In a second phase, a meta-analysis was performed to calculate the overall GSK’s rotavirus VE, which was further discriminated through pre-defined stratified analyses.

Results

Of 2,890 references screened for title/abstract, 261 full-text articles were evaluated for eligibility and 29 case-control studies were included in the meta-analysis according to pre-defined criteria. Whereas the overall two-dose VE estimate across all studies was 69% (95% confidence interval [CI]: 62%–75%), stratified analyses revealed non-negligible impact of confounders such as study design or geographical settings. Depending on the control groups used in the study, the two-dose VE ranged from 63% (CI: 52%–72%) to 81% (CI: 69%–88%) for unmatched and matched rotavirus negative controls, respectively. The VE following two-dose vaccine varied according to the socio-economic status: 81% (CI: 74%–86%) in high-income countries, 54% (CI: 39%–65%) in the upper-middle-income countries and 63% (CI: 50%–72%) in the lower-middle-income countries. Age, rotavirus strain and disease severity were also shown to impact the VE, but to lesser extent.

Conclusions

This meta-analysis of real-world studies demonstrated that a two-dose GSK’s rotavirus vaccine is effective in preventing hospitalizations and/or emergency department visits due to rotavirus infection.

Funding: GlaxoSmithKline Biologicals SA

Systematic Review Registration (Please input N/A if not registered)

N/A
ANTIBIOTIC PRESCRIPTION FOR RESPIRATORY TRACT INFECTIONS IN CHILDREN IS HOSPITAL DEPENDENT

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Background

Children with respiratory tract infections (RTIs) are often prescribed antibiotics. While the large variability in prescription rates between settings suggests that interventions could reduce antibiotic prescription, the implementation of such interventions requires knowledge of how population characteristics (case mix) and hospital characteristics influence prescription rates. We aimed to explain variability in antibiotic prescription rates for RTIs in children at European emergency departments (EDs) by differences in case mix and hospital characteristics.

Methods

Our prospective observational study included children with a working diagnosis of RTI – as part of the SHIVER registry of febrile children visiting the ED of 27 European hospitals in 12 countries. We collected data on clinical presentation, diagnostics and treatment between 2014 and 2016. A multilevel logistic regression model calculated variability in antibiotic prescription rate between hospitals, corrected for specific hospital characteristics (hospital type, resource use, crowding, availability of guidelines, mode of supervision) and for case mix (age, gender, duration of fever, vital signs, CRP level, focus of infection, season).

Results

Of the 3316 children (median age 2.4 years, 54% male) included in the study, 2829 (85%) had infections of the upper respiratory tract and 487 (15%) of the lower respiratory tract. Overall antibiotic prescription rate was 36% (35% for upper RTI, 47% for lower RTI), varying 16–63% between hospitals. After correction for specific hospital characteristics and for case mix, antibiotic prescription rates remained significantly different between hospitals (p<0.01).

Conclusions

Differences in antibiotic prescription for RTIs are hospital dependent and cannot be explained by differences in case mix or specific hospital characteristics. This should guide the design of intervention studies on antibiotic prescription and emphasizes the importance of performing multicentre trials.

Clinical Trial Registration (Please input N/A if not registered)
02A. SCIENCE: ANTIMICROBIALS: RESISTANCE AND PHARMACOLOGY

NEPHROTOXICITY OF ONCE-DAILY DOSING GENTAMICIN IN CHILDREN

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Background

Aminoglycosides are frequently used for gram negative bacilli infections. The aminoglycosides once-daily dosing (ODD) was increasingly reported in favor of efficacy and safety among adults and neonates compared to traditional three-times daily dosing. Experiences in aminoglycosides ODD are still limited in children outside of neonates. Our aim of the survey was to evaluate nephrotoxicity in children who were treated with gentamicin ODD.

Methods

A single-center, retrospective cohort study was conducted at Tokyo Metropolitan Children’s Medical Center between April 2010 and March 2017. Children treated with gentamicin ODD were included for analysis. Exclusion criteria were children admitted to neonatology, children required renal replacement therapy and children without gentamicin level testing. Nephrotoxicity was evaluated according to the staging 1-3 of KDIGO guideline for acute kidney injury. Patients’ demographic data and gentamicin level were collected.

Results

A total of 268 cases with gentamicin ODD were observed. Boys were 53.0%. Median age was 21 (IQR 5-100) month-old. Duration of ODD treatment was median 5 (IQR 3-7) days. Gentamicin trough level for the first time after initiation was median 0.53 (IQR 0.33-0.76) μg/mL. Trough level exceeded safe range of 1μg/mL was observed in 25 cases (9.3%). Acute kidney injury of stage 1, 2 and 3 occurred in 3.7%, 0.8% and 0%, respectively. All of them were transient and recovered.

Conclusions

Only mild and transient nephrotoxicity was observed in minority of patients at equivalent rate of traditional three-times daily dosing. Severe acute kidney injury was not observed in our study cohort. ODD has advantages in theoretical efficacy and safety along with less labor for nurses. Although we did not examine efficacy, gentamicin ODD may be an option with sufficient safety in children.
VARIABILITY OF LENGTH OF THERAPY FOR POSSIBLE EARLY ONSET SEPSIS (EOS) AND LATE ONSET SEPSIS (LOS): IDENTIFYING OPPORTUNITIES FOR ANTIBIOTIC STEWARDSHIP IN THE NEONATAL INTENSIVE CARE UNIT (NICU)


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Background

Antibiotic resistance is a global public health threat and is associated with increased morbidity, mortality and healthcare costs. Antimicrobial stewardship is considered a core action in reducing antimicrobial resistance and is being advocated by all major health organizations globally. We sought to describe prescribing patterns in neonates treated for possible EOS and LOS and negative cultures.

Methods

15 public NICUs participated (September 2016-June 2017) and captured demographic, clinical, laboratory and antibiotic use data. The first 15 antibiotic initiations for unique patients were recorded each month. Cases with negative cultures were selected. Length of therapy (LOT) was calculated for each unit and described by median and IQR. Antibiotic consumption was measured for the first 7 days of each episode of EOS or LOS. Possible EOS was defined as one occurring within the first 2 days of life.
Results

1330 cases of possible EOS were recorded with a median LOT of 7 days (IQR:5-7.5). Median LOT, at the unit with the lowest value, was 3 days (IQR:2-4) while at the one with the highest 11 (IQR:9-15).

260 cases of possible LOS were identified with a median LOT of 7 days (IQR:5-7.5). Median LOT, at the unit with the lowest value, was 4 days (IQR2-5) while at the one with the highest 10 (IQR6-13).

Median antibiotic consumption was: a) glycopeptides 2.7% (range:0-12.6%) for EOS and 21.7% (range:8.8%-34.8%) for LOS. b) meropenem 0.4% (range:0-4.8%) (EOS) and 8.6% (range:0-16.8%) (LOS), c) cefotaxime 1.2% (range:0%-12.5%) (EOS) and 2.2% (range:0-26.8%) (LOS)

Conclusions

Benchmarking data on the variability of antibiotic use for common neonatal and pediatric indications is critical in identifying targets for antibiotic stewardship. We identified significant variability in the duration of therapy for EOS and LOS in the NICU. We are currently utilizing these data to design an intervention to improve antibiotic use in the NICUs nationally.
Background

Bloodstream infections are an important cause of morbidity and mortality in neonates and account for the majority of neonatal sepsis episodes. This study aims to outline the epidemiology of early and late onset neonatal bloodstream infections in Malta over a ten year period between 2008 to 2017.

Methods

Blood culture results for all neonates were retrieved from the Infection Control Unit at Mater Dei Hospital, Malta. The organisms were analysed to exclude contaminants. Coagulase negative staphylococci were only considered significant in patients with indwelling devices or central lines. Bloodstream infections were defined as early onset if occurring in the first 72 hours and as late onset in patients aged between 3 to 28 days. Annual birth rate was obtained from the Maltese National Statistics Office. Poisson regression was used to test for significance of trends.

Results

The rate of positive blood cultures was 4.11% (126/3062), with 36.5% being early onset neonatal bloodstream infections. The mean incidence of neonatal bacteraemia over the ten year period was 2.94/1,000 live births. *Streptococcus agalactiae* was isolated in 50% (23/46) of early onset bacteraemias and coagulase negative staphylococcus in 25% (20/80) of late onset bacteraemias, followed by *Staphylococcus aureus* in 16.3% (13/80).

There was a trend toward an increase in the incidence of neonatal late onset bacteraemias which however did not reach statistical significance (p = 0.058).

Conclusions

Group B streptococci remain the predominant cause of early onset bloodstream infections in neonates. Coagulase negative staphylococci account for a modest proportion of late onset bacteraemias especially in neonates having central lines.
IMPACT OF AN ANTIMICROBIAL STEWARDSHIP PROGRAM ON CARBAPENEM PRESCRIPTION IN A TERTIARY HOSPITAL IN FRANCE

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Background

Antimicrobial stewardship programs aim at reducing the overuse of broad-spectrum antibiotics. To restrict the use of carbapenem in our university hospital, the approval of the antibiotic stewardship team (AST) is needed. The objective of this study was to evaluate the carbapenem use in our pediatric and adult wards.

Methods

Patients receiving carbapenems were identified using a computer-generated alert system, and underwent a prospective review by the AST for eligibility for de-escalation. Clinical and microbiological data were collected. We then analyzed all carbapenem prescriptions and subsequent AST intervention in pediatric and adult wards during one year (2014).

Results

In total, 383 carbapenem prescriptions for 158 children and 140 adults were reviewed. Most of the patients had underlying diseases (97%) and 51% had known carriage of extended spectrum beta-lactamase enterobacteriaceae (ESBLE). Most of the prescriptions came from intensive care wards (26%) and were initiated for urinary tract (29%) and lung (19%) infections. Carbapenems were initiated empirically in 272 (71%) of cases. The 264 documented infections were mostly caused by Klebsiella spp. (33%), 51% of the isolated organisms were ESBLE, 8% were not susceptible to carbapenem, and there were appropriate alternatives to carbapenem in 59% of cases. AST prospectively reviewed 323 prescriptions, 38% of them were considered non appropriate necessitating either antibiotic discontinuation (8%) or de-escalation (30%). Inappropriate prescriptions were mainly observed in pediatric wards (46% vs. 34%, p<0.05).

Conclusions
Carbapenem therapy was generally initiated in severely ill patients or with risk factors of drug resistance. However, more than one third of carbapenem prescriptions were considered inappropriate and discontinued by the AST, mostly in pediatric wards. The study suggests that AST implementation is essential to better control pediatric antibiotic use and subsequent antimicrobial resistance.
Background

Bacterial pneumoniae is still one of the most dangerous infection diseases and causes serious complications and mortalities in children. The aim of present study was to identify the most common of bacterial agents causing pneumoniae in children less than 12 years old and detection of their resistance to current antibiotics in Hamadan.

Methods

Overall 242 children suspected to pneumoniae were investigated for results of pleural fluid cultures and antibiogram patterns. Frequency of age, sex and seasons of patients were also studied from 1999 to 2003. The data were gathered through a questionnaire and analysed using Epi6 system. The species were identified by biochemical and serological methods. Antibiogram tests were also performed by Kirby-Bauer method.

Results

Out of 242 children suspected to pneumoniae, 33 cases (13.2%) had positive bacterial culture that 54.4% were gram negative and 43.6% were also gram positive bacteria. The most common species were: Staphilococcus aureus 18.6%, Streptococcus pneumoniae 16.9%, Klebsiella ozaenae 12.3%, Pseudomonas aeruginosa 11.8%, Streptococcus β-haemolytic 6.1%, E. coli 4.9%, Acinetobacter species 3.2% and other gram negative bacteria 23.3%. The most positive cultures were observed in children 1-4 years age group (31.3%), male (52.4%) and during winter (41.8%). The results of antibiogram showed that the most effective antibiotics were cefixime, ceftriaxone, gentamycin, ciprofloxacin for both gram positive and gram negative bacteria, but they showed high resistance to tetracyclin, amoxicillin and ampicillin.

Conclusions

The present study showed that some gram positive bacteria in particular, Staphilococcus aureus and Streptococcus pneumoniae are predominant causes of bacterial pneumoniae in children less than 12 years old in these regions. Most species showed high resistance to routine antibiotics such as tetracyclin, amoxicillin and ampicillin.
01B. EDUCATION: RATIONAL USE OF ANTIBIOTICS

ANTIBIOTIC PRESCRIPTION PRACTICES FOR CHILDREN ADMITTED WITH RESPIRATORY ILLNESSES IN ANSONGO HOSPITAL, NORTHERN MALI: A RETROSPECTIVE STUDY

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Background

Inappropriate use of antibiotics has been identified as one of the multiple causes of antimicrobial resistance. Sub-Saharan Africa is not spared by this worldwide issue. Since 2012 MSF is working with the ministry of Health in the reference health centre (CSREF) of Ansongo, an ongoing conflict area of Northern Mali where there is a significant gap of knowledge about antibiotic prescription.

Methods

Retrospective cohort of patients under 15 years of age admitted to the CSREF in 2015. Respiratory conditions were stratified into 2 groups. Group 1 for which antibiotics prescription could be generally expected (tonsilitis, otitis, pneumonia, respiratory distress, tuberculosis) and Group 2 for which routine use of antibiotics is usually not recommended (Asthma, Bronchiolitis, bronchitis, upper respiratory tract infections, “flu”)

Results

Respiratory conditions represented 35.2% of the total 398 patient files reviewed. In both groups 100% received antibiotics while the majority of these patients (G2, 81.4%) would normally not benefit from them. 53.8% in G1 and 54.4% in G2 received 2 antibiotics or more. 15.39% in Group 1 and 13.15% in Group 2 received 3 antibiotics or more. In both groups, most frequent antibiotics used were ampicillin and gentamicin followed by ceftriaxone.

Conclusions

There is an indiscriminate and inappropriate use of antibiotics among children diagnosed with respiratory illnesses in Ansongo CSREF. This can be explained to some extend by, a lack of reliable, accessible and affordable diagnosis tools, an inadequate training of prescribers, a false assumption that antibiotics will prevent superinfection or reduce hospital length of stay.

Context adapted, rational antibiotic use programmes and promotion of illness-specific treatment need to be put in place urgently in order to contribute to the reduction of development of antibiotic resistance.
SHINGLES IN VARICELLA VACCINATED CHILDREN WITHOUT HISTORY OF PREVIOUS CHICKENPOX INFECTION. NAVARRA, SPAIN

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Background

Navarra, Spain, initiated universal varicella (VZ) vaccination in 2007. Herpes zoster (HZ) is uncommon in children under 10 years, and is rare in VZ-vaccinated. From 2013, strain identification of all HZ confirmed cases in VZ-vaccinated children with no previous chickenpox is carried out.

Methods

Samples of HZ cases of children from vaccinated cohorts, with positive PCR for VVZ (RealCycler universal, Progenie Molecular) and no previous history of chickenpox were sent to the CNM for strain identification. PCR and Sanger sequencing of a VZV ORF62 fragment was carried out in order to characterize vaccine-specific OKA strain. Fisher’s exact tests and Non-parametric tests used to variable comparison.

Results

14 vaccinated children with confirmed HZ, without previous chickenpox. 50% males. Age ranged 1-12 yrs (mean: 5.4 ± 4.0 yrs). 57.1% of cases received two doses of vaccine; time since last dose ranged 5-92 months (median 62 mo).

Samples from three cases were not sent to the CNM. Results in the other 11 cases were: 2 cases "indeterminate", 5 cases "wild-strain", 4 cases "OKA-strain".

80% of HZ-Wild cases had received two doses of vaccine; All HZ-OKA cases received one dose (p=0.04). Median time since last dose: HZ-OKA cases, 48.5 months; HZ-WILD cases, 68 months (p=0.52).

13/14 healthy children; one with immunosuppressive therapy. Two cases admitted in hospital (one HZ-OKA and other not tested). 10/14 cases antiviral treatment. All cases recovered.

Conclusions

Both, OKA and wild strain might cause shingles in VZ vaccinated without history of chickenpox. Although few cases were studied no differences were observed except for the number of vaccine doses received.
Clinical Trial Registration (Please input N/A if not registered)

N/A
Background

Establishing microbial diagnosis in pneumonia is difficult and rationalizing empiric antimicrobial use is fraught with challenges. We present a case of severe necrotising pneumonia with empyema in a previously healthy child from community.

Case Presentation Summary

A 2 ½ y girl was referred for treatment of left sided complicated pneumonia with pleural effusion.

The child had received oral coamoxiclav and IV cefoperazone sulbactam and Piperacillin tazobactam, 3 days each

Investigations revealed neutrophilic leucocytosis and and CRP of 200. CT scan of the chest revealed consolidation with areas of breakdown in left midzone with loculated pleural effusion.

The child was started on Ceftriaxone and Vancomycin + Clindamycin and underwent VATS.

24 hr post VATS xray revealed satisfactory expansion of the left lung . WBC and CRP improved. The child developed fever ,increasing tachypnea with reduced air entry on the left side with increase in the CRP. A repeat CT scan of the chest showed a huge loculated pocket of air outside the ICD with consolidation with necrotic areas , in the mid zone on the left side. The loculated pneumothorax and fluid were drained with another ICD.

In the absence of isolation of any pathogen from blood or pleural fluid/debris, and the deteriorating lung parenchymal lesion, Flucloxacillin and and Meropenem were added to cover MSSA and Klebsiella respectively .

The child improved clinically over a period of 7 days, the ICD tube was removed and the child was discharged on Ofloxacin and Linezolid. There was complete resolution at follow up at 4 weeks
Necrotising pneumonia can pose a therapeutic challenge in absence of bacteriological evidence and may need agents to cover MSSA, MRSA and Klebsiella in such a setting.
HISTONE DEACETYLASE INHIBITION REVERSES SEPSIS-INDUCED SUSCEPTIBILITY TO PSEUDOMONAS AERUGINOSA PNEUMONIA

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Background

There is growing evidence that sepsis induces long lasting alterations of transcriptional programs that may lead to sepsis-induced immune suppression (SIIS), secondary infections and death. We hypothesized that epigenetic changes contribute to the pathophysiology of SIIS. To test this hypothesis, we studied the effects of histone deacetylases (HDAC) inhibition with trichostatin A (TSA) in a double-hit murine model of SIIS and secondary pneumonia.

Methods

C57BL/6 mice were treated with TSA (2 mg/kg ip) or saline serum (CTL) 30 min before induction of sepsis by cecal ligation and puncture (CLP). Surviving mice underwent intratracheal instillation of 1.5x10⁶ CFU of Pseudomonas aeruginosa 8 days after CLP. Survival and bacterial clearance were assessed. Cellular responses and apoptosis were assessed by flow cytometry 1 and 8 days after CLP. We also evaluated the effect of TSA on H3K9 acetylation in T-cells.

Results

Whereas treatment with TSA did not change survival after CLP, TSA improved survival and bacterial clearance in the bronchoalveolar lavage after tracheal instillation of P. aeruginosa (p=0.009 and p=0.04, respectively). Treatment with TSA significantly reduced T-cell apoptosis induced by sepsis 1 and 8 days after CLP (p=0.03 and 0.04, respectively). TSA also decreased T-cell expression of PD1 and PDL-1 (key role in regulating T-cell activation and immune tolerance) at day one of sepsis (p=0.03). Whereas TSA increased H3K9 acetylation in isolated T-cells at day one of CLP, treatment with TSA decreased the H3K9 hyper-acetylation observed at day 8 of sepsis.

Conclusions

TSA has an impact on T-cell phenotype and H3K9 acetylation, which might be involved in improved survival in our murine model of secondary pneumonia. These results confirm that sepsis-induced epigenetic changes contribute to the advent of SIIS.
DENGUE WITH HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS - CLINICAL FEATURES AND MANAGEMENT

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Title of Case(s)

Dengue associated HLH - clinical features and management

Background

Infection associated hemophagocytic lymphohistiocytosis (HLH) is an increasingly recognized unusual complication of dengue fever. There is little published data in literature on its clinical course and there are controversies in the most appropriate management.

Case Presentation Summary

A retrospective study of admitted with dengue fever in a university teaching hospital in South India between July and Dec 2017 was done. Children in whom the fever > 38.5 °C persisted and platelet counts continued to drop beyond 7 days were evaluated with serum ferritin levels, fasting triglycerides and fibrinogen levels. Those with serum ferritin > 500 µg/ and hypertriglyceridemia/hypofibrinogenemia were considered to have HLH. The clinical course in hospital and management has been described.

Out of 952 children with dengue fever, in 36 fever continued beyond 7 days. 31 (3.3%) were diagnosed to have HLH. Of these, 26 had severe dengue and 5 had dengue with warning signs. 21 children received only supportive treatment. Dexamethasone was used in 7 children. IVIG was used in 3 patients. 13 received blood products. In view of typical history and absence of family history, genetic test for familial HLH was not done. The children are under follow-up for over 3 months and are doing well.

Learning Points/Discussion

Dengue associated HLH should be considered if fever/cytopenia does not resolve in 7 days. All children with infection associated HLH do not need the standard therapy (HLH 2004 protocol). Most patients recover with supportive management with a minority requiring Steroids or IVIG.
VACCINATION STRATEGIES AGAINST HEPATITIS A IN CATALONIA: VACCINATION COVERAGE AND IMPACT ON THE DISEASE.

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Background

In Catalonia, systematic vaccination against hepatitis A (HA) began in 1999 at 11-12 years with combined hepatitis AB vaccine. In 2014, vaccination with first dose was started in two cohorts in 2nd and 6th year of life. The second dose is scheduled after 5y of the first (in 2019). Given the high effectiveness of a single dose of vaccine, it is proposed to limit vaccination regimen to a single dose.

To assess vaccination coverage against HA in vaccinated cohorts according to the program and to estimate the impact of HA vaccination on the disease.

Methods

Vaccination coverage and the declared incidence of HA was obtained from Health Department of Catalonia records. Vaccination coverage will be estimated and the incidence rate will be compared before (2013) - after (2017) introducing the vaccine by percentage variation.

Results

Incidence rate in children between 0-4y decreased by 56.8% and in children aged 5-9y by 69.23% (Table 1) in a context of increased global incidence. Vaccination coverage was higher than 85% in the 2nd year of life and than 65% in the 6th year of life.

Table 1. Incidence rates of HA 2013 and 2017 and variation by age groups, Catalonia

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>2013</th>
<th>2017</th>
<th>% variation</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4</td>
<td>4.4 per 100000</td>
<td>1.9 per 100000</td>
<td>- 56.8</td>
</tr>
<tr>
<td>5-9</td>
<td>7.8 per 100000</td>
<td>2.4 per 100000</td>
<td>- 69.2</td>
</tr>
<tr>
<td>Total</td>
<td>1.4 per 100000</td>
<td>4.9 per 100000</td>
<td>+ 250</td>
</tr>
</tbody>
</table>

Conclusions

There is a significant reduction in the incidence rate in cohorts vaccinated with a single dose, despite the context of increased global incidence caused mainly by an outbreak in MSM. It is necessary to assess vaccine effectiveness in order to change the vaccination strategy and reduce the schedule to a single dose.
03B. SCIENCE: COMM.ACQ. INVASIVE BACTERIAL INFECTIONS (NON-RESPIRATORY)

PREVALENCE AND DENSITY OF MENINGOCOCCAL CARRIAGE AMONGST PARTICIPANTS IN THE “STUDY TO EVALUATE PREVALENCE OF MENINGOCOCCAL CARRIAGE IN TEENAGERS” (SPIT)

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Background

SPIT is a prospective observational pilot cohort study, investigating feasibility and to permit power calculations for a larger study, to measure the effects of Bexsero vaccination on meningococcal carriage in sixth-form school students.

Methods

Subjects received two vaccine doses, one month apart, with oropharyngeal swabs (OPS) taken prior to each dose (visits V1 and 2) and 3 months later (V3). Saliva samples were also collected at weekly intervals. The study was done in 2 schools in Bristol, UK, between November 2016 and March 2017.

Following automated DNA extraction (QIAsymphony SP), real-time quantitative PCR (QuantStudio7, Thermo), for sodC, was used to detect (Ct values ≤ 36) and quantify meningococci. OPS results are reported here.

Results

The study population was predominantly white (80%) non-smokers (92%) and 61% female. 416 students attended V1, 295 completed all three visits.

Carriage rates at V1, V2 and V3 were 8.7%, 6.3% and 6.4%, respectively. The median densities of meningococci amongst carriers were 5.9, 10.6 and 7.4 gene copies/ml, at V1-3, respectively. There was one high density carrier (>1000 gene copies/ml) at V1, there were 3 at V2 and none at V3.

Conclusions

As expected, the trends observed in this small study do not achieve statistical significance. The apparent 26.4% observed fall in carriage between V1 and V3 is similar to that seen in the only previous study of carriage following Bexsero. An estimated subject group size of 2200 would detect this, however noting the drop-out rate of 29% in this study; it would be prudent to recruit at least 2900. If replicated in a larger study, the absence of high density carriage at V3 could be important, as such episodes may drive onward transmission events.

Clinical Trial Registration (Please input N/A if not registered)

N/A
CONTRIBUTION OF BOCAVIRUS, METAPNEUMOVIRUS AND CORONOVIRUS TO LOWER RESPIRATORY TRACT INFECTION IN HOSPITALIZED CHILDREN

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Background

Lower respiratory tract infections (LRTIs) are the most important cause of hospitalization in children under the age of 5. Most LRTIs are caused by viral pathogens, and modern multiplex real-time polymerase chain reaction assays (qPCR) now allow a sensitive detection of viral nucleic acids in respiratory specimens. For some viruses, in particular human bocavirus (hBoV), human coronavirus (hCoV) and human metapneumovirus (hMPV), the relative incidence and contribution to LRTI is still under debate. The objective of our study is to assess the contribution of individual viruses, and in particular hBoV, hCoV and hMPV to LRTI in children hospitalized with ARTI.

Methods

We prospectively reported medical data and multiplex qPCR results from >1000 children hospitalized with LRTI, upper respiratory tract infection (URTI) and other admission diagnosis with concomitant respiratory tract infection to a tertiary referral hospital in Germany. Unadjusted and multivariate odds ratios (ORs) were calculated with logistic regression to assess the association between viruses and LRTI. Because the risk associated with one virus can be confounded by coinfection with other viruses, we adjusted for infection with other viruses in a multivariate regression model which was constructed including age, viruses, and Mycoplasma pneumonia.

Results

At least one viral respiratory pathogen was detected in 82%, and viral coinfection occurred in 20% of our patients. hCoV, hBoV and hMPV were detected in 11% (114/1068), 5% (57/1068) and 4% (41/1068) of patients, respectively. Infection with hMPV was associated with LRTI (OR 2.01, P = 0.04). Children with hCoV infection had a lower likelihood of LRTI (model OR 0.66), even though this was not statistically significant (P=0.05).

Conclusions

hMPV is associated with LRTI, and is thus likely to be causative of severe respiratory disease in children.

Clinical Trial Registration (Please input N/A if not registered)

N/A
Background

Characterizing household transmission of H1N1 influenza virus is critical for the design of effective public health measures to reduce spread. Our objective was to estimate the secondary attack rates within households on the basis of active clinical follow-up of household contacts of children hospitalized with influenza like illness.

Methods

We conducted a prospective observational study during the period Jan-Feb 2017 in Chennai, South India. During this period a total of 56 children (index case in the family) were hospitalized with influenza like illness. Out of these, the nasopharyngeal swab tested H1N1 positive by RT-PCR in 36 cases. We assessed the transmission in the 100 household contacts (Group 1) of the 36 hospitalised children with H1N1 Influenza and the 57 households contacts (Group 2) of those with non H1N1 acute respiratory illness.

In both groups, cough hygiene and hand hygiene were taught. In addition group 1 received the recommended chemoprophylaxis with oseltamivir. Clinical data was prospectively collected by serial phone calls (fever and cough or sore throat). Secondary cases were identified by clinical criteria.

Results

We identified 21 secondary cases (21%) in 17 households in Group 1 and 9 (16%) in 5 households Group 2. The mean interval between onset of primary and secondary cases was 3.16 days (median interval of 3 days) in both groups. Infectivity did not vary with age.

Conclusions

Even when chemoprophylaxis is appropriately instituted, household transmission is substantially greater than that of non H1N1 respiratory infection.
INTESTINAL PARASITOSIS IN CHILDREN REFERRED TO A TERTIARY-CARE CENTER IN A LOW-ENDEMICITY AREA OF NORTHERN ITALY

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Background

Intestinal parasitoses represent a major global health concern, especially in developing countries. In industrialized countries, groups like immigrants are at high risk, but limited data are available on indigenous children. We aimed to investigate demographic factors and the etiology of intestinal parasitoses in a low-endemicity area with a high migration rate.

Methods

We performed a retrospective analysis based on the 205 confirmed cases of intestinal parasitoses (macro- and microscopical stool examination, and scotch test for E. vermicularis eggs) in children referred to the Pediatric Infectious Diseases Outpatient Clinic at Luigi Sacco Hospital, Milan, in the period 2012-2017. After data collection, statistical analysis evaluating the demographic data of the patients and the correlation with the specific etiology of the infection was performed.

Results

107/205 patients (52.19%) were Italian, with a mean age of 7.8 years. Of the total, 72.3% were symptomatic. The major presenting symptom was abdominal pain (55% of symptomatic children) followed by diarrhea (26.7%). E. vermicularis was the prevalent finding (35.12% of the total) and the commonest among Italian children (54.2%). Giardia lamblia was the second most frequent pathogen (21.9% of the total), being more frequently isolated in immigrants (30/98 vs 15/107, p<.01). A co-infection, defined as the detection of more than one parasite/stool sample, was found in 20% of the patients. Prevalence of co-infection was found to be significantly higher in non-Italian children (35/98 vs 6/107, p<.00001).

Conclusions

Our data suggest that the commonest intestinal parasitoses in Italian children is E. vermicularis. Immigrants are at risk for polyparasitism. Further investigations are needed to clearly determine whether parasites were acquired locally or imported.
CASES OF SEVERE RESPIRATORY INFECTIONS IN PEDIATRIC INTENSIVE CARE UNIT
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²Hippokration Hospital Thessaloniki, Paediatric Intensive Care Unit, Thessaloniki, Greece
³Hippokration Hospital Thessaloniki, 3rd Paediatric Department of University, Thessaloniki, Greece

Background

The appearance of cases with severe infection of the respiratory tract seems to increase in recent years. A lot of incidences need the helpful treatment of PICU- mechanical ventilation, non invasive mechanical ventilation-, while a percentage of these are very serious with a long hospital stay.

Methods

The files of patients hospitalized with severe respiratory infections in PICU from January 2015 until December 2017, were retrospectively reviewed. 31 patients (14 girls and 17 boys) were admitted to the PICU during this time. The mean age was (45 days to 14 years). All patients presented to the pediatric departments of various hospitals with symptoms of the respiratory tract system, such as tiredness, cough, some of them with fever, necessitating transfer to PICU for respiratory support.

Results

All of them required intubation, except 2 of them. Most of them 26 (83.87%) patients had an excellent response to treatment and were extubated, while 5 died. The mean duration of PICU hospitalization was 24.6 days for the survivors and 14.4 days for the fatal cases. 4 of them (12.9%) were patients with known psychomotor retardation, while a lot of them (13/31 41.9%) had at first symptoms of bronchiolitis (age less than 2 years). 4 of them (4/31 12.9%) were involved with severe pneumonia and extensive pleural effusion.

Conclusions

Infections of the respiratory tract system may be particularly threatening the lives of young patients. Early diagnosis and treatment is paramount to deal with it, especially with babies having bronchiolitis. The duration of hospitalization according to our data is valuable, so the more you prevent the less you cure.
N-ACETYL CYSTEINE IN THE PREVENTION OF AMPHOTERICIN-INDUCED ELECTROLYTE IMBALANCES: A RANDOMIZED, CLINICAL TRIAL
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¹Hacettepe University -Faculty of Medicine, Pediatric infectious disease, Ankara, Turkey
²Izmir Tepecik Research and Training Hospital, Pediatric infectious disease, Izmir, Turkey

Background

Amphotericin B (AmB) is one of the most potent antifungal agents, but nephrotoxicity and consequent electrolyte imbalances can restrict its clinical utility.

Methods

In this prospective study 87 patients who received amphotericin B between January 2002 and December 2017 were included. Thirty seven patients were randomly selected and given N-acetyl cysteine (NAC) concomitant with amphotericin B. NAC was given 600 mg to patients with body weight <40 kg, 900 mg to patients with body weight ≥40 kg per oral once daily during AmB treatment. Blood renal and liver function tests at the time of AmB treatment, at the 3rd, 7th and 14th days and weekly morning urinary electrolytes were recorded.

Results

Median age of the 37 patients who received NAC concomitantly with AmB was 115 months (6-227 months), median age of the 50 patients who received AmB without NAC was 94 months (1-216 months). Blood hemoglobin, leukocyte, thrombocyte values at the first day, 3rd day, 7th day and 14th day of AmB treatment were not different between two groups. Serum magnesium values at the 7th and 14th day of AmB treatment was higher in NAC-given group (p<0.05). Serum sodium levels at the 14th day of AmB treatment was in normal values and statistically significantly different in NAC-given group. Hypokalemia was noted in 26 of 37 (70.3%) patients in NAC given group, versus 44 of 50 (88%) patients in group without NAC. In group without NAC, mortality was found 2,3
Table 1. Demographics and laboratory characteristics of group 1 receiving AmB without NAC and group 2 receiving AmB with NAC

<table>
<thead>
<tr>
<th></th>
<th>AmB without NAC (n=80)</th>
<th>AmB with NAC (n=37)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sociodemographic characteristics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (mean, median, min-max)</td>
<td>94 (1,216)</td>
<td>115 (6,227)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Gender (m/f)</td>
<td>25 m/55 f (64%)</td>
<td>19 m/18 f (51.4%)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td></td>
<td>21 f (942)</td>
<td>18 f (48.6%)</td>
<td></td>
</tr>
<tr>
<td><strong>Laboratory parameters</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>At the time of AmB treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum sodium (mEq/L)</td>
<td>123±44±44.6</td>
<td>132±33±19.87</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Serum potassium (mEq/L)</td>
<td>3.9±40.71</td>
<td>4.6±40.45</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Serum magnesium (mg/dL)</td>
<td>1.5±40.37</td>
<td>1.9±40.29</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Serum calcium (mg/dL)</td>
<td>9.4±40.76</td>
<td>9.0±40.61</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Serum phosphorus (mg/dL)</td>
<td>3.7±40.23</td>
<td>4.0±40.94</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Serum creatinine (mg/dL)</td>
<td>0.5±40.35</td>
<td>0.5±40.32</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Days after</td>
<td>Serum sodium (mEq/L)</td>
<td>128±44±44.25</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>3rd day</td>
<td>132±33±19.1</td>
<td>132±33±19.1</td>
<td>&gt;0.05</td>
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<td></td>
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</tr>
<tr>
<td></td>
<td>Serum potassium (mEq/L)</td>
<td>3.7±40.6</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td></td>
<td>3.7±40.34</td>
<td>3.7±40.34</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td></td>
<td>Serum magnesium (mg/dL)</td>
<td>1.5±40.12</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td></td>
<td>1.9±40.26</td>
<td>1.9±40.26</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td></td>
<td>Serum calcium (mg/dL)</td>
<td>8.4±40.7</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td></td>
<td>9.6±40.36</td>
<td>9.6±40.36</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td></td>
<td>Serum phosphorus (mg/dL)</td>
<td>5.3±40.83</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td></td>
<td>4.3±40.95</td>
<td>4.3±40.95</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td></td>
<td>Serum creatinine (mg/dL)</td>
<td>0.5±40.21</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td></td>
<td>0.5±40.21</td>
<td>0.5±40.21</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td></td>
<td>14th day</td>
<td>Serum sodium (mEq/L)</td>
<td>135±44±44.1</td>
</tr>
<tr>
<td></td>
<td>138±33±19.4</td>
<td>138±33±19.4</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td></td>
<td>Serum potassium (mEq/L)</td>
<td>3.5±40.26</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td></td>
<td>3.5±40.26</td>
<td>3.5±40.26</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td></td>
<td>Serum magnesium (mg/dL)</td>
<td>1.5±40.46</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td></td>
<td>1.9±40.33</td>
<td>1.9±40.33</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td></td>
<td>Serum calcium (mg/dL)</td>
<td>5.6±40.7</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td></td>
<td>5.7±40.81</td>
<td>5.7±40.81</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td></td>
<td>Serum phosphorus (mg/dL)</td>
<td>4.3±40.28</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td></td>
<td>4.6±40.96</td>
<td>4.6±40.96</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td></td>
<td>Serum creatinine (mg/dL)</td>
<td>0.6±40.26</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td></td>
<td>0.6±40.26</td>
<td>0.6±40.26</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td></td>
<td>Need for potassium supplementation (n,%)</td>
<td>44 (32)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td></td>
<td>24 (64.9)</td>
<td></td>
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</tbody>
</table>

Conclusions

We conclude that NAC treatment decreased tubulopathic effects of AmB, when given concomitantly and during AmB treatment. More prospective studies are needed for routine use of NAC in AmB receiving patients.

Clinical Trial Registration (Please input N/A if not registered)

N/A
NARCOLEPSY TYPE 1 IN AN ADOLESCENT WITH VERTICAL-ACQUIRED HIV INFECTION - COINCIDENCE OR POTENTIAL TRIGGER?

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²University Children's Hospital Zurich- Zürich- Switzerland, Department of Pediatric Neurology, Zürich, Switzerland

Title of Case(s)

Weight gain in an adolescent with HIV infection: did you say narcolepsy?

Background

The underlying pathogenic mechanism of narcolepsy type 1 (NT1) is thought to be an autoimmune-mediated loss of hypocretin-secreting neurons. Epidemiological data reveal a clear association between NT1 and various infections. However, the association of HIV infection and narcolepsy has not been described so far. We present the case of an adolescent with vertically-acquired HIV infection under effective antiretroviral treatment who was diagnosed with NT1.

Case Presentation Summary

The 15-year-old boy was diagnosed with HIV-infection at the age of 8 years in Kinshasa. Under effective antiretroviral therapy (abacavir/lamivudine/ritonavir-boosted-atazanavir) the patient showed an uncomplicated course of HIV infection with fully suppressed viral load and no opportunistic infections. Seven years after HIV diagnosis, the patient presented with excessive daytime sleepiness and weight gain. Investigations revealed no signs of anemia, thyroid gland dysfunction or Cushing-Syndrome; screening for illicit drug intake was negative. A cerebral MRI was normal showing no signs of HIV encephalopathy and no HIV replication in the CSF was detected. Results of polysomnography and multiple sleep latency test were highly suggestive for narcolepsy. Moreover, the patient was tested positive for HLA-DQB1*06:02. Eventually the finding of a pathologically low hypocretin CSF level confirmed the diagnosis of NT1.

Learning Points/Discussion

The presented case raises the hypothesis that HIV infection in a host with a distinct genetic susceptibility may trigger autoimmune-mediated destruction of hypocretin-secreting neurons leading to NT1. This association has not been described so far possibly because NT1 is underdiagnosed in children and adolescents due to its less typical presentation in this population. Analysis of large HIV cohorts might answer the question whether there is a significant association with narcolepsy in children and adolescents infected with HIV.
Information, comprehension and competence: key elements in children’s assent for vaccine research

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¹Universidad Católica de Valencia San Vicente Mártir, School of Nursing, Alzira, Spain
²FISABIO, Hospital Lluís Alcanyís, Xátiva, Spain
³FISABIO - Public Health, Vaccine Research Area, Valencia, Spain

Background

Research on vaccines with minors requires their assent to participate. The project I-Consent investigates three aspects of assent: the information offered; the understanding of that information and; their decision-making capacity.

Methods

Systematic search using PubMed of experimental, observational and theoretical articles that include aspects of information, comprehension and capacity for assent in research with minors published since 2007. A first blind review of the resulting articles was made by two reviewers (by title and summary). Critical reading and summary were made of the selected articles. Articles about research in vaccines were analyzed independently.

Results

Seven publications (none about vaccine research) dealt with the information. This must be adapted to the age, development and emotional state of the subject. The importance of the communicative aspect between the child and the researcher during the assent process is highlighted.

The understanding was studied in eighteen publications, nine of them referring to vaccine research. They study it with none validated interviews or surveys and analyze various methods to improve understanding. Contradictory results regarding understanding when using new technologies and improved models. The communicative abilities when contributing the information on the study improve the understanding.

The child's capacity to give consent was studied in six publications (one of them on vaccine research). The validity of the MacCAT-CR test was confirmed to assess the capacity of assent, although theoretical studies support methods based on communication. Age is still the most important variable to judge the capacity of assent.

Conclusions

There is insufficient evidence of which information the children are interested in knowing and should be included in the assent processes in research, as well as tools that evaluate the understanding of said information and the child's capacity for decision making.

Systematic Review Registration (Please input N/A if not registered)
N/A
EPIDEMIOLOGY AND MICROBIOLOGY OF INVASIVE SALMONELLOSIS DURING A 12-YEAR PERIOD

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\textsuperscript{1}National and Kapodistrian University of Athens, 1st Department of Pediatrics, Athens, Greece
\textsuperscript{2}“Aghia Sophia” Children’s Hospital, Department of Clinical Microbiology, Athens, Greece

**Background**

Salmonellosis is an infection that is a major global problem for public health. *Salmonella* spp. causes two clinical syndromes, non-typhoid salmonellosis and typhoid fever. Non-typhoid salmonellosis causes gastroenteritis that usually carries on but has sometimes complications, such as bacteraemia. The aim of the study was to investigate the epidemiology of invasive salmonella infections in blood among children aged 0-16 years in a tertiary pediatric hospital during a 12-year period.

**Methods**

This is a retrospective study of children aged 0-16 years who were hospitalized at “Aghia Sophia” Children’s Hospital with invasive salmonella during 2004-2016. Epidemiological, demographic and laboratory data were recorded and statistical analysis was performed.

**Results**

During the 12-year study period, 73 children were hospitalized due to invasive salmonellosis. The median age of the hospitalized children was 2.8 years (IQR: 1.00-4.75). Thirty children were girls (41.9%) and 43 boys (58.9%). Forty-six children were of Greek origin (61.6%), while 13 of them were Roma (17.8%) and 15 were foreigners (20.5%). Increased incidence was observed during the summer months. The most frequently isolated serotypes in blood cultures were *S. enteritidis*, *S. group B* and *S. group C*.

**Conclusions**

In our study salmonella bacteremia is caused mainly by non-typhoid serotypes, such as *S. enteritidis*, *S. group B* and *S. group C*, and was found to have increased incidence in infancy, especially during summer months. Further investigation of invasive Salmonella infections will substantially contribute to improving public health and preventing food-borne infections.
Palatal Abscess in a Pediatric Patient: Report of a Case

Background

Palatal abscess in childhood is very rare condition. Genesis, clinical expression and local findings are very atypical so it can be easily misdiagnosed. Goal is to point out the role of paediatrician in such difficult cases in order to make prompt diagnose and treatment of this condition to prevent further complications.

Case Presentation Summary

3.5 year old girl came to healthcare professional office with pain in the mouth, high body temperature and large lymph nodes on the neck. Basic laboratory findings were done, inflammatory markers and parenteral therapy with third generation cephalosporin was administered in the hospital. After 7 days, pain was still persistent.

Further investigations were done and consultation with ORL specialist and maxillofacial surgeon. CT on the head confirmed palatal abscess as a complication of molar tooth infection. Drainage and pulpectomy was performed by the maxillofacial surgeon and per os antibiotic therapy was recommended.

Laboratory findings: HGB-122 g/L; RBC – 4.45x10^12/L; WBC – 13.27x10^9/L; PLT – 223x10^9/L; HCT-35.1%; CRP-95.3mg/L

Urine analysis: ALB ++; Sugar-neg; Sed Le-4-6; acetone ++; bilirubin neg.; urobilinogen neg.; nitrites neg.; blood neg.; Specific weight-1030; ph-5

Hepatogram: bilirubin-12.3umol/L; direct bilirubin-5.9umol/L; indirect bilirubin-6.4umol/L, AST-24U/I; ALT-10U/I; LDH-213U/I; GGT-9U/I

Computed tomography on the head.

Learning Points/Discussion

The taking of the history and intraoral examination are valuable diagnostic tools in conjunction with radiographic examination for the evaluation of palatal abscess.
Malignant Pertussis: Emphasis on early leucoreduction

Background

Pertussis is a leading cause of respiratory illness leading to significant mortality in developing nations. There has been a rise in its incidence even in developed countries. Malignant pertussis or critical pertussis is defined as a combination of pneumonia, respiratory failure, leucocytosis and pulmonary hypertension. It requires intensive care and may have a mortality of up to 80%. We report an infant who presented with malignant pertussis, and underwent leucoreduction by leucopheresis but unfortunately succumbed to the illness.

Case Presentation Summary

An 8 weeks old baby presented with acute onset of respiratory distress in the form of paroxysms of cough with fever and lethargy. Investigations revealed hyperleucocytosis with total leucocyte count of 114000 cells/cumm. A clinical possibility of pertussis was kept. Azithromycin was added, throat swab was sent for pertussis PCR which came positive. As the child had persistent tachypnoea, tachycardia in tune of 200, with high TLC, malignant pertussis was diagnosed. Leucoreduction by leucopheresis was done. Three hours post procedure, baby developed repeated bouts of cough with increased work of breathing and saturation dips, requiring mechanical ventilation. There was subsequent development of shock and the child succumbed to the illness.

Learning Points/Discussion

Malignant pertussis is a life threatening disease in infancy. Strict immunization practices, especially in developing countries like India are vital to prevent it. In affected infants, early recognition of critical pertussis and timely leucoreduction are the key for survival. Leucoreduction can be done by leucopheresis or exchange transfusion. Mortality remains high despite optimum management hence focus should be on prevention.
Background

CLABSIs are a common complication in the inpatient pediatric oncology setting. CLABSIs are associated with significant mortality, morbidity, and healthcare costs. The majority of the literature focuses on CLABSIs in the hospital setting but less known about the epidemiology of CLABSIs in the pediatric oncology ambulatory setting (Community Onset CLABSIs: COCLABSIs). Our aim was to describe the burden and nature of COCLABSIs in children with cancer.

Methods

A prospective study was conducted at a large pediatric oncology hospital in Athens, Greece. All patients (12/2015-12/2017) with a central line (CL) and a bloodstream infection (BSI) within the first 48 hours of admission without a focus of infection, were prospectively studied. Patients discharged within 5 days prior to entry to the study were excluded. Clinical and demographic data including length of antibiotic therapy, central line removal, ICU admission within 72 hours, chemotherapy delay and death within 30 days, were collected. CLABSI surveillance data were also collected for inpatients using CDC definitions.

Results

Thirty-one COCLABSIs cases were identified with a median hospitalization duration of 10 days (IQR: 6-11) and a median antibiotic course of 10 days (IQR: 10-10). The infection resulted in a delay in chemotherapy in 8/29 (27.6%), catheter removal in 4/31 (12.9%) and 1 patient 1/31 (3.2%) required ICU admission. No deaths were recorded. During the same period, 12 CLABSIs occurred in the hospital. Pathogens isolated are shown in Table 1. Gram negative organisms were responsible for the majority COCLABSIs in contrast to CLABSIs which were caused predominately by Gram positive.
Conclusions

COCLABSIs were not uncommon in pediatric oncology patients in the ambulatory setting and were associated with significant morbidity including delays in chemotherapy for the underlying malignancy. The different pathogen distribution compared to hospital-acquired CLABSIs may provide clues to the pathogenesis and inform future prevention efforts for these infections.
Background

Fever and neutropenia (FN) is a common complication in children who receive chemotherapy for cancer and hematopoietic stem-cell transplantation recipients and is associated with high morbidity and mortality. Proper initiation of empiric treatment can be crucial to a favorable outcome. The aim of this study was to evaluate the empiric antimicrobial use in these patients in order to identify possible targets for antibiotic stewardship.

Methods

We conducted a prospective study in 5 public pediatric oncology units in Greece (9/2016-6/2017). Data collected included demographic, clinical, laboratory, and use of antibacterial and antifungal antibiotics. The first antibiotic initiations for up to 15 unique patients were recorded each month and patients were followed for 7 days. Episodes with FN were extracted. Fever was defined as a recorded axillary temperature of ≥37.5°C and neutropenia as absolute neutrophil count (ANC)≤500 cells/μL (recorded or expected by the physician). Empiric antibiotic use on the first day and antifungal use within the first 4 days was analyzed.

Results

Among 258 FN episodes, initial empiric therapy was monotherapy in 50 cases (19.3%). In 34% of all FN cases an antipseudomonal b-lactam with a second gram-negative agent and a glycopeptide was administered. There was variability in antibiotic and antifungal use among the units (Table 1).

45.7% of the cases received at least 1 antifungal agent within the first 4 days of the course.
The median rate of de-escalation/discontinuation of antibiotic therapy on the 6th day in cases with negative cultures was 27.8% (IQR: 5.3%-46.9%) (see table 1).

### Conclusions

Variability of empiric antibiotic and antifungal use among pediatric oncology units in Greece for children with FN was detected. These results are important for identifying targets for antimicrobial stewardship in the setting of increasing resistance and the limited arsenal of new antibiotics.
IMMUNOLOGICAL AND VIROLOGICAL OUTCOME OF HIV-INFECTED ADOLESCENTS AFTER THEIR TRANSFER TO ADULT CARE SERVICES IN BELGIUM

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1Université de Mbuji-Mayi, Faculté de Médecine, Mbuji-Mayi, Democratic Republic of the Congo
2Université Libre de Bruxelles, Faculté de Médecine, Brussels, Belgium
3CHU Saint-Pierre- Université Libre de Bruxelles, Pédiatrie, Brussels, Belgium
4Oita University, Faculty of Medicine, Yufu, Japan
5Cliniques universitaires Saint-Luc, Pediatric infectious diseases - Pediatric Department, Brussels, Belgium
6Institut de Recherche Expérimentale et Clinique, Secteur des Sciences de la Santé, Brussels, Belgium

Background

There are scarce data regarding health outcome of HIV-infected adolescents after their transfer from pediatric to adult care.

Methods

This study included patients from nine pediatrics centers transferred to adult care between 1st January 1996 and 31st December 2013. Socio-demographic, clinical, immunological, and viral loads (VL) have been recorded at the time of the transfer and 2 years after transfer. A multivariate logistic regression model was used to identify factors predicting poor immunological status at two-years post transfer.

Results

70 HIV-infected patients were transferred during the study period. Median age at transfer was 18 years (range: 15-25) with a 1:1 sex-ratio. At transfer, 83% of HIV-infected adolescents were on cART. The median number of T lymphocytes was higher after transfer ($p=0.04$) compared to before, but the median CD4 cell count did not differ before and after transfer. However, the proportion of patient with CD4 < 200/mm$^3$ (Low CD4 cell count) increased from 13% to 20% after transfer towards adult care without reaching significance ($p=0.366$). Low CD4 cell count after transfer was associated with detectable VL before transfer (aOR=16.4 [2.1-27.2]; $p = 0.0073$), detectable VL 2 years post transfer (aOR=15.5 [2.1-17.5]; $p = 0.0054$), and female gender (aOR=0.02 [0.002- 0.3]; $p = 0.004$). Factors associated with detectable viral load at 2 years post-transfer were concomitant low CD4 cell count (aOR=11.0 [3.4-35.4]; $p=0.0001$) and African origin (aOR=1.8 [1.1-3.0]; $p=0.0315$).

Conclusions

Among patients who were transferred, the proportion of patients with virological suppression and preserved immune function was not different before and after transfer. African origin, female gender and detectable VL at the time of transfer might serve as markers for patients requiring more careful attention by health care providers.
BURDEN OF PROLONGED DIARRHOEA AND ITS RISK/ASSOCIATED FACTORS AMONG UNDER-FIVE CHILDREN: A CASE-CONTROL STUDY IN BANGLADESH

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1icddr-b, NCSD, Dhaka, Bangladesh
2icddr-b, Nutrition and Clinical Services Division, Dhaka, Bangladesh

Background

Prolonged episodes of acute diarrhoea (ProD, duration 7–13 days) are common problem in the hospitalized children in Bangladesh. The epidemiology and risk or associated factor of ProD is not clearly known.

Methods

A secondary analysis was carried out on data collected between 1996-2014 in a hospital-based Diarrhoeal-Disease-Surveillance-System (DDSS) in the Dhaka-Hospital of icddr,b. The DDSS enrolls a 2% systematic sample, regardless of age, sex, and diarrhoea severity. The data included information on socio-demographic factors, environmental history, clinical characteristics, immunization status, feeding practices, and diarrhoea pathogens.

Results

After cleaning of data, relevant information of 13027 children aged <5-years were available who admitted with diarrhoea with ≤ 13 days duration, and they comprised the study sample. Of them, 997 children admitted with ProD and considered as cases. The rest 11884 children, were admitted < 7 days diarrhoea (acute diarrhoea; AD), and they were considered as controls. In both the groups 40% were female children. In the ProD cases and AD controls the mean±SD age was 12.6±9.5 vs. 15.1±11.8 months (p<0.001), HAZ was -1.62±1.43 vs. -1.43±1.45 (p<0.001), and case fatality rate was 0.3% (n=5) vs. 0.1% (n=22) (p<0.001) respectively. Variables found significantly associated with ProD in bi-variate analysis were used in backward logistic regression analysis, which revealed that malnutrition status; prior use of any drug, admission with abdominal pain, and Shigella or other non-cholera-bacteria isolated from stool were the associated/ risk factors of ProD.

Conclusions

The above mentioned associated or risk factors of ProD in under-five children would help to differentiate prolonged diarrhoea from acute diarrhea who usually does need better care.
A POPULATION STUDY OF THE EPIDEMIOLOGY OF INVASIVE BLOODSTREAM INFECTIONS IN HOSPITALISED CHILDREN IN MALTA

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Background

Invasive bloodstream infections are a significant cause of morbidity and mortality in children. Identification of the causative pathogen from blood cultures is crucial in determining antibiotic susceptibility and rationalising treatment. We aimed to determine the incidence and epidemiology of bloodstream infections in hospitalised children more than 3 months old.

Methods

Results of all blood cultures taken from children aged 3 months-<16 years hospitalised on the paediatric medical wards and the neonatal intensive care unit at Mater Dei Hospital, Malta from 2010-2017 were retrieved from the Infection Control Unit. All isolates were analysed to differentiate pathogens from contaminants. Annual birth rate was obtained from Maltese National Statistics Office.

Results

Over the 8 year study period, 63 pathogens were isolated from a total of 5,044 blood cultures resulting in a positive rate of blood cultures of 1.25%. The mean annual incidence of septicaemia in children (median age: 1 year) was 12.34/100,000 children.

The most common pathogen was *Staphylococcus aureus* (n=14, 22.2%), 42% (n=6) of which were methicillin resistant. This was followed by *Streptococcus pneumoniae* (n=11, 17.5%), *Escherichia coli* (n=6, 9.5%) and *Enterococcus faecalis* (n=6, 9.5%).

Conclusions

*Staphylococcus aureus* is the most prevalent invasive pathogen in children >3 months old. Despite being recognised as a significant cause of invasive disease in children, its importance as a source of community acquired blood stream infection is increasing in contrast to the decline in the incidence of vaccine preventable invasive bacterial infections.
Vancomycin is a frequently used antibiotic in paediatric inpatient care. Recent data suggests that target trough levels should be 10-20 mg/L to achieve bacterial killing of MRSA, enterococci and coagulase negative staphylococci. The recommended paediatric dose (40-50mg/kg/day) is often insufficient to reach these levels leading to significant delays in reaching target trough levels with potential increase in morbidity/mortality. The aim of this study was to evaluate administered vancomycin doses and therapeutic drug monitoring(TDM) at the Children’s Hospital Iceland from 2012-2016.

Methods
This was a retrospective study investigating all children (younger than 18 years) who received ≥1 intravenous dose of vancomycin at the Children’s Hospital Iceland, during the study period, using electronic medical records. Student t-test and dichotomous regression analysis were used for statistical analysis.

Results
105 children received 163 vancomycin treatments during the study period. Average daily starting dose outside the NICU was 39.7 mg/kg/day and a starting dose above 45mg/kg/d was associated with a therapeutic TDM(p=0.027). TDM were never done in 58 treatments (35.6%) and of 275 TDM levels done, 144 (52.4%) were <10mg/L. In 44 treatments did a TDM lead to changed dose (38 increased dose). Malignancy was associated with increased risk of subtherapeutic levels compared with all other children(88.2% vs 65.1%, p=0.086).

Conclusions
In more than a third of started vancomycin treatments, no TDM was done. Malignancy was associated with lower TDM(only 11.8% had levels between 10-20mg/L). A subtherapeutic level only led to increased doses in 38/144(26.4%) of cases, potentially delaying bactericidal effects of the antibiotic. This study suggests that starting doses of vancomycin in children should be reconsidered, especially in relation to malignant diseases and supports the importance of antibiotic stewardship to ensure optimal antibiotic use.
FACTORS ASSOCIATED WITH LOW VITAMIN A COVERAGE AMONG YOUNG CHILDREN ADMITTED IN AN URBAN DIARRHEAL TREATMENT FACILITY IN BANGLADESH

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Background

This study was carried out to find out the factors affecting low vitamin A coverage among the young children admitted to a diarrheal hospital.

Methods

We extracted data from Diarrhoeal Diseases Surveillance System (DDSS) on children aged 12-59 months admitted in the Dhaka Hospital of icddr,b from 1996-2014. Logistic regression model was used to identify the factors that were significantly associated with non-compliance to vitamin A supplementation (VAS). Strength of association was determined by calculating adjusted odds ratio (aOR) and their 95% confidence intervals.

Results

A total of 8,649 children aged 12-59 months were enrolled in the DDSS during the period comprised the analyzable sample. Their mean±SD age was 25.2±12.8 months and 40% were female. Around 68% of them had VAS in the previous 6 months. In logistic regression analysis, older (>24 months) children (aOR: 1.39; 95% CI: 1.25-1.54), children having illiterate mother (aOR: 1.45; 95% CI: 1.27-1.64), illiterate father (aOR: 1.32; 95% CI: 1.16-1.50), coming from two lowest quintiles of wealth index (aOR:1.13; 95% CI: 1.02-1.27), parents having below average monthly income (<10,000 BDT, 1 USD=60 BDT (average during the study period) and children who had not received measles vaccination (aOR: 1.89; 95% CI: 1.63-2.19) were more likely to miss VAS in the preceding six months. We also observed an increase in VAS from 61% to 76% over the last 20 years (p<0.001).

Conclusions

Non compliance to VAS was found to be associated with older children, uneducated parents, poorest household wealth quintile, low family income and lack of measles vaccination. Specific programmatic approaches including prioritizing vulnerable children may enhance VA coverage.
Background

The vaccination against pneumococci is a part of NIP since 2009 in Slovakia. Currently both conjugated vaccines are involved to the NIP, thus PCV-13 as well as PCV-10. The National Reference Centre for Pneumococcal and Haemophilus Infections has been established, in the Regional Authority of Public Health in Banská Bystrica, two years after the implementation of vaccination to the NIP. The National Guideline has been approved since September 2011. The aim was to summarize actual epidemiological situation in IPD and in the IPD serotype distribution during the NRC activity 2011-2017 in Slovakia.

Methods

According to the National Guideline all confirmed cases of IPD have to be reported to the Slovak Epidemiological Information System (EPIS) and strains from laboratory confirmed cases have to be sent to the NRC for serotyping. Serotyping is usually carried out using the latex agglutination, quellung reaction and the multiplex PCR.

Results

Although the surveillance of IPD has a long-term character in Slovakia, serotyping is regularly carried out since 2011 after the NRC establishment. Before the introduction of vaccination to the NIP only two limited studies with serotype distribution analysis were performed. Data available from these studies suggest that the most prevalent \textit{S. pneumoniae} IPD serotypes before the vaccination were 14, 19A, 6A, 19F and 6B. In the years 2011-2017 the most prevalent IPD serotypes in Slovakia were serotypes 3 and 19A. During the 2011-2017 these two serotypes accounted 33.3% of all laboratory confirmed IPD cases.

Conclusions

Average IPD incidence in Slovakia represents 1.86/100,000 and is still influenced by underreporting. Therefore ongoing surveillance of IPD serotypes in Europe and Slovakia as well, remains essential for the monitoring of serotype replacement after implementation of mandatory vaccination.

Systematic Review Registration (Please input N/A if not registered)
N/A
RISK FACTORS FOR COMMUNITY ONSET CENTRAL LINE ASSOCIATED BLOODSTREAM INFECTIONS (CO-CLABSIS) IN PEDIATRIC ONCOLOGY PATIENTS

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Background

CLABSI is a well described complication linked to higher morbidity, mortality, longer length of stay and higher costs in childhood cancer. Although CLABSI management is well studied, there is paucity of data on bloodstream infections (BSIs) in ambulatory oncology patients (Community onset CLABSIs: COCLABSIs). Our aim was to identify risk factors for the development of COCLABSIs.

Methods

We conducted a case-control(1:2) study at a pediatric oncology hospital in Athens, Greece (12/2015-12/2017). Cases were defined as all patients with a central line (CL) and a BSI on the day of admission or the day after without a secondary focus of infection. Controls were selected from patients that visited the outpatient clinic (OC) the same day. Clinical and demographic characteristics including type of CL, time since placement, underlying disease, number of OC visits and the number of times the CL was accessed the previous week were recorded. Associations were evaluated using the chi-square test of independence and the Mann-Whitney test.

Results

Thirty-one cases and 56 controls were identified. Univariate analysis showed that factors found to be correlated with a higher probability of a COCLABSIs were a) Acute non lymphoblastic leukemia (AnLL) (88.89%) Vs. other cancer type, p=0.002 b) double lumen tunneled CL (42.62%) Vs. single, p=0.014 and c) neutropenic status (50.00%, p=0.007) (Table 1). Conditional multivariate logistic regression revealed that AnLL patients are 38 times more likely to develop a COCLABSIs (95%CI 1.87-772, p=0.018), patients with a double lumen CL 27 times (95%CI 1.71-431, p=0.019) and neutropenic 5 times (95% CI 1.11-24.02, p=0.036).
Conclusions

Factors such as Acute non-Lymphoblastic Leukemia, double lumen tunneled catheter and neutropenia increase the likelihood for a COCLABSI. After multivariate analysis AnLL, CL type and neutropenic status were independently associated with a COCLABSI. However the sample size may have limited our ability to detect other significant risk factors.
BLOOD CULTURE PACKS, A POLICY AND TRAINING ARE EFFECTIVE MEASURES IN REDUCING CONTAMINATION RATES IN CHILDREN

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Background

In an attempt to decrease blood culture contamination rates, a blood culture policy was launched in Mater Dei Hospital in February 2011. Paediatric blood culture packs as well as efforts at training doctors in the correct blood culture technique were introduced in 2014.

A previous study showed that following these measures, a decrease in blood culture contamination rates was observed (from 17.8% in 2012 to 8.4% in 2014; p=<0.0001). The aim of this study was to assess if the accepted blood culture contamination rate of 2-3% was reached.

Methods

Records of all blood cultures taken from children (0-<16 years) hospitalised between 1st January 2010 and 31st December 2017 were obtained. Blood cultures taken from children admitted to the oncology, surgical wards, day care unit and intensive care as well as those taken from a central line were excluded. The proportion of contaminants for each year was calculated and differences between the study years were analysed by means of a two tailed Z test.

Results

The mean blood culture contamination rate from 2010 to 2011 was 19.2% and this went down to a mean contamination rate of 3.72% between 2014 and 2017. The proportion of contaminants in 2012 – 17.8%, had decreased to 4.3% in 2014. This value has continued to decrease from 2014 to 2017 (contamination rate of 3%) and this decrease was found to be statistically significant with a p value of <0.0001.

Conclusions

Standardisation of blood culture techniques resulted in a decrease in the proportion of blood culture contamination to the observed international rates within 5 years. Efforts in education and training of hospital staff working with children should continue in order to sustain the low rates of blood culture contamination rates.
A CASE OF BRAIN ABSCESSES IN A PATIENT WITH OSTEOPETROSIS; A RARE COMPLICATION

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Title of Case(s)

A case of brain abscess in a patient with osteopetrosis; A rare complication

Background

Osteopetrosis is a congenital disorder characterised by thickened, dense bone predisposing to recurrent fracture resulting from defective osteoclast function. Many otolaryngological, neurological and haematological complications seen. Brain abscess formation is a very rare entity in osteopetrosis patient. Herein we discuss a case of viridans streptococci brain abscess who has osteopetrosis diagnosis.

Case Presentation Summary

An 14-year old boy with a previous diagnosis of osteopetrosis presented with the complaints of confusion and generalised convulsion. He had history of recurrent suppurative otitis media in the last year. On physical examination he had reduced consciousness and abnormal involuntary contractions in left arm. Laboratory examination revealed white blood cells 17,500/mm³ (80% neutrophil %20 lymphocyte), hemoglobin 8.5 g/dL and platelet count 456,000/mm³. C-reactive protein was 9.2 mg/dL. Computed tomography scan of head shows brain abscess formation so intravenous ceftriaxone, vancomycin and metronidazole started. In the fourth day of treatment he referred to our clinic for neurosurgical intervention. Contrast enhanced magnetic resonance imaging of the brain showed a multiloculated and multilobulated lesion with perilesional oedema and slight contrast enhancement in the right temporal lobe which was approximately 6x5x4.5 cm in diameter. Patient underwent abscess drainage through temporal lobe burr hole craniostomy. After surgery he follow up in paediatric intensive care unit but he had unfavourable clinical progress and after 24 hours of admission in PICU he was exitus. Surgical drainage culture showed growth of viridans streptococci sensitive to β-lactam antibiotic.

Learning Points/Discussion

Middle ear infections of patients diagnosed with osteopetrosis should be carefully monitored and treated for prevent possible life-threatening complications. Our case represents one of the unusual complications of osteopetrosis in the literature.
Increasing rates of antibiotic resistance have led to efforts to ensure appropriate antimicrobial utilization. Antimicrobial stewardship programs (ASPs) are essential components of this. Our centre has a paediatric ASPs (PROA-NEN), institutionalized since 2015.

Improving surgical antibiotic prophylaxis (SAP) use is fundamental in controlling resistance. Although the evidence basis for defining appropriate SAP is robust, the compliance is unsatisfactory.

Aims: 1) evaluate SAP in a tertiary paediatric hospital, 2) detect points of improvement, 3) develop strategies to increase quality of SAP. All from PROA-NEN

Methods

It is a uni-centric observational ambispective study. Semi-annual cross sections (each lasting 21 days) of the paediatric surgeries were made (excluding: neonates, ambulatory surgery) to evaluate the quality of paediatric SAP. Quality assessment of SAP was achieved through indicators of process (ECDC 2013) and pre-defined clinical indicators.

Results

165 patients and 96 SAP administrated. 65% of surgeries were clean and 20% clean-contaminate. In about 5-10% of the cases, they had unregistered data. The antibiotic was suitable in 73% of cases and 90% of patients received antibiotics during procedures where SAP was indicated. The initial time of antibiotic prophylaxis (within 60 minutes of surgical incision) was wrong in 60% of the cases and SAP exceeded 24 hours in 55%. A fully adequate SAP was considered in 57% of the procedures.

Conclusions

Despite the PROA-NEN project and its involvement in the optimization of PAP, there is still a wide range for improvement. The main problems detected were the initial time of antibiotic and the recorded data. PROA-NEN has initiated optimization strategies, based on educational intervention and the improvement in the quality of the computerized prescription. Furthermore, the implication of the team responsible of the patient is crucial.
04A. EDUCATION: SEVERE PNEUMONIA IN CHILDREN

POLYMERASE CHAIN REACTION IDENTIFYING PNEUMOCOCCAL COMMUNITY ACQUIRED PNEUMONIA IN CHILDHOOD

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Background

The utilization of the polymerase chain reaction (PCR) methods can increase the identification of the etiologic diagnosis of community acquired pneumonia (CAP).

Methods

We have included patients admitted due to severe CAP that were tested by lytA targeted PCR for Streptococcus pneumoniae detection. Chest X-rays were analysed by radiologists, blindly.

Results

Between January 2012 and December 2017, we have included 97 patients with CAP. The median age was three years (IQR=1-6 years), the median length of stay 13 days (IQR=7-22 days) and 3 (3.2%) deaths. There were 24.2% (n=23) patients that had used antibiotics previous to admission. Pleural effusion occurred in 46.4% (n=45) of the children, and it was associated with positive serum PCR (p=0.002). Pneumococcus was detected in 12.5% (n=11) of the cases by PCR, all of them with pleural effusion. There were six positive blood cultures, 2 of them with S. pneumoniae identified, 3 with Haemophilus sp and 1 with S. aureus. Of the patients with positive blood culture, two of them had positive PCR: one with S.pneumoniae in the blood culture and the other with Haemophilus sp.

Conclusions

The use of PCR increased the diagnosis in patients with culture-negative community-acquired pneumonia. The method seemed to be more sensitive in those with most severe pneumonia.
BURDEN OF DISEASE AND SOCIETAL COSTS DUE TO MENINGOCOCCAL DISEASE IN DENMARK – A NATIONAL REGISTER BASED STUDY

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Background

Detailed information on the burden and the associated societal costs of meningococcal disease in Denmark is limited. The objective of this study was to estimate the societal costs of meningococcal disease in Denmark as well as the burden of disease.

Methods

The study was designed as a retrospective study based on national Danish registries. Incident patients with meningococcal disease between 1980 and 2015 were identified in the National Patient Register and matched with two controls using direct matching on age, gender and level of education. Siblings constituted a secondary control population. Costs related to health care in the primary and secondary sector, prescription medicine, municipality homecare services, and costs of production loss were included. The burden of disease was assessed by analyses on mortality, sequelae a posteriori and follow-up on labour market status.

Results

Patients diagnosed with meningococcal disease have more sequelae, lower employment rates in the first year after diagnosis, and the mortality is significantly affected in the period immediate after the diagnosis. Actual health care costs are high (Table 1). The differences in costs between cases and controls are most significant in the baseline year (case: €3,439; control: €1,563) and the first year after diagnosis (case: €14,925; control: €1,279). Most plausibly the increased costs in the baseline year are explained by more prior comorbidities among cases compared to controls. Having a life time perspective and adding the loss due to premature death further increases the costs of meningococcal
disease.

Table 1. Actual costs per person in the baseline year (year 0) and the first five years after diagnosis with meningococcal disease among patients diagnosed 1997-2015 and their matched controls and sibling controls, respectively, Euros 2015 prices

<table>
<thead>
<tr>
<th>Year</th>
<th>Case</th>
<th>Control</th>
<th>Year</th>
<th>Case</th>
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<td>Year 3</td>
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Note: a) controls matched on age, gender and level of education. b) sibling controls are siblings to patients with meningococcal disease with same registered mother and father and ≤5 years difference in age between control sibling and case. If more than one control sibling exists, the one closest in age to the case individual was chosen. c) For the analyses on home care costs we only have data access after 2007. This means that only persons diagnosed from 2008-2015 are included in the analysis for that subcategory.

Conclusions

The costs and burden of meningococcal disease are substantial. The data presented in this study provides a cost of event estimate that may be informative in evaluating the impact of preventive interventions targeting meningococcal disease.
04A. EDUCATION: SEVERE PNEUMONIA IN CHILDREN

POLYMERASE CHAIN REACTION IDENTIFYING PNEUMOCOCCAL COMMUNITY ACQUIRED PNEUMONIA IN CHILDREN WITH SICKLE CELL DISEASE

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Background

Children with sickle cell disease (SCD) have a higher risk for encapsulated bacterial infection, particularly invasive pneumococcal disease. Despite the use of preventive care, pneumococcal community-acquired pneumonia (CAP) is still the most important cause of hospitalization in this patients.

Methods

Samples from children diagnosed with severe CAP were tested by lytA targeted PCR for Streptococcus pneumoniae detection. Chest X-rays were analysed by radiologists, blindly.

Results

It has been included 22 patients with SCD hospitalized due to CAP between January/2016 and December/2017. Those patients were compared with a cohort of 75 previously healthy patients also admitted due to CAP. The mean age was 5.5 years (CI95% = 3.56 – 7.44 years), the mean length of stay was 13.1 days (CI95% = 9.24 – 17.04 days) and there was 1 (4.5%) death. Pleural effusion occurred in 27.3% (n=6), five of them needed ICU care. S. pneumoniae was detected in 9% (n=2), one of them by pleural effusion PCR and the other by both serum PCR and blood culture. No other bacteria were detected. There were no statistically significant differences when comparing healthy, and SCD children with CAP regarding sex, age, and hospitalization in ICU, etiological diagnosis by PCR or blood culture, pleural effusion or previously antibiotics use.

Conclusions

Although the frequent utilization of prophylactic antibiotic and pneumococcal vaccines, SCD patients can have as severe pneumonia as the general population.
Background

Respiratory Tract Infections (RTI) are the most common disease in children. They range from short, auto-limited infections to severe disease requiring admission, with great economic and social impact. The majority of RTI are caused by viruses with overlapping clinical manifestations. Knowledge of the etiology of RTI may help to create a better understanding of the natural history of each virus, and eventually improve diagnosis and treatment. Real-time (RT) multiplex PCR is a highly accurate molecular test useful for identification of respiratory viruses.

Methods

Prospective observational study, from December 2016 to May 2017 of patients admitted in a Pediatric inpatient service with respiratory symptoms. Demographic data were collected. RT-PCR was performed on aspirated nasopharyngeal secretions for the following viruses: respiratory syncytial virus (RSV), adenovirus, influenza, parainfluenza, rhinovirus, human bocavirus, metapneumovirus, enterovirus, echovirus and coronavirus.

Results

83 patients were included, and at least one virus was isolated in 87.95% (73/83) of children. In patients with negative RT-PCR, only two had less than 12 months. Seventy-one percent (52/73) had one virus identified, 21% (15/73) two and 8% (6/73) three or more viruses. The most common viruses isolated in children with less than six months were RSV (24/46) and rhinovirus (12/46). In older children, RSV (20/56) and adenovirus (9/56) were the most frequent. Three patients needed intensive care: one month old with RSV and enterovirus; newborn with RSV and one year old with Influenza A.

Conclusions

RT-PCR was useful to identify the etiology of the RTI in a majority of patients and about one third had co-infections. We found no relation between age, etiologic agents, number of viral agents and severity of disease. This multiplex technique can help to understand the role of etiologic agents in RTI.
WEST SYNDROME IN INFANTS WITH SUSPECTED CONGENITAL ZIKA SYNDROME: UNEXPECTED ASSOCIATED PARTNERS?

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Title of Case(s)

WEST SYNDROME IN INFANTS WITH SUSPECTED CONGENITAL ZIKA SYNDROME: UNEXPECTED ASSOCIATED PARTNERS?

Background

Zika virus (ZIKV) has been associated with microcephaly and neuro-developmental abnormalities. West syndrome (WS) is a severe epileptic syndrome characterized by the triad of infantile spasms, hypsarrhythmia, electroencephalogram (EEG), and mental retardation. ZIKV laboratory diagnosis in pregnant women is difficult in low-middle resource countries. Overall, 143 infants born to suspected ZIKV-infected mothers are followed-up in a tertiary pediatric hospital in Guayaquil (Ecuador). We report the diagnostic and treatment challenges of the first four cases of WS associated with congenital ZIKV syndrome (CZS).

Case Presentation Summary

All cases had CZS signs/symptoms, seizures and hypsarrhythmic EEG compatible with WS (table). No mothers, except for case 4, had laboratory evidence of ZIKV during pregnancy. Blood, CSF and/or urine tested negative for CMV, Toxoplasma and ZIKV in all the children. Seizures did not respond to valproate, and imported vigabatrin controlled them.

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex (M/F)</th>
<th>Mother's symptoms during pregnancy (yes/no)</th>
<th>Gestational Age at birth (weeks)</th>
<th>Head Circumference at birth (cm(z-score))</th>
<th>Age at seizure onset (months)</th>
<th>Age at WS diagnosis (months)</th>
<th>Brain CT scan findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>yes</td>
<td>39</td>
<td>31(-3.4)</td>
<td>4</td>
<td>12</td>
<td>ventriculomegaly, calcifications in basal nuclei</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>no</td>
<td>40</td>
<td>32(-2.5)</td>
<td>3</td>
<td>11</td>
<td>ventriculomegaly, thin cortices, calcifications in basal nuclei</td>
</tr>
</tbody>
</table>
Learning Points/Discussion

ZIKV-infected mothers have difficulties to be diagnosed in low-middle resource countries. We report four cases of WS associated with suspected CZS diagnosed in Ecuador, in whom delayed treatment could have led to more severe neurological outcomes. The lack of vigabatrin in Ecuador potentially worsened the clinical condition of these children.
ROTAVIRAL INFECTION AT INFANTS AND TODDLERS IN CENTRAL ROMANIA, A SIX YEAR STUDY

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Background

Rotavirus infection is one of the most common causes of diarrheal disease in young children. The aim of the study was to assess the prevalence of rotavirus infection in Brasov area along with the particularities of lab exams in children admitted at the Clinic Children's Hospital Brasov during 2011-2016.

Methods

A retrospective study has been conducted over a six-year period, between 1st of January 2011 and 31st December 2016 at the Clinic Children's Hospital, Brasov, Romania. The study included a number of 716 patients aged ten days to 7 years old, having the diagnosis of rotaviral infection.

Results

23% of patients received antibiotics prior to admission. Prevalence of the infection during the studied time-frame was 26.9% during autumn months.

69% have been encountered in caucasians population and 25% lived in extremely poor life conditions.

Iron deficiency was encountered at 53% of patients (normal value 50-120 mg/dl), 13% had anemia.

Furthermore, 46% of patients were treated with antibiotics, out of which only 4% had criteria for antibiotic treatment (CRP higher than 5mg/dl). 11.3% of patients were discharged from the hospital in the week prior to the rotavirus infection.

Average hospitalization period per patient was 4.53 days.

Conclusions

Prevalence of rotaviral infection is high in Brasov, central Romania during autumn and winter. Particular for our study population is the presence of anemia and iron deficiency.
A pediatric case of pneumococcal meningitis due to Streptococcus pneumoniae serotype 10A

Background

Streptococcus pneumoniae is a leading causative agent for bacterial meningitis, pneumonia and septicemia. 13-valent pneumococcal conjugate vaccine are routinely used for children in Turkey from April, 2011. After vaccination has been introduced non-vaccine serotypes began to isolated from children with invasive disease more often as a result of serotype replacement. Herein we report a pediatric meningitis case due to S. pneumoniae 10A with no underlying condition.

Case Presentation Summary

A 6 month old girl presented with complaints of fever, lethargy and sudden abnormal contractions of the muscles. She was sleepiness and anterior fontanel bulging seen in physical examination. On admission, body temperature was 36.9 °C, heart rate 130/bpm and blood pressure was 90/60 mmHg. Laboratory examination revealed white blood cells 36.400/mm³ (82% neutrophil), C-reactive protein 12.6 mg/dL and procalcitonin 4.21 ng/mL. The cerebrospinal fluid was clear, colorless with leukocyte count at 500/mm³, protein levels at 93 mg/dL, and glucose levels at 55 mg/dL (blood glucose 117 mg/dL). Patient was diagnosed as meningitis and intravenous ceftriaxone and vancomycin started. The cerebrospinal fluid culture yielded penicillin-resistant pneumococci and the isolate was identified as serotype 10A. On the fourth day of treatment convulsive contractions seen in left arm and left leg. Intravenous phenytoin was started immediately, and computed tomography scan of head shows no pathology. Patient treated with ceftriaxone and vancomycin for fourteen days and fully recovered. During follow ups no complications seen.

Learning Points/Discussion

While the effect of pneumococcal vaccine in reducing invasive pneumococcal disease is known, necessity of surveillance for serotype replacement is also evident. Routine surveillance for meningitis cases confirmed with PCR, will be helpful to maintain strategy to further pneumococcal immunization program.
09C. SCIENCE: INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS

NOROVIRUS INFECTION – FREQUENCY AND DURATION OF VIRAL SHEDDING IN PAEDIATRIC HAEMATO-Oncologic PATIENTS
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²Medical University of Graz, Institute of Hygiene- Microbiology and Environmental Medicine, Graz, Austria

Background

Noroviruses (NV) cause severe gastrointestinal infections. Incidence and duration of shedding in paediatric haemato-/oncologic patients has not been studied so far.

Methods

We retrospectively analysed results of NV reverse transcription PCRs from stools obtained from haemato-/oncologic patients from 2010 to 2016. NV PCRs were performed as screening in stem cell transplantation recipients or in patients with symptoms of gastroenteritis.

Results

997 results from 152 patients (age 0.2-33.6, median 8.2 years, female 44.7%) were evaluable of which 241 PCRs (24.2%) were positive for NV. 39/152 patients (25.7%, age 0.3-21.5, median 6.9 years, 33.3% female) were tested positive at least once. In 23 (59.0%) of 39 positive tested patients, end of shedding could be defined and was documented for 2 to 170 (median 25) days.

In 7/39 (17.9%) positive tested patients end of shedding could not be defined (despite multiple testing), with documented shedding for at least 4 to 160 (median 11) days. A 15-year-old female patient with primary immunodeficiency has been shedding up to now for at least 5.2 years. In 8/39 (20.5%) positive tested patients, no follow-up examination was performed. In 19/39 positive tested patients (48.7%), shedding of more than 2 weeks and in 15/39 patients (38.5%) shedding of more than 4 weeks was documented without persistence of norovirus-typical symptoms during this period.

Conclusions

NVs in stool were detected in a quarter of patients tested. Duration of shedding was variable and was documented for up to 6 months - for one patient longer than 5 years. Nearly 40% of the positive tested patients showed shedding of more than 4 weeks. These mostly asymptomatic shedders may be a major source of infection for other patients.
Background

Late-onset neonatal sepsis is a healthcare-associated infection and a major cause of neonatal mortality, with the incidence of 1-5:1000 newborns. Risk factors for this disease include prematurity, low birth weight, use of central venous catheters and other devices.

Methods

We conducted a retrospective descriptive study performed on a Brazilian NICU from January/2011 to December/2016. We included all newborns in NICU with late-onset neonatal sepsis and bacteraemia.

Results

The admission rate in this NICU is around 300 newborns per year. The cohort was 107 newborns admitted in NICU, which had 147 episodes of late-onset neonatal sepsis during the six years study. The mean gestational age was 31.6 weeks (95% CI 30.7 - 32.5 weeks); the frequency of low birth weight was 82.2% (n=89) and the lethality rate was 26.2% (n=28) in 30 days. Invasive devices were used in 79.4% (n=85) and parenteral nutrition was received in 70.1% (n=75) of the newborns. The most prevalent etiology was Coagulase-negative Staphylococcus (CNS) with 40.5% (n=60) of cases and 71.7% (n=38) oxacillin resistance. The second most prevalent etiologic agent was Klebsiella with 29.7% (n=44) of cases and 54.5% (n=24) extended-spectrum beta-lactamase. Only one of the gram-negative bacteria was carbapenem-resistant.

Conclusions

Most of the bacteria causing late-onset neonatal sepsis were antibiotic-resistant strains. Strategies to improve the management of these neonates remain a concern to reduce healthcare-associated infection and the antibiotics resistance.
Background

Now (2018) there is no universal vaccination against rotavirus infection in Ukraine. Making vaccination for the parents' expense has led to coverage of only 0.15-0.6%.
We tried to study whether rotavirus infection incidence may decrease in children without using of vaccination.

Methods

Children 0-59 months of age who were hospitalized for AGE at 2 sentinel sites in Kyiv and Odesa were enrolled into the active, prospective surveillance program. In Odesa, the surveillance period was during 2007-2015 and in Kyiv, it was during 2011-2015. Stools were tested for rotavirus and positive specimens were genotyped.

Results

During July 2007-June 2015, 12,350 children were enrolled in the surveillance programs and had stool specimens collected and tested for rotavirus. Overall, rotavirus infection was diagnosed in 5412/12350 (44%) of children, 929/1734 (54%) of those in Kyiv and 4483/10616 (42%) in Odesa. These data have not changed during all observation period in conditions of absence of universal vaccination. Rotavirus infections peaked during the winter months. Children with rotavirus AGE displayed more severe clinical symptoms than those without rotavirus. The predominant genotypes identified were G1P[8], G2P[4], G3 P[8], G4 P[8] and G9 P[8].

Conclusions

Active epidemiologic surveillance of AGE in hospitalized children younger 5 years in two large Ukrainian cities reveals a significant burden of rotavirus infection. The proportion of rotavirus-associated hospitalizations remained high during all years of observation.

Clinical Trial Registration (Please input N/A if not registered)
PREVALENCE AND IMPACT OF CO-INFECTIONS IN PEDIATRIC PATIENTS WITH RESPIRATORY INFECTIONS ATTENDING PRIMARY CARE HEALTHCARE (FLUGAL)

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²Hospital Clínico Universitario de Santiago, Translational Pediatrics and Infectious Diseases, Santiago de Compost, Spain
³Centro Saude Lousame, Pediatra de Atención Primaria, A Coruña, Spain
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⁶Hospital Clínico Universitario de Santiago de Compostela, Servicio de Microbiología, Santiago de Compostela, Spain
⁷Instituto de Ciencias Forenses- Facultade de Medicina- Universidade de Santiago de Compostela, Unidade de Xenética- Departamento de Anatomía Patolóxica e Ciencias Forenses, Santiago de Compostela, Spain

Background

The impact of co-infections in primary care healthcare is poorly known. The aim of the present study was to analyse the clinical patterns and phenotypes of co-infections in paediatric patients attending primary care consultations for acute respiratory infections (ARI).

Methods

A prospective, controlled, multicentre study was carried out through a network of primary care centres (ReGALIP; www.regalip.org) during 2016-2017 in children <18 years of age attended due to an ARI. A polymerase chain reaction (PCR) was carried out in nasopharyngeal swabs for the detection of influenza (AH1, AH1pdm09, AH3, B), metapneumovirus, respiratory syncytial virus, parainfluenza (1-4), rhinovirus, enterovirus, adenovirus, bocavirus and coronavirus (NL63, 229E, OC43) and also for Mycoplasma pneumoniae, Chlamydyphila pneumoniae, Legionella pneumophila, Haemophilus influenzae, Streptococcus pneumoniae, Bordetella pertussis, Bordetella parapertussis.

Results

A total of 343 samples were collected, 277 patients with ARI and 66 controls. 10.1% (n=28) of the patients vs. 66.6% (n=44) of the controls were negative. In patients with ARI, the most frequently identified microorganism were rhinovirus (n=119), H. influenzae (n=91) and S. pneumoniae (n=87). Virus-bacteria co-infections were detected in 38.1%. Rhinovirus (n=14, 21.2%) was the pathogen most frequently found in controls, while RSV, influenza, metapneumovirus or adenovirus were not detected. Bacteria appeared in 10.6% (n=7) of the controls. The presence of co-infections in patients with ARI occurred in 49.8% (n=138) of the cases, while in asymptomatic children occurred in only 7.6% (n=5) of
Conclusions

Molecular techniques applied to the primary care context reveal very frequent co-infection in children with ARI. A pathogen can be detected in about 90% of patients requiring consultation for ARI of which the diagnosis is generally based on clinical symptoms. The impact of different co-infection patterns on clinical course deserve further research.

Clinical Trial Registration (Please input N/A if not registered)
HOW PREDICTIVE 2 NEGATIVE CRPs (<5) ARE OF NEGATIVE BLOOD CULTURES IN SUSPECTED NEONATAL SEPSIS AND ITS POTENTIAL ROLE SHORTENING HOSPITAL STAY FOR WELL NEWBORNS

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Background

In asymptomatic neonates treated for suspected sepsis, NICE recommend having blood culture (BC) reports negative at 36-hours before ceasing antibiotics/permitting discharge. Many hospitals even require 48-hour reports. Research suggests most pathogenic BCs are positive within 24-hours. Unnecessarily prolonged hospital stays burden resources and families. We assessed the local impact of stopping antibiotics at 24-hours following 2x CRP results <5 and negative BCs.

Methods

We locally identified 445 newborns treated with antibiotics for suspected sepsis between May-December 2017. Each had a BC sample and CRP taken at birth, with a second CRP at 18-hours. Taking positive BCs as indicative of true sepsis, we assessed the negative-predictive-value (NPV) of 2x ‘negative’ (<5) CRPs in predicting negative BCs.

Results

Of 297 babies with 2x negative CRPs, 98% were BC negative (NPV=0.98). There were 5 positive BCs within this CRP negative group; all assessed as contaminants/clinically insignificant. All 10 other positive cultures had at least 1 positive CRP. Sampling the CRP negative cohort, having excluded babies needing transfer and <35-weeks gestation (19% of total), we found 84% of the remaining were asymptomatic and awaiting negative 48-hour cultures for discharge. The average total time of antibiotic administration was 56-hours (average of 4.7 doses per baby). With an earlier discharge at 24-hours, we extrapolate, a total potential saving of 622 doses, 6220 nursing-minutes, and 124 bed-days between May-December.

Conclusions

Had all asymptomatic babies with 2x negative CRPs stopped antibiotics following a negative BC at 24-hours, no bacteraemic cases would have been missed in our series and would have resulted in significant savings, strengthening the case for a change in practice.
Management of refractory Chikungunya arthritis with methotrexate

Background

In 2014 the Brazilian Ministry of Health confirmed autochthonous transmission of Chikungunya virus (CHIKV) in the country. The disease is characterized by fever associated with severe and debilitating arthralgia, headache, rash, and myalgia. Polyarthralgia generally improves after ten days but may last for months to years, in up to 4 to 63% of the cases. The clinical presentation of CHIKV in children differs from adults, only 20% developing arthralgia. CHIKV-induced arthritis is also significantly less prominent in children than in adults.

Case Presentation Summary

A 12-year-old healthy boy presented to our service with intermittent joint pain, fever, and odynophagia that began during a trip to Northeastern Brazil, 2016. The patient later presented vomiting, major arthralgia, diffuse erythematous macules and pain-induced abnormal gait. Serological testing confirmed CHIKV infection. During follow-up, the patient presented improvement of the systemic symptoms but maintained chronic, worsening arthralgia, affecting several joints, mainly knees and ankles, but also wrists and shoulders, mostly associated with physical effort. He also presented edema, hyperemia and heat in some joints, morning stiffness and Raynaud’s phenomenon about three times a day. There was no improvement with common analgesics and nonsteroidal anti-inflammatories. Methotrexate was started with significant symptom improvement. The patient remains well, without arthritis, with occasional arthralgia during important efforts, without the need for analgesia.
CHIKV infection has emerged with major arthritic epidemics, leading to chronic and severe pain, with an important impact on patients’ quality of life. Evidence-based therapy is still limited, especially for children. Studies are underway to assess the treatment of such cases with methotrexate. Our case shows a child with an important joint impairment after chikungunya infection, with a successful outcome after methotrexate therapy.
Background

One important key-point of antimicrobial stewardship programmes is the measurement of the appropriateness and quality of hospital antibiotic usage. Although a number of quality indicators (QI) has been described and evaluated in adults, little is known for children.

Aim: A systematic literature review on QI for antibiotic usage in children.

Methods

We performed a literature review using PUBMED to identify studies regarding the development or evaluation of QIs for antibiotic use in hospitalized children. The terms used were: “quality indicators and antibiotic prescribing”, “quality indicators and anti-bacterial agents”, “quality indicators and antibiotic”, “process indicators and anti-bacterial agents”, “process indicators and antibiotics”, “process indicators and antibiotic prescribing”. There was no limit for period time and languages used were English, German, Portuguese, Spanish.

Results

The initial search identified 3949 articles. After application of several filters, 1887 articles were selected and 912 of them were excluded because of duplication. The remaining 975 articles were analysed and 845 were excluded (not related to hospital care/antibiotic use or not related to quality/process indicators for QI ATBs). The following analysis selected 78 articles and from these, 26 articles were selected, containing 131 QI. An additional 106 articles were excluded (55 for adult setting and 51 because of duplication, and 25 QI were included for final analysis. We identified 10 general recommendations for antibiotic use in children, two for recommendation for community-acquired pneumonia in children, two for antibiotic prophylaxis and three for urinary tract infections.

Conclusions

Quality indicators are important components in antimicrobial stewardship programmes and identification of these recommendations should be used in paediatric healthcare institutions.

Systematic Review Registration (Please input N/A if not registered)
N/A
EVALUATING THE POTENTIAL CLINICAL UTILITY OF A HOST-PROTEIN SIGNATURE FOR DISTINGUISHING BETWEEN BACTERIAL AND VIRAL DISEASE IN FEBRILE CHILDREN

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²MeMed Diagnostics, n/a, Tirat Carmel, Israel
³Schneider Children’s Medical Center of Israel, Infectious Diseases, Petach Tikva, Israel

Background

A novel assay (ImmunoXpert™) that integrates the serum levels of three host-response proteins (TRAIL, IP-10, and CRP) was developed to assist in differentiation between bacterial and viral disease. The assay exhibited high performance in double blind validation studies. We sought to evaluate the assay’s potential clinical utility.

Methods

The study was conducted at the emergency department of a pediatric tertiary care facility. As part of the interim analysis of the ongoing “ROSETTA” study, we performed a sub-analysis of prospectively recruited children ≥3 months, presenting with upper and lower respiratory tract infections or fever without source. For every participant, the managing physician completed a questionnaire indicating whether they suspected a bacterial or viral etiology after the initial history and physical examination. We analyzed the concordance between ImmunoXpert™ results and (a) the physician assessment at presentation and (b) a reference standard diagnosis, determined by three independent experts based on comprehensive clinical and laboratory investigation, including a nasal swab multiplex-PCR and patient follow up.

Results

Out of 127 children, 37% presented with fever without source, 42% with upper and 21% with lower respiratory tract infection. As shown in the figure, senior physicians’ diagnoses were with better concordance with ImmunoXpert™ results than residents’ diagnoses. Notably, the assay had a concordance of 95% to the reference standard, significantly higher than that of the residents and
senior physicians (P=0.01).

Figure 1. ImmunoXpert™ concordance increases with physician's seniority and when compared with reference standard

Conclusions

The ImmunoXpert™, taken at presentation, demonstrated a higher concordance rate with expert panel diagnosis, compared with initial clinical suspicion. This supports the assay's potential clinical utility in facilitating timely and accurate diagnosis, thereby reducing diagnostic work-up and antibiotic misuse.

Clinical Trial Registration (Please input N/A if not registered)

N/A
HAVE YOU COME MADE A VACCINATION ERROR? KNOWLEDGE AND PERCEPTION OF IMMUNIZATION ERRORS IN CATALONIA.

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²Departament de Salut Generalitat de Catalunya, CIBERESP, Barcelona, Spain

Background

Immunization is the procedure through which a person is vaccinated by a healthcare professional (HP), to induce specific immunity. Vaccination error (VE) awareness may be important because of possible reduction in vaccine efficacy, presentation of adverse effects and confidence impairment in HPs and vaccines, according to patient safety perspective. It is important to assess the scope of VE in order to plan HP training in order to reduce its impact. To know the degree of error perception, perceived frequency, conditioning factors, level of knowledge about VM prevention and the actions to be taken in front of each one of them.

Methods

On-line survey carried out on HP in vaccination centers (VC) of 2 health regions of Catalonia.

Results

720 surveys were sent and the response rate was 31%. 92.7% were responded by nurses. 52.6% were older than 20 yo. Degree of perception of VE was 66.1%, 22.2% had personal perception it happened some time ago, while 84.5% believed it happened in the VE to other HP. The main reasons declared for EV were work overload, similar packagings and brand changes. 60% knew the procedure for post-EV.

Conclusions

Majority of HP are aware of the fact that VE is committed. Errors occur because HP are not aware of the nature of VM and because there is no knowledge of an existing notification system for VE reporting. We believe that training of VE and VE notification systems are necessary.
The Brazilian Ministry of Health (BMH) offers, since 2014, HPV vaccination for healthy girls (ages 9 to 14), and people living with HIV (PLHIV; ages 9 to 26). Since 2017 it is also offered for boys from 11 to 13 yrs. BMH data show a coverage rate of 45% in girls. Data on vaccine coverage in PLHIV is scarce. We aim to evaluate this vaccine coverage in healthy individuals and PLHIV and assess factors associated with non-vaccination.

Methods

Retrospective study analyzing two groups: [Group 1] 26 PLHIV, ages 9 to 26, following at the pediatric infectious diseases outpatient clinic. Adequate vaccination: 3 doses or vaccination underway. [Group 2] 111 healthy individuals, ages 9 to 17, from a local private school. Adequate vaccination: 2 doses or vaccination underway.

Results

Among [Group 1], 73% were adequately vaccinated, with little difference between men and women. Among [Group 2], 68.5% were adequately vaccinated, 74% among girls and 65% among boys.
In Brazil, there is a low HPV vaccination coverage, despite its contribution to reducing cervical and other cancers. Our study showed a higher coverage rate in both groups. A long-term follow-up with the same medical team, with a well-established doctor-patient relationship, can lead to better coverage of the patients in [Group 1]. The BMH, in a partnership with the Ministry of Education, created a national programme for HPV vaccination in schools. The patients in [Group 2] had the opportunity of being vaccinated at their school, which could have increased coverage of this group. Educational campaigns involving healthcare workers and the general populations are fundamental in improving HPV vaccine coverage.

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n=26)</th>
<th></th>
<th>Group 2 (n=111)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>♀ n=19</td>
<td>♂ n=7</td>
<td>♀ n=88</td>
<td>♂ n=23</td>
</tr>
<tr>
<td>Adequate vaccination</td>
<td>73%</td>
<td></td>
<td>68,5%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>♀ 73,6%</td>
<td></td>
<td>♀ 73,9%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>♂ 71,4%</td>
<td></td>
<td>♂ 65,2%</td>
<td></td>
</tr>
<tr>
<td>Vaccination completed</td>
<td>53,8%</td>
<td></td>
<td>55,8%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>♀ 68,4%</td>
<td></td>
<td>♀ 67,04%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>♂ 14,2%</td>
<td></td>
<td>♂ 13,04%</td>
<td></td>
</tr>
<tr>
<td>Vaccination underway</td>
<td>19,2%</td>
<td></td>
<td>16,2%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>♀ 5,2%</td>
<td></td>
<td>♀ 6,8%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>♂ 57,1%</td>
<td></td>
<td>♂ 52,2%</td>
<td></td>
</tr>
<tr>
<td>Vaccination late</td>
<td>15,8%</td>
<td></td>
<td>9,9%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>♀ 15,7%</td>
<td></td>
<td>♀ 12,5%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>♂ 14,2%</td>
<td></td>
<td>♂ 0%</td>
<td></td>
</tr>
<tr>
<td>No vaccine doses</td>
<td>11,5%</td>
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<td>18%</td>
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<td></td>
<td>♀ 10,5%</td>
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</tr>
<tr>
<td></td>
<td>♂ 14,2%</td>
<td></td>
<td>♂ 34,78%</td>
<td></td>
</tr>
</tbody>
</table>

Table 1. Vaccine coverage in each group, divided by sex.

Conclusions

In Brazil, there is a low HPV vaccination coverage, despite its contribution to reducing cervical and other cancers. Our study showed a higher coverage rate in both groups. A long-term follow-up with the same medical team, with a well-established doctor-patient relationship, can lead to better coverage of the patients in [Group 1]. The BMH, in a partnership with the Ministry of Education, created a national programme for HPV vaccination in schools. The patients in [Group 2] had the opportunity of being vaccinated at their school, which could have increased coverage of this group. Educational campaigns involving healthcare workers and the general populations are fundamental in improving HPV vaccine coverage.
CEFOTAXIME-INDUCED DRUG REACTION WITH EOSINOPHILIA AND SYSTEMIC SYMPTOMS (DRESS) COMPLICATED BY HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS (HLH)

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Title of Case(s)

Cefotaxime-induced drug reaction with eosinophilia and systemic symptoms (DRESS) complicated by hemophagocytic lymphohistiocytosis (HLH)

Background

Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is a rare, life-threatening syndrome with rash, fever, eosinophilia, lymphadenopathy and internal organ involvement; the incidence is 0.9 / 100,000. In majority of the patients, the reaction begins two to six weeks after the initiation of the medication. It is frequently associated with anticonvulsants, allopurinole and rarely antibiotics. Skin biopsy findings are consistent with nonspecific drug hypersensitivity. Four pediatric patients with cefotaxime-induced DRESS has been reported. This case is the first report of cefotaxime-induced DRESS complicated by HLH in a child.

Case Presentation Summary
Five-year old male with a cochlear implant due to congenital bilateral hearing loss was hospitalized for *Streptococcus pneumoniae* mastoiditis abscess and received cefotaxime. On the 14th day of the treatment, he developed 39°C fever, maculopapular rash, hepatomegaly, pancytopenia, eosinophilia and increased levels of transaminases. HLH was considered due to high levels of ferritin, triglyceride and hemophagocytosis in bone marrow aspiration and IVIG was given at 1 gr / kg. Fever persisted and the patient developed rash and eosinophilia on the 4th day of follow, that's why DRESS was considered. Skin biopsy findings were compatible with DRESS. For treatment 1 mg / kg / day systemic methylprednisolone was initiated, the fever dropped rapidly, the rash disappeared and the laboratory values quickly returned to normal.

**Learning Points/Discussion**

DRESS is a rare clinical syndrome and there is no previous report of cefotaxime induced DRESS complicated by HLH. In patients with severe fever and rash at least 2 weeks after drug use, DRESS should be kept in mind and the patient should be followed for signs and symptoms of HLH.
CLINICAL CHARACTERISTICS ASSOCIATED WITH RESPIRATORY SYNCYTIAL VIRUS IN CHILDREN HOSPITALIZED WITH ACUTE RESPIRATORY TRACT INFECTION

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Background

Respiratory Syncytial Virus is a frequent cause of hospitalization in young children. Unfortunately, RSV is difficult to diagnose on a clinical basis. First, RSV causes a wide spectrum of clinical disease, ranging from relatively mild upper respiratory tract infection to severe pneumonia. Second, bronchiolitis, which is the classical clinical manifestation of RSV infection in young infants, is not specific to RSV infection but can be caused by other viruses. The objective of our study was to identify clinical parameters associated with RSV in children hospitalized with acute respiratory tract infection.

Methods

We prospectively collected medical data and multiplex real-time PCR results from children hospitalized with acute respiratory tract infection (aRTI). Logistic regression was applied to identify clinical parameters independently associated with RSV infection. Between November 2014 and March 2017, 1068 children with ARTI were enrolled in our study.

Results

At least one viral respiratory pathogen was detected in 82% (875/1068). RSV infection was identified in 41% (n=440). Duration of clinical symptoms ≥ 2 days on admission, month of admission, cough, younger age and rale were independently associated with RSV infection. We developed a RSV risk score. Children with a score >22 had an RSV pretest probability of 64% (95% CI 59 – 69%), children with a score 12 – 22 of 36% (95% CI 31-41%), and a score <12 reduced the risk of RSV infection to...
7% (95% CI 4 – 12 %).

Risk score for RSV infection in children hospitalized with ARTI. The green letters indicate the individual risk points for a patient 12-23 months old, admitted in March, with the clinical symptoms of rale and cough and a duration of clinical symptoms of 2 days or more (on admission).

<table>
<thead>
<tr>
<th>Risk points</th>
<th>Total score (max.25)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
</tr>
<tr>
<td>0-5 months</td>
<td>5</td>
</tr>
<tr>
<td>6-11 months</td>
<td>4</td>
</tr>
<tr>
<td>12-23 months</td>
<td>3</td>
</tr>
<tr>
<td>≥ 2 years</td>
<td>2</td>
</tr>
<tr>
<td><strong>Admission month</strong></td>
<td></td>
</tr>
<tr>
<td>november</td>
<td>0</td>
</tr>
<tr>
<td>december</td>
<td>5</td>
</tr>
<tr>
<td>january</td>
<td>5</td>
</tr>
<tr>
<td>february</td>
<td>5</td>
</tr>
<tr>
<td>march</td>
<td>2</td>
</tr>
<tr>
<td>april</td>
<td>0</td>
</tr>
<tr>
<td>rale</td>
<td></td>
</tr>
<tr>
<td>yes</td>
<td>5</td>
</tr>
<tr>
<td>no</td>
<td>2</td>
</tr>
<tr>
<td>cough</td>
<td></td>
</tr>
<tr>
<td>yes</td>
<td>5</td>
</tr>
<tr>
<td>no</td>
<td>0</td>
</tr>
<tr>
<td>duration of symptoms at admission</td>
<td></td>
</tr>
<tr>
<td>≤1 day</td>
<td>0</td>
</tr>
<tr>
<td>2 days or more</td>
<td>5</td>
</tr>
<tr>
<td>Total risk score</td>
<td>20</td>
</tr>
</tbody>
</table>

**Conclusions**

A simple clinical score identifies children with high pretest probability of RSV infection, and might thus guide clinicians in the responsible application of RSV test assays.
**Background**

Tuberculous meningitis (TBM) is a severe, but uncommon presentation of tuberculosis (TB) disease. The published data on TBM in children in Europe are limited. This study aimed to determine the performance of immune-based and microbiological tests in routine clinical practice in this patient population.

**Methods**

Members of ptbnet, a network comprising >180 members in 29 European countries, reported TBM cases treated at their healthcare centre using a web-based instrument collecting a standardised dataset for each case.

**Results**

A total of 120 paediatric patients with TBM were included in the final analysis; 54 (45.0%) were definite, 41 (34.2%) probable and 25 (20.8%) possible cases. The median age was 2.6 (IQR: 1.1-6.1) years. 108 (90.0%) were born in Europe, of whom 57 (52.8%) had ≥1 parent originating from a high TB incidence country. Of 110 cases who underwent cranial imaging with CT and/or MRI, 54 (49.1%) had hydrocephalus, 45 (40.9%) basal meningeal enhancement, 33 (30.0%) tuberculomas and 14 (12.7%) cerebral infarcts. Of 84 cases with quantitative tuberculin skin test (TST) results, 53 (63.1%) had a positive test result at the 5mm cut-off and 46 (54.8%) at the 10mm cut-off. Of 74 cases with interferon-gamma release assay (IGRA) results, 55 (74.3%) had a positive, 9 (12.2%) a negative and 10 (13.5%) an indeterminate test result (no significant difference between TST at lower cut-off and IGRA sensitivity). On cerebrospinal fluid testing, 3/77 (3.9%) cases were acid-fast bacilli stain-positive, 47/96 (48.9%) culture-positive, 24/74 (32.4%) PCR-positive. Culture had significantly higher sensitivity than PCR (95%CI 39.2-58.8% vs. 22.9-43.7%; p=0.0412).

**Conclusions**

Existing immune-based and microbiological tests have suboptimal sensitivity in children with TBM. Tests with better performance characteristics are urgently needed to enable early diagnosis of TBM.
BRODIE ABSCESS IN A PATIENT PREVIOUSLY HEALTHY BOY

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Title of Case(s)

Brodie abscess in a patient previously healthy boy

Background

Brodie abscess is a subacute form of hematogenous osteomyelitis and defined as any infectious process in the bony tissue persisting for more than 2 weeks without any symptoms of acute illness. Here we report brodie abscess localizing in the right distal tibia who previously healthy boy.

Case Presentation Summary

A 17 years old boy presented with progressive right leg pain and swelling for 1 month. He had no history of fever or recent trauma. Physical examination showed swelling and local redness in the anterolateral part of his right ankle. Laboratory examination revealed that white blood cells 9.200/mm³ (70% neutrophil), hemoglobin 14.2 g/dL and platelet count 272.000/mm³. Eritrocyte sedimentation rate was 53 mm/h and C-reactive protein was 4.69 mg/dL (<0.5 mg/dL). Magnetic resonance imaging of right ankle revealed a 4 cm diameter intramedullary lesion located in the distal right tibial metaphysis with sclerotic margins. The central part of the lesion was iso-hypointense while peripheral lining of the lesion was hyperintense on T1-weighted images and lesion hyperintense on T2-weighted images. Extensive bone marrow edema, periosteal thickening and deep soft-tissue edema were observed surrounding the lesion margin. He was diagnosed as Brodie abscess, and intravenous teicoplanin and imipenem started. The patient planned to undergone a surgical procedure for excision of the abscess cavity after a preoperative course of antibiotic therapy.

Learning Points/Discussion

Brodie abscess diagnosis is clinically difficult because patients generally have mild local symptoms with nearly normal laboratory values. Radiological evaluation plays an important role in the diagnosis but also Brodie's abscess may mimic various benign or malignant condition. Systemic antibiotics and surgical debridement is the main corner of treatment.
TYPHOID FEVER OUTBREAK IN SÃO PAULO, BRAZIL

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¹Santa Casa São Paulo, Pediatrics Infectious Diseases, São Paulo, Brazil

Title of Case(s)

TYPHOID FEVER OUTBREAK IN SÃO PAULO, BRAZIL

Background

Typhoid fever is a severe systemic illness presenting with fever and abdominal pain, caused by Salmonella enterica serotype Typhi. It affects mainly children and young adults in impoverished areas with poor sanitation and unsafe food and water. In Brazil, the incidence coefficient of typhoid fever is lower than 0.5/100.000 inhabitants. Here we report a typhoid fever outbreak that occurred in the city of Sao Paulo, Brazil, on May 2017.

Case Presentation Summary

Six suspected cases were admitted to the Pediatric Department, all children studied at the same school and were between 4 and five years of age. They presented with fever and abdominal pain for as long as 23 days. Hepatosplenomegaly was found in five patients, along with increased liver enzymes. The treatment choice was intravenous 3rd generation cephalosporin, which sometimes was switched to oral therapy with Trimethoprim-Sulfamethoxazole when the patient was ready to be discharged. Three patients had a Salmonella enterica serotype Typhi isolated from blood culture, and one patient had it isolated on a stool sample. The other patients without laboratory confirmation were suspected and treated because of the similarities between clinical presentation and strong epidemiology. (see table 1). There was a 41-year-old woman that worked as a cook at the school that
was identified as an asymptomatic chronic carrier of the bacteria.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Symptoms onset</th>
<th>Fever duration</th>
<th>Abdominal Pain</th>
<th>Hepatosplenomegaly</th>
<th>AST/ALT</th>
<th>Treatment</th>
<th>Blood culture</th>
<th>Stool sample</th>
<th>Epidemiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>07/05/17</td>
<td>11 days</td>
<td>++</td>
<td>Yes</td>
<td>291/275</td>
<td>3rd Gen. Cefalosporin (8 days)</td>
<td>Negative</td>
<td>Negative</td>
<td>Yes</td>
</tr>
<tr>
<td>Patient 2</td>
<td>10/05/17</td>
<td>8 days</td>
<td>+++</td>
<td>Yes</td>
<td>260/425</td>
<td>3rd Gen. Cefalosporin (13 days)</td>
<td><em>Salmonella enterica</em> serotype Typhi</td>
<td>Negative</td>
<td>Yes</td>
</tr>
<tr>
<td>Patient 3</td>
<td>12/05/17</td>
<td>23 days</td>
<td>+++</td>
<td>Yes</td>
<td>97/44</td>
<td>3rd Gen. Cefalosporin (10 days)</td>
<td><em>Salmonella enterica</em> serotype Typhi</td>
<td>Negative</td>
<td>Yes</td>
</tr>
<tr>
<td>Patient 4</td>
<td>10/05/17</td>
<td>14 days</td>
<td>+++</td>
<td>Yes</td>
<td>125/337</td>
<td>3rd Gen. Cefalosporin (13 days)</td>
<td>Negative</td>
<td><em>Salmonella enterica</em> serotype Typhi</td>
<td>Yes</td>
</tr>
<tr>
<td>Patient 5</td>
<td>17/05/17</td>
<td>10 days</td>
<td>++</td>
<td>Yes</td>
<td>38/25</td>
<td>3rd Gen. Cefalosporin (6 days) + TREP+SMX (4 days)</td>
<td><em>Salmonella enterica</em> serotype Typhi</td>
<td>No data</td>
<td>Yes</td>
</tr>
<tr>
<td>Patient 6</td>
<td>24/05/17</td>
<td>11 days</td>
<td>+</td>
<td>No</td>
<td>No data</td>
<td>TREP+SMX (7 days)</td>
<td>No data</td>
<td>No data</td>
<td>Yes</td>
</tr>
</tbody>
</table>

**Learning Points/Discussion**

Typhoid fever outbreaks are a threat to public health because of the severity and duration of symptoms. Fever and abdominal pain are the most common findings. In the light of an outbreak, it is important to identify all suspected cases and to remember the possibility of an asymptomatic chronic carrier.
Background

Vaccination can protect against life-threatening infectious diseases. This is even more important for immunocompromised children because of their increased risk of complications upon exposure to vaccine-preventable diseases. We assessed vaccination coverage and seroprotection rate for measles, mumps and rubella (MMR) and diphtheria, tetanus and pertussis (DTP) in immunocompromised children in a university hospital in Flanders, Belgium.

Methods

Antibody titers were determined by ELISA (MMR) and multiplex assay (DTP) in patients with pediatric immunodeficiencies (n=88) and solid organ transplant recipients (n=35), aged 2-16 years. Titers were classified as seropositive if above cut-off value. Vaccination data were retrieved from documents provided by the parents and the general practitioner and verified against the Flemish vaccination register. Patients were considered fully vaccinated if they had been correctly vaccinated for their age according to the recommended Belgian immunisation programme.

Results

Vaccination rates are lower compared to the general population of Flemish children. Moreover, as can be expected, seroprotection rates for all investigated diseases were lower in immunocompromised children compared to literature data on healthy children. However, vaccination is still associated with a better protection for measles, mumps, rubella and tetanus, but only for rubella statistical significance was reached (table). Seroprotection rates were slightly lower in the transplant group.
Conclusions

Up to 50% of immunocompromised children remain susceptible to vaccine preventable diseases. This can be explained by the nature of their disease, the immunosuppressive medication in SOT, and to the relatively low vaccination coverage (74 to 79%). These results highlight the importance of herd immunity and the need for better follow-up of the vaccination status in immunocompromised patients.

Clinical Trial Registration (Please input N/A if not registered)

N/A

<table>
<thead>
<tr>
<th>Immunocompromised children (n=123)</th>
<th>Antibody titer cut-off value for protection</th>
<th>Percentage protected</th>
<th>Percentage fully vaccinated</th>
<th>Of those fully vaccinated, percentage protected</th>
<th>OR (95% CI) for seroprotection (fully vs incompletely vaccinated patients)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measles</td>
<td>≥ 350 mIU/ml</td>
<td>87.5%</td>
<td>78.9%</td>
<td>70.1%</td>
<td>1.72 (0.69–4.18)</td>
<td>0.23</td>
</tr>
<tr>
<td>Mumps</td>
<td>≥ 150 I.U/ml</td>
<td>54.5%</td>
<td>78.9%</td>
<td>66.7%</td>
<td>1.52 (0.64–3.71)</td>
<td>0.34</td>
</tr>
<tr>
<td>Rubella</td>
<td>≥ 10 I.U/ml</td>
<td>76.4%</td>
<td>78.9%</td>
<td>81.4%</td>
<td>3.22 (1.20–8.2)</td>
<td>0.04</td>
</tr>
<tr>
<td>Diphtheria</td>
<td>≤ 0.1 IU/ml</td>
<td>62.6%</td>
<td>74.5%</td>
<td>63.7%</td>
<td>1.11 (0.47–2.55)</td>
<td>0.81</td>
</tr>
<tr>
<td>Tetanus</td>
<td>≥ 1.0 IU/ml</td>
<td>91.1%</td>
<td>74.5%</td>
<td>93.4%</td>
<td>2.10 (0.51–7.90)</td>
<td>0.28</td>
</tr>
<tr>
<td>Pertussis</td>
<td>≥ 5 IU/ml</td>
<td>51.2%</td>
<td>73.8%</td>
<td>51.1%</td>
<td>0.92 (0.41–2.07)</td>
<td>0.84</td>
</tr>
</tbody>
</table>
HPV-VACCINATION COVERAGE IN FLANDERS REMAINS HIGH IN THE VACCINATION PROGRAMME FOR YOUNG GIRLS

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²Flemish Agency for Care And Health, Prevention, Brussels, Belgium

Background

In September 2010 HPV-vaccination for young girls was added to the vaccination programme of Flanders. Vaccines are made available free of charge to all vaccinators. All vaccinations with free vaccines should be registered in the vaccination registry. The availability of the new partially reimbursed 9-valent HPV-vaccine caused some concern the participation degree in the vaccination programme might decrease with a fall in vaccination coverage as a result (91% in 2016).

Methods

To evaluate the impact of the new situation on the vaccination coverage, we compared the number of ordered and delivered free HPV-vaccines for the vaccination programme from the last years. On the other hand we extracted registrations of all given HPV-vaccinations in the target groups to see to what extent 9-valent HPV-vaccines are registered and might compensate a possible decrease in amount of delivered vaccines in the vaccination programme.

Results

In the first trimester of the new school year, the number of ordered vaccines by all vaccinators had decreased with 3310 vaccines compared to the same period in 2016. Nevertheless, a total number of 2081 vaccinations with other brands of HPV-vaccines were registered, 1905 of which with 9-valent vaccines. Considering the non-obligation for registration of these other vaccinations, there might be some degree of under-registration.

Conclusions

The availability of a partially reimbursed 9-valent HPV-vaccine besides the organised vaccination programme (free of charge) has reduced the number of delivered vaccines for the programme. However, there is an increase in registered other HPV-vaccinations. Considering the amount of vaccines registered in the target group of girls, this situation doesn’t seem to alter vaccination coverage substantially, but needs a careful follow-up.
CLOSTRIDIUM DIFFICILE INFECTION IN CHILDREN: EXPERIENCE IN A TERTIARY CARE HOSPITAL

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Title of Case(s)

CLOSTRIDIUM DIFFICILE INFECTION IN CHILDREN: EXPERIENCE IN A TERTIARY CARE HOSPITAL

Background

*Clostridium difficile* infection (CDI) has increased in children, although its diagnosis in <3 years-old is controversial due to high rates of colonization.

Retrospective study to describe the characteristics of CDI diagnosed in children <16 years-old during 2013-2017.

CDI in <1 years-old were excluded following the recommendations of the literature.

Case Presentation Summary

Over the period, 30 episodes of CDI were diagnosed. 2 cases were excluded for being <1 years-old. The remaining 28 were diagnosed in 23 children. Mean age at diagnosis: 6.79 years (SD 4.68). 39.1 % were between 1-3 years-old. Risk factors (RF) for CDI are presented in figure 1.

Abdominal pain (57.9%), diarrhea (46.3%) and fever (10.5%) were the predominant symptoms. 75% had mild-moderate colitis, no one presented as fulminant colitis. CD toxin was positive in 67.9% and Nucleic-Acid Amplification Test in 78.6%; both resulted positive in 46.4%.

Most of the first episodes were treated with metronidazole (68.4%); rifaximine was used in 14.3% of them. The length of treatment was 10 days in 68 %. Two patients were not treated (7.1%), with good outcome.

Six children developed recurrences (22.2%), generally treated with metronidazole (33%). One patient presented multiples recurrences and fidaxomicin therapy was indicated, without more relapses. The use of gastric acid-suppressing agents (GASA) or a previous episode of CDI was associated with the development of recurrence (p<0.05 and p=0.06). No statistically association were observed between
other RF and recurrence.

<table>
<thead>
<tr>
<th>Risk Factors of CDI (n=28)</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RF</td>
<td></td>
</tr>
<tr>
<td>Immunosuppressive treatment</td>
<td>14 (50%)</td>
</tr>
<tr>
<td>Previous hospitalization</td>
<td>9 (32.1%)</td>
</tr>
<tr>
<td>Inflammatory bowel disease</td>
<td>8 (28.6%)</td>
</tr>
<tr>
<td>Gastric acid-suppressing agents</td>
<td>8 (28.6%)</td>
</tr>
<tr>
<td>Previous antbiotherapy</td>
<td>8 (28.6%)</td>
</tr>
<tr>
<td>Previous CDI episode</td>
<td>6 (21.4%)</td>
</tr>
<tr>
<td>Broad spectrum antibiotic therapy</td>
<td>6 (21.4%)</td>
</tr>
<tr>
<td>Oncologic diseases</td>
<td>5 (17.9%)</td>
</tr>
</tbody>
</table>

*Figure 1. Risk factors of CDI. RF: Risk Factors, CDI: Clostridium difficile Infection*

**Learning Points/Discussion**

Most CDI presented with mild-moderate colitis, as in other paediatric studies.

39.1% CDI happened in <3 year-old children, although some of them could be simple colonization.

Use of GASA was associated with relapsing CDI.
YELLOW FEVER VACCINE-ASSOCIATED NEUROLOGIC DISEASE IN SÃO PAULO, BRAZIL: TWO CASES REPORT

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Title of Case(s)

YELLOW FEVER VACCINE-ASSOCIATED NEUROLOGIC DISEASE IN SÃO PAULO, BRAZIL: TWO CASES REPORT

Background

Yellow Fever (YF) is an acute febrile disease, endemic in many regions of Brazil. Since 2005, there has been an expansion of the affected areas, with an increase in the number of cases. The main strategy for preventing the disease is through vaccination with a YF vaccine (YFV).

YF vaccine-associated neurologic disease (YEL-AND) is a serious adverse event, (IR 0.4-0.8/100,000 vaccines doses) presenting as different clinical syndromes, including meningoencephalitis, Guillain-Barré syndrome (GBS), acute disseminated encephalomyelitis (ADEM). The diagnostic criteria for YEL-AND is the presence of YF IgM antibody in the CSF and is more sensible than RT-PCR. In 2017, 56 cases YEL-AND were reported in the state of São Paulo.

We present two cases of meningoencephalitis after first dose of YFV. Other two suspected cases are being investigated.

Case Presentation Summary

Patient 1: Healthy 4 year old boy presented with headache, fever, dysarthria, muscle strength decrease in the right upper limb and ataxic gait after 25 days of YFV. Patient presented fever for 5 days and remained hospitalized for 10 days.

Patient 2: Healthy 3 year-old girl presented with headache, fever, irritability and partial seizures after 20 days of YFV. Fever duration was 14 days. Patient remained for 15 days in hospital care.

Both patients presented positive serology in CSF (YF IgM antibodies). Clinical outcome was favorable, without sequelae, patients remain completely asymptomatic after 1 month of clinical follow-up.

Learning Points/Discussion

YFV adverse events are mostly mild. However, an increase in the number of vaccine doses administered leads to more serious adverse events. Therefore, the decision to vaccinate must be individualized according to the epidemiological and if possible individual risk factors of each patient.
ESP18-0840
E-POSTER VIEWING - MAY 28-JUNE 2 - EXHIBITION HOURS

04B. SCIENCE: COMMUNITY ACQUIRED INFECTIONS: RESPIRATORY TRACT INFECTIONS

COMPARISON AND ANALYSIS OF THE IMPACT OF CO-INFECTIONS IN PEDIATRIC PATIENTS WITH RESPIRATORY INFECTIONS ADMITTED TO HOSPITAL OR IN PRIMARY CARE HEALTHCARE

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Background

Molecular diagnostic techniques frequently reveal the presence of several microorganisms in respiratory patients. However, the importance of co-infections has not been well established. The aim of this study was to compare the clinical patterns of co-infection in pediatric patients hospitalized with patients attending primary care healthcare (PC) units for acute respiratory infections (ARI) in the same epidemic period.

Methods

A prospective, multicenter study was developed through a network of primary care centers (ReGALIP; www.regalip.org) and the Hospital Clínico Universitario de Santiago (Galicia, Spain) during 2014-2015 in children<14 years old attended and hospitalized respectively due to an ARI. A polymerase chain reaction (PCR) was performed in nasopharyngeal swabs to detect influenza (A, B), metapneumovirus, respiratory syncytial virus, parainfluenza (1-4), rhinovirus, enterovirus, adenovirus, bocavirus and coronavirus (NL63, 229E,OC43, HKU1) and Chlamydotrophila pneumoniae, Legionella pneumoniae, and Mycoplasma pneumoniae.

Results

A total of 189 samples were collected, namely, n=109 PC and n=80 hospitalized. At least one pathogen was identified in a similar percentage in both groups (PC: 81.6% vs. hospitalized: 82.5%), although the pattern of microorganisms found was different in both groups. Rhinovirus appeared as the most frequent pathogen in PC (n=49, 44.9%), while RSV was the most common pathogen in hospitalized patients (n=31, 38.8%). Number of co-infections were similar in PC (n=31, 28.4%) and hospitalized (n=19, 23.8%) patients.

Conclusions

The present study shows that molecular techniques in primary care and hospital healthcare are able to detect a pathogen in at least 80% of the patients. Rhinovirus was found to be more prevalent in
patients attending PC units and RSV in those hospitalized. The presence of co-infections in both groups of patients is very frequent although the clinical importance of this finding still remains to be elucidated.

Clinical Trial Registration (Please input N/A if not registered)
MEDICO-SOCIAL ISSUES OF PEDIATRIC INFECTIOUS DISEASES IN NORTH-EASTERN BULGARIA

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Background

The authors analyze a number of various infectious diseases in children in North-Eastern Bulgaria for the period 2015-2018.

Methods

A thorough analysis of the social effect on the health of children suffering from those three major pathology conditions is performed by using up-to-date statistical evaluation.

Results

The accent is on the infections with definite social importance, such as respiratory diseases.

A statistical analysis is performed on the epidemiologic distribution of influenza, common cold and upper respiratory tract infections.

The age groups indicate that altogether 148 children from kinder gardens (aged between 3 and 5 years) suffer more often than those 236 from the primary schools (aged between 6 and 9 years) in the region of Varna (48 from kinder gardens, 92 from primary schools), Shoumen (46 from kinder gardens, 62 from primary schools), Dobrich (34 from kinder gardens, 42 from primary schools) and Silistra (20 from kinder gardens, 40 from primary schools).

Conclusions

The statistic evaluation of all investigated children shows prevalence of common cold (49%) as major pathologic condition, followed by upper respiratory tract infections (32%) and influenza (19%).

Systematic Review Registration (Please input N/A if not registered)

N/A
OSELTA\textsc{mivir} SUSPENSION RELATED QUERIES FROM INTERNET MEDICAL DATABASES BY HEALTHCARE PROFESSIONALS COINCIDE WITH CHILDREN’s INFLUENZA OUTBREAKS

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Background

While Internet searching behaviour has been characterized in detail previously, little data exist on healthcare professionals’ queries on medical information relating to outbreaks. In Finland, healthcare professionals use mainly one medical database, Physician’s Databases (PD). Every keyword or opened article is included in the PD log file. Log files were assessed to evaluate the usability of log data in identifying influenza outbreaks among children.

Methods

The data were collected retrospectively from the log files of PD during 2013-2016 across Finland. Openings of the information page on oseltamivir suspension was used as the indicator. We compared these data to the diagnoses and seropositive findings on influenza A and B in under 7-year-olds in the Hospital Discharge Register and in the National Infectious Disease Register, respectively.

Results

We found an annually similar pattern in oseltamivir suspension web-page openings that coincide with the register of children’s influenza diagnoses and seropositive findings (Figure).
Conclusions

Healthcare professionals' information seeking behaviour on oseltamivir suspension from Internet medical databases resembles epidemiological patterns on children's influenza and could eventually be used to supplement existing disease surveillance methods.
Henöch-Schönlein purpura following influenza and adenovirus infection; two cases

Background

Henöch-Schönlein purpura is a small vessel IgA-predominant vasculitis which commonly affects skin, gastrointestinal tract, joints and kidneys. The etiology is diverse; infection, drug, food allergy, malignancy, autoimmune connective disease can be a trigger factor. Viral infection thought to be one of the most predisposing factor.

Case Presentation Summary

Case 1: A 7 year old boy was presented with fever, rashes on hands and foot and mild abdominal pain. Physical examination showed swelling in bilateral ankle and purpuric rashes were on his extremities. Laboratory examination revealed white blood cells 10.100/mm³ (90% neutrophil), hemoglobin 11.1 g/dL and platelet count 448.000/mm³. Renal and liver function tests were normal. Urine dipstick test was negative for hematuria and proteinuria. Serum C3 was 118 mg/dL (90-118) and C4 level was 8.86 mg/dL (10-40). The patient was diagnosed clinically as Henöch-Schönlein purpura vasculitis and treated with ibuprofen. Clinical finding improved gradually within six days and discharged. Nasopharyngeal PCR evaluation showed influenza A (H1N1).

Case 2: A 5 year old girl was presented with swelling and rashes on bilateral ankle. Physical examination showed swelling in bilateral ankle and purpuric rashes were on her lower extremities. Laboratory examination revealed that white blood cells 5.900/mm³ (50% neutrophil), hemoglobin 9 g/dL and platelet count 509.000/mm³. Renal and liver function tests were normal. Urine dipstick test was negative for hematuria and proteinuria. The patient was diagnosed clinically as Henöch-Schönlein purpura vasculitis and treated with ibuprofen. In the fourth day she had abdominal pain; methylprednisolone started. Clinical finding improved gradually and patient discharged at seventh day. Nasopharyngeal PCR evaluation showed adenovirus.

Learning Points/Discussion

Viral respiratory infections can be stimulant factor for HSP so should be considered in differential diagnosis.
Title of Case(s)

Mycobacterium bovis arachnoiditis

Background

Tuberculous meningitis is rare in areas of low TB incidence. Diagnosis is challenging due to the non-specific presenting symptoms, the difficulty in culturing the organism and the low yield of CSF PCR. Mycobacterium bovis is associated with a worse prognosis.

Case Presentation Summary

An 11-year old, HIV-negative, caucasian Irish girl presented with 2-weeks of intermittent fever, worsening headaches and vomiting. She was previously well, without history of travel, known TB contacts, exposure to farm animals or unpasteurised dairy products. Admission bloods and CT brain were normal. LP showed: WCC, 443/cmm (77% monocytes); RCC, 40/cmm; protein, >2500mg/L; glucose, 1.7mmol/L. Gram and AFB stains, culture and multiplex bacterial PCR were negative. Empiric ceftriaxone and aciclovir were started. An EVD was inserted for worsening encephalopathy and increased ventricular dilatation on repeat CT brain. Repeat CSF showed: WCC, 63/cmm; protein, 333mg/L; glucose, 3.1mmol/L. AFB stain, Filmarray, and MTB complex PCR were negative. The discrepancy in lumbar and ventricular CSF parameters prompted MRI brain and spine with contrast. This showed extensive enhancement of spinal cord subarachnoid space and brainstem and basal cisterns pial surfaces. She underwent lumbosacral laminectomy and nerve root biopsy for suspected malignancy. Histology was negative for malignancy but showed granulomas and a single AFB stain positive organism. Anti-mycobacterial chemotherapy and high dose dexamethasone was commenced for presumed MTB infection confirmed on positive MTB complex PCR and subsequent culture identification as Mycobacterium bovis. She is now well 6 months into treatment.

Learning Points/Discussion

This case underlines the difficulties inherent in diagnosis of tuberculous meningitis and particularly arachnoiditis. Repeat CSF MTB complex PCR samples were negative with diagnosis ultimately depending on spinal neuroimaging and tissue biopsy.
AN ACUTE HYPTERTENSIVE UVEITIS IN A CHILD WITH EBSTEIN-BARR INFECTION

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Title of Case(s)

An acute hypertensive uveitis in a child with Ebstein-Barr infection

Background

Posner-Schlossman syndrome (PSS) is an acute uveitis characterised by unilateral recurrent episodes of mild intraocular inflammation associated with an elevated intraocular pressure and more rarely by fine white keratic precipitates. We report a case of paediatric PSS, associated with recent Ebstein-Barr infection (EBV).

Case Presentation Summary

A 6-year-old previously healthy male was evaluated due to the sudden onset of headache, blurring vision in the left eye with anisocoria. An ophthalmological visit revealed white keratic precipitates and an increased intraocular pressure. No signs of anterior chamber angles obstruction were noted. Laboratory tests showed a mild increase of alanine aminotransferase. The infectious disease work-up showed EBV serology compatible with recent infection as demonstrated by detectable level of viral capsid antigen (VCA) IgG antibodies and negativity of VCA IgM and nuclear antigen IgG. Blood PCR for EBV was positive (2000 copies/mL); however, PCR was not performed on aqueous humor sampling due to the invasiveness of this test and the prompt clinical response. The patient was started on topical treatment with prompt response. At 6-months follow-up the ophthalmological evaluation was normal.

Learning Points/Discussion

PSS is underreported due to the silent course and only few cases have been reported in adolescent. To our knowledge this is the first case described in a child below 10 years of age. The majority of the cases are associated with CMV and rarely with HSV and VZV infection.

In our case EBV infection have been supposed to act as a trigger for PSS. However, this association could not be proved as EBV PCR on aqueous humor was not performed. No other cases of EBV-associated PSS have been published, so further studies are needed to confirm this association.
THE CLINICAL UTILITY OF WHOLE BLOOD TRANSCRIPTOMIC SIGNATURES FOR THE DIAGNOSTIC EVALUATION OF ACTIVE TUBERCULOSIS

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Background

Tuberculosis (TB) is the leading infectious killer globally, with up to 500 children dying of the disease each day. A large proportion of cases of TB, particularly in children, lack definitive microbiological diagnosis because of low bacterial burden and/or difficulty in obtaining site-of-disease samples. Measurement of host responses in the blood is an attractive alternative approach, which may provide increased sensitivity in hard to diagnose groups. Several studies have identified whole-blood transcriptomic profiles that discriminated between active TB cases and controls in adults with high sensitivity and specificity. However, their ability to diagnose the full spectrum of TB disease (including culture-unconfirmed and extra-pulmonary cases), among a range of differential diagnoses presenting in a real life clinical setting, has not yet been determined.

Methods

We used genome-wide gene-expression microarray to validate the performance of six published transcriptomic signatures in a prospective cohort of 628 adults presenting with suspected TB to multiple hospital sites in routine practice in England.

Results

The proportion of TB within our cohort was 48%, of which 31% were culture-unconfirmed. The published signatures provided a maximum area under the curve (AUC) of 0.81 for detecting all TB cases, and 0.79 for detecting highly-probable (culture-unconfirmed) TB. When we used the data to derive novel signatures, the performance was similarly poor.

Conclusions

In a real-life cohort of patients representing the full clinical spectrum of suspected TB recruited in routine practice, whole-blood transcriptomic signatures were not clinically useful, especially in hard-to-diagnose groups. These findings are especially relevant to TB in children, where the proportion of highly-probable culture-unconfirmed TB is high, and a new diagnostic approach is sorely needed.

Clinical Trial Registration (Please input N/A if not registered)

N/A
Schistosomal myeloradiculopathy: report of two cases

Background

Schistosomiasis is a public health issue in Brazil, with a broad geographic distribution of cases. Less than 20% of infected individuals present central nervous system involvement. We describe two imported cases of Schistosomal myeloradiculopathy from an endemic area, successfully treated and without sequelae.

Case Presentation Summary
Patient 1: a healthy 11-year old boy presented with pain in right popliteal fossa area, neuropathic gait, and urinary retention. On examination patient presented grade 4 muscle strength in lower limbs and absent Achilles reflex. Spinal cord MRI showed an intramedullary lesion expansion between T10 and conus medullaris, associated with vasogenic edema compatible neuroschistosomiasis. Patient 2: a healthy 6-year-old girl presented with intermittent fever, and weakness and pain in lower limbs. Deep tendon reflexes were absent in the lower limbs, associated with decreased tactile sensory, and sensory loss of pain and temperature. Spinal cord MRI evidenced a nodular lesion in the conus medullaris compatible with neuroschistosomiasis.

Patients had lived in northeast Brazil (an endemic area for Schistosomiasis), where swimming in ponds and rivers was frequent to both children. Serology was positive in blood and CSF in both cases, Kato-Katz stool examination was positive only for patient 1. We used a 5-day course of high-dose corticosteroid followed by praziquantel. Both patients were discharged with low dose oral corticosteroids after clinical improvement. Patient 1 is asymptomatic for >12 months, and steroids were weaned and tapered after six months. Patient 2 is under follow up at our outpatient clinic.

Learning Points/Discussion

Schistosomal myeloradiculopathy is an important etiology of spinal cord compression in endemic countries. Accurate medical history and extensive epidemiological assessment, neuroimaging, and complementary exams are essential for early diagnosis. Treatment leads to full recovery of symptoms.
CONGENITAL TOXOPLASMOSIS: A CHALLENGING DIAGNOSIS
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Background

It is estimated that 3 to 20 newborns per 10,000 live births are born with congenital toxoplasmosis. About 70% are asymptomatic, presenting a subclinical infection, though they may develop late sequelae, mainly visual and neurologic manifestations. Spiramycin is used to prevent and reduce vertical transmission. Sulfadiazine and pyrimethamine should be started on any evidence of fetal compromise since they cross the placenta and can minimize further damage to the fetus. We describe data on diagnosis and treatment of toxoplasmosis during pregnancy, as well as clinical and laboratory characteristics of those infants.

Methods

We’ve conducted a retrospective study with infants with suspected or confirmed congenital toxoplasmosis, born between 2014 and 2017, in the pediatric infectious diseases outpatient clinic in our hospital. We evaluated data on maternal infection and clinical and laboratory data of the infants.

Results

Our cohort consisted of 31 infants born to mothers diagnosed with toxoplasmosis during pregnancy. Spiramycin treatment was initiated for 16 (51.6%) women. None had amniocentesis for prenatal diagnosis by PCR. Only 16% of newborns were symptomatic at birth, and only 19.3% had a positive IgM for toxoplasma, all of which presented chorioretinitis and cerebral calcification. Furthermore, 9.5% presented symptoms despite a negative IgM. Among all newborns, 29 (93%) were submitted to fundoscopy (5 chorioretinitis), 14 to lumbar puncture (4 CSF abnormalities), 26 (83%) to neuroimaging (4 calcifications, 2 ventricular dilatation), 14 (45%) to otoacoustic emissions (all normal) and 8 (25%) to BERA (1 auditory deficiency). Eighteen (58%) were treated with sulfadiazine and pyrimethamine.

Conclusions

Our data show the importance of additional investigations in infants at risk of congenital toxoplasmosis. An improvement in prenatal care is fundamental to diagnosis and treatment of pregnant women with toxoplasmosis, decreasing mother-to-child transmission.
SPECIFIC T-CELL IMMUNITY AGAINST HHV-6 IN HEALTHY CHILDREN AND ADOLESCENTS

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Background

Primary infection with human herpes virus 6 (mainly HHV-6B) commonly occurs in the first two years of life leading to persistence and the possibility of virus reactivation later in life. Consequently, a specific cellular immune response is essential for effective control of virus reactivation. We have studied cell-mediated immune response to HHV-6 in healthy children and adolescents.

Methods

By flow cytometry, the amount of cytokine (interferon gamma – IFN-γ, interleukin 2 – IL-2, tumour necrosis factor alpha – TNF-α) secreting T-cells after 10 days of pre-sensitization and 6 hours of re-stimulation were measured with mixtures of pooled overlapping peptides from HHV-6 specific protein U54, staphylococcal enterotoxin B (SEB, positive control) or Actin (negative control) in healthy children and adolescents without any underlying immune disorder or infectious disease.

Results

All 25 tested individuals (age 3.1-18.3, median 8.2 years, 28% female) showed a virus-specific response for at least one cytokine in either CD4+ or CD8+ cells. Percentages of individuals with HHV-6-specific TNF-α response in CD4+ (48% of individuals) as well as CD8+ (56% of individuals) were almost the highest. Our data show significantly higher frequencies of HHV-6-specific TNF-α producing CD8+ T-cells in individuals older than 10 years of life (n=12, p=0.033). Additionally, the frequency of TNF-α producing CD8+ T-cells positively correlated with the age of the individuals (Spearman-Rho, r=0.465) on a two-sided significance level of p=0.019.

Conclusions

HHV-6 specific T-cells are commonly present, expandable, and detectable in healthy children and adolescents with higher frequencies of antigen-specific T-cells in older children and adolescents possibly reflecting repeated stimulation by viral persistence and subclinical reactivation.

Clinical Trial Registration (Please input N/A if not registered)

N/A
EMERGENCE OF ROTAVIRUS G8P[8] IN SANTIAGO CHILE, A COUNTRY WITHOUT PROGRAMATIC ROTAVIRUS VACCINATION

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Background

Five distinct rotavirus genotypes, differing in their VP7 (G1-G4 and G9) and/or VP4 (P[8] and P[4]) outer capsid proteins, cause >90% of rotavirus infections in humans. During the past 10 years, G8P[8] and G12P[8] genotypes have emerged in different countries, but reports in South America have been scarce. In addition, the occurrence of less common genotypes in areas with widespread rotavirus vaccine use has led to claims of possible “vaccine selection”. In Chile, a country where rotavirus vaccines have not been incorporated into the national program, genotypes G1P[8], G4P[8], and G9P[8] have intermittently predominated over the past decade.

Methods

In May 2016, we initiated a prospective surveillance study of acute gastroenteritis in 100 families with ≥1 infant in Colina, a low-middle income city on the outskirts of Santiago. Rotavirus was genotyped by semi-nested polymerase chain reaction associated to reverse transcription using genotype specific primers.

Results

Through December 2017, a total of 135 gastroenteritis episodes were detected, of which 22 (16%) were caused by rotavirus. A first genotypic analysis identified 4 G9P[8], 2 G2P[4], 2 G12P[8], 1 G2P[8], 1 G8P[8], 2 non-identified strains and a 10 isolates with a double band using the G12 primer. Reanalysis with a G8 specific primer, followed by sequencing, determined that these strains were G8P[8], sharing >99% identity with each other and with prototype sequences recently described in Asia. None of the infants participating in the surveillance received the rotavirus vaccine.

Conclusions

Rotavirus G8P[8] emerged and predominated in Colina, Chile during 2016 in a country where rotavirus vaccines are not programmatically used. The commonly used G12 primer may misidentify G8 strains.

Clinical Trial Registration (Please input N/A if not registered)
CEFTRIAXONE AS A NEW POSSIBLE DRUG THERAPY FOR CONGENITAL SYphilis

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Background

Penicillin is the drug of choice in the treatment of syphilis. Since 2015, there has been a worldwide shortage due to the difficulty in acquiring its raw material. Brazilian Ministry of Health recommended ceftriaxone, as an alternative, for the treatment of congenital syphilis (CS), although without scientific evidence for its use. We aimed to evaluate the incidence of CS, the number of newborns with CS treated with ceftriaxone and its adverse effects. We also assessed clinical and laboratory follow-up during the first two years of life.

Methods

We conducted a prospective transversal study evaluating medical charts of newborns whose mothers were diagnosed with syphilis during pregnancy, treated with ceftriaxone, born between January 2015 and December 2016. These infants are followed at our pediatric infectious diseases outpatient clinic, for clinical and laboratory follow-up.

Results

We observed a very high prevalence of CS in our cohort (29 cases per 1000 live births) compared to other Brazilian data. Despite it being a 100% preventable disease, CS remains a public health issue in Brazil and around the world. These data point to a failure in pre-natal care and could be related to the social vulnerability profile of these women, 43.9% of which were addicted to alcohol and other drugs, and 19.5% were homeless. This is the first study that evaluated ceftriaxone for CS treatment, assessing 41 newborns. No adverse effects, including jaundice, were related. We observed that 97% of newborns were asymptomatic at birth, but 3.2% presented CSF abnormalities compatible with neurosyphilis. We could follow-up 18 patients, all with good clinical outcome and negative VDRL.

Conclusions

Despite the small number of patients, our data show that ceftriaxone use was associated with good clinical and laboratory outcomes.
ANTIBIOTIC PRESCRIPTIONS IN HOSPITALIZED ITALIAN CHILDREN: DATA FROM THE GARPEC PROJECT.

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Background

Antibiotics are the most prescribed drugs for children and there is a strong correlation between antibiotic over-prescribing and the spread of resistant organisms. The aim of this study, as part of the Global Antimicrobial Resistance, Prescribing and Efficacy in Neonates and Children (GARPEC) project, is to describe antimicrobial prescriptions amongst hospitalised children in four tertiary care hospitals in Italy.

Methods

Three one-day point prevalence surveys (PPS) were conducted between February 2016 and February 2017, enrolling children admitted on the participating wards at 8am on the selected day with an ongoing antimicrobial prescription.

Results

From the preliminary analysis, 565 children (37.9% of all inpatients) receiving 851 antibiotics were included (median age 24 months; IQR: 3-96). One hundred and fourteen children (20.2%) were enrolled in the first PPS (May-June 2016), 220 (38.9%) in the second (September-October 2017) and 231 (40.9%) in the third (December-February 2017). Most children were received antibiotics for lower respiratory tract infections treatment (160/565; 28.3%), followed by medical and surgical prophylaxis (153/565; 27%), and fever/fieberle neutropenia (47/565; 8.3%). The most commonly prescribed antibiotics were cephalosporins (27%), penicillins (23%), and aminoglicosides (16%). Carbapenems were used in 6% of patients, of those 58% were prescribed for health-care associated infections. Only 163/851 (19.1%) antibiotics were prescribed according to susceptibility tests.

Conclusions

By comparing our analysis with the previous study published in 2016 as part of the Antibiotic Resistance and Prescribing in European Children project (ARPEC), the same percentage of ongoing antibiotic prescriptions in inpatients (37.9% vs 38.9%) was observed. From a preliminary analysis, it appears that nothing has changed since the last PPS. Serial PPS can be part of antimicrobial
stewardship programmes (ASP) but not sufficient alone to produce changes in clinical practice. Further studies are needed to implement ASP according to local patterns.
Background

Bacterial meningitis is associated with a significant burden in Brazil. In 2010, both 10-valent pneumococcal conjugate vaccine and meningococcal capsular group C conjugate vaccine were introduced in the routine vaccination schedule. Haemophilus influenzae type b (Hib) vaccine was previously introduced in 1999. We observed a decrease in incidence and an epidemiological shift in bacterial meningitis. Currently, N. meningitidis is the leading etiological agent. We’ve evaluated the epidemiological, clinical and laboratory characteristics of patients with bacterial meningitis presenting at our hospital.

Methods

Descriptive study of a historical cohort, based on data withdrawn from the meningitis investigation charts of our national notification system. Children and adolescents with bacterial meningitis presenting at our hospital between January 2005 and December 2015 were included.

Results

191 cases of bacterial meningitis were notified by our hospital. The mean age was 58 months, and 43% of the patients were younger than 12 months. N. meningitidis was the main etiological agent (29%), followed by S. pneumoniae (11%). Meningococcal serotyping was performed in 19 cases: 63.1% C and 26% B. We observed a decrease of serotype C since 2011. In 25 cases, PCR for meningococcus, pneumococcus, and Hib was performed alongside CSF culture. It allowed an etiological diagnosis in 12 (48%) culture-negative episodes. Overall mortality was 12.6% but reached 33% in meningococcal disease and 20% in pneumococcal meningitis.
Conclusions

Meningococcal disease was responsible for the majority of the cases, with group C the most common serotype. Bacterial meningitis remains a significant health care issue, with high mortality. This study emphasizes the importance of vaccination in young infants.
WE SEE MORE OFTEN NOW. A HIV INFECTED ADOLESCENT WITH SECONDARY SYphilis

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Title of Case(s)

HIV infected adolescent with syphilis coinfection

Background

Human Immunodeficiency Virus (HIV) infection incidence among adolescents has been rising, both globally and in our country. Sexually transmitted diseases like syphilis can also be encountered in these patients. Here in we present a 16 year old male with HIV-syphilis coinfection.

Case Presentation Summary

On admission; he was conscious, well in appearance, with height and weight percentiles appropriate for age. There were no aphthous lesions in his mouth. He had bilateral cervical multiple lymphadenopathies with maximum diameter of 1.5 cm plus right axillary 1 cm mobile lymphadenopathy. No hepatosplenomegaly was palpated. He had widespread maculopapular rash, which was more intense on extremities. Genital examination was compatible with pubertal male development; it revealed neither lesion nor inguinal lymphadenopathy. Laboratory examination revealed white blood cell count as 1800/mm³ (absolute neutrophil counts: 800/mm³, absolute lymphocyte counts: 900/mm³). Liver transaminases and renal function tests were within normal range. C-reactive protein was slightly elevated, 25 mg/L (<5 mg/L). Urinary analysis was normal. Epstein - Barr virus and Cytomegalovirus polymerase chain reaction tests, rubella IgM, rubella IgM and parvovirus IgM were negative. Viral respiratory panel [ResPlex II Panel v2.0 (Qiagen, Hilden, Germany)] was negative. The Rapid Plasma Reagin (RPR, Spinreact, Girona, Spain) titer for syphilis was reported as positive with a titer of 1/128. He was successfully treated with intramuscular benzatine penicillin G.

Learning Points/Discussion

Considering HIV infected adolescent patients are under increased risk of sexually transmitted diseases like syphilis, they should serologically be tested during their follow-up.
CLINICAL FEATURES AND OUTCOMES OF CHILDHOOD LYMPHADENOPATHIES IN A THIRD-LEVEL CHILDREN’S HOSPITAL


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Background

Lymphadenopathy is defined as an abnormality in size, number or consistency of one or more lymph node(s). Up to 44% of children below five years of age develop a lymphadenopathy. The aim of the present study is to describe the clinical features and outcomes of childhood lymphadenopathies and to find out prognostic factors.

Methods

We considered all the children evaluated in our third-level children's hospital because of lymphadenopathy between January 1st 2014 and March 31st 2016. For each patient the following characteristics have been included: clinical examination, blood tests and ultrasound features, histological and infectious diseases investigations on biopsy or surgical materials and treatment.

Results

Three hundred and twenty-two children (median 4.5; interquartile range 2.5-9) years were enrolled. A specific diagnosis was achieved in 159 (49.4%) cases. Among those with a defined diagnosis, Epstein Barr virus and non-tuberculous mycobacteria were the most common etiological agents among acute/subacute and chronic lymphadenopathy, respectively. Two hundred and forty-one children (74.8%) received an antibiotic therapy and 73 (22.7%) had a surgical operation. At the end of the study period, two-third (220, 68.3%) of the patients were cured. Malignancies and non-tuberculous mycobacteria infections had the longest time to resolution.

Conclusions

Our data suggest that lymphadenopathy is a benign condition in most cases. However, in our study, 2.5% were due to oncologic diseases. The most frequent infective causes were Epstein Barr virus, bacteria and non-tuberculous mycobacteria infections. No haematic or ultrasound features were enough by itself to make a conclusive diagnosis. However, the combination of those items with the clinical evaluation can guide the physicians.
ASSESSMENT OF PAEDIATRIC THERAPY IN THE INTENSIVE CARE UNIT AT A PRIVATE HEALTHCARE FACILITY

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Background

In all developing economies, infants and children constitute large proportion of the population and establishing safe and effective therapeutic regimen for children is challenging. This study is an attempt to assess the pharmacotherapy in the neonatal intensive care unit (NICU) at a private paediatric healthcare facility with special reference to the use of antimicrobials.

Methods

A cross-sectional record based study was conducted at a private healthcare facility catering to the paediatric segment. Patients who had received at least one antimicrobial and were admitted in the ICU for at least 24 hours were included. The prescribing pattern for 142 patients was analyzed.

Results

89 male and 53 female neonates comprised the sample. The average age of patients was found to be 2.70±0.33 days. The average weight of patients was 2.05±0.06 kg. As many as 76 were pre-term, 48 term, 15 late pre-term and 3 late term. The most common diagnosis was sepsis, affecting over 55% of the neonates, followed by neonatal jaundice and respiratory distress. The average number of antimicrobials prescribed was 2.82±0.10; and, the average duration of this treatment was 6.48±0.23 days, with average LoS of 10 days. Over 85% of the antimicrobials were prescribed by the generic name. Cefotaxime and amikacin (22% each) were the most commonly prescribed antimicrobial followed by vancomycin, meropenem, gentamicin and ampicillin. 166 cultures ordered from 114 cases. Klebsiella was the most common isolate followed by Acinetobacter. In this study, a large number of gram positive and gram-negative bacteria exhibited variable resistance to many of the clinically useful antimicrobials. Gram-negative isolates showed a high level of resistance to all cephalosporins.

Conclusions

This small study reinforces the caution to be exercised while using drugs, especially antimicrobials, in the neonates.
LONGITUDINAL ANALYSIS OF ANTIMICROBIAL CONSUMPTION IN NEONATAL INTENSIVE CARE UNIT: THE USE OF DEFINED DAILY DOSES

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Background

Monitoring of antimicrobial consumption in neonates is essential, but there are limited longitudinal data because of the absence of standardized metrics. Defined daily doses (DDD) are recommended by the World Health Organization for monitoring antimicrobial consumption currently only for adults. The aim of this study was to use the methodology of DDD and assess the pattern and time trends of antibiotic consumption (AMC) in a NICU for 15 years.

Methods

This retrospective study was conducted in a 44-bed neonatal unit (15 NICU beds) in a tertiary-care level hospital. The study was divided in 3 time periods: 2002-2006, 2007-2011, 2012-2016. Data of antimicrobial consumption were obtained from the hospital pharmacy and expressed as defined daily doses per 100 bed-days (DDD/100BD). Number of bed-days was obtained from Hospital Office of Statistics.

Results

The median total AMC ranged between 21.2 and 24.8DDD/100BD. Ampicillin had the highest consumption among all antimicrobials and had a non-significant decrease especially during the third period (from 9.9 to 9.0DDD/100BD). Aminoglycosides consumption ranged between 3 and 4DDD/100BD and followed ampicillin consumption. During the first period 3rd and 4th generation cephalosporins were frequently used; however, their consumption reduced from 4.3 to 1.8DDD/100BD at the third time period. Carbapenem consumption had no significant change (2.4-2.6DDD/100BD). Glycopeptide use showed an increase during the second period (from 2.3 to 3.1DDD/100BD) and then a reduction to 2.5DDD/100BD. The same trend was observed for fluoroquinolones, which had the lowest consumption: increased from 0.2 to 0.8DDD/100BD and then reduced to 0.6DDD/100BD. Metronidazole consumption was constantly low (0.1-0.2DDD/100BD).

Conclusions

Longitudinal analysis of antimicrobial consumption in NICU using the DDD methodology was feasible and provided analyzable data. Pattern and trends of antimicrobial consumption may be used for designing antimicrobial usage guidelines.
SEPTIC ARTHRITIS OF SALMONELLA ENTERITIDIS IN A PATIENT WITH MULTIPLE SCLEROSIS
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Title of Case(s)
Septic Arthritis of Salmonella Enteritidis in a Patient with Multiple Sclerosis

Background
Septic arthritis causes severe joint destruction in childhood and if not properly treated that causes permanent sequel. The number of septic arthritis cases due to Salmonella is low in literature. Salmonella is frequently associated with sickle cell anemia osteomyelitis. To the best of our knowledge, this is the first report of septic arthritis due to Salmonella enteritidis under interferon 1-β.

Case Presentation Summary
A 13-year-old girl was diagnosed with multiple sclerosis because of sudden visual loss in her right eye 8 months ago; received pulse methylprednisolone 3 times, continuation therapy methylprednisolone 1 mg / kg / day and interferon 1-β during this period. The case was hospitalized with a fever of 38.6ºC and pain in the left hip. MRI revealed septic arthritis, vancomycin and ceftriaxone treatment were initiated. Salmonella enteritidis was detected in blood and fluid cultures. Treatment was switched to ampicillin due to antibiotic susceptibility results. In our case, antibiotic treatment was continued for 8 weeks. Our case’s findings of the infection regressed in the follow-up is still in the physical therapy program.

Learning Points/Discussion
In our case septic arthritis of salmonella enteritidis developed while using steroid and interferon 1-beta treatment. Early initiation of antibiotic therapy is very important to prevent long-term sequelae. Delayed and inappropriate treatment has led to serious complications in Salmonella infections that’s why it should be kept in mind that in endemic areas, especially in patients with underlying immunosuppressive conditions, Salmonella may be a cause of septic arthritis.
16C. SCIENCE: TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

AN INTERESTING CASE OF CHRONIC OSTEOMYELITIS FROM RURAL NORTHEASTERN INDIA
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Title of Case(s)
An interesting case of chronic osteomyelitis from rural Northeast India.

Background
Chronic osteomyelitis in children from India can be due to TB, brucellosis, melioidosis etc. Our patient had varied epidemiological risk factors and was finally diagnosed with drug resistant TB.

Case Presentation Summary
6 year old boy, previously healthy with h/o bilateral cervical adenopathy, pain and swelling of his right elbow of 1.5 years duration. Treated with ATT (HRZE) for 1 year (following FNAC of cervical node showing granuloma) with no clinical improvement. From a rural area in North East India. Consumes unpasteurized milk. H/o near drowning in a lake 2 years ago with trauma to right thumb. Exposed to his maternal uncle with Pulmonary TB 2.5 years ago. He had not taken regular treatment and died 1 year ago. Received BCG, OPV, DPT, Hib and Measles vaccines - no adverse reactions. Only child of a non-consanguineous marriage with no family h/o immunodeficiency. Had bilateral anterior cervical nodes with draining sinuses, flexion deformity of right elbow with cutaneous ulcers, deformed right thumb.

Differential Diagnosis: Chronic osteomyelitis with cutaneous ulcers/abscesses with no improvement on ATT:

TB- MDR
Melioidosis
Brucellosis
Non-tuberculous mycobacteria
Nocardiosi

Labs:
Mantoux – 30mm, HIV – non reactive. Brucella serology- negative. Bone biopsy : Multiple epitheloid granulomas and giant cells. Gene Xpert MTB complex detected, Rifampicin resistance detected. Fungal and bacterial cultures were sterile, PCR for Meliodosis was negative. T and B cell flow cytometry, MSMD and CGD workup was negative.
**Course:**

Started on MDR TB regimen with Pyrazinamide, Ethambutol, Levofloxacin, Amikacin, Cycloserine, Ethionamide and PAS. He is 4 months into the treatment and currently improving.

**Learning Points/Discussion**

1. Drug resistant TB should be considered in chronic osteomyelitis in children from India.
2. Gene Xpert MTB clinches the diagnosis.
3. Other aetiologies like brucellosis and melioidosis should be considered.
04A. EDUCATION: SEVERE PNEUMONIA IN CHILDREN

NECROTIZING PNEUMONIA: THE CHALLENGE OF MAKING THE DIAGNOSIS
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Title of Case(s)
Necrotizing pneumonia: The challenge of making the diagnosis

Background
Necrotizing pneumonia (NP) is an emerging and severe complication of community acquired pneumonia in children. Despite being uncommon, its incidence is rising. The most common pathogens associated with NP in children are Streptococcus pneumoniae and Staphylococcus aureus.

Case Presentation Summary
A two-year-old female with personal history of epilepsy, due to a probable tuberous sclerosis, medicated with levetiracetam and vigabatrin, presented to the emergency room with a four-days history of fever, anorexia and lethargy. Physical examination revealed prostration and dehydration signs. A complete blood count showed haemoglobin 8.9 g/dL, leukocytes 6,200/mm³ (neutrophils 4200/mm³, lymphocytes 1200/mm³), C reactive protein (CRP) 326 mg/L. Chest radiography revealed a hypotransparency in the upper two-thirds of the right hemithorax. She was empirically treated with ampicillin and azithromycin and transferred to High Dependency Unit Care. At day-three, due to clinical deterioration with persistent fever and prostration, it was decided to change antibiotics to amoxicillin/clavulanate and clindamycin. At day-six, with persistence of the fever and elevation of CRP, antibiotherapy was switched to meropenem and vancomycin. A chest CT, performed at day-eight, showed necrosis of the right upper lobe and a small pleural effusion on the right, which thoracic echography confirmed “a maximum thickness of 2mm”. There was favourable clinical outcome: remained afebrile from day-thirteen, general condition improved and only required intermittent oxygen therapy during sleep, maximum 1L/min. She was discharged after 21-days of ev antibiotics with amoxicillin/clavulanate for ten days. The etiological agent remains unknown: tuberculosis was excluded, blood cultures-serologies were negative.

Learning Points/Discussion
The hallmark of this case is a striking dissociation between the radiological findings and the respiratory symptoms. NP diagnosis should be considered when, despite appropriate antibiotics, the child remains febrile and unwell.
A Recurrent Retropharyngeal Abscess in a Patient Carrying MBL2 Homozygous Mutations

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Title of Case(s)

A Recurrent Retropharyngeal Abscess in a Patient Carrying MBL2 Homozygous Mutations

Background

Retropharyngeal abscess is a rare but potentially fatal deep neck infection and recurrence is rarely occur. To investigate the underlying cause of recurrence, genetic analysis was performed. The c.52T>C variant in the MBL2 gene is first reported in this study and predicted to be pathogenic in in-silico analysis. This case is presented to emphasize the rarity and the necessity of investigating immunodeficiency in recurrent infections.

Case Presentation Summary

A 4-year-old male admitted to emergency department with the complaints of 38.2°C fever and limitation of neck movements. Neck CT was compatible with retropharyngeal abscess and clindamycin therapy was initiated. Drainage was performed by department of otolaryngology, but no abscess material could be obtained. Cefotaxime was added because of fever persistence and increased levels of acute phase reactants. Therapy was continued for 14 days. In previous medical history, he had two episode of retropharyngeal abscess. To investigate the underlying cause of recurrence, neck MRI revealed no anatomic disorder. Immunoglobulins and lymphocyte panel were normal. To investigate if there was an underlying genetic defect of immune deficiency in the patient we performed molecular genetic test including a panel of immune deficiency genes using next generation sequencing. Molecular analysis revealed a compound heterozygous mutations, c.161G>A (p.G54D) and c.52T>C (p.S18P), in the MBL2 gene of the patient. Segregation analysis showed that the mother carried the c.52T>C (p.S18P) and the father c.161G>A (p.G54D) variant heterozygously.

Learning Points/Discussion

Molecular analysis of the underlying hereditary immunodeficiency in our case revealed a compound heterozygous c.161G>A (p.G54D) and c.52T>C (p.S18P) variants in the MBL2 gene, c.52T>C variant was first reported in this study.
CULTURE NEGATIVE MULTIFOCAL OSTEOMYELITIS IN A 13 YEAR OLD GIRL

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Title of Case(s)

Culture negative multifocal osteomyelitis in a 13 year old girl

Background

Osteomyelitis is a frequent infection in children with *Staphylococcus aureus* and *Kingella kingae* as the common bacterial pathogens. Multifocal and culture negative cases, which have received a biopsy, are less frequent.

Case Presentation Summary

We present a case of an otherwise healthy 13 year old girl with a 7 weeks history of pain of the right femur and hip. She had no fever, no history of trauma, weight loss, night sweat or *M. tuberculosis* contact. No clinical improvement after 7 weeks of antiinflammatory medication under the initially suspected diagnosis sporting injury was seen. A MRI revealed an inflammatory process in the proximal femur as well as the sacrum with the differential diagnosis of malignancy. The histologic examination of the biopsy revealed a chronic, osteo-destructive histiocytic-granulomatous osteomyelitis. No bacteria or fungi could be detected.

At this point, the girl presented in our clinic for evaluation. The laboratory results showed only slightly elevated infection parameters with negative serological testing for *Yersinia enterocolitica/pseudotuberculosis*, *Salmonella enteritidis/typhi* and *Coxiella burnetti*. Tuberkulin Skin Test was negative. We found high IgG titer for *Bartonella henselae* of 1:320 with a negative IgM. In the total-body MRI there was additional evidence of a multifocal osteomyelitis (Ulna, Tibia, Femur and Sacrum) in the absence of localized pain in other regions.

Under oral treatment with Clarithromycin and Rifampicin for 3 weeks she showed clinical improvement and a gradual drop of *Bartonella henselae* IgG titers to 1:80 after 4 weeks was observed.

Learning Points/Discussion

In patients with culture-negative uni- or multifocal osteomyelitis with low infection parameters *Bartonella henselae* should be considered as a possible cause and serological testing performed. This may avoid invasive diagnostic procedures.
19B. SCIENCE: OTHER

OSTEOARTICULAR INFECTIONS IN PEDIATRICS: EPIDEMIOLOGICAL UPDATE
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Background

Acute osteoarticular infections (OAI) is a potentially severe disease that affect mainly children younger than 5 years old. Early diagnosis and treatment reduce the risk of complications and sequelae. This study evaluated the etiology, clinic and laboratory characteristics, and treatment of OAI in children.

Methods

We accessed medical records from children under 16 years old with OAI admitted at our hospital between January 2002 and December 2016.

Results

Our study included 64 children. An agent was identified in 62% of the cases: in blood culture (31%), joint secretion (10%), peripheral blood culture plus joint secretion or bone fragment (20%). The main etiologic agent was S. aureus (40%), followed by S. pyogenes (8%). In the susceptibility profile, 73% of the S. aureus were methicillin-sensitive (MSSA) and 27% were resistant (MRSA). All MRSA, except one, was considered community associated (CA)-MRSA by phenotypic profile. All patients were treated with endovenous antibiotic and was used in 46% of the patients.

Conclusions

We could identify a high rate of agents (62%), with the highest positivity observed in patients who had osteomyelitis. The rate of MRSA raises the question whether oxacillin should still be maintained as the first choice as empirical therapy for OAI. Kingella kingae, considered one of the most frequent agent in pediatric group, was not observed in our cases; possibly because we do not routinely use identification methods for this agent. All patients were hospitalized. Socioeconomic-cultural conditions of our population can explain the longest hospitalization and antibiotic use.
A CASE OF YOUNG INFANT HPeV1 INFECTION WITH INTRAVENTRICULAR HEMORRHAGE

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Title of Case(s)

A case of young infant HPeV1 infection with intraventricular hemorrhage

Background

Human parechoviruses (HPeVs) are RNA viruses that are classified in the family Picornaviridae and 16 genotypes are confirmed. HPeVs usually cause mild respiratory or gastrointestinal symptoms, but HPeV1 and HPeV3 are known that they can provoke sepsis and meningoencephalitis leading to neurological sequelae in neonates and young infants.

Case Presentation Summary

We report a case of HPeV1 infection with Intraventricular hemorrhage. The patient was 2 months' male infants who have no abnormality in perinatal history. He was hospitalized with complaint of looked pale and was presented irritability and neck stiffness. Empirical antimicrobial treatment was started immediately as a serious infectious disease and was combined anticoagulant therapy. His general condition improved on day 5, but intraventricular hemorrhage was detected by Computed Tomography scan. HPeV1 was detected by blood and fecal PCR and it was thought that a series of symptoms were caused by viremia of HPeV1. There is no abnormal neurological finding on examination at discharge, it is necessary careful follow-up observation.

Learning Points/Discussion

HPeVs infection in neonatal and young infants, especially HPeV3 can be severer and cause cerebral hemorrhage as a neurological complication. Compared with HPeV3, HPeV1 symptoms are relatively mild and there are few central nervous symptoms. There is no report of HPeV1 that caused cerebral hemorrhage so far. This case is important that it can merge intraventricular hemorrhage even with HPeV1 infection.
CARDIOMYOPATHY AND MID AORTIC SYNDROME IN HIV INFECTED CHILD

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Title of Case(s)

HIV Cardiomyopathy

Background

Cardiomyopathy and vascular disorders are life-threatening complications of HIV infection. As far as we know, mid-aortic syndrome (MAS), the localized narrowing of the distal thoracic or abdominal aorta, has not been reported with HIV in the literature yet. Herein we present a first case of MAS in an 11-year old congenital HIV infection.

Case Presentation Summary

An 11-year-old girl with the diagnosis of congenital HIV infection presented with palpitation and respiratory distress. In history, she had been diagnosed to have HIV infection at 15 months of age, but could not get antiretroviral therapy, regularly. On admission; she was pale, hypertensive, tachypneic and tachycardic, 2/6 pansystolic murmur and S3 was heard. Hepatomegaly and crackles on lower lobes were noted. Laboratory examination revealed lymphopenia, low CD4⁺ count with HIV viral load of 309 copies/mL and increased hs-Troponin T and pro-BNP. Echocardiography detected mitral and aortic insufficiency, decreased left cardiac output (ejection fraction: %47). She was started on furosemide, enalapril and carvedilol. Abdominal Doppler sonography and MR angiography, revealed occlusion within the proximal segment of the superior mesenteric artery, along with distal collateral retrograd flow and moderate stenosis in the celiac truncus orifice in addition to poststenotic dilatation. Decreased caliber in the left renal artery was found due to severe ostial stenosis. Diffuse intimal thickening from the celiac artery level to just before the bifurcation compatible with MAS. Cardiac MRI revealed increased trabeculation secondary to dilated cardiomyopathy. Detailed work-up revealed high EBV load and decreased serum selenium levels.

Learning Points/Discussion

HIV associated cardiomyopathy and vasculopathy can be due to several reasons including direct effects of HIV, cardiac autoimmunity, opportunistic infections, and nutritional deficiencies. Detailed evaluation should be performed especially in cases with facilitating risk factors.
03A. SCIENCE: SEVERE BACTERIAL INFECTIONS

EXTENSIVE RETROPHARYNGEAL ABSCESS EXTENDING INTO THE MEDIASTINUM - A SEVERE MANIFESTATION OF INVASIVE GROUP A STREPTOCOCCUS INFECTION

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Title of Case(s)

Extensive retropharyngeal abscess extending into the mediastinum - a severe manifestation of invasive group A Streptococcus infection

Background

Streptococcus pyogenes is a common bacterial organism associated with a wide spectrum of disease in children. Here we present a case of an unusually extensive abscess caused by the organism.

Case Presentation Summary

A previously healthy 13-month-old girl presented to her local hospital with five days of fever and URTI symptoms. Inflammatory markers were raised (CRP 410, WCC 34.6, Neutrophils 28.0) and she showed signs of shock. She was transferred to PICU at Evelina Children's Hospital where she was treated for sepsis of unknown origin.

Chest wall ultrasonography demonstrated a large retrosternal abscess with extension beyond the scope of the imaging modality. Cross-sectional CT neck/thorax revealed a retropharyngeal abscess (3 x 1.2 cm) extending into a large, septated, mediastinal collection. The mediastinal components measured 7x2 cm anteriorly and 2.5x2.3 cm posteriorly, with displacement of the oesophagus.

Surgical drainage by ENT and Cardiothoracics removed more than 25 millilitres of pus, with ongoing drainage post-operatively.

Oral swabs, blood cultures, and fluid cultures yielded no growth. 16S PCR analysis identified Streptococcus pyogenes in Surgically drained fluid.

Treatment included 8 weeks of parenteral antibiotics (ceftriaxone and clindamycin) followed by 4 weeks orally (co-amoxiclav and clindamycin). 6 weeks of the parenteral therapy were delivered by p-OPAT using a PICC. The patient subsequently made a full recovery.

Learning Points/Discussion
Microbiology samples taken after antibiotic commencement failed to grow any organisms, however PCR analysis identified the likely causative organism. This enabled confidence in antibiotic choice, facilitating p-OPAT.

*Streptococcus pyogenes* remains a pathogen capable of causing severe disease in otherwise well children.

p-OPAT is an effective tool to reduce hospital stays in children with severe bacterial infections.
THE PAEDIATRIC ANTIMICROBIAL STEWARDSHIP PROGRAMME IN BRISTOL ROYAL HOSPITAL FOR CHILDREN: IMPACT ON PRESCRIBING HABITS.

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Background

Antimicrobial stewardship programs (ASPs) enhance surveillance on antibiotic prescribing and aim to improve the prudent use of antimicrobial therapy, shown by adult data. Data from paediatric settings are sparse and this report describes a snapshot of the ASP in a UK paediatric hospital (Bristol Children's Hospital).

Methods

The ASP in Bristol children hospital include education sessions and weekly antimicrobial stewardship rounds in the general paediatric, surgical and adolescent wards. All antimicrobial prescriptions are reviewed. The stewardship team includes pharmacists and the paediatric infectious diseases team. We present data from 320 patients from two time periods (Aug-Sept 2016 and Apr-Jun 2017). We produced a “discordance rate” indicating a difference between antimicrobials prescribed in the treatment chart and recommended by the stewardship team. The discordance rate represented the number of discordant prescriptions divided by the total prescriptions.

Results

Co-amoxiclav was the most commonly prescribed antibiotic representing 22% of prescriptions and had a discordance rate of 40%, mostly due to the stewardship team suggesting a stop of therapy. The second most common antimicrobial prescribed was amoxicillin (12% of total prescriptions).

Discordance rate was highest for macrolides (59%) mostly prescribed for community acquired pneumonias. The number of discordant prescriptions fell over the two periods analysed for all indications except for the treatment for surgical disease.

Conclusions

This report shows that a substantial number of prescriptions can be optimised with a weekly ASP word round (to ensure use of the narrowest antimicrobial spectrum is used according to current local evidence, guidelines and sensitivities). The programme appears to be successful in improving prescribing according to the reduction of discordant prescriptions in the second period. More data are required to substantiate this initial observation.
COMPARATIVE EVALUATION OF LIVER, SPLEEN, KIDNEY AND THYROID IN HIV-MONOINFECTED PEDIATRIC PATIENTS VIA SHEAR WAVE ELASTOGRAPHY

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Background

To evaluate the elasticity of liver, spleen, both kidneys and thyroid gland in Human Immunodeficiency Virus (HIV)-monoinfected children taking antiretroviral treatment (ART) via shear wave elastography (SWE) and to compare the results with healthy subjects.

Methods

Twenty-one HIV-monoinfected children with median age of 12.6 (0.5-18.5) years and 37 health subjects with median age of 10 (0.5-18) years were included in this prospective study. Liver, spleen, both kidneys and thyroid gland of all of the participants were examined via SWE. Routine laboratory tests of HIV-monoinfected children were also recorded. Elasticities of these organs were compared between patient and control groups. T test was used for statistical analysis.

Results

Elasticity of liver, spleen and both kidneys of HIV-monoinfected children was significantly higher than healthy subjects. No statistical significance was observed between patient and control group in terms of elasticity of the thyroid gland. When the patients with high and undetectable viral load and the patients with the disease duration of more and less than 5 years were compared within each other; no significant difference was observed in terms of elasticity values of liver, spleen, both kidneys and thyroid gland.

Conclusions

Elasticity of liver, spleen and kidney in HIV-monoinfected children who are on ART treatment was increased. SWE can be used as a noninvasive technique to determine the cytotoxic effect of HIV and ART on liver, spleen and kidneys, before the laboratory parameters deteriorate. More studies should be performed in order to comment the availability of SWE on thyroid gland in this manner.
STUDY ON COMPLIANCE TO ANTIBIOTICS IN CHILDREN

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Background

Antibiotics are an extremely important weapon in the fight against infections. For children, the parents assume the responsibility of administering the antibiotics. An attempt was made to assess the extent of compliance to antibiotic therapy and identify the patterns of non-compliance.

Methods

This 6 month long prospective questionnaire based study was conducted at a pediatric outpatient clinic in pediatric patients who were prescribed antibiotic. Patient details were collected at the time of visit and they were followed up telephonically after the completion of the antibiotic course. The compliance to antibiotic therapy was indirectly assessed through parents because parents were responsible for administering the medication to children. All pediatric patients visiting the clinic in the age group from 2 month to 14 years, prescribed with an antibiotic, and willing to participate were included.

Results

Out of 85 patients, 80 were successfully followed up with a response rate of 97.5%. The average age of children prescribed antibiotics was found to be 2.05±0.23 years. Two third of the infants’ parents were compliant to the prescribed antibiotic therapy. Postgraduate parents were found to be more compliant to prescribed therapy (62%). The joint families were found to be more compliant than nuclear families. Administering measure were not used adequately in 43.7% of the patients and it was found to be the most common reason for non-compliance. The other reasons included cessation of therapy when bottle was empty even if complete course was left (40.6%). It was found that compliance to shorter antibiotic therapy was better than the longer therapy.

Conclusions

The outcome of the therapy depends a lot on the perception and medication usage behaviour of the parents.
IMPACT OF NECROTIZING ENTEROCOLITIS IN MORTALITY AND NEURODEVELOPMENTAL IMPAIRMENT.
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Background

Necrotizing enterocolitis (NEC) is still one of the most catastrophic intestinal emergencies in preterm very low-birth weight infants (VLBW). NEC is associated with increased mortality and short and long-term morbidity, including growth and neurodevelopmental

Aim: to evaluate the impact of NEC in mortality, neurodevelopment and growth in VLBW infants with gestational age < 32 weeks.

Methods

Observational, analytical and retrospective case-cohort study of infants with NEC ≥ grade II, admitted in a Neonatal Intensive Care Unit between January/2005 and December/2015. Outcomes at 24 months included: anthropometric measurements, Griffiths Mental Development Scales and major neurosensory abnormality. It was considered severe neurodevelopmental impairment: cerebral palsy, neurodevelopmental delay (developmental quotient <2sd), hearing impaired and/or blindness. WHO growth charts were used to determine growth status at follow-up (weight, length, and head circumference). Growth impairment was defined by < -2sd for gender and age.

Results

This study included 434 preterm infants: 21 with NEC and 395 controls without NEC. In univariate analysis, difference between cases vs controls were identified for: gestational age (26.8± 1.6w vs 28.5±1.8, p<0.001), birth weight (900± 242g vs 1096±251g, p=0.002), hypotension (p<0.001), persistence ductus arteriosus (p<0.001), red cell transfusion (p<0.001), mechanical ventilation >7 days (p<0.001), antibiotic therapy D1 (p=0.019), bronchopulmonary dysplasia (p=0.022), enteral feeding <3d (p=0.026), weight at 24 months(p=0.001), and mortality/neurodevelopmental impairment (p<0.001). After adjusting for birth weight, gestational age, antenatal steroids, mode of delivery and gender, preterm with NEC had an increased risk to mortality/neurodevelopmental impairment (p<0.001; OR: 6.6 IC95%: 2.4-18.2) and growth impairment (p=0.024, OR: 4.6 IC95%: 1.2-17.7).

Conclusions

Conclusion: NEC is associated with mortality and long-term adverse outcome in growth and developmental impairment.
CASE REPORT - SEPTIC ARTHRITIS OF THE KNEE IN A NEWBORN

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Title of Case(s)
Case report - Septic arthritis of the knee in a newborn

Background

Septic arthritis represents an intra-articular infection caused by pyogenic bacteria, being rare in neonates. Delay in diagnosis or treatment may result in irreversible damage to the joint.

Case Presentation Summary

A newborn girl with 24 days of life, born at 40 weeks of gestation via eutocic birth, with negative maternal serologies performed in the 3rd trimester, and negative b group Streptococcus, researched in cultured rectal exudate after 35 weeks of gestation, was admitted in the emergency department due to decreased mobility of the left lower limb and intense crying when mobilized, without fever, vomiting or diuresis changes. Physical exam showed edema on the left knee, increased temperature and flushing, with the limb preferably in flexion and impaired range of movement. Blood workout showed 12,900/ul leukocytes (4360/ul neutrophils), C-reactive protein 29mg/L and procalcitonin 0.2ng/ml. Radiography of the knee and MRI showed no signs of osteomyelitis. With the suspicion of septic arthritis, an arthrotomy with drainage and lavage was performed and she started flucloxacillin (200mg/kg/day) and cefotaxime (200mg/kg/day). Joint fluid was positive for multisensitive group b Streptococcus and blood cultures were sterile. Antibiotics were replaced to ampicillin (200mg/kg/day) and it was maintained for 4 weeks with a positive clinical and analytical outcome.

Learning Points/Discussion

Septic arthritis in the neonate is a serious condition which could result in permanent dysfunction or deformity of the limbs. Staphylococcus aureus is the most frequent agent but others like group b Streptococcus can cause septic arthritis, particularly at this age. This case reminds that group B streptococcus can colonize birth canal and be negative when searched during pregnancy, so although rare, has to be considered in newborns.
MAINTENANCE OF TETANUS, DIPHTHERIA AND PERTUSSIS ANTIBODIES AFTER PRIMARY IMMUNIZATION IN CHILDHOOD AND HUMORAL IMMUNE RESPONSE TO A Tdap BOOSTER IN VERTICALLY HIV-INFECTED ADOLESCENTS

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Background

Response to a Tdap booster has not been previously assessed in vertically HIV-infected adolescents.

Methods

Thirty HIV adolescents with CD4>200 on combined antiretroviral therapy (cART) and 30 healthy CONTROLs were immunized with Tdap, after prior DTwP vaccine primary scheme. Blood samples were collected immediately before and 28 days after Tdap. Tetanus, diphtheria and pertussis toxin antibodies were assessed by ELISA.

Results

Adolescents from both groups received baseline vaccine regimens with 3 doses of DTwP vaccine and 2 to 3 booster doses before study entry (p=0.255). Median time interval between the last vaccine dose and Tdap was 7.0 years and 7.7 years for HIV and CONTROL group, respectively (p=0.405). Pre-Tdap, diphtheria and pertussis antibodies were comparable in the two groups, but tetanus antibodies were significantly higher in HIV group. After Tdap, tetanus, diphtheria and pertussis antibodies increased significantly in both groups. Tetanus and pertussis antibodies were comparable in both groups on day 28, but HIV group responded with lower diphtheria antibodies (Table). All CONTROL individuals seroconverted to the three antigens; in HIV group, one adolescent (3.3%) did not seroconvert to tetanus, three (10.0%) did not seroconvert to diphtheria and 12 (41.4%) did not seroconvert to pertussis. We assessed variables that could justify the unexpected higher levels of tetanus toxoid antibodies in HIV group on day 0: 21/30 (70.0%) HIV and only one CONTROL individual (1/30, 3.3%) had received a meningococcal C tetanus toxoid conjugate vaccine between
2001 and 2015 (p<0.0001).

**Conclusions**

Vertically HIV-infected adolescents on cART respond to a Tdap booster with lower humoral immune response, especially to diphtheria and pertussis antigens. Meningococcal tetanus toxoid conjugate vaccines might influence maintenance of tetanus antibodies after primary vaccine scheme.

<table>
<thead>
<tr>
<th>Parameter (IU/mL)</th>
<th>Day</th>
<th>HIV</th>
<th>CONTROL</th>
<th>Mann-Whitney (p)</th>
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<tr>
<td>Tetanus antibodies</td>
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<td>0</td>
<td>0.4 (0.1-1.2)</td>
<td>0.1 (0.5-0.3)</td>
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<tr>
<td></td>
<td>28</td>
<td>26.7 (13.7-42.4)</td>
<td>29.3 (8.8-46.5)</td>
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<tr>
<td>Diphtheria antibodies</td>
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<td>0</td>
<td>0.2 (0.0-0.6)</td>
<td>0.7 (0.1-1.3)</td>
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<tr>
<td></td>
<td>28</td>
<td>4.0 (1.0-15.5)</td>
<td>22.9 (11.6-42.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pertussis toxin antibodies</td>
<td></td>
<td>0</td>
<td>8.7 (2.7-37.0)</td>
<td>7.1 (4.7-17.1)</td>
</tr>
<tr>
<td></td>
<td>28</td>
<td>31.5 (10.5-73.8)</td>
<td>48.1 (23.9-140.1)</td>
<td>0.185</td>
</tr>
</tbody>
</table>
Escherichia coli relapsing meningitis.

Background

Relapsing meningitis (Rme) due to E. coli is very uncommon, although some anatomic defects and immunodeficiencies have been described as predisposing factors.

This is a retrospective study to describe the characteristics of Rme diagnosed in children <14 years-old in a tertiary care hospital during 2008-2017.

Case Presentation Summary

Over the period, 4 cases of Rme were diagnosed. Male/female: 3/1.

Three of them were preterm (30-33 weeks of gestational), 2 related to a maternal chorioamnionitis.

The first episode of meningitis happened between 2-22 days of life, with isolation of E. coli in CSF (3 cases) and blood culture (1 case) without resistance to cephalosporins. They were treated with cefotaxime in two cases and meropenem in the remaining ones at correct doses, which were admitted to Neonatal Intensive Care Unit at the moment of the first episode of meningitis. Treatment duration was between 13-30 days.

The mean of days between first and second meningitis was 28.5 (range 4-50), without resistances in CSF cultures. Three of the relapsing cases were treated with cefotaxime combined with ampicillin, meropenem or ciprofloxacin; the last case was treated with meropenem plus ciprofloxacin. One patient developed subdural empyema and required surgical drainage. The mean days of treatment was 41 (range 30-54). Three patients received oral ciprofloxacin after the hospital discharge during 30 days. A brain-spinal cord MR and immunological tests were normal in all these patients. No more relapses were described. Two patients developed neurological sequels, which were severe in one patient.

Learning Points/Discussion
Meningitis by E. coli may relapse after adequate antibiotic treatment. Half of our patients developed neurological sequels after the RMe.

None of them had identified anatomical defect or immunodeficiency as predisposing factors.
THE ACTUAL CAUSE IN AN ADOLESCENT PATIENT FOLLOWED UP FOR VESICOURETERAL REFLUX: RENAL TUBERCULOSIS

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Title of Case(s)

Adolescent with renal tuberculosis

Background

Genitourinary tuberculosis is a rare form of extrapulmonary tuberculosis in childhood. Patients may present with recurrent sterile pyuria and non-specific urinary system findings. Hydronephrosis due to granuloma formation may develop in the collecting system. We present a case of adolescent girl with renal and pulmonary tuberculosis who had previously been misdiagnosed as vesicoureteral reflux (VUR).

Case Presentation Summary

A 15-year-old girl was admitted to another facility with the complaint of frequent urination and hematuria, two years ago. She had been operated with the preliminary diagnosis of VUR related hydronephrosis. After the operation, sterile pyuria persisted and the patient was referred to our clinic with the suspicion of urinary system tuberculosis. On admission; She had minimal sensitivity at the left lumbar region and the left kidney palpated under the rib. Laboratory study revealed lymphopenia, mild anemia, high ESR, proteinuria and hematuria. Tuberculin skin test was negative and quantiferon was positive. Chest X-ray showed reticulonodular infiltration on upper lobes. Computerized chest tomography revealed “tree in bud” appearance. Urinary culture yielded *Mycobacterium tuberculosis* growth. Contrast enhanced magnetic resonance imaging of the abdomen revealed dilatation and blunting in the left urinary system, together with diffuse thickening and fibrosis throughout the whole ureter. Renal pathology was considered to be compatible with renal tuberculosis. Antituberculous therapy including isoniazid-rifampicin-pyrazinamide and ethambutol was started. She was planned to have a catheter insertion operation due to obstructive hydronephrosis. But the operation delayed because of severe edema and obstruction in the urinary system. The patient was scheduled to receive methylprednisolone 2 mg/kg/day for 6-8 weeks.

Learning Points/Discussion

Although renal tuberculosis is rare in childhood, patients with recurrent urinary tract symptoms and sterile pyuria must be evaluated in terms of tuberculosis.
03B. SCIENCE: COMM.ACQ. INVASIVE BACTERIAL INFECTIONS (NON-RESPIRATORY)

PEDIATRIC OSTEOARTICULAR INFECTIONS

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Title of Case(s)

PEDIATRIC OSTEOARTICULAR INFECTIONS

Background

Pediatric osteoarticular infections (OAI) are rare but important diseases to identify early and treat appropriately in order to avoid associated acute complications or long-term morbidity.

Methods:
Retrospective and descriptive study of children<14 years of age hospitalized for OAI between January-2016 and December-2017.

Case Presentation Summary

We report 41 patients with OAI. Twenty-four were diagnosed with osteomyelitis and seventeen with septic arthritis. The incidence was 18-20/100.000, higher than what we observed from 2002 to 2015 (4-11/100.000).

The median age was 26 months and 68% were younger than 5 years. The sex distribution was similar.

Drainage, culture and PCR testing for \textit{Kingella kingae} was performed in twenty-one patients (seventeen arthritis and four osteomyelitis), but 30\% of them received prior treatment with antibiotics. In relation to arthritis cultures, only one out of seventeen was positive (\textit{Kingella Kingae}), and two out of four osteomyelitis cultures were positive (1 \textit{S. aureus}, 1 MRSA).

Blood culture was taken from all patients but only one was positive (\textit{S. aureus}). Cefotaxime and cloxacillin were the main antibiotics, especially in younger children, but cefuroxime as individual therapy was the second in frequency.

Median duration of intravenous antibiotic was 9 days, followed by oral therapy. The average stay was nine days. Two patients required re-entry, both had calcaneal osteomyelitis. Long-term evolution was favorable in all patients with normal physical examination after 6months.

Learning Points/Discussion

Although pediatric OAI are relatively rare, our study suggests an increased incidence in the last two years, which requires in-depth study.
Due to the low diagnostic yield observed in our series, a protocol will be established to identify the problem and achieve a more accurate diagnostic.
Primary cutaneous aspergillosis in an immunocompromised patient with acute myeloid leukemia after bone marrow transplant

Background

Aspergillus species are among the most common fungi causing fungal infections in immunocompromised patients. Invasive aspergillosis occurs in 5-13% of bone marrow transplant recipients. Although, invasive aspergillosis is common, primary cutaneous aspergillosis (PCA) is rare.

Case Presentation Summary

A 17-year old boy with acute myeloid leukemia, in second relapse after allogeneic bone marrow transplantation (BMT), presented with an erythematous plaque at his right thigh. He remained afebrile. Ultrasound revealed cellulitis. After skin biopsy, the plaque became black in the centre with violaceous areola. Culture revealed infection of aspergillus fumigatus, sensitive to amphotericin B, voriconazole and posaconazole. Due to liver damage (Child – Pugh B) related to chemotherapy and BMT, he initiated antifungal therapy with posaconazole. Blood cultures, chest X-rays and CT scan and abdominal ultrasound were negative for fungal infection. The lesion kept expanding despite the treatment, so a surgical debridement was performed. Although declining at first, the lesion resumed expansion soon afterwards. Another surgical debridement was performed. The second culture also revealed infection of aspergillus fumigatus, with the same antifungal susceptibility. Treatment was modified to liposomal amphotericin B (5mg/kg) because of poor response to treatment and aggravated liver damage. Another extensive scan revealed no signs of invasive aspergillosis. He resumed with liposomal amphotericin B and underwent 2 more surgical debridements before being transferred to BMT ward. This course lasted about two months. Soon after receiving the transplant, he developed invasive aspergillosis with lung involvement and multiple skin lesions. He passed away approximately
1 month later due to illness progression.

**Learning Points/Discussion**

PCA is a rare but extremely difficult infection to treat, requiring prolonged antifungal treatment and multiple surgical debridements.
TRADITIONAL PRACTICES USED IN CHILDREN CARE MAY LEAD TO INFECTION: A CASE OF TURKEY

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Background and Objective

The aim of this review is to state the traditional practices used in children care which may lead to infection.

Methods

Traditions are collecting habits from society and society, habits, information, customs and behaviors cultural heritages that have been gathered from society and society. Sometimes those traditions may cause health problems involuntarily. Children are a vulnerable population. In the conducted studies, it is stated that salting, washing body with urined water and applying indigo may cause damage in the sensitive skin. Additionally, towing and lemon squeezing to eyes may cause conjunctivitis, late breastfeeding, giving sugared water, using baby powder for curing rash may lead to aspiration and lung problems, applying mother’s hair to moniliasis (in that case recovery of moniliasis delays and both in baby’s mouth and on mother’s breast may cause infection), using breast milk and olive oil for umbilical cord care, putting under baby eart and wrapping the baby in this way (that case may cause tetanus), rubbing swollen breast to shrink it are stated as leading to infection. Infection is one of the important death causes in the developing countries. Although World Health Organisation recommends breastfeeding in the first six months, it could be seen delaying to start breastfeeding, interruption of breastfeeding and giving sugared water. Those applications increases the tendency to infections by weakening the immune system.

Learning Points Discussion

Midwives and nurses should plan the care for preventing children from infections originating from traditional practices. Mothers who have low education level and are at a young age should be given education about children care.
A REVIEW OF DATA ON ANTIMICROBIAL RESISTANCE IN PNEUMOCOCCI ACROSS NORTHERN EUROPE AND ITS RELATIONSHIP TO ANTIBIOTIC CONSUMPTION AND THE USE OF PNEUMOCOCCAL CONJUGATE VACCINES

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Background and Objective

The most common reason for prescribing antibiotics to children is otitis media. Antimicrobial consumption drives antimicrobial resistance (AMR). Vaccination leads to reductions in antimicrobial use, which can result in declining rates of AMR. AMR rates in pneumococci vary considerably across Europe with northern European countries maintaining relatively low rates. Our objective was to review data on AMR, antimicrobial consumption and relevant interventions across northern Europe.

Methods

Publications were identified through Medline and Embase searches, limited to human, English language and last 10 years using “Pneumococcus OR Streptococcus pneumoniae OR Pneumococci AND Antimicrobial Resistance OR AMR OR penicillin OR erythromycin OR tetracycline OR macrolides AND UK OR Ireland OR Denmark OR Sweden OR Norway OR Finland OR Latvia OR Lithuania OR Estonia OR Netherlands OR Iceland OR Greenland.” We also reviewed data from the European Surveillance for Antimicrobial Consumption Network (ESAC-Net) and the European Antimicrobial Resistance Surveillance Network (EARS-Net).

Learning Points Discussion

210 articles were identified and of those we deemed 95 warranted further review based upon title. In 2016, EARS-Net reported pneumococcal penicillin resistance rates across northern Europe ranged from 2.2% (The Netherlands) – 16.5% (Ireland). Macrolide resistance rates ranged from 0% (Iceland) - 18.1% (Lithuania). In the same year ESAC-Net reported consumption of antibacterials in the community ranged from 10.4 (The Netherlands) – 21.0 (Iceland) defined daily dose/ 1,000 inhabitants/day. All northern European countries recommend pneumococcal conjugate vaccine (PCV) immunisation in children. The Joint Committee on Vaccination & Immunisation in the UK stated immunisation is an important strategy for tackling AMR and recommended future reviews of vaccination programmes should include the potential benefits of vaccines in reducing antimicrobial use. We encourage other national immunisation technical advisory groups (NITAGs) to follow this policy.
A RARE FUNGAL AGENT IN SEPTIC ARTHRITIS: CANDIDA ALBICANS

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Title of Case(s)

Fungal Septic arthritis

Background

In the course of septic arthritis, microorganisms are invasive to the joint space and the morbidity can be quite high when proper treatment is not given. Although it may be seen in all joints, it is frequently seen in the hip and knee joint, and the most common cause is Staphylococcus aureus. Etiology rarely causes fungal agents. Here we present a case of septic arthritis caused by Candida albicans.

Case Presentation Summary

A 6 month old girl was brought the outpatient clinic with the complaint of fever and swelling of right knee. She was born at 28th gestational week (1000-gr birth weight) and was hospitalized for 70 days in neonatal intensive care unit. She was diagnosed to have septic arthritis and was started on teicoplanin and sultamycin treatment. After the determination of Candida albicans growth in the joint aspirate; she was referred to our clinic. Her physical examination was unremarkable other than swelling, redness and the disability of right knee. Laboratory examination revealed slightly elevated white blood cell count. According to aspirate fluid culture sensitivity, micafungin treatment was started. Contrast-enhanced MRI revealed thickness 7 mm suprapatellar bursa level enhancement was interpreted in favor of arthritis, osteomyelitis was not detected. Immunological studies were normal. Appropriate physiotherapy support was given. On the 15th day of treatment since the effusion persisted, control aspiration was performed. On serial ultrasound imaging, the effusion disappeared and second aspiration fluid became sterile. After the treatment was completed for 42 days, the patient was discharged with complete recovery.

Learning Points/Discussion

Septic arthritis is an important cause of morbidity in childhood; fungal pathogens should be considered even in healthy children who do not carry a risk factor when they are diagnosed.
RATIONAL ANTIBIOTIC USE IN PEDIATRIC INTENSIVE CARE UNITS
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²Çukurova University, Child Health and Diseases Nursing, Adana, Turkey

Background and Objective

The aim of this review is paying attention to the use of rational antibiotics in pediatric intensive care units (PICU).

Methods

Infection is an important problem in PICU. Developing infection in a critically ill child leads to increased mortality and morbidity, prolongation of hospital stay, and increased hospital costs. Rational antibiotic use in PICU has two main targets. Firstly, it is the effective treatment of the infection in the patient and the prevention of infection-related mortality and morbidity. The second is to minimize the development and spread of resistant microorganisms. Among the applications that have been shown to achieve these goals are; the correct diagnosis of infection, follow up and use of local data, selection of antibiotics for pathogenesis, establishment of treatment protocols, restriction of antibiotic use, continuous education about infectious diseases and antibiotic use. Clinical and laboratory findings are important for the diagnosis of infection. According to these findings, diagnostic protocols should be established, in which cases infection should be diagnosed and empirical antibiotic therapy should be started. Local data, that is; the follow-up and use of factors and resistance patterns seen in PICU is important in reducing mortality and morbidity due to infection. At the same time, the development of guidelines for the use of glycopeptides, broad spectrum penicillin and cephalosporin, quinolone and carbapenem drugs by hospital infection committees will reduce the frequency of antibiotic use. In addition, regular training of health personnel on infectious diseases and antibiotic use will increase the correct use of antibiotics.

Learning Points Discussion

Unnecessary or irrational antibiotic use in PICU results in increased morbidity and emergence of resistant microorganisms. The establishment of rules for antibiotic use will reduce the frequency of antibiotic use and antibiotic resistance.
UMBILICAL CORD STUMP INFECTIONS AMONG UGANDAN NEONATES IN A PRIMARY HEALTH CARE SETTING

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Background

Infections are one of the major causes of morbidity and mortality among neonates and 99% of these deaths occur in low income countries. Infection of umbilical cord stump is a known risk factor of neonatal septicemia. We conducted a descriptive cross sectional study on a cohort of neonates in an ongoing trial to describe pathogens causing umbilical stump infections among 3 day old neonates.

Methods

This study was conducted at three primary health care facilities in and around Kampala. Umbilical swabs were collected in Amies transport medium from all neonates including those presenting with clinical signs of cord sepsis; redness or swelling or foul smell and pus discharge on day 3 after birth. The Validated questionnaires were used to obtain sociodemographic and clinical information using mobile based Open data kit. We used conventional culture methods and Kirby Bauer disk diffusion method for antimicrobial susceptibility testing.

Results

The prevalence of umbilical cord infections was 6.1%. The mean birth weight of the studied neonates was 3.12 (SD 4.9) kgs and 51.4% of the cases had applied at least one unhygienic substance to the cord stump after birth. The commonest organisms isolated from cases include E.coli 35.1%, K.pneumoniae 16.2% and Enterobacter spp 8.1%. They were all resistant to ampicillin and amoxicillin-clavulanic acid. However, they were susceptible to gentamycin. Half of the K.pneumoniae isolates were resistant to 3rd generation cephalosporins. One MRSA isolate of among the cases.

Conclusions

The commonest bacterial cause of umbilical cord infections among neonates born at primary health care facilities in Uganda were E.coli, K.pneumoniae and Enterobacter spp. Clinicians should take note of the increasing resistance to commonly available and affordable antibiotics used to empirically treat common infections in resource limited settings.
Parapneumonic pleural effusion (PPE) and empyema are complications of bacterial pneumonias. The epidemiology of these diseases suffered important variations coinciding with the introduction of pneumococcal conjugate vaccines (PCV). The aim of this study is to assess the possible effect of the introduction of heptavalent (VCN7) and thirteenvalent (VCN13) vaccines.

Methods

Data was collected from patients admitted with PPE in our center from 1995 to 2017 confirmed by thoracic ultrasound and excluded secondary to other pathologies. PPE of pneumococcal origin was defined as one that had blood culture, culture of LP (LP), Ag or PCR of LP positive for pneumococcus. For analytical purposes, we consider the prevacunal period from 1995 to 2001, period VCN7 from 2002 to 2010 and period VCN13 from 2011 to 2017. The statistical analysis was carried out using the student's t test to compare incidences (cases / 100,000 under 15 years).

Results

We collected 356 patients with PPE of which 119 were pneumococcal. An increase in PPE was observed significantly (p <0.05) in the PCV7 period compared to the prevacunal in all ages. Also increases in pneumococcal PPE in all ages except in <2 years were found. When comparing the PCV13 era with the PCV7, a decrease in PPE was observed in all age groups except 5-15 years (p = 0.067). The incidence of pneumococcal PPE decreased significantly in <15 years and in 2-5 years.

Conclusions

The data analyzed suggest that the introduction of PCV7 influenced the increase in pneumonias associated with PPE and caused by pneumococcus. They also suggest that VCN13 has influenced the decrease of these pathologies.
Background

Children with Acute Myeloid Leukemia (AML) are in increased danger of fungal infections of various types.

Case Presentation Summary

Materials – Methods: All children of our center diagnosed with AML between 1/1/2010 and 31/12/2017 were evaluated retrospectively. We selected only those with confirmed FIs at any site.

Results: A total of 33 patients were diagnosed during this period of time. A FI was confirmed in 7 of them (21.2%). Five patients (71.4%) receive chemotherapy after initial diagnosis and 2 (28.5%) after relapse. The site of infection was lungs for 3 patients (42.8%), fungemia for 2 (28.5%) – although one with both fungemia and lung involvement, soft tissue for 1 (14.2%) and nasal mucosa for 1 (14.2%). Aspergillus spp (3 fumigatus, 1 terreus, 1 niger) was responsible for the infection in 5 patients (71.4%), Candida parapsilosis in 1 (14.2%) and Alternaria alternata in another one (14.2%). Liposomal amphotericin B was given initially in all patients for a median of 25 days/patient (3-7mg/kg). After confirmation of the sensitivity tests, treatment was modified to voriconazole in 5 patients for a median of 77.8 days/patient and to posaconazole in 2 patients for a median of 35.5 days/patient. Five patients were cured from FI and survived (71.4%) whereas 2 (28.4%) died due to disease progression with signs of FI.

Learning Points/Discussion

Almost one out of 4 children with AML develops an apparent FI. Aspergillus spp is the main pathogen in our patients. Proper antifungal treatment resulted in a successful outcome for our patients. Disease progression was the main cause of death among those who died.
Background: Enteroviruses are associated with various clinical symptoms. Enterovirus D68 (EV-D68), primarily causes respiratory illness. Many areas of the United States experienced increased reports of severe respiratory illnesses among children. There are no previous description of respiratory disease by this agent in Brazil.

Methods

We screened 715 children < 2 years old with acute respiratory tract infections admitted to an urban hospital for respiratory virus using polymerase chain reaction (PCR) assays. We retrospectively analyzed the cases diagnosed as EV-D68. The chart reviews evaluated medical history, clinical presentation, and hospital course.

Results

EV-D68 was detected in nasopharyngeal specimens in 7 children 5 male and 2 female. All of the children have wheezing as the main symptom. In 3 of these patients EV-D68 was associated with other respiratory virus. One child was admitted in intensive care. Patients presenting with wheezing and EV-D68 infection had similar medical histories and clinical presentations comparing with children with other viral respiratory infections.

Conclusions

Patients presenting with wheezing and EV-D68 infection had similar medical histories and clinical presentations to those without EV-D68.
IDENTIFICATION OF NEW BIOMARKERS TO DISTINGUISH BETWEEN A BACTERIAL OR VIRAL INFECTION IN CHILDREN

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Background

The biggest cause of death in children under 5 years is infection. The most common symptom presenting the infection is fever. Most of the febrile illnesses are caused by viral infections, but a small number are life-threatening bacterial infections, such as meningitis, pneumonia or osteomyelitis. In the clinic it is nowadays difficult to distinguish between a bacterial or viral infection based on clinical grounds. This results in treatment with antibiotics when they are suffering from a viral infection out of fear of missing a bacterial infection, leading to unnecessary use of antibiotics. There is an urgent need of the development of improved methods to distinguish between bacterial and viral infections.

Methods

Here, we focus on the identification of new discriminators of bacterial and viral infection. This is done a Luminex assay with candidate markers and by ELISA to validate known biomarkers.

Results

In our cohort of 150 bacterial and viral plasma samples we have confirmed by ELISA that C-reactive protein (CRP) and neutrophil protein elastase is increased in bacterial infections compared to viral infections. The Luminex showed us several macrophage proteins elevated in children with meningococcal infection. Also, S100A12 is significantly increased in bacterial infections, compared to viral infection.

Conclusions

Further research into these markers is needed to get insight in these findings. We hope to develop a reliable diagnostic tool which will lead to more accurate diagnosis to reduce hospital admissions and antibiotic use.

Clinical Trial Registration (Please input N/A if not registered)
N/A
A CASE OF LISTERIA MONOCYTOGENES MENINGITIS IN AN IMMUNOCOMPETENT 16-MONTH-OLD CHILD.

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Title of Case(s)

A case of *Listeria monocytogenes* meningitis in an immunocompetent 16-month-old child.

Background

*Listeria monocytogenes* (LM) is a gram-positive bacteria transmitted to humans through ingestion of contaminated food. It causes severe infections in immunocompromised patients, but it is rarely reported in previously healthy and immunocompetent subjects.

Case Presentation Summary

A previously healthy, immunocompetent, 16-month-old girl was hospitalized for high grade fever, vomiting and irritability. On admission, the patient was in good clinical conditions and the clinical examination was normal with no sign of meningitis. Laboratory tests showed white blood cell (WBC) counts of 14090/mmc (75.7% neutrophils) and C-reactive protein (CRP) of 5.76 mg/dl (normal value < 0.5 mg/dl); renal and liver function and coagulation tests were within the normal range. Intravenous ceftriaxone was started. The patient’s clinical and neurological conditions rapidly worsened. The computed tomography (CT) scan of the brain was normal. A lumbar puncture was performed and cerebrospinal fluid (CSF) analysis revealed 840 cells/mmc with neutrophilic predominance, glucose and protein concentration of 38 and 44 mg/dl respectively. The real-time polymerase chain reaction (RT-PCR) for bacteria and the culture of CSF were positive for LM Ceftriaxone was discontinued and intravenous ampicillin plus gentamicin were started and continued for a total 21 days. A brain magnetic resonance imaging scan showed mild meningeal enhancement without parenchyma involvement. The patient improved rapidly and she was discharge after 22 days. She had not any neurological sequelae.

Learning Points/Discussion

LM represents a rare cause of meningoencephalitis in previously healthy and immunocompetent children, but it could progress rapidly and may be associated with severe complications and a high mortality rate. Prompt diagnosis is essential to start adequate antibiotic treatment.
Visceral leishmaniasis in Greece: Under-reported or Under-estimated?

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Title of Case(s)

Visceral leishmaniasis in Greece: Under-reported or Under-estimated?

Background

Visceral leishmaniasis (VL) has been characterized a neglected tropical disease, endemic in over 98 countries worldwide. Greece is considered an endemic country with visceral leishmaniasis being the predominant form. L.infantum is the species responsible while the vectors transferring the parasite are Phlebotomine sandflies. Dogs are considered the main reservoir hosts and humans are basically accidental hosts.

Leishmaniasis is a mandatory notifiable disease in Greece. During the years 2004-2014, 606 new cases of VL were reported. The annual incidence of VL ranged from 0,27-0,78 new cases per 100,000 population. Lakonia is a Regional Unit in Peloponesse, South Greece with a population of 89,138 residents. The annual incidence of VL in the area is estimated between 0,71-1,00 per 100,000 population.

Case Presentation Summary

During 2017, we report four new cases of VL diagnosed in the General Hospital of Lakonia- Nursing Unit of Sparta. The three new cases were children aged 3, 5 and 8 years old respectively. The fourth case was a 42-year-old male. All four cases presented with fever, hepatosplenomegaly and pancytopenia and positive rK39 antigen. The diagnosis was sealed by demonstration of the parasites in bone marrow sample.

All four patients were treated with liposomal amphotericin B with excellent response and no relapses. The three children were reassessed within one month after release and their laboratory exams were normal.

Learning Points/Discussion

During 2017, VL incidence in Lakonia was 4,487 per 100,000 population, 4-6 times increased comparing to the reported data in the region and 5-16 times comparing to the country's annual incidence. So, is that an actual increase in the incidence of VL in Lakonia or the country's recording system needs re-evaluation?
Primary sternal osteomyelitis with mediastinitis in a neonate.

Background

Primary sternal osteomyelitis is an extremely rare condition in children and develops in the absence of a contiguous focus of infection. S. aureus remains the usual causative organism.

Case Presentation Summary

We report a case of primary sternal osteomyelitis with mediastinitis in a 16-day-old female infant who presented with fever of 39.3-40 degrees Celsius and no obvious source. White cell count (29,000 with 75% neutrophils) and C-reactive protein (CRP, 95mg/L) were raised. She was started on meningitic doses of IV Ampicillin and IV Gentamicin. An erythematous patch was noted over her upper chest wall the following morning, which quickly became fluctuant and tender. There was no prior history of skin breakage or insect bites. Blood cultures grew MSSA. She was empirically changed to IV Vancomycin then switched to IV Cloxacillin. An ultrasound scan of her chest wall showed a cystic echogenic lesion measuring 23 x 15 x 14mm abutting the underlying bone. Cultures from an ultrasound-guided needle biopsy yielded MSSA. An MRI scan of the chest wall showed a chest wall abscess and mediastinitis. Surgical drainage and debridement was performed, where a sternal sequestration was identified and removed. An immunodeficiency work-up returned negative. She received a total of 6 weeks of IV Cloxacillin until resolution of infection on repeat imaging.

Learning Points/Discussion

Rare severe infections in a neonate beg a closer look for risk factors including structural abnormalities and immunodeficiency. The "fixation point theory" may explain the sternal involvement where slow blood flow through a porous sternal matrix facilitating microthrombosis and bacterial stasis. MRI remains imaging of choice and surgical debridement should be first-line treatment to direct antibiotic therapy following culture results.
A SNEAKY BUT FAMILIAR BACTERIUM IN ACUTE ABDOMINAL PAIN: MYCOBACTERIUM TUBERCULOSIS

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Title of Case(s)

Abdominal Tuberculosis

Background

Tuberculosis, which continues to threaten public health, can affect all tissues and organs. Although pulmonary form is more common, extrapulmonary forms are also seen; confronts with non-specific clinical findings and makes diagnosis difficult and continues its existence.

Case Presentation Summary

A previously healthy 17-year-old male patient admitted to an outpatient clinic with the complaint of nausea and abdominal pain increasing in severity with walking. Because of increased acute phase reactants and sonographic suspicion of acute appendicitis he was scheduled to undergo surgery. Since preoperative chest x-ray had revealed widespread infiltration he was referred to our department with the suspicion of concomitant tuberculosis. He was told that he smoked 5-6 cigarettes a day for 1-2 years and his family had an active tuberculosis story. Physical examination revealed minimal sensitivity in the right lower quadrant. In the laboratory study, mild leukocytosis and mild anemia was noted. CRP was 104 mg/dL. Chest x-ray, revealed bilateral diffuse infiltrates. In abdominal tomography appendix is 7 mm and inflame; intraabdominal diffuse lymphadenopathy was detected. In chest tomography; extensive lymphadenopathy involving calcification foci and reactivation tuberculosis with cavitation in both upper lung lobes. Findings in the image of the abdomen were also reported to develop tuberculosis secondary. Acid-resistant bacilli was found in the sputum of the patient. Tuberculous culture yielded M. tuberculosis complex growth which was susceptible to traditional 4-drug regimen. He was started on antituberculous therapy; abdominal pain disappeared and no other complication was observed.

Learning Points/Discussion

Although tuberculosis is an infectious disease that frequently affects the lungs, extrapulmonary tuberculosis is also an important clinical problem. Since the incidence in our country is high, it should be remembered in patients with unusual symptoms such as abdominal pain and nausea.
Background

Congenital Zika virus (ZIKV) syndrome has been thoughtfully described, as it causes severe clinical manifestations. But long-term consequences to healthy infants exposed to ZIKV in uterus remains unclear. A standardized specific follow up assessment of these infants is crucial. Our aim is to describe an up-to-date physical, neurological and psychomotor developmental follow up of infants with a possible exposure to ZIKV in uterus from pregnant women returning from endemic areas to Southern Europe.

Methods

An active surveillance system was established at Hospital Clínic Barcelona (HCB) and Hospital Sant Joan de Dèu (HSJD) with the aim to thoughtfully follow up all infants born to mothers with a possible exposure to ZIKV. The one-year follow up consisted on neuroimaging, ocular, hearing and psychomotor assessment and concluded with the Bayley Scale for development of infants and toddlers at 18 months of age. All variables were collected in standardized questionnaires.

Results

From the cohort of 43 children born to ZIKV positive and/or suspected mothers, 9 children (21%) were lost to follow up. So far, none of the infants presented growth retardation, nor delay in the psychomotor development. There are not major pathological findings in the cerebral ultrasound, but two cases with choroid plexus cysts and another with cerebral ventricular asymmetry identified as a variant of normality. One two-month infant is under close follow-up since birth due to a non-affiliated hepatitis.

Conclusions

The follow up of healthy infants with a possible exposure to ZIKV in uterus represents a challenge. Efforts are needed to comprehensively understand the neurological findings of these infants and its possible clinical consequences in the long term.

Clinical Trial Registration (Please input N/A if not registered)
National Institute of Public Hygiene is a reference center for immunization in Côte d'Ivoire. Within this structure, the International Vaccinations Center (IVC) aims to protect people against vaccine-preventable diseases such as yellow fever and typhoid fever. In many developing countries, the risk of post-immunization manifestations and/or vaccine inefficiency remains high. Since October 2017, the IVC is one of the only immunization services certified ISO 9001 version 2015 in West Africa. The objective of this work is to describe the control-quality approach implemented around the "Achieve individual immunization" process.

Methods

For the IVC one of the challenges of the certification was the drafting of operational procedures and work instructions covering the various tasks to be carried out from the reception to the validation through the issue of the invoices, the payment and the administration of quality vaccines. To realize this work, we analyzed all these procedures, instructions and internal report.

Results

The first procedure called "pre-registration procedure of the client" consists of an interview with the client to collect his needs, analyze his card or vaccination book, identify the vaccines to be administered and look for any contraindications. Other procedures for vaccine storage and good injection practices help ensure safe and effective immunization. The control-quality approach favored a better organization of the center, a more fluid and clear circuit for all the customers. Notable improvements include the control of process-related risks (risk of impaired vaccine quality, post-immunization events and blood exposure). No post-immunization events have been reported since certification.

Conclusions

Control-quality of services is essential in immunization services not only to ensure safe and effective immunization but also to reduce drop-out rates.
Cytomegalovirus (CMV) is the most common congenital infection in both developed and developing countries. Both maternal primary and non-primary infection can lead to intrauterine fetal infection and long-term complications.

Methods

We systematically reviewed articles from the Medline and Scopus Database, published since 1980, which described neonatal symptomatology and long-term sequelae of cCMV infected infants and compared incidence and/or severity among children born to mothers with primary and non-primary CMV infection. The long-term sequelae of interest included sensorineural hearing loss (SNHL) and neurologic sequelae (microcephaly, seizures).

Results

From the 202 articles found, 10 articles met the criteria of our systematic review. These included 9 cohort studies and one cross-sectional study. Overall, our database included 579 and 305 cCMV infected children born post primary and non-primary maternal infection respectively. Duration of follow-up varied significantly and ranged between 1 to 5 years. The prevalence of symptomatic neonatal disease in cCMV infected infants born to mothers with primary and non-primary maternal infection was 14.3% (34/238) and 7.6% (10/131) respectively. The incidence of SNHL (unilateral, bilateral, severe) and long-term neurologic sequelae were comparable in the two groups of children.

Conclusions

To answer whether maternal type of CMV infection is associated with long-term sequelae in cCMV infected children, a meta-analysis of the collected data will be performed.

Systematic Review Registration (Please input N/A if not registered)

N/A
introduction of PVC13 in the National Immunization Program PNEUMOCOCCAL MUCOSAL DISEASE RESISTANCE PATTERN IN CENTRAL ROMANIA AFTER INTRODUCTION OF PCV13 IN THE NATIONAL IMMUNIZATION PROGRAM

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Background

*Streptococcus pneumoniae* is a common cause of community-acquired alveolar pneumonia (CAAP) and acute otitis media (AOM) in children. Romania has one of the highest known rates of *S. pneumoniae* antibiotic resistance pattern. Starting with September 2017 - PCV 13 was introduced in the National Immunization Plan for all the newborns.

Methods

Retrospective prospective - ongoing study was designed at the Clinical Children Hospital Brasov, Central Romania starting with January 2016 throughout 2017, January 2018 respectively. Comparative analyzes, before and after introduction of PCV13, was performed for all admitted patients with *S. pneumoniae* positive isolates (nasal swabs, conjunctival secretion, ear secretion, laryngo tracheal secretion).

Results

Overall 622 strain of *S.pneumoniae* were isolated during the studied period, 276 cases (%)in 2016, 316 (%) in 2017. Analyzing the same period of year by comparison, there are no significant statistical differences between the studied years with 21 isolates in January 2016, 30 in 2017 respectively 29 in 2018. Before PCV13 implementation, from September 2016- January 2017 – 142 strains were isolated, with a decreased of 21% with a total of 109 positive isolates from September 2017 until January 2018. The median age was 21 months and boys were encountered in 56% cases while the resistance pattern remained the same.

Conclusions

At 5 moth of continuous surveillance after PCV 13 implementation we observed a slow but continuous decrease in *S.pneumoniae* incidence. Further analyses need to be made in order to observe the changes in the antibiotic resistance pattern.
Primary immunodeficiency disorders remain under diagnosed in developing countries. Despite several limitations and challenges, there has been significant progress in the diagnosis and management of these conditions.

**Methods**

To study the clinical & laboratory profile of children with primary immunodeficiency in a tertiary care center in India.

Retrospective study over a period of 5 years of children up to 16 years diagnosed with primary immunodeficiency at Manipal Hospital, Bangalore, India.

**Results**

Out of the total 47 children with primary immunodeficiency, 22 children were found to less than 12 months. 25 were males and 22 were females. 18 children were diagnosed with severe combined immunodeficiency. 6 cases of hypogammaglobulinemia, 5 cases of familial HLH, 3 cases of leucocyte adhesion defect, 3 cases of hyper IgM syndrome, 3 cases were mandelian susceptibility to mycobacterial disease. 3 cases of digeorge syndrome, 2 cases of ataxia telangiectasia, 2 cases of wiskott aldrich syndrome & 2 cases of hyper IgE syndrome.

The clinical presentation of these cases was recurrent sinopulmonary infections in 18 cases, persistent fever among 6 cases and failure to thrive in 9 cases, 8 cases of recurrent & deep skin infections, 3 cases of BCG adenitis. These conditions are appropriate laboratory screen like immunoglobulin levels CD4 & CD8 counts flow cytometry & NBT test. These cases were treated with IvIg & bone marrow transplantation. BMT was done in 12 cases & on regular follow ups with good recovery.

**Conclusions**

Primary immunodeficiency conditions are frequently diagnosed in developing countries like India. Lack of awareness & non availability of diagnostic facilities is a major hurdle. Cost constraints to treatment like access to immunoglobulin replacements & HSCT are major barriers in the management in underdeveloped countries.
THE SAFETY AND EFFICACY OF FIRST-LINE ART REGIMENS IN CHILDREN
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Background

Active antiretroviral therapy (ART) as treatment for HIV infection refers to the use of a combination of three or more ARV drugs for treating HIV infection with the aim of preventing long-term toxicity and increasing treatment adherence. In this study, we evaluated first-line ART regimens in children for safety and efficacy address the longterm metabolic implications, virologic response and immunological response.

Methods

HIV-infected patients under 18 years were included. Primary outcomes of interest include serious adverse events, virologic response to ART, immunologic response and secondary outcome of interest is development of ART drug resistance.

Results

Twenty seven patients under 18 years of age admitted at the Pediatric Infectious Department were enrolled between 2001-2016. The mean age of patients at start of treatment was 69.2 (1–204) months, where 44.4 % of patients under 3 years, 37.1 % of patients 3 to less than 10 and 18.5 % of patients older than 10 years.

LPV/r-based regimen (AZT + 3TC + LPV/rb) as first-line ART was started in 22 patients (81.4 %). Patients above 15 years old (n:2) were prefered fixed dose combinations for first-line ART.

The mean time of follow up period was 67.1 (6–192) months. Nine teen patients (76%) received same first line ART. Six patients were changed the first line therapy due to toxicity (n:1), antiviral resistance (n:4). One of a patient developed non-compaction cardiomyopathy and ART was changed to reduce cardiac toxicity.

Conclusions

Despite of small number of patients to assess the safety and efficacy first-line ART regimes in children our results show that NRTI and PI-based regimes are good option for children in immune recovery.
CANDIDEMIA IN INTESTINAL INSUFFICIENCY AND INTESTINAL TRANSPLANTATION

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Background

The most important complication in the management of children with intestinal insufficiency is catheter-related bloodstream infections depending on total-parenteral-nutrition which is the main stay in the management of children with intestinal insufficiency.

Methods

In our study, between January 2011 and December 2015, 75 episodes of candidemia were examined in our clinics. Patients were divided into two groups according to underlying diseases as intestinal insufficiency and other causes to show the differences between groups.

Results

A total of 22 candidemia episodes were developed in 11 children who had intestinal insufficiency and a total of 7 intestinal transplantations were performed on 5 of them. When the datas of 22 candidemia episodes developed on the intestinally insufficient cases compared to the 53 candidemia episodes developed on the other patients with no intestinal insufficiency. Candidemia incidence on intestinally insufficient cases was found 6.1/1000 catheter days while incidence on the catheter applied cases with no intestinal insufficiency was found 3.7/1000. (p=0.001). In particular, recurrent candidemia episodes were more frequent in the group of intestinal insufficiency group whereas 5 cases of candidemias (22.7%) were caused by C.albicans and 17 cases of non-albicans candidemia episodes (77.3%) had developed with non-albicans candida species. In the non-albicans candidemia episodes, C.parapsilosis was the main cause in 13 (59.1%), C.tropicalis in 3 (13.6%) and C.glabrata in one (4.5%) episode. While 6 (54%) of those isolates were susceptible to fluconazole, 5 (46%) were semi-susceptible or resistant. In other group (n=53), 41(78.8%) of the candidemia episodes were susceptible to fluconazole (p<0.05).

Conclusions

Close follow-up of local epidemiological data and antifungal susceptible patterns should be essential in determining the empirical antifungal approaches in these cases

Clinical Trial Registration (Please input N/A if not registered)

N/A
INTRAVENTRICULAR VANCOMYCIN IN STAPHYLOCOCCAL VENTRICULOOPERITONEAL SHUNT INFECTIONS IN PEDIATRIC PATIENTS

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Title of Case(s)

INTRAVENTRICULAR VANCOMYCIN IN STAPHYLOCOCCAL VENTRICULOOPERITONEAL SHUNT INFECTIONS IN PEDIATRIC PATIENTS

Background

Treatment of post-neurosurgical meningitis, ventriculitis or central nervous system (CNS) shunt infections is challenging and associated with a high morbimortality rate. The emergence of methicillin-resistant strains of Staphylococcus (MRS) difficults even more treatment options.

Case Presentation Summary

We report four pediatric neurosurgical patients with meningitis and VPS infection due to MRS treated with intraventricular vancomycin.

Case 1 - a fifteen-months-old boy submitted to ventricular-peritoneal shunt (VPS) replacement the month before, with Staphylococcus aureus methicillin-resistant isolated on cerebrospinal fluid (CSF). After twelve days of intravenous vancomycin and rifampin the CSF cultures remained positive; case 2 - a five-month-old girl, with Staphylococcus epidermidis methicillin-resistant (MRSE) VPS infection. On the tenth day of vancomycin and rifampin the fever persisted and the inflammatory parameters increased; case 3 – a five-month-old boy submitted do VPS placement 3 months before with CSF Staphylococcus epidermidis (DNA16S) infection. Alterations in CSF biochemical exam persisted after vancomycin for 10 days; case 4 - A six-month-old boy submitted to multiple VPS and shunt revisions, with a MRSE isolated on CSF. He was treated with vancomycin and rifampin with no improvement and CSF cultures remained positive. Intraventricular vancomycin (5-10mg/day) was associated in all patients.

The duration of intraventricular treatment after clinical and bacteriologic improvement was variable (median of 11 days). Successful clinical outcome was achieved in all patients, with no side effects or relapses.

Learning Points/Discussion

Although there are only a few pediatric case reports in the literature, intraventricular vancomycin seems to be an effective, well tolerated treatment and should be considered when conventional therapy fails. Further studies are needed to determine the appropriate vancomycin dosage and duration of therapy in these patients.
FEVER, ABDOMINAL PAIN AND APPENDICITIS, DIAGNOSTIC CHALLENGES IN THE PAEDIATRIC EMERGENCY DEPARTMENT
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Background

In children presenting with fever and abdominal pain, appendicitis continues to be a diagnostic challenge resulting in significant risk of perforation and abscess formation. Reliable diagnostic tests are required for the timely diagnosis.

Methods

A prospective patient record review embedded in MOFICHE (PERFORM H2020) identified 220 children aged 0-17 years with fever (≥ 38.0) and abdominal pain presenting to a tertiary centre paediatric emergency department from April - December 2017. Demographic and clinical data was extracted from medical and electronic hospital records.

Results

12(26.1%) appendicitis 4(2.3%) non-appendicitis presented with central pain migrating to right iliac fossa. 82.2% appendicitis and 31.6% non-appendicitis cases sought medical attention prior to admission. There were no other differences in presentation.

Mean C-Reactive Protein(CRP) was significantly higher in appendicitis versus non-appendicitis (111.9mg/L versus 32.8mg/L; p<0.001). 26 abdominal ultrasounds were performed, 16 in appendicitis cases (12 abnormal, 4 normal).

Mean Length of stay: appendicitis six days, non-appendicitis 14 hours. 20(45.5%) had perforated appendix, they did not differ from non-perforated cases in presentation or length of symptoms.

Conclusions

Differentiating appendicitis in this group is a diagnostic challenge. There was no clear difference in presentation or investigations apart from CRP. Incidence of perforation was higher than in reported literature and concern exists that the majority had sought prior medical assistance. New diagnostic tests to differentiate this group are urgently needed and abdominal ultrasound may have a role as a useful point of care test but more evidence is required.
PROGNOSIS OF VARICELLA INFECTION IN IMMUNOCOMPROMISED CHILDREN

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Title of Case(s)

PROGNOSIS OF VARICELLA INFECTION IN IMMUNOCOMPROMISED CHILDREN

Background

Varicella infection in immunocompromised patient could cause fatal complications that lead to death. Risk of varicella transmission is higher in developing countries where varicella vaccine is not established as part of national immunization program.

Case Presentation Summary

Retrospective analysis has done for hospitalized patients from 2016 to 2017 in national referral hospital at Indonesia. Analysis was focused on course and outcome of patients with varicella in immunocompromised condition.

There were 11 varicella cases in immunocompromised children, 7 of them had underlying hematologic malignancy, while others were non hematologic malignancy, lupus nephritis, chronic kidney disease and biliary atresia patient. Six patients were treated by intravenous Acyclovir, 3 patients by oral Acyclovir, and 2 patients by combination therapy of oral and intravenous Acyclovir. Mean duration of Acyclovir treatment was 7.5 (Range 1-10) days. Clinical resolution achieved at day 5 (range 0-10).

Complications were developed in 2 of 11 hospitalized patients, such as pneumonia and sepsis. Patients with complication would lead to death. Only one patient with sepsis complication had died. All patients have never received varicella immunization. Varicella immunization is not yet included in Indonesia’s national immunization program until now.

Learning Points/Discussion

Varicella in immunocompromised patient may result complications which can lead to death. Prevention of complications through proper treatment is important in increasing the survival of varicella in immunocompromised patients.
Background

*Dientamoeba fragilis* is a flagellated protozoa with a questioned role in gastrointestinal pathology but it is increasingly related to digestive symptoms with an unknown real prevalence. The use of molecular tests would improve its diagnosis.

Methods

We present a prospective cohort study on *D. fragilis* in children aged 1-17 years from October 2017 to February 2018 in the Hospital Germans Trias i Pujol, Badalona, Spain. Stool samples from children with gastrointestinal symptoms (exposed) and without symptoms (not exposed) in whom other etiologies have been excluded were collected. A real-time PCR for *D. fragilis* (Viasure *D. fragilis*, Zaragoza, Spain) was performed. Data about diarrhea, abdominal pain, abdominal distension, weight loss, peripheral eosinophilia were recorded and have been analyzed for a plausible statistical association with *D. fragilis* infection.

Results

A total of 44 samples were tested for the presence of *D. fragilis*. Out of the exposed group, 10 were positive (37%) and 17 were negative (63%). In the not exposed group, 5 were positive (29.4%) and 12 negative (70.6%). The relative risk of the exposed compared to the not exposed was 26%. Abdominal pain was the most frequent symptom (7/10) followed by meteorism (6/10). Diarrhea, abdominal distension and peripheral eosinophilia were present in 2 over 10. None of the patients had weight loss.

Conclusions

Detecting DNA of *D. fragilis* in stool samples using PCR is regarded as the gold standard diagnostic test. Although the small sample size, the results suggests that there is a positive tendency between intestinal symptoms and *D. fragilis* infection. Treatments for the eradication of the parasites could be justified for the improvement of the symptoms in children. **Further works are required to establish the** etiopathogenic role of *D. fragilis* in gastrointestinal disorders.
ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS) CAUSED BY INFLUENZA A/H1N1 INFECTION IN A 10-YEAR-OLD GIRL TREATED WITH ANTIVIRAL THERAPY AND EXTRACORPORAL MEMBRANE OXYGENATION (ECMO)

Background

Acute respiratory distress syndrome (ARDS) is a devastating disorder that presents with overwhelming pulmonary inflammation leading to hypoxia and respiratory failure. It has been reported to be one of the most devastating complications of the Influenza A/H1N1 infection.

Case Presentation Summary

We report a case of a 10 years old girl presented in emergency room in January 2018 with a 24 hrs history of shortness of breath following several days of an influenza-like illness. At presentation, she was admitted in intensive care unit because of respiratory failure requiring urgent intubation and mechanical ventilation. The initial chest radiograph revealed complete consolidation of the left lung with atelectasis. Influenza A/H1N1 virus was confirmed by real-time polymerase chain reaction (RT-PCR) on respiratory secretions. Bacterial cultures were negative. He was treated with oseltamivir. Within 48 hrs after hospital admission the patient had severely impaired gas exchange despite maximum respiratory support on the ventilator and the chest radiograph showed bilateral consolidation. For this reason veno-venous ECMO (VV-ECMO) and prone positioning had to be established. VV-ECMO was provided for a total of 10 days and could afterwards be successfully explanted. The patient rapidly improved and control chest radiograph showed normal lung morphology. The girl could be discharged from the hospital after a total of 22 days with full resolution of symptoms.

Learning Points/Discussion

These findings suggest that anti-viral drugs and ECMO can play an important role in the improvement of ARDS caused by Influenza A/H1N1. However, influenza vaccination remains the best strategy to prevent complicated influenza.
NEONATAL MELIOIDOSIS: A CASE OF MULTIFOCAL OSTEOMYELITIS?

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Title of Case(s)

Neonatal melioidosis: a case of multifocal osteomyelitis?

Background

Melioidosis is a tropical infectious disease caused by *Burkholderia pseudomallei*, which is endemic in parts of Southeast Asia and Australia. The presentation of melioidosis varies widely, both with age group and geographic location. Clinical diagnosis is often problematic, yet the condition can be fatal. The spectrum of neonatal infections is not extensively described, and cases of neonatal multifocal osteomyelitis have not yet been identified.

Case Presentation Summary

A full-term neonate was admitted on day eleven of life due to fever, respiratory distress, and irritability. The child had severe respiratory acidosis and a chest radiograph revealed an opacity in the right lower lobe. He was admitted to intensive care for mechanical ventilation and received ceftriaxone for treatment of pneumonia. Blood cultures at 24 hours grew *Burkholderia pseudomallei*, and antibiotics were changed to meropenem accordingly. After a difficult 3-week stay on intensive care, his clinical condition improved and he was transferred to the ward. On follow-up chest radiograph, four weeks after admission, lesions were noted in the humerus. Further imaging revealed a multifocal osteomyelitis, presumed to be caused by *B. Pseudomallei*. The patient completed four weeks’ of meropenem in total, and was discharged with a further four weeks’ of co-trimoxazole.

Learning Points/Discussion

Melioidosis can vary in presentation and severity, but in some cases can be fatal. In endemic areas it should be considered as a differential in cases of neonatal sepsis. Although not proven as the cause of multifocal osteomyelitis in this case, it seems that *Burkholderia pseudomallei* was the most likely organism responsible.
05D. SCIENCE: CONGENITAL AND PERINATAL INFECTIONS

KNOWLEDGE, ATTITUDES AND PRACTICES OF MATERNITY CARE PROVIDERS CONCERNING PREVENTION OF CONGENITAL AND NEONATAL INFECTIONS

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Background

Pregnant women are at risk for influenza-related complications, while their children are at risk for influenza or pertussis associated morbidity. Influenza and pertussis vaccination is proven safe and effective during pregnancy, while recommendation from maternity care providers is strongly associated with vaccine uptakes. Moreover, counseling of pregnant women on congenital infections is important. The aim was to investigate providers' knowledge, attitudes and practices (KAP) around congenital and neonatal diseases' screening, prevention and vaccination strategies.

Methods

A KAP survey was performed, using a questionnaire e-mailed through Survey Monkey to a convenience sample of Obstetricians/Gynecologists.

Results

102 Obstetricians/Gynecologists responded; 76.3% males and 72.5% over 40 years old. Most claimed discussing congenital infection prevention strategies (98%) during prenatal visits, in particular hand hygiene (92.2%), eating properly washed vegetables and well-cooked meat (98%), while fewer providers advised women to avoid young children’s saliva and gardening without gloves (62.4% and 65.7% respectively). Moreover, 99% of providers tested pregnant women during the first trimester for antibodies against CMV and Toxoplasma, and 94.1% retested if seronegative. Regarding pregnancy, postpartum and family vaccination, many providers suggested influenza vaccine (88.2%, 78.2% and 70.6% respectively) but not pertussis vaccine (60.8%, 71% and 65.7% respectively). Univariate analysis revealed that providers suggesting avoidance of young children's saliva were more likely to recommend gardening with gloves (p=0.016) and those who retested a seronegative woman were more likely to retest her every trimester (p<0.001). Vaccinating pregnant women against influenza was also associated with postpartum and family influenza vaccination (p<0.001 both).

Conclusions

Despite these encouraging results, further education of Obstetricians/Gynecologists is indicated to increase vaccine awareness and recommendation. Further research should focus on pregnant women to examine whether these results reflect actuality.
ESP18-0930
E-POSTER VIEWING - MAY 28-JUNE 2 - EXHIBITION HOURS

16C. SCIENCE: TUBERCULOSIS AND OTHER MYCOBACTERIAL INFECTIONS

THE EVALUATION OF PEDIATRIC EXTRAPULMONARY TUBERCULOSIS: A SINGLE CENTER EXPERIENCE
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Background
Extrapulmonary tuberculosis (EP-TB) is more common in children than adults since the risk of lymphohematogenous spread is higher in the former. It can cause serious life-threatening complications in the childhood. The demographic and clinical characteristics in addition to treatment outcomes of children followed-up in our clinic with EP-TB were assessed in this study.

Methods
Seventy children aged 0-18 years, followed-up with the diagnosis of EP-TB in our department between the years of 2008-2017 were enrolled. Data of the patients were evaluated retrospectively.

Results
Thirty-three patients (47.1%) were female. There were 37 patients (38.6%) between 0-4 years, 15 patients (21.4%) 5-9 years, 28 patients (40%) 10-18 years of age. Forty four patients (62.9%) had EP-TB, while 26 patients (37.1%) had pulmonary and EP-TB. The most common form of EP-TB was extrathoracic lymphadenopathy (n=22, 31.4%). The others were musculoskeletal-TB (n=10), gastrointestinal-TB (n=9), miliary TB (n=8), intra-thoracic LAP (n=7), renal TB (n=6), central nervous system (CNS)-TB (n=5) and pleural TB (n=3). Close contact with TB was determined in 20 patients (28.6%). Positivity of tuberculin skin test (TST) and interferon gamma-release assay (IGRA) were 60% (39/65) and 54.1% (33/61), respectively. Of 58 patients whom had been tested for both TST and IGRA; TST positivity ratio was more than IGRA (p=0.012). Median duration of treatment was 12 (6-24) months. The most common preferred regimen was isoniazid+rifampicin+pyrazinamide (n=32, 45.7%). Complete recovery was observed in 52 patients (74.2%), sequel [hydrocephalus (n=2), kyphosis (n=3) and hydronephrosis (n=1)] occurred in 6 patients (8.5%). Two patients (2.8) with the diagnosis of CNS-TB died secondary to herniation.

Conclusions
Tuberculosis can affect any organ system. Diagnosis of EP-TB in children can be more difficult than adults. Further investigations are warranted in the case of suspicion.
HAEMOPHAGOCYTIC SYNDROME ASSOCIATED WITH EPSTEIN-BARR VIRUS INFECTION – A TREATABLE CONDITION
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Title of Case(s)

HAEMOPHAGOCYTIC SYNDROME ASSOCIATED WITH EPSTEIN-BARR VIRUS INFECTION – A TREATABLE CONDITION

Background

Hemophagocytic lymphohistiocytosis (HLH) is characterized by dysregulated activation and proliferation of lymphocytes and macrophages. It can appear in patients with a known dysregulation of the immune system or previously healthy. Known triggers include malignancies, auto-immune disorders or infection with innumerous agents, such as Epstein-Barr Virus (EBV).

Case Presentation Summary

1) Previously healthy 6-year-old female, with a 7-day history of fever and odinophagy, treated with amoxicillin, diagnosed with infectious mononucleosis. She had cervical adenopathies, hepatomegaly and elevated liver enzymes and was discharged with symptomatic treatment. At day 9, her general appearance worsened with difficulty breathing and palpebral edema. On physical exam, she had large hepatosplenomegaly. Laboratory findings revealed: no cytopenias, CD8 elevation, EBV viral load 144.900 copies/ml, low fibrinogen (120mg/dl), high ferritin (539ng/ml) and soluble CD25 (5448ng/ml). She had favorable evolution on immunoglobulin and rituximab therapy.

2) A 17-year-old male with allergic rhinitis, presented with infectious mononucleosis on day 9 of fever and adenopathies and jaundice for the last 24 hours. He had leukocytosis (31.9090/ul) with lymphocytosis, cholestasis, hepatitis and positive EBV IgM. On day 12, his condition worsened with higher fever, large adenopathies, skin rash and progressive hepatosplenomegaly. Leukocyte count was 30.011/ul with atypical lymphocytes, elevated triglycerides (468 mg/dl), ferritin (1963 ng/ml) and soluble CD25 (6331ng/ml). EBV viral load was 402.000 copies/ml. He was treated with Rituximab and immunoglobulin with clinical and laboratory improvement.

Learning Points/Discussion

Early diagnosis and prompt medical treatment allows a favorable outcome in an otherwise fatal condition. Rituximab provides a safe and effective treatment of HLH associated with EBV infection. In a child or adolescent with a presumed or confirmed EBV infection with unfavorable evolution, HLH should be considered.
LONG-TERM IMPACT OF PCV10 VACCINATION ON NASOPHARYNGEAL CARRIAGE IN CHILDREN AFTER 7 YEARS OF VACCINE INTRODUCTION IN BRAZIL
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Background

Brazil introduced the PCV10 into the routine infant immunization program in March/2010, with a 3+1 dose schedule, changing to 2+1 in January/2016. We evaluated the impact of vaccination on pneumococcal carriage of PCV10-types after 7 years of vaccination.

Methods

The nasopharyngeal carriage survey was conducted from 16-19/Sep2017 in 498 children aged 12-23 months recruited in the vaccination rooms in the municipality of São Paulo during a campaign to update the vaccine immunization. \textit{S.pneumoniae} was identified by standard methods. Isolates were serotyped by Quellung reactions and PCR. Vaccine status was assessed by the vaccination card. Prevalence of pneumococcal carrier and PCV-10 types were compared with a previous survey conducted with same methodology in 2010 among unvaccinated children (baseline).

Results

The median age of children was 17 months (IQ-range=6.0). \textit{S.pneumoniae} was detected in 58.4% of children and 1.2% were PCV10-types. The most prevalent serotypes were 6C/6D (N=89), 15B/15C (N=34), 19A (N=28), 16F (N=19), 15A/15F (N=18), 11A/11D (N=13), 23A (N=12), 23B (N=12). A total of 327 (65.7%) children had received 2+1 (64.3%) or 3+1 (1.4%) doses. Only two children carried PCV10-types [14 (2+0 doses); 23F (2+1 doses)]. When comparing with the baseline these findings show: (i) an increase of the overall pneumococcal carriage (from 40.3% to 58.4%; \(p=0.000\)) driven primarily by a rise in non-PCV-types; (ii) a significant reduction of PV10-types (from 19.8% to 1.2%, \(p=0.000\)); (iii) an increase in 19A (from 1.8% to 5.6%, \(p=0.001\)).

Conclusions

After 7 years of PCV10 vaccination in Brazil we observed a significant decrease in PCV10-types in the nasopharyngeal of children target by the immunization program, and a clear serotype replacement in pneumococcal carriage calling attention to the high proportion of 6C/6D, 15B/15C and 19A types.
ACCIDENTAL POISONING WITH ISONIAZID IN AN INFANT
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Title of Case(s)
ACCIDENTAL POISONING WITH ISONIAZID IN AN INFANT

Background
Isoniazid (INH) has been widely used for prophylaxis and treatment of tuberculosis. The most common side effect of isoniazid is reversible hepatic toxicity. Acute INH intoxication manifests by seizures, metabolic acidosis, coma refractory to standard therapy and even death.

Case Presentation Summary
A 6-month-old boy born in Belgium to Syrian parents was admitted to our unit for work-up after close contact with smear-positive pulmonary tuberculosis presented by his father. Cough represented the main symptom and on physical examination, weight loss was noted.

Chest X-ray showed right hilar enlargement. Tuberculin skin test demonstrated 18 mm induration. According to fully sensitive drug susceptibility pattern of father’s Mycobacterium tuberculosis, treatment with isoniazid and rifampicin was started.

Accidentally, he received, after being fasted, 400 mg of isoniazid on first day of treatment. Eight hours later, the intoxication was discovered by checking administered doses. Clinically the child developed no symptoms and normal vital signs were observed. Continuous cardio-respiratory monitoring and fluid perfusion were started immediately. Blood test showed normal hepatic and kidney functions, as well as normal electrolyte and creatinine kinase levels. Capillary blood gas excluded metabolic acidosis. Isoniazid serum concentration measured 9 hours after ingestion, showed a value of 5.2 µg/L.

Learning Points/Discussion
INH toxicity is reported for doses as low as 10 mg/kg but doses over 20 mg/kg are more likely associated with severe complications and death above 50 mg/kg

The reported cases did neither show any symptoms nor abnormal laboratory findings with doses as high as 50 mg/kg, suggesting a fast acetylator status associated with less toxicity.

Clinicians should be aware of the high risk of acute toxicity, and inversely also of the impact of age and acetylation rate on the choice of optimal therapeutic doses.
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E-POSTER VIEWING - MAY 28-JUNE 2 - EXHIBITION HOURS

13A. SCIENCE: PUBLIC HEALTH | EPIDEMIOLOGY

PREVALENCE AND RISK FACTORS FOR EARLY ESBL-PRODUCING ENTEROBACTERIACEAE FECAL CARRIAGE AMONG NEWBORNS FROM CAMBODIAN COMMUNITY SETTINGS

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Background

In low resources settings, where the burden of neonatal sepsis is the highest, the spread of extended spectrum beta-lactamase-producing enterobacteriaceae (ESBL-E) in the community is a public health concern. However, data regarding the early digestive acquisition of ESBL-E in newborns are scarce. Here, we aimed to determine early prevalence of ESBL-E fecal carriage in newborns, identify risk factors and investigate ESBL genes in Cambodia.

Methods

From July 2016 to January 2017, 145 mother-child couples from two urban and rural community settings were enrolled. Socio-demographic data, dietary habits, health-care, environmental and antibiotics exposures were collected as well as a fecal sample at day 3 of life. Cefotaxime-resistant enterobacteriaceae were identified by Maldi-Toff. ESBL genes were sought by PCR/sequencing. Risk factors were analyzed using logistic regression.

Results

At day 3 of life, the prevalence of ESBL-E fecal carriage among newborns was 53.1% [95%IC: 44.8-61.2]. Ninety-eight ESBL isolates from 77 newborns were recovered. Escherichia coli were the most frequently isolated species (n=61, 62.2%), followed by Enterobacter cloacae (n=16, 16.3%) and Klebsiella pneumoniae (n=14, 14.3%). Eighteen newborns (23.4%) carried at least 2 different ESBL-E isolates. The bla-CTX-M-15 gene was the most frequently detected from 42 isolates (42.9%), followed by bla-CTX-M-55 (n=16, 16.3%) and bla-CTX-M-27 (n=15, 15.3%). In multivariate analysis, urban setting (OR 3.4; 95%IC 1.4-8.0), delivery at hospital (OR 6.4; 95%IC 1.8-21.8) or in a private clinic (OR 5.7; 95%IC 1.7-19.4) and a household of less than 6 people (OR 2.3; 95%IC 1.1-4.9) were positively associated to ESBL-E carriage.

Conclusions

In Cambodia, we found a particularly high proportion of community newborns colonized by ESBL-E very early in life, increasing the risk of ESBL-E neonatal infection and raising the issue of resistance to antibiotics recommended in low-resource settings.
INTRATHECAL COLISTIN THERAPY FOR MENINGITIS DUE TO CARBAPENEM-RESISTANT KLEBSIELLA PNEUMONIAE

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Title of Case(s)

Intrathecal colistin therapy for meningitis due to carbapenem-resistant Klebsiella pneumoniae

Background

The rising incidence of multidrug-resistant organisms in post-neurosurgical central nervous system shunt infections mostly results in treatment failure. Intrathecal colistin therapy has limited data for routine usage but its bypassing blood-brain barrier and providing higher concentration at infected site are its advantage.

Case Presentation Summary

An 11 month old girl with a previous diagnosis of hydrocephalus presented with the complaints of fever. She has ventricular-peritoneal shunt replacement history two weeks ago. Physical examinations were normal except neurodevelopmental delay. Laboratory examination revealed that white blood cells 13,900/mm³ (%65 neutrophil), hemoglobin 10.1 g/dL and platelet count 590,000/mm³, C-reactive protein was 20.1 mg/dL. The cerebrospinal fluid showed 20 cells/mm³, protein 71.8 mg/dL, glucose 37 mg/dL (serum glucose 84 mg/dL). Patient was diagnosed as meningitis and ampicric intravenous cefotaxime and linezolid started. Extended spectrum β-lactamases producing K. pneumoniae was identified in cerebrospinal fluid culture so intravenous antibiotherapy changed to meropenem and colistin. After five days of meropenem and colistin cerebrospinal fluid cultures still remained positive so shunt removed. On the tenth day of meropenem and colistin, after shunt removal, patient still had fever and leucocytosis seen. Patient did not improve with intravenous antibiotic therapy so intraventricular colistin (5 mg) was given via external ventricular drainage, then catheter was clamped for 1 hour. Colistin continued for 14 days. Cerebrospinal fluid culture on third day of colistin was sterile. No adverse effects seen due to IVT colistin therapy and patient progressively improved.

Learning Points/Discussion

Efficacy and safety of intrathecal or intraventricular colistin is unclear in pediatric population but intrathecal/intraventricular colistin can be a alternative treatment for patient with multidrug-resistant central nervous system shunt infection who are nonresponsive to standard intravenous therapy.
Background

Pediatric population is the most affected during influenza season, having the highest risk of complications children under 5 years of age. The aim of this study was to identify risk factors associated with severe infections among children hospitalized with laboratory confirmed influenza in a tertiary university hospital in Barcelona (2015-2017).

Methods

To describe demographic, virological and clinical variables in patients <16 years old hospitalized due to influenza and to analyze its association with severity (admission to intensive care unit (ICU), high flow therapy (HFT), sepsis, pneumonia and death). Crude and multivariate statistical analysis were performed.

Results

We included 194 hospitalized patients (mean age 3.88 years): 117 (60.31%) were males. The median admission length was 5 days (IQR 3-8). Underlying chronic diseases were reported in 45.87% patients (immunodeficiency was the most frequent, 17%). Influenza vaccine coverage among those who had indication was 23%. We identified 62 (32%) severe cases: 5 ICU-admitted, 20 required HFT, 4 with sepsis and 50 with pneumonia. No deaths reported.

Only clinical onset with wheezing was a significant predictor for severe infection (p=0.019; ORc, 2.48; 95% CI, 1.10 - 5.53). Respiratory tract malformations were associated with higher risk for pneumonia (p= 0.003; ORc, 12.41; CI, 1.87 - 133.51). No association was observed between severity and age, vaccine status or influenza viral subtypes.

Conclusions

The identification of risk factors in the most susceptible population is important to reduce complications. Despite the high proportion of children with underlying disease that required hospitalization due to influenza, a low influenza vaccine coverage was reported.
11C. SCIENCE: SYSTEMIC VIRAL INFECTIONS

INFLUENZA IN CHILDREN – CLINICAL FORMS IN THE 2017 – 2018 SEASON

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Background

Seasonal influenza epidemics are potentially serious health issue in the paediatric population. In Romania, many cases of influenza with various symptoms are registered yearly because of low vaccination rates.

Methods

We performed a retrospective review on cases of influenza in children who were hospitalized in the 9th Paediatric Department of the National Institute for Infectious Diseases during October 2017-January 2018. In all patients we checked sex, background, age, severity of the infection and if there were complications of this pathology. The diagnosis was built up on epidemiological data, signs and symptoms and the results of the laboratory investigations.

Results

Amid the examined period, we have registered 120 instances of influenza. The etiology of most cases consisted of type B influenza virus. H1 subtype of type A influenza virus was responsible for 35% of the illnesses. RT-PCR was the criterion standard that confirmed this pathology. The majority of cases were moderate forms 56%, 26.66% were mild forms and 16.66% represent the severe forms. The most vulnerable age group was under 2 years and most of them were male. Type B was most commonly associated with encephalitis reactions and myositis and type A with interstitial pneumonia and digestive manifestations. There were no deaths.

Conclusions

Influenza infection can present various form of disease, at times with an unfavourable evolution with complications and sequelae. We emphasize on the importance of non-specific and specific preventive measures and formulation of an early and precise diagnosis of influenza in paediatric patients.
01A. EDUCATION: PAEDIATRIC ANTIBIOTIC STEWARDSHIP

PREVALENCE OF PATIENTS WITH A RAPIDLY FATAL MCCABE SCORE AND THE PREVALENCE OF HEALTHCARE ASSOCIATED INFECTIONS IN PEDIATRIC SPANISH HOSPITALS: A SUBGROUP META-ANALYSIS

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Background

The EPINE study is a point prevalence survey (PPS) of healthcare associated infections (HAI) conducted annually in Spanish hospitals. In 2012 the EPINE was adapted to the ECDC HAI s PPS protocol, which uses the McCabe Score (MS) to adjust for the severity of patient conditions. MS categories are: 1. non-fatal disease (expected survival ≥5 years); 2. ultimately fatal disease (expected survival 1-5 years); 3. rapidly fatal disease (expected death ≤1 year).

We aimed to investigate if the proportion of pediatric inpatients with a rapidly fatal McCabe Score is related to the HAI prevalence in Spanish hospitals.

Methods

We undertook a meta-analysis of the 2016 EPINE studies of 23 pediatric hospitals that included ≥50 individuals. We combined the HAI prevalences using the Freeman-Tukey Double Arcsine transformation. We performed a subgroup meta-analysis according to the percentage of patients with MS-3 (<5% vs ≥5%).

Results

246 hospitals reported 4,802 pediatric inpatients. 23 hospitals included ≥50 individuals, with a total of 2,088 patients. 42 (2.01%) of them had a MS-3. Only 4 hospitals had ≥5% of inpatients with MS-3. The global HAI prevalence was 5.86 (95%CI 4.12-7.85) with an I-squared statistic of 66.78% (p-value<0.001). In the subgroup analysis, hospitals with ≥5% of patients with MS-3 had a combined HAI prevalence of 13.66 (95%CI 10.09-17.64) with an I-squared statistic of 0% (p-value=0.64). In hospitals with <5%, the prevalence was 4.71 (95%CI 3.23-6.42) also with a reduction in between-study heterogeneity: I-squared=55.01% (p-value<0.001) (Figure 1).
Conclusions

McCabe Score appears to be a useful estimate of HAI risk in pediatric Spanish inpatients. Hospitals with a high proportion of severe McCabe Score have higher HAI prevalences. This should be taken into account if using HAI prevalences for hospital benchmarking.

Systematic Review Registration (Please input N/A if not registered)

N/A
Title of Case(s)
Severe clinical presentation of human metapneumovirus; three cases

Background
Human metapneumovirus generally causes upper respiratory tract infection in healthy people. Sometimes it can be associated with lower tract infection and also been recognized as an important cause of severe viral infections.

Case Presentation Summary
Case 1: A seven month old girl was presented with fever. Physical examination was normal. Laboratory examination revealed that white blood cells 37.900/mm³ (70% neutrophil), hemoglobin 10.4 g/dL and platelet count 671.000/mm³, procalcitonin was 0.492 ng/dL. The cerebrospinal fluid finding showed normal protein and glucose levels, gram staining was negative. Intravenous cefotaxime treatment started. Cerebrospinal fluid culture, blood culture and urinary culture was negative but nasopharyngeal PCR evaluation showed human metapneumovirus.

Case 2: A 5 years old boy was presented to pediatric department with fever, cough and wheezing. Physical examination showed severe respiratory distress and he needed mechanical ventilation in the intensive care setting for nine days and was treated with vancomycin, meropenem and oseltavimir. Chest radiograph showed diffuse bilateral infiltrates with no sign of cardiogenic edema and patient clinically diagnosed as acute respiratory distress syndrome. Nasopharyngeal PCR evaluation showed human metapneumovirus.

Case 3: A 5 years old boy was presented with fever, cough and respiratory difficulty. After endotracheal intubation he sent to our intensive care unit department. Body temperature was 39.4 °C, heart rate was 140/bpm and blood pressure was 84/63 mmHg. He clinically diagnosed as septic shock and pneumonia. He needed mechanical ventilation for four days and was treated with cefotaxime and oseltavimir. Chest radiograph showed bilateral infiltrates. While blood culture was negative nasopharyngeal PCR evaluation showed human metapneumovirus.

Learning Points/Discussion
The role of viral infections in patients presenting with clinical sepsis is underestimated. Diagnosing viral infections may reduce unnecessary antibiotic use.
COMPARISON OF TWO METHODS OF COLLECTING BACTERIOLOGICAL SAMPLES FROM DONOR BREAST MILK
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Background

To compare two methods – scraping the surface of the frozen unpasteurized donor breast milk from every batch (method A) and the aseptic sampling technique of pooled thawed (+4 °C for 12 hours) donor breast milk (method B).

Methods

Two parallel samples using both methods were collected from donations of fresh human breast milk from eight women. The samples were cultured, incubated, colonies counted and bacteria identified by a microbiologist blinded for the sample collecting method. The results of bacteriological analysis of the sample pairs received by using the two collecting methods were compared, McNemar test was utilised.

Results

Bacterial growth occurred in both samples in seven from eight pairs. Altogether, 14 bacteria species were identified, 11 of them grew in both parallel samples. In two cases the bacteria identified in samples collected by method B were missing in parallel samples collected by method A; in one case bacteria growing in the sample collected by method A failed to grow in the sample collected by method B. The difference between sampling methods was not statistically significant. In cases where there was bacterial growth in both parallel samples, the number of colonies did not differ substantially.

Conclusions

Scraping the surface of the frozen portion and the aseptic sampling technique of pooled thawed liquid are two methods for collecting microbiological samples from donor breast milk before pasteurization in Human Milk Bank. The current study failed to demonstrate a significant difference in bacterial outgrowth diversity between sample pairs collected from the same donations by different methods. If the difference cannot be demonstrated in further studies, the technically less demanding method might be suggested for breast milk sampling in most cases.
Severe acute cytomegalovirus hepatitis in an immunocompetent child - Case report

Background

The clinical course of the infection is usually mild, although a small percentage of patients suffer from protracted and severe fever. CMV infection in immunocompetent hosts may rarely be able to lead to severe organ specific complications. Most cases of CMV induced hepatitis occur in adults with severe immune deficiency. Only a few cases involving immunocompetent patients have been reported. Severe hepatitis is an uncommon presentation.

Case Presentation Summary

We present the case of a 6-year-old child presented with a 1-week history of recurrent fever and nonspecific maculo-papular rash. Her initial evaluation physical revealed fever, angina and moderate hepatosplenomegaly. Laboratory tests showed newly increased transaminase activity (x 300N) and serum bilirubin and prothrombin time were also severely impaired. She was admitted for evaluation of acute hepatitis in the 9th Paediatric Departamen at the National Institute for Infectious Diseases „Pof. Dr. Matei Bals” – Bucharest, Romania.

Learning Points/Discussion

Serology for hepatitis A, B, C, E and HIV were negative. Abdominal imaging indicated moderate hepatosplenomegaly. Cultures were sterile. Additional tests for uncommon viral hepatitis included herpes simplex virus, cytomegalovirus and Epstein-Barr virus. Subsequently, cytomegalovirus serology showed an initial IgM positive and negative IgG titre and repeated titres of cytomegalovirus serology showed seroconversion. Cytomegalovirus DNA qualitative PCR was negative in the day 10 after the onset of the simptome. No antiviral medication was given, but she required fresh plasma suport for the coagulation impairement. She continued to have intermittent daily fever but reported no associated symptoms. She was discharged 10 days after admission in good condition, her serum hepatic profile returned to normal and she reported no more episodes of fever or rash.
SEPTIC ARTHRITIS: A CHANGING TREND – A TERTIARY CENTER’S EXPERIENCE

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Background

Septic arthritis is one of the most common deep seated infection in neonates. However, incidence of septic arthritis is increasing in high risk referral NICU. Hence this study was planned to know the etiology, clinical profile, antibiotic susceptibility and prognostic factors in neonates with septic arthritis.

Methods

This is a retrospective observational study of all neonates admitted with diagnosis of septic arthritis from Jan 2016 to Aug 2017 at Indira Gandhi Institute of Child Health, Bangalore. Data was collected from case records and analyzed using standard statistical methods.

Results

A total of 116 neonates were admitted with diagnosis of septic arthritis. Decreased movement of involved limb (100%) followed by swelling of joints (90%) were the common presenting features. Single joint was involved in 66(57%) babies and Hip joint 80(69%) was most commonly involved followed by knee joint 36(31%). Unilateral joint involvement was seen in 83(71) % cases and bilateral in 33(28%) cases. Gram negative infections accounted for majority of cases among which klebsiella was most common organism followed by candida infection. Low birth weight, anemia, Prolonged NICU stay, prematurity, leukocytosis and male sex were strongly associated with septic arthritis.

Conclusions

The incidence of septic arthritis due gram negative infections and fungal infections is increasing. Prematurity and low birth weight with prolonged NICU stay increases the risk of developing septic arthritis.
TIME OF APPEARANCE AND TYPE OF BCG SCAR REACTIONS IN CHILDREN WITH KAWASAKI DISEASE: A 3-YEAR PROSPECTIVE MULTICENTER DESCRIPTIVE STUDY AT 17 MEXICAN REFERRAL HOSPITALS


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Background

BCG scar acute skin changes can be helpful in the clinical suspicion and diagnosis of Kawasaki disease (KD) in countries where BCG vaccine is administered. Most publications come from Asia, where BCG scar changes occur in 10-50% of pts. We describe the first prospective multicenter descriptive study of BCG scar changes in Mexican children with KD.

Methods

Prospective descriptive analysis of local BCG scar skin changes (erythema, edema, crust and/or ulcer formation) in patients less than 13 years with a discharge diagnosis of classic or incomplete (atypical) KD. Pts were attended at 17 main pediatric or general referral Mexican hospitals from the REKAMLATINA Network (Red de Enfermedad de Kawasaki en America Latina), from June-1\textsuperscript{st}-2014 to May-31\textsuperscript{st}-2017.

Results

Among 304 enrolled KD pts, 260 (85.5\%) had been vaccinated with BCG, from which 96 (36.9\%) developed acute scar reactions. 15.6\% pts had incomplete KD. 12 (12.5\%) and 75 (78.1\%) pts were <6 and 24 months respectively, and only 4 (4.2\%) pts were >60 months. Median length of fever at admission was 6(2-28) days. Specific details on the type and onset of scar reaction were available in 92 (95.8\%) pts as follows: erythema, 90/92 (97.8\%) pts; edema, 72 (78.3\%); crust formation, 19 (20.7\%); and ulcer, 10 (10.9\%). According to the chronological order of appearance since day 1 of fever; erythema, edema, crust and ulcer formation were seen from days 1 to 4 in 73/90 (81.1\%), 57/72 (79.2\%), 3/19 (15.8\%), and 5/10 (50\%) pts, respectively.

Conclusions

In children <2 years, acute BCG scar changes can be a useful clinical finding to suspect KD, especially from days 1-4 of fever. Our results describe the highest percentage of BCG scar changes found in Latin American KD pts.

Clinical Trial Registration (Please input N/A if not registered)

N/A
16A. SCIENCE: TUBERCULOSIS

COMPARISON OF SOCIO-DEMOGRAPHIC AND CLINICAL FACTORS AND TREATMENT OUTCOME OF PULMONARY AND EXTRA PULMONARY PEDIATRIC TUBERCULOSIS

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Background

This study assesses the socio-demographic and clinical factors and treatment outcomes associated with pulmonary and extra pulmonary pediatric tuberculosis cases.

Methods

This retrospective study was carried out between the period of January 2001 and January 2015, for a total of 125 pediatric TB cases diagnosed and treated in the Department of Pediatric Infectious Diseases in Balcali Hospital of Cukurova University in Adana, Turkey.

Results

Of the total 125 patients (median age: 62 months, range: 3-252 months), 37 (58%) were males, 56 (44.8%) were aged <5 years and 63 (50.4%) had history of contact with infectious TB adults. Number of patients who have a scar for BCG vaccination was 89 (71.2%). Tuberculin Skin Test (TST) was positive in 52 (41.6%) patients with TB. Of all the patients, 54 (43.2%) were pulmonary TB (PTB), 71 (56.8%) were extra pulmonary TB (EPTB). The contact source was defined in 32 (59.3%) PTB cases and 31 (43.7%) EPTB cases. Of the total 54 patients with PTB, 19 (35.2%) were bacteriologically-confirmed; 14 (25.9%) were smear-positive. Ten of 109 (9.2%) bacteriologically-confirmed cases’ isolates showed resistance to isoniazid or rifampicine. Seven (70%) of 10 resistance isolate was in PTH, 3 (30%) in EPTB (p<0.05). The ratio of the completion of treatment at the end-of-therapy was 85.2% in PTB cases while it was 61.9% in EPTB cases. Of the total 6 death outcome, 1 (16.7%) was PTB and 5 (83.3%) were EPTB (p<0.01).

Conclusions

Our findings revealed that over half of the cases had TB contact history and half of them were under 5 years old. As a result, all family members of people with adult TB diagnosis, particularly children, should be screened for TB.
13A. SCIENCE: PUBLIC HEALTH | EPIDEMIOLOGY

TUBERCULOSIS SCREENING WITH TUBERCULIN SKIN TEST IN CRETE, GREECE, 1990-2014
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Background

Childhood tuberculosis remains a leading health problem worldwide. The tuberculin skin test (TST) is the most common tool to detect infection with *M. tuberculosis*. The aim of this study was to estimate the prevalence of *M. tuberculosis* infection and to explore the value of TST tuberculosis screening among elementary school first graders in Crete, Greece.

Methods

All first graders, that underwent TST during the 25-year study period (1990-2014), as part of the national screening programme, were retrospectively included in the study. Positive TST was defined as the presence of induration of >10 mm.

Results

A total of 82,402 children (92.3% of Greek nationality; 51.0% male) underwent TST. The mean rate of positive TST result was 0.48% (95% CI 0.36 - 0.60, median 0.41). The tuberculin index ranged from 1.42 (1991-1992) to 0.13 (2009-2010) and declined significantly between 1990-1994 and 2010-2014 (0.74 vs 0.27; RR 2.73, 95% CI 1.82-4.09; p<0.0001). Positive TST result was significantly higher in the immigrant than the native group (0.66% vs 0.24%; RR 3.76 95%, CI 2.89-4.84; p<0.0001). Tuberculin positivity was independent of gender or prefecture of residence.

Conclusions

The prevalence of *M. tuberculosis* infection declined during the study period in the study area and mainly affected children from immigrant families. In the last five years of the study, TST should be performed in 408 children (in particular, 517 children of Greek nationality) in order 1 to be found positive. These findings question the massive tuberculin testing and point to screening of individuals at high risk.

Acknowledgements. This study required support from with the State Tuberculosis Clinics in all 4 prefectures of Crete.
Title of Case(s)

AN ATYPICAL MANIFESTATION OF CAT SCRATCH DISEASE: PARINAUD’S OCULOGLANDULAR SYNDROME

Background

Cat scratch disease (CSD) is a common benign disease in children, caused mainly by Bartonella henselae. Parinaud's oculoglandular syndrome appears to be the most common ocular complication of CSD, affecting approximately 5% of symptomatic patients. This syndrome occurs when B. henselae bacilli are inoculated onto the conjunctiva of the patient, resulting in a conjunctival disease characterized by a unilateral granulomatous follicular conjunctivitis associated with ipsilateral regional lymphadenopathy.

Case Presentation Summary

A 13 old-girl presented with a 2-week history of swelling of the right parotid region. The patient was afebrile, with no other symptoms. She had received per os treatment with amoxicillin/clavulanic acid with no signs of improvement. Physical examination revealed unilateral mild papular lesions of the lower eyelid of the right eye that had been presented 17 days before admission. There was, also, 3x3 cm swelling present just anterior to the right tragus. The swelling was firm and attached to the skin. There was no local tenderness. Ultrasound showed a round hypoechoic intraparotid node measuring 1 X 1.5cm in diameter. These features were considered virtually diagnostic of CSD. On subsequent questioning there was clear history of being scratched by their recently acquired kitten. Diagnosis was confirmed by serological tests. The patient received per os clarithromycin with uncomplicated clinical course and full recovery one month later.

Learning Points/Discussion

Slow-growing painless neck masses in children are generally alarming and physicians frequently rush into biopsy or resection to exclude a neoplastic etiology. However, apart from the cervical lymphadenopathy itself, history taking and physical exam should always look for a portal of entry of an infectious agent in the head and neck region, leading to a much less invasive diagnostic and therapeutic management.
Beyond protection: Neisseria meningitidis serogroup B in a vaccinated child - Case Report

Background

Invasive meningococcal disease (IMD) can be life threatening if not approached properly. Serogroup B meningococcus is now the main cause of IMD in Portugal. 4CMenB was the first broad-coverage group B meningococcal vaccine and was approved for individuals 2 months of age and above, although it is not included on the Portuguese immunization program.

Case Presentation Summary

A 4-year-old girl, with no relevant past medical history, with a vaccination schedule plus 2 doses of 4CMenB taken at the age of 2 years and 5 months, and 2 months later. She had an 18 hour fever history (40 °C maximum), flu-like symptoms, right ankle pain and a simultaneous and sudden onset of a rash from the head to lower limbs. Clinical examination revealed a maculopapular eruption with a petechial rash on the trunk and lower limbs, with no signs of meningeal irritability or respiratory distress.

Laboratory evaluation showed leukocytosis with neutrophilia without thrombocytopenia and C-reactive protein levels rising from 39,5 mg/L to 140 mg/L in 14 hours. Chemistry and cytologic findings of the cerebrospinal fluid (CSF) were normal. Coagulation tests were only slightly altered (Prothrombin Time 15,3s; Fibrinogen 552 mg/dL).

Blood cultures were negative, but Neisseria meningitidis serogroup B was cultured on the CSF. Evaluation of complement function and immunoglobulins were normal.

She completed 10 days of ceftriaxone, given immediately within 5 hours after admission, with an excellent outcome.

Learning Points/Discussion

The authors stress out the particular interest of this case as it occurred in a previously healthy immunized child. This should be taken in account by clinicians, as a 2017 study shows that the estimated 4CMenB strain coverage in Portugal is 67,9%.
A RARE CASE OF CERVICAL EPIDURAL ABSCESS IN A YOUNG CHILD WITHOUT RISK FACTORS

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Title of Case(s)
A rare case of cervical epidural abscess in a young child without risk factors

Background

Spinal epidural abscesses are rare bacterial infections in the pediatric population, with possible devastating neurologic sequelae. Localization in the cervical segment is distinctly unusual. The typical treatment of SEA is surgical decompression and long antibiotic treatment, although no consensus on management has been reported.

Case Presentation Summary

We describe a case of a previously healthy 30-month old boy presenting with fever and pain in the cervical area. Clinical examination revealed nuchal rigidity, meningeal signs and exudative tonsillitis. Brain CT was performed with normal findings and lumbar puncture followed which revealed pleocytosis (1400 WBCs/mm³, 79% neutrophils, 21% monocytes), hypoglycorrhachia (28mg/dL), and elevated protein (218.5mg/dL).

With the initial diagnosis of meningitis the boy was started empirical treatment with ceftriaxone and vancomycin. Blood cultures yielded Group A Streptococcus, CSF and urine cultures were sterile. PCR tests in the cerebrospinal fluid for bacteria were negative. After remaining afebrile for 48 hours, fever, headache and neck stiffness recurred. Gadolinium enhanced MRI imaging of the brain and spine revealed a posterior epidural abscess at C3-T2 level (figure).

The antibiotic regimen was modified to IV vancomycin, IV meropenem and PO rifampicin, which received for three weeks. Repeated MRI showed resolution of the collection. The child received PO amoxicillin and rifampicin for 3 more weeks. In follow-up visit after two months, the child was neurologically intact.

Learning Points/Discussion

We report a rare case of cervical epidural abscess in an immunocompetent child with no risk factors. Our case highlights the need for a high index of suspicion in order to make a timely diagnosis of this rare disease. Conservative management under close monitoring can be successful in selected pediatric patients.
CLINICAL AND NEURORADIOLOGICAL SPECTRUM IN NEONATAL CHIKUNGUNYA: A TERTIARY CENTRE EXPERIENCE

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Background

Chikungunya viral infection has emerged as a significant arboviral disease with significant neonatal mortality and morbidity. Most of the cases in neonates are treated as sepsis like syndrome and meningitis with unnecessary antibiotic exposure and prolonged hospital stay. Some of these cases are also investigated like inborn error of metabolism, resulting in exorbitant investigation costs and improper prognostication. There is lack of sufficient literature about these cases from karnataka state, which accounts for more than 50% of all the cases from india.

Methods

This is a prospective observational study carried out from july 2017 to December 2017 over a period of 6 months. The diagnosis of chikungunya was confirmed by serologic testing for CHIK-IgM and detection of the viral genome by reverse transcriptase polymerase chain reaction (RT-PCR). Neonatal details including demographic and base line characteristics, clinical features, laboratory and radiological features were recorded. Results were analysed by standard statistical methods.

Results

A total of 11 neonates were included. There was no major difference in baseline and demographic factors. Most common presenting clinical feature was encephalopathy (82%) followed by classical hyperpigmentation (72%), specially over perioral area, fever (57%) and seizures (57%). Hyperpigmentation more commonly affected male babies. In nearly half of the cases the diagnosis was retrospective after appearance of classical hyperpigmentation. Maternal fever was present in nearly half of the cases. Thrombocytopenia (66%) and anemia (54%) were the most common laboratory manifestations. Diffusion restriction in subcortical area and periventricular white matter was the most common radiological abnormality.

Conclusions

Neonatal chikungunya is a serious infection with high incidence of neurological sequelae. A high index of suspicion of should be kept in any neonate presenting with fever encephalopathy and delayed hyperpigmentation.
PSEUDOMONAS SOFT TISSUE INFECTION IN A CHILD WITH WISCOTT ALDRICH SYNDROME

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Title of Case(s)

PSEUDOMONAS SOFT TISSUE INFECTION IN A CHILD WITH WISCOTT ALDRICH SYNDROME

Background

The aims of these study was to present the important of earlier and adequate treatment of soft tissue infections in children with immunocompromised system.

Case Presentation Summary

In this study was described a boy 21-months with Wiscott-Aldrich Syndrome complicated with soft tissue infection. He presented with a purulent lesion on first lumbar vertebra. He had petechial lesions on the skin. It started two days ago, with high temperature, productive cough, nasal congestion and purulent discharge from ears. The lumbar lesion was about 1 cm diameter, raised above the skin and looked like a macular-papular lesion with black scrub in center. During the next two days the lesion enlarged at 2.5 cm diameter, swollen, warm with hyperemic borders and a necrotic central crust. On the pulmonary auscultation is heard bronchial crackles. The child had a history of frequent hospitalization for recurrent infections and bleeding diathesis and was diagnosed for Wiscott-Aldrich Syndrome. There was no family history for any genetic disorder. In the initial laboratory values is noted: thrombocytopenia (64,000), low red blood count (2760), low hemoglobin (8.2). C-Protein Reactive was elevated and there is a moderate increase at the enzymes of catalysis LDH (374) and AST (135). There was an augmentation of IgA, and the IgM was at normal range. Antinuclear antibodies resulted to be positive ANA (+++). Pseudomonas Aeruginosa was isolated from culture of lesions. The initial therapy was intravenous ceftazidime, amicacyn, IV Imunoglobulin. The hospitalization lasted 12-days

Learning Points/Discussion

From the child history (several infections and the bleeding diathesis) and the results of the laboratory tests (thrombocytopenia, anemia, augmentation of IgA, ANA positive) was concluded that it might be a Wiscott-Aldrich Syndrome
THE EFFECTS AND SUSTAINABILITY OF CLINICAL PATHWAYS AS PART OF ANTIMICROBIAL STEWARDSHIP PROGRAM IN THE PEDIATRIC EMERGENCY DEPARTMENT

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Background

Italian pediatric antimicrobial prescription rates are among the highest in Europe. Clinical Pathways (CP) defining optimal prescribing are effective components of antimicrobial stewardship programs. The primary aim of this study was to assess changes in antibiotic prescription immediately and one year after pediatric CP implementation; secondary aim was to assess treatment failure changes.

Methods

CPs for acute otitis media (AOM), pharyngitis and community-acquired pneumonia (CAP) were implemented on October 1st 2015 in a large Italian pediatric emergency department (PED) in collaboration with Children’s Hospital of Philadelphia. We conducted a pre-post quasi-experimental study assessing changes in antibiotic prescribing from the 6-month period pre-CP implementation (15/10/2014-15/04/2015), to the 6-month period after (15/10/2015-15/04/2016) and 1 year after (15/10/2016-15/04/2017). Interrupted Time Series analysis was used to determine intervention effect, chi squared test to assess treatment failure and Kruskal Wallis test to compare antibiotic dosages and durations.

Results

AOM: an increase in “wait and see” (21.7% pre- vs. 33.1% post- vs. 28.9% 1y post-, p=0.08) and amoxicillin prescriptions (32% vs. 51.6% vs. 52.8%, p<0.001) was reported. Broad-spectrum antibiotics were prescribed in only 4.7% of cases of uncomplicated AOM 1-year post-intervention (29.8% pre- vs. 7.2% post-, p<0.001). Pharyngitis: post-CP, amoxicillin was the first choice (53.6% vs 93.4% vs 93.2%, p<0.001). CAP: amoxicillin prescriptions increased (52.1% vs. 69.9% vs. 82.5% , p<0.001) and macrolide prescriptions decreased (19.7% vs. 6.5% vs. 2.1%, p<0.001). No statistically significant difference in treatment failure observed for any condition.

Conclusions

A reduction in broad-spectrum antibiotic prescriptions with sustainability of the results indicates promise for CPs in this setting.
ASSISTED TRANSITION OF SEROPOSITIVE CHILDREN TO ADULTHOOD: RESULTS OF TOSCA STUDY
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Background

The HIV pandemic involves a growing number of adolescents. Clinical, psychological and social HIV-related problems are amplified during adolescence, which coincides with transition of patients with vertically-acquired HIV infection to the management by infective disease specialists of adult patients. To reduce this burden, a joint medical and psychological intervention was set up and the impact on the viro-immunological status and on the quality of care was measured.

Methods

Thirteen vertically-acquired HIV patients aged between 13-20 years were included and followed-up for 20 months by a multidisciplinary team including pediatricians, infectious diseases specialists, psychologist, gynaecologist and nurses with multiple scheduled meetings. Clinical and psychological evaluations were performed at 0, 6 and 12 months. Compliance to treatment and psychological outcomes were assessed using standardized questionnaires for quality of live (PGWB).

Results

In 11/13 participants the drug regimen was optimised, significantly reducing the pill number/day (4.18 + 1.72 vs 2.0 + 1.1, p <0.002) and the number of administrations/day (1.82 + 0.4 vs 1.09 + 0.3, p< 0.0001). The percentage of patients with undetectable vital load and CD4+ >25% increased from 61.5% to 69% (p 0.68) from 61.5% to 92% (p 0.06), respectively. The percentage of patients classified with “severe” psychological distress according to the PGWB index decreased from 34% to 15% (p 0.18).

Conclusions

Transition is a delicate step for patients with vertically-acquired HIV infection. An improvement in the immunological and psychological outcomes after the intervention was observed. Results are not statistically significant due to the small population size, but show a positive trend. Long term follow-up is needed to assess ART adherence and psychological outcomes.
Efficacy of an adult tablet based individualized ARV combination suspension for paediatric HIV/AIDS patients: The first 5 years

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Background

Assuring a reliable supply chain for paediatric formulations remains a major problem especially in Africa. To overcome this difficulty and compliance/adherence issues as well as the huge dosing steps offered by the few fixed dose combinations (FDC) available in 2011, we developed and tested an individualized ARV combination (IACS) for the treatment of HIV+ children. Based on each child’s body weight and body surface area respectively, every month individual numbers of adult Lamivudine, Abacavir and Nevirapine tablets were dissolved in sorbitol to allow constant administration of 5mL BID up to a body weight of 15 kg.

Methods

The study involved HIV-positive children <15 Kg followed at the St.Camille Hospital in Ouagadougou, Burkina Faso, between 2012 and 2017 who were assigned to IACS or one of two classic therapies (CT): 3 distinct syrups, or FDC. Follow-up was monthly for 1.5 years. We collected clinical (stunting-wasting-clinical stage), immunological (CD4%- immunological stage), compliance (liquid measurements and pill count), hospitalization and survival data.

Results

62 children were analyzed: 32 received IACS and 30 CT. Both groups were similar at baseline. Though the compliance was significantly better with IACS (>95% in 81% of patients receiving IACS vs 53% among those on CT; p: 0.006), both showed constant improvement in clinical and immunological parameters over time. There were less hospitalizations among the IACS-group. Survival was 90% in both groups after 18 month of follow-up.

Conclusions

Due to ease of administration and the better availability of adult tablets as compared to paediatric formulations, IACS showed better compliance and probably because of that also less hospitalizations. However, the more precise dosing of each ARV component did not translate in better immunological efficacy and survival as compared to FDC.
ESP18-0967
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05D. SCIENCE: CONGENITAL AND PERINATAL INFECTIONS

CONGENITAL CYTOMEGALOVIRUS INFECTION ASSOCIATED WITH THYMIC DYSPLASIA WITH LYMPHOID DEPLETION: CHICKEN-AND-EGG DILEMMA.
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Title of Case(s)

Congenital Cytomegalovirus infection and immunodeficiency

Background

There is limited information about interference of host defense mechanisms by Cytomegalovirus. We report a case of congenital cytomegalovirus infection, which probably ended in severe immunodeficiency.

Case Presentation Summary

Baby J, 2 months male child was admitted with jaundice and hematochasia for 15 days. He was passing high colored urine and clay colored stools. His parents had non-consanguineous marriage, without any contributory family history. In immediate perinatal period, he had unconjugated hyperbilirubinaemia managed with phototherapy. His examination revealed stable vitals, normal weight (3.7 Kg), microcephaly (35 cm), pallor, jaundice and petechiae. The systemic examination revealed abdominal distention and hepatosplenomegaly with normal respiratory, cardiovascular and neurological examination. His laboratory examination revealed bicytopenia (Hb- 4.1 gm%, platelets-72000/mm³), haemolysis on peripheral blood film (Rh incompatibility), lactate dehydrogenase (4241 U/L), conjugated hyperbilirubinaemia (total 10 mg% and conjugated 9.1 mg%), transaminitis (AST 559 u/L, ALT- 172 U/L), serum alkaline phosphatase (631 IU/L), normal coagulogram (PTI- 12 sec, PTTK-33 sec), total proteins and albumin (4.4 gm%/ 2.1 gm%), normal TMS/GCMS, normal immunoglobulin profile, and negative serology for Cytomegalovirus, Rubella, and Herpes. His cholestasis and transaminitis partially improved during hospital stay, however bicytopenia persisted. Baby developed healthcare associated infection leading to multiorgan dysfunction and he succumbed on 28 days of hospital stay. His autopsy revealed disseminated CMV disease with involvement of Lungs, liver, GIT, adrenals, heart, lymph node, kidneys and spleen; non-syndromic paucity of intrahepatic bile ducts, pneumocystis jiroveci pneumonia, thymic dysplasia with lymphoid depletion in lymph nodes, spleen, and appendix.

Learning Points/Discussion

This case reports reiterates that conventional serology might miss CMV infection. Furthermore congenital cytomegalovirus can lead to profound immunodeficiency, which needs to be proven by further studies.
ANAPHYLAXIS AFTER IMMUNIZATION

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Title of Case(s)

Anaphylaxis after immunization

Background

Control, record and analysis of side effects after immunization play a vital role in ensuring the safety of vaccination. For the period 2012-2017 in Belarus 5 cases of anaphylaxis were recorded after immunization.

Case Presentation Summary

In the first 31-year-old male the reaction in the form of an isolated critical blood pressure drop was caused by the planned RV adsorbed diphtheria tetanus caprinized anatoxin (ADSM) in the first minute (prevalence is not calculated). In the second 42-year-old male anaphylaxis developed due to emergency tetanus prophylaxis for 1 hour after the administration of anti-tetanus anatoxin and antitetanus serum (prevalence is not calculated). In a third 58-year-old male anaphylaxis in the form of cardiovascular and respiratory manifestations developed 10 minutes after the administration of anti-botulinum serum type A (prevalence was 1 to 28 doses administered).

In a 17-year-old girl anaphylaxis developed on RV ADSM 15 minutes after the administration of the vaccine in the form of gastrointestinal and cardiovascular symptoms.

In a 7-year-old girl severe refractory anaphylaxis manifested on RV MMR in the first minute after subcutaneous administration of the vaccine. The clinical picture developed fast, the symptoms included weakness, pallor, a single vomiting, rapid loss of consciousness with a lack of pulse and respiration. Resuscitation during 1 hour was unsuccessful, a fatal outcome has been reported. The girl did not have a background pathology, including allergic.

Emergency care was provided to patients in accordance with the national protocols for managing patients with anaphylaxis.

Learning Points/Discussion

As can be seen from the above in Belarus, the prevalence of anaphylaxis after immunization in children is 4.34 cases per 1,000,000 doses of MMR administered and 0.67 cases per 1,000,000 administered doses of ADSM.
Background

Bacterial meningitis remains a major cause of morbidity and mortality in childhood worldwide, though epidemiology has dramatically changed over the past decades following the introduction of effective vaccines.

Methods

We analyzed the epidemiological trends of childhood bacterial meningitis during a 25-year study period in Crete, Greece. All immunocompetent patients aged 1 month to 14 years with bacterial meningitis were included in the study.

Results

Between 1991 and 2015, 234 cases of bacterial meningitis were recorded; 18 suspected by the clinical presentation and 216 confirmed by latex agglutination test, culture, and PCR. N. meningitidis was the leading cause for all periods and all age groups. The mean annual incidence rate (IR) was 9.01/100,000 children for bacterial meningitis (16.1 in children <4 years old), 5.20/100,000 for N. meningitidis (7.95 in children <4 years old), 2.17/100,000 for S. pneumoniae (4.08 in children <4 years old), 1.92/100,000 for H. influenzae type b (Hib) before vaccination (5.52 in children <4 years old) and 0/100,000 after Hib vaccination in 1992. Among 136 meningococci, 30.1% were serogroup B, 16.1% C, 5.14% A and 2.94% W. MenC, the leading cause of meningococcal meningitis for the period 1991-2000 (average rate of 24.6%), dropped significantly to 8.45% (RR 2.07; 95% CI 0.89-4.93) following MenC vaccine in 2001, while MenB became afterwards the predominant serogroup (RR 2.46; 95% CI 1.314.71; p=0.004). The S. pneumoniae IR was not considerably affected by the introduction of PCV7 while the effect of PVC13 is still unclear.

Conclusions

Our results confirm post-vaccine changing trends in the epidemiology of childhood bacterial meningitis with disappearance of Hib and decrease in MenC. Nowadays, MenB is the leading cause in the study area.
NEONATAL GASTROENTERITIS: PREVALENCE AND ANTIMICROBIAL SUSCEPTIBILITY

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Background

The purpose of our study was to determine the incidence and the antibiotic resistance of enteropathogens isolated from infants and to compare them with those from children >1 month of age in Crete.

Methods

This study included all neonates, outpatients and inpatients, taken care for diarrhea from January 1993 to December 2016 at Heraklion University Hospital, Crete, Greece. Bacterial isolates from their stool cultures were analyzed and antimicrobial susceptibilities were determined.

Results

Of the 33 neonatal bacterial enteropathogens isolated, 18 (54.5%) were diarrheagenic E. coli, 7 (21.2%) were Campylobacter spp. and 8 (24.2%) were Salmonella spp. During the same period, 1669 children from 0 to 14 years old treated for diarrhea in our hospital were positive for bacterial enteropathogens. Susceptibility rates to imipenem, ceftriaxone, ciprofloxacin, co-trimoxazole and amoxicillin in neonates were 100%, 100%, 91.8%, 75.8%, and 63.6%, respectively, without significant differences through the study period. As compared to older children, isolates from neonates were more susceptible to ciprofloxacin (9.1% vs. 25%, p <0.05) and more resistant to cefotaxime (6.1% vs 0.3%, p<0.01). No Shigella spp, Aeromonas spp or Yersinia spp was detected in neonates.

Conclusions

Our findings suggest that neonatal enteropathogens may well differ from isolated from older infants and children, both in terms of microbiology and of susceptibility to antibacterials.
Acute rheumatic fever (ARF) is a major public health problem in Morocco and other developing countries, because of the high prevalence of its principal complication which is rheumatic heart disease. The aim was to evaluate epidemiology, clinical features, treatment and outcome of acute rheumatic fever.

Methods

A retrospective study of 210 cases of acute rheumatic fever (ARF) older than seven years was conducted in a cardiopaediatric department at Hassan II Universitary hospital center, among a 7-years period (2009—2015). We was included patients with age under 18 years. The diagnosis of ARF was based according to diagnosis Jones criteria.

Results

The mean age was eleven years. There was a leger feminin predominance (sex ratio:0.89). 88% was of urban origin and 12% wad of rural origin. ARF occured throughout the year especially during the cold period (81.5%), with a slight predominance in spring (32.4%) and winter (26.7%). The history of ARF in the family was found in 2 patients and recurrent pharyngitis in 92 patients (73%, n = 126). Arthralgia was reported in 84.78% (n = 138) and arthritis in 24 patients (11.43%). 72.73% of cases have a fever> 37.5. Carditis was found in 134 patients which 88% age was between 5 and 15 years. Laboratory tests showed evidence of inflammation in the majority of cases (ASO>300 found in 60 patients and VS>20 noted in 60 cases). All patients received antibiotherapy and antiinflammatory treatment. Corticosteroid therapy was used in 64 patients: 51 carditis (79.69%) and 12 arthritis (18.75%).

Conclusions

Carditis was very hight in our series, which confirm that ARF is a real public health problem in our country. As long as this disease is not reported, it's the principal source of mortality.
AN IMPORTED SEVERE CASE OF MEASLES WITH AN ATYPICAL RASH AND MULTI-SYSTEM COMPLICATIONS

Background

Measles, as a public health problem in areas where active immunization is not done adequately, can cause serious complications. In this article, we present a case of measles which has an atypical severe course from beginning that results in death.

Case Presentation Summary

A 5-year-old girl referred to our hospital from the Cerablus region of Syria due to extensive skin rash, high fever and general condition impairment. She had generalized red-purple maculopapular rash with broad-based bullous formation (Figure 1). Additionally, conjunctivas were hyperemic, there were peeling on her lips and severe mucositis in her mouth. Fever, hypotension and altered state of consciousness were other findings. From the story, we learned that our case and her two siblings developed rash after having a fever consecutively in two weeks ago. Her condition went worse within the last two days before admission. There was pancytopenia and CRP, procalsitonin, transaminases and creatinine kinase levels were high. She had coagulopathy and renal impairment also. Chest X-ray showed an increased opacity in right upper lobe. Antibiotherapy with vitamin A supplementation started immediately. Measles IgM and serum PCR tests were positive. During the first week we saw extensive blistering and sloughing on the back (Figure 2A and 2B). A skin biopsy done for differential diagnosis. In the second week pancreatitis and angioedema developed additional to pneumonia and she deaths on the fourteenth day of admission because of metabolic decompensation.
Learning Points/Discussion

Pneumonia, haemorrhagic exanthema, mucositis, disseminated intravascular coagulopathy can be seen in severe measles cases. Pancreatitis is also a very rare complication. Despite reported experimental success with ribavirin, there is still no approval for using ribavirin in treatment.

Background

Measles is one of the most contagious infectious diseases, that although it consists a primarily childhood illness, can affect people of all ages. Measles is caused by the measles virus, an RNA virus within the family Paramyxoviridae. It typically enters with high fever, coryza, conjunctivitis and cough and is followed by the appearance of Koplik spots and characteristic maculopapular rash, that lasts up to 5-7 days. Measles virus induces transient immunosuppression that occasionally leads to fatal secondary infections. It has been found that at the onset of rash, remarkable lymphopenia has already occurred with reduction of CD4+ T, CD8+ T, B cells, neutrophils and monocytes. The severity and duration of the lymphopenia are found to be age-dependent; less severe in young children and more severe in infants under one year of age, adolescents and adults.

Case Presentation Summary

A measles outbreak has occurred in Europe that is still ongoing. During the period 2016-2017, more than 20,000 cases have been recorded in Europe. In Greece, till 31st of December 2017, 968 cases have been recorded, especially in the southern part of the country.

In our hospital, 21 cases of measles presented from October 2017 till January 2018, aged from 8 months up to 44 years old. In 14 of them we performed laboratory examinations. All of them had lymphopenia immediately after rash eruption, but adolescents and adults (11-44 years old) did have more severe lymphopenia, with lymphocyte absolute number from 200 up to 900 than young children (12m-5 years), who presented with lymphocyte absolute number from 600 up to 4,050.

Learning Points/Discussion

From our clinical cases, measles virus causes immunosuppression and lymphopenia, that is indeed more severe in adolescents and adults. No complications were reported in our series.
AN EVALUATION OF THE APPROPRIATENESS OF ANTIMICROBIAL THERAPY FOR EARLY ONSET NEONATAL INFECTION ON THE POSTNATAL WARD

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Background

A number of new born infants are prescribed intravenous antimicrobial therapy for treatment of Early Onset Sepsis (EOS). In August 2016 Evelina London Children's Hospital set up a Neonatal Outpatient Parenteral Antibiotic Therapy (OPAT) service. This prompted a review of the overall antimicrobial stewardship within this patient cohort to ensure antimicrobial prescribing was in adherence with the Trust guidance based on the National Institute for Health and Care Excellence (NICE) guidance.

Methods

Retrospective data collection for new born infants born between June and July 2017 who received intravenous antimicrobial therapy for treatment of EOS. Data including demographics, maternal risk factors, neonatal risk factors, microbiology, and antimicrobial details.

Results

Sixty four infants included for analysis. In 34% of infants antimicrobial prescribing was found not to adhere to the Trust guidance, 15% of infants were initiated on antimicrobial therapy unnecessarily and 19% were continued unnecessarily. The main reasons identified for non-adherence to the Trust guidance was incorrect classification of maternal risk factors such as pyrexia and duration of rupture of membranes. All babies were found to have negative blood cultures. Just two babies were discharged under the neonatal OPAT service.

Conclusions

The results have promoted the need for a review of obstetric management of pyrexia in labour as a number of new born infants were incorrectly identified as having maternal risk factors for EOS. The current Trust guidance requires a degree of clinical interpretation and understandably there does appear to be a preference to over treat rather than under treat. To ensure a more consistent approach to septic screening of new born infants the Trust guidance should be reviewed and attempts made to remove areas of ambiguity.
LYME BORRELIOSIS IN CHILDREN OF THE CITY OF MINSK
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Background

In recent years, Lyme Borreliosis (LB) in terms of incidence rates in the Republic of Belarus is one of the first among all natural focal transmissible zoonoses

Methods

The study included 110 patients with LB who received treatment at the City Children's Clinical Infectious Disease Hospital in Minsk from 2010 to 2017. The diagnosis of LB was verified by ELISA and immunoblot methods.

Results

Preventive therapy with amoxicillin or amoxicillin / clavulanic acid, or cefuroxime received only 9 (11.8%) patients. Later, they developed an early localized stage of LB. Therapy of patients in the stage of migrating erythema was carried out by one of the following antibiotics: amoxicillin, ceftriaxone, doxycycline, azithromycin, cefuroxime, cefdinir, cefixime for 14 days at age dosages. Therapy of patients with LB in the stage of early dissemination was carried out by ceftriaxone for 21-28 days.

Conclusions

The low efficacy of amoxicillin and cefuroxime for prevention of LB was revealed, which requires further study. Chronic course of LB is not revealed.
CLINICAL SEVERITY AND COST OF RESPIRATORY SYNCYTIAL VIRUS HOSPITALIZATIONS

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Background

Respiratory syncytial virus (RSV) is the leading cause of lower respiratory tract infections among infants and young children. We aimed to determine clinical features and cost of hospitalization due to RSV among children <5 years.

Methods

Children with acute respiratory tract infection whose respiratory samples were positive for RSV with fluorescent immunoassay rapid test (Sofia™) were retrospectively identified in a tertiary center. Age, sex, underlying illness, use of mechanical ventilation, duration of hospital stay, and cost of hospitalization were recorded.

Results

From Jan 2016 through 2018, 200 children were identified to have RSV infection. Among them 41 (20%) were hospitalized, and 8% of all children (n=16) had intensive care unit (ICU) admission. 28 (68%) patients had no underlying illnesses. 7 were preterm, 2 had Down syndrome, 3 had chronic lung disease, 2 had congenital heart disease. The mean age at presentation was 3.7 months (13 days-14 months). Male-to-female ratio was 1.05. Only one death was reported in a child with immunodeficiency. Mean hospital stay was 7.8 days Antibiotics were given in 75.6% of patients. The median direct cost for hospitalization was US$ 282 per case.

Conclusions

RSV hospitalizations constitute a considerable economic burden among children less than 5 years of age.
10A. SCIENCE: FUNGAL INFECTIONS

DIFFICULTIES IN THE MANAGEMENT OF INVASIVE FUNGAL INFECTION IN CHILDREN

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Background

Systemic fungal infection is still an important cause of mortality through health care associated infections (HCAI) in children. The management of this pathology it is more difficult as the age is lower, the nutritional and immune status affected, the associated pathology is severe with vital risk and the sensitivity to the common antifungals compromised. **Aim:** identification the incidence of fungal sepsis in HCAI, risk factor and therapeutic management difficulties to them.

Methods

**Method:** retrospective study of 982 cases of HCAI during the period 2012-2017 at the Emergency Hospital for Children Iasi, from which 53 cases (21.58%) of Candida albicans and non-albicans infection were identified, out of which 18 cases (33, 96%) with sepsis (blood culture by Backton-Dickinson system).

Results

**Results:** age group: <1 month -50% of which premature-33.33%, 1-11 months-22.22%, 1-4 years -16.66%, 5-10 years -11.11%; clinical areas: neonatal intensive care unit (ICU) - 50%, paediatric ICU-22.22%, pediatric surgery-16.66%, oncology-11.11%; associated diseases: malnutrition -55.55%, renal disease with hemodialysis-11.11%, malformations with various localizations-66.66%, oncologic disease-11.11%, pulmonary infection-16.61%, infectious endocarditis-16.61%, total parenteral nutrition-61.11%; invasive medical device: mechanical ventilation-44.44%; venous central catheter-66.66%; length of stay (days)in the ICU: >14-72.22%; <14-27.78%; etiology: Candida albicans-61.11%, non-albicans (parapsilosis; tropicalis) -27.77%, Trichosporon beigeli-5.55%, Rhodotorula mucilaginosa; pure candidemia -72.22%, mixed candidemia and bacteriemia-27.78%; sensitivity spectrum: Candida albicans: only Amphotericin B (Amf B) and 5 fluorocytosine; non-albicans: azole derivates (Fluconazol, Voriconazol, Itraconazol), Amf B, Caspofungin, Mycafungin, Anidulafungin.

Conclusions

**Conclusions:** Management of fungal sepsis remains a challenge by correctly assessing the timing and type of treatment appropriate to age and associated pathology, directly influencing the mortality rate.
CONFRONTING MEASLES OUTBREAK: PUBLIC HEALTH INTERVENTION POLICIES IN CRETE

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Background

Measles has re-emerged in several European countries, including Greece, creating a need for vigilance, epidemiological observation, and enforcement of vaccination.

Aim: In this study we describe the policies applied in Crete in order to confront this re-emergence of measles.

Methods

In collaboration with the regional state health and education authorities, we checked immunization records of all children attending primary school. Families of children with missing doses were called by telephone and advised on the importance of and the practicalities of fulfilling the vaccination schedule. A hotline for healthcare professionals was launched, aiming both to timely record new cases and to provide consultation on diagnosis and management issues.

Results

Starting from November 2016, 24,665 vaccination records have been checked from children attending all primary schools in Crete. 2 doses of measles vaccine were documented in 22,954 (94.2%), 1 dose in 1305 (5.36%) and no doses in only 89 (0.37%) children. A total of 1200 families were advised on the missing doses. Medical contra-indication was confirmed in 18 cases and vaccine hesitancy in 4. In 9 cases parents asked for more information by an Infectious Disease expert. Up to the beginning of February 2018, only 7 measles cases (none fatal) were recorded in Crete (instead of 79 expected), as compared to 1362 (including 2 deaths) in Greece as a total. The intervention is still active targeting to cover the whole child population of 43,392 children.

Conclusions

Following an intervention with hotline and telephone reminders, measles prevalence in the study area was minimal, suggesting that intensive prevention policies may work well in vaccine-preventable diseases.
Background

Urinary Tract Infections (UTI) is the second most common infections in childhood. In this study we compared the antimicrobial resistance pattern of pathogenic agents of primary and recurrent UTI in children referring nephrology clinic of Ali-Ebne-Abitaleb hospital in Zahedan in 2015-16.

Methods

This cross-sectional study was conducted in 2015-16 on 456 children with a positive U/C referring nephrology clinic of Ali-Ebne-Abitale hospital. Data were collected using information forms and analyzed using SPSS v.22 and by $X^2$ test.

Results

In this study 456 children were evaluated. 387 (84.9 %) were girls and the mean age of the boys and girls was 3.40 ± 3.47 and 4.53 ± 3.51 years (P=0.014). 81 % of UTIS in boys was primary and 19 % was recurrent and in girls, 93 % was primary and 7 % was recurrent. The most common cause of UTI was E. Coli (79.8 %), followed by Entrobacter, Psodomonas, Klebsiella, Citrobacter. The highest level of sensitivity was to Ciprofloxacin and Amkacin and highest level of resistance was to Ampicillin and Co-Trimoxazole.

Conclusions

The most common cause of UTI was E. Coli. The highest level of sensitivity was to Ciprofloxacin and Amkacin.
BLOODY STOOLS IN AN IMMIGRANT CHILD: INFECTIOUS OR INFLAMMATORY COLITIS?

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Title of Case(s)

BLOODY STOOLS IN AN IMMIGRANT CHILD: INFECTIOUS OR INFLAMMATORY COLITIS?

Background

Diarrhea and bloody stools can be manifestations of both infectious and noninfectious diseases; particularly infection caused by bacterial pathogens, inflammatory bowel disease or ischemic bowel.

Case Presentation Summary

This is a 7-year-old boy, from São Tomé and Príncipe, living in Portugal since 6-year-old, previously healthy, that presented with bloody stools and intermittent diarrhea for 12 months. Physical examination was normal except for a vague right iliac fossa pain with palpation. Laboratory studies showed a microcytic and hypochromic anemia, eosinophilia, elevated fecal calprotectin levels, equivocal ASCA and negative ANCA. The stool culture was sterile and parasite stool tests were negative. Strongyloides and schistosoma serology were negative. Abdominal ultrasonography revealed parietal thickening of the cecum, ascending colon and distal ileum and moderate amount of intraperitoneal fluid. Colonoscopy was performed and revealed macroscopically abnormal findings with mucosal nodularity in the terminal ileum and multiple ulcers and erosions throughout the entire colon. Biopsies were conducted and pathological examination revealed numerous parasites on the luminal surface with histological characteristics of amebiasis.

The diagnosis of amebic colitis was made and the condition was successfully treated with metronidazole and paromomycin. At this time, with 6 months follow-up, the child is asymptomatic.

Learning Points/Discussion

In our case the diagnosis of amebic colitis was made based on histological examination of biopsies from colonoscopy.

Pediatricians should be aware that foreign-born immigrant children have a higher incidence of some infectious diseases such as amebiasis and other parasitosis, that are rare in developed countries. Screening should be optimized and a high suspicious index is necessary so that this diagnosis is not missed.
A RARE CAUSE OF GRANULOMATOUS HEPATITIS: TULAREMIA

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Title of Case(s)

A RARE CAUSE OF GRANULOMATOUS HEPATITIS: TULAREMIA

Background

Tularemia is a potentially fatal, multisystemic, zoonotic infectious disease that is especially seen in the north hemisphere and caused by *Francisella tularensis*. Although *Francisella tularensis* has been shown in previous experimental studies leading to necrotizing hepatic granulomas, we could not find any case report of granulomatous hepatitis associated with tularemia published in the medical literature. In this study, we report a rare case of granulomatous hepatitis in a pediatric case with tularemia.

Case Presentation Summary

An 8 year-old male patient had had fever complaints intermittently since January 2016. The patient applied with a stomach-ache in upper right side of the abdomen 2 months ago. Family was using water supply network of their village and the patient had a habit of eating snow. Abdominal ultrasonography, we identified partly patchy, partly nodular, non-sharply circumscribed hyper-echogenic lesions in right lobe of liver. Many hyper dense lesions with millimeter diameter were reported in abdominal MRI (Picture 1). Granulomatous hepatitis was identified in liver biopsy (Picture 2). Tularemia Micro-Agglutination Test (MAT) was reported 1/320 positive. We started treatment of patient with streptomycin and ciprofloxacin for tiphoidal tularemia. Streptomycin was discontinued on the 14th day and ciprofloxacin therapy was continued. Intramuscular gentamicin was added to the treatment of the patient because there was no improvement in the abdominal ultrasound examination on day 21 of ciprofloxacin therapy. Ciprofloxacin was given 1 month gentamicin for 10 days. After 6 months, the findings were completely resolved.

Learning Points/Discussion

We think of a water-based mode of tularemia transmission in our patient due to snow-eating habit and residence in the village. This rare granulomatous hepatitis complication of the disease should be kept in mind for regions with endemic tularemia.
ASSESSING THE FREQUENCY OF URINARY INFECTION RECURRENCE AND ITS RELATED FACTORS IN CHILDREN WITH URINARY TRACT INFECTION IN ZAHEDAN

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Background

Recurrent urinary tract infection (UTI) is one of the major health problems in children because of its high rate of occurrence. This study aimed to evaluate the frequency of recurrent urinary tract infection and related factors in children aged 2 months to 15 years refereed to pediatric nephrology clinic in Zahedan City.

Methods

In this descriptive study, 270 children with urinary tract infection were studied. Sampling was convenient. Information gathered from patients' files. Data analyzed by SPSS Ver. 18 using Chi Square and T-test.

Results

The mean age of children was 4.3±3.7 years. Thirtyfour children (12.6%) were boys and 236 (87.4%) girls (P>0.05). 109 children (73.6%) with recurrent UTI and 53 children (44.2%) without recurrent UTI had abnormal ultrasonography (P=0.001). 115 children (76.7%) with recurrent UTI and 100 children (83.3%) first UTI had positive results for E.coli culture (P=0.177). 79 children (54.5%) with recurrent UTI and 61 children (39%) first UTI diagnosed to have elimination syndrome (P=0.067). Abnormal VCUG found in 39 children (47.6%) of 82 children with recurrent UTI but in children with first UTI had normal VCUG (P=0.001).

Conclusions

There was no difference regarding age, sex, elimination syndrome and urine culture in children with recurrent UTI compared to those first UTI, but abnormal VCUG and ultrasonography were much higher in children with recurrent UTI.
FREQUENCY OF HYPOMAGNESEMIA IN CHILDREN THAT ADMITTED IN PICU
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Background

Magnesium is the fourth most abundant cation in the human body only after sodium, potassium and calcium and is the third intracellular cation. Magnesium is essential for human body health for the reason that ionized magnesium is involved in the interaction of more than 300 enzyme reactions and is important for electrolyte homeostasis, membrane stability, cell division, and generation of action potentials.

Hypomagnesaemia is one of the most common electrolyte disturbances in hospitalized patients (12%), especially in the critically ill. The incidence of hypomagnesemia varies from 20% to 65% in patients admitted to ICU.

Methods

In this study we searched about serum levels of magnesium in 150 children admitted to the PICU of Aliebne Abitaleb peace be upon him hospital and it's relationship with outcome and risk factors. We found information with data forms and used SPSS software to analyse this data.

Results

In this study the incidence of hypomagnesemia in first day of hospitalization was 35.3%. And incidence of hypomagnesemia in dead patients was more than others.

Conclusions

Hypomagnesemia in patients admitted to intensive care unit is common and have relationship to outcomes.
01A. EDUCATION: PAEDIATRIC ANTIBIOTIC STEWARDSHIP

IMPACT OF A 12-MONTH ANTIMICROBIAL STEWARDSHIP PROGRAM IN ANTIMICROBIAL USE IN A PEDIATRIC REFERRAL CENTER


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Background

Antimicrobial stewardship programs (ASP) are critical in preventing the development of antimicrobial resistance. Results of the first 12 months of an ASP based on postprescription review with feedback (PPRF) as core strategy in a referral pediatric hospital are presented.

Methods

Quasi-experimental study. Comparison of antimicrobial use (in days of treatment [DOT] per 100 bed-days) in the inpatient area of Hospital Sant Joan de Déu (314 beds; Barcelona, Spain) during 2016 and 2017, before and during the implementation of a PPRF-based ASP, respectively. In 2017, the quality of prescriptions was also evaluated by means of quarterly cross-sectional surveys.

Results

Global systemic antimicrobial use remained stable overtime (median [IQR] DOT/100 bed-days: 70.9 [67.6-73.1] in 2016 and 68.1 [66.2-69.9] in 2017, \(p=0.147\)). Antibacterial use decreased in non-PICU patients (\(p=0.041\)), due to a reduction in the use of broad-spectrum anti-gramnegative drugs (meropenem, \(p=0.045\); piperacillin-tazobactam, \(p=0.022\)) and in surgical prophylaxis duration (cefazolin, \(p=0.002\)). Antifungal use plateaued (\(p=0.119\)), with variations in specific drug use related to local protocol changes. In 2017, 4,533 prescriptions were reviewed after a median admission time of 2.4 (IQR 1.5-3.5) days. The main group were antibacterials (n=4,093, 90.3%) administered intravenously (n=3,688, 81.4%). Recommendations were given in 843 (18.6%) prescriptions that were considered 'non-optimal' because of: non-compliance with local guidelines (n=412, 48.9%) administered intravenously (n=3,688, 81.4%). Recommendations were given in 843 (18.6%) prescriptions that were considered 'non-optimal' because of: non-compliance with local guidelines (n=412, 48.9%), inadequate treatment duration (n=436, 51.7%), antimicrobial spectrum (n=231, 27.4%) or dosage (n=222, 26.3%). The percentage of 'optimal' prescriptions increased from 73.0% in 2017 1st quarter to 85.6% in 2017 4th quarter (\(p=0.04\)).

Conclusions

In our experience, a PPRF-based ASP led both to a decrease in the use of broad-spectrum antibacterials and to an improvement in the quality of antimicrobial prescription.
Clinical Trial Registration (Please input N/A if not registered)

N/A
A CASE OF ACUTE OSTEOYELITIS DUE TO PANTON- VALENTINE LEUKOCIDIN (PVL) – POSITIVE COMMUNITY- ACQUIRED METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS (MRSA) IN 3-YEARS-OLD CHILD
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Title of Case(s)
A CASE OF ACUTE OSTEOYELITIS DUE TO PANTON- VALENTINE LEUKOCIDIN (PVL) – POSITIVE COMMUNITY- ACQUIRED METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS (MRSA) IN 3-YEARS-OLD CHILD

Background
Osteomyelitis is defined as an infection of the bone, bone marrow, and the surrounding soft tissues. Most cases of acute hematogenous osteomyelitis in children are caused by Gram-positive bacteria, principally Staphylococcus aureus (SA). Most community-acquired methicillin-resistant Staphylococcus aureus (CA-MRSA) infections affect skin or soft tissues, while invasive and life-threatening illnesses including osteomyelitis are less common. Paediatric acute hematogenous osteomyelitis (AHOM) is a serious disease requiring early diagnosis and treatment.

Case Presentation Summary
A case of acute osteomyelitis of the femur caused by Panton-Valentine leukocidin (PVL)-positive CA-MRSA in a 3-year-old girl in good health is presented. She had an acute onset of fever, decreased movement of his left leg with limping and increased irritability. PVL-positive MRSA was isolated also from blood culture. She accidentally falled down and developed swelling of the leg. Drenaige of the abscess was positive for PVL-MRSA. Because of recurrence of fever and worsening of inflammatory indexes, MRI was done showing femur osteomyelitis. A pure bone biopsy revealed extensive inflammation with no evidence of neoplasm, and PVL-positive MRSA was isolated from the culture. Antibiotic treatment, with 8 weeks of intravenous vancomycin and meropenem. One years after treatment completion, there has been no relapse of infection.

Learning Points/Discussion
This case strongly suggests that we need to be aware of CA-MRSA osteomyelitis, which requires a high level of suspicion, prompt diagnosis, and appropriate antibiotic treatment.
EPIEDEMOLOGICAL CHARACTERISTICS OF HOSPITALIZED CHILDREN DIAGNOSED WITH
INFLUENZA DURING 2 CONSECUTIVE SEASONS IN A TERTIARY PEDIATRIC DEPARTMENT

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Background

Influenza is a serious public health problem and is associated with severe morbidity and mortality in children and adults. Signs and symptoms of upper and/or lower respiratory tract involvement are common, but the presentation varies. The aim of this study was to describe the epidemiological and clinical characteristics of children hospitalized for influenza during two consecutive seasons in a tertiary pediatric department.

Methods

This is a retrospective study. Data were collected from medical records of children who were hospitalized at the Second Department of Pediatrics, “P.&A. Kyriakou” Children’s Hospital, Athens during 2015-2016 and 2016-2017 flu seasons. Only children with laboratory confirmed influenza were included. Data regarding clinical and epidemiological characteristics, immunization coverage, treatment and complications were analyzed and compared between the two flu seasons.

Results

100 children (62 male) were included. Virus type A prevailed during 2015-2016 (70,5%), while type B during 2016-2017 (58,9%). Type B was associated with older children (p-value: 0,013). Children were presented with fever (88%), gastrointestinal complaints (12%), respiratory distress (41%), neurological symptoms (23%) and muscular weakness (34%). Muscular weakness was associated with type B influenza (p-value: <0.001). 83 children received antiviral treatment. 43,21% of them within the first 48h of symptoms onset. Complications were observed in 55 children (58% musculoskeletal, 20% neurological). Only 1 child was immunized for influenza.

Conclusions

Influenza epidemiology varies every year because of viral antigenic shifts and drifts. Older children seem to be at higher risk of type B influenza and musculoskeletal complications. More data are needed regarding the need for universal influenza vaccination in childhood as well as for antiviral treatment and whether antiviral treatment is associated with a shorter length of hospitalization or a lower risk of complications.
ANTIBIOTIC THERAPY AND PROPHYLAXIS IN GERMAN PAEDIATRIC HOSPITALS: DATA FROM THE GLOBAL ANTIMICROBIAL RESISTANCE, PRESCRIBING, AND EFFICACY IN NEONATES AND CHILDREN (GARPEC) PROJECT

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Background

Monitoring of antibiotic prescribing data helps to identify where antibiotic stewardship interventions are most needed. The GARPEC project is a global surveillance network focused on collection of data on neonatal and paediatric antimicrobial prescribing and resistance. This study aimed to assess antibiotic utilisation and prophylactic and therapeutic prescribing practices through Point Prevalence Surveys (PPS) in 4 German tertiary care hospitals.

Methods

Detailed antimicrobial prescribing data were collected through 3 PPS in 4 German tertiary care hospitals between May 2016 and February 2017. This analysis included paediatric inpatients receiving at least one systemic antibiotic on the day of PPS. Data were collected in the web-based database REDCap™ and included age, gender, weight, antimicrobial agents, dose, frequency, mode of administration, and reasons for treatment.

Results

625 antibiotic prescriptions in a total of 1060 inpatients were recorded covering 110 wards. 37% of all patients were on at least one antibiotic. We analysed 526 prescriptions in 337 children, excluding neonates. 293 (56%) prescriptions were for therapeutic use, 168 (32%) for medical and 65 (12%) for surgical prophylaxis. Overall, utilisation of narrow-spectrum penicillins to cephalosporins ranged from 1 to 2.2-3.0. Penicillins/β-lactamase-inhibitor combinations (23%) were most frequently prescribed for therapeutic indications. For prophylaxis, TMP/SMX (46%) was most frequently used. 32% of
Prophylactic antibiotics included aminoglycosides and broad-spectrum antibiotics.

**Conclusions**

This study identified frequent use of cephalosporins and broad-spectrum antibiotics in German tertiary care hospitals. A high proportion of antibiotics was prescribed for prophylaxis, including antibiotics not routinely used for prophylactic indications. We conclude that interventions to improve cephalosporin and broad-spectrum antibiotic prescribing practices are most needed. Furthermore, indications for appropriate antibiotic prophylaxis provide a key target for antibiotic stewardship interventions.
KIKUCHI-FUJIMOTO DISEASE: AN UNUSUAL CAUSE OF RECURRENT EPISODES OF PROLONGED FEVER, HEADACHE AND VOMITING IN A SEVEN-YEAR OLD GIRL

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Title of Case(s)

KIKUCHI-FUJIMOTO DISEASE: AN UNUSUAL CAUSE OF RECURRENT EPISODES OF PROLONGED FEVER, HEADACHE AND VOMITING IN A SEVEN-YEAR OLD GIRL

Background

Kikuchi-Fujimoto disease (KFD) or histiocytic necrotizing lymphadenitis is often self-limiting and usually characterized by cervical lymphadenopathy and fever. Recurrent KFD with extranodal manifestation in young children is rare. We report an unusual case of a young girl with recurrent KFD presenting with two episodes of prolonged fever, severe headache and vomiting.

Case Presentation Summary

A seven-year old Sri Lankan girl was hospitalized for recurrent fever, headache and vomiting for two months. Past medical history revealed a similar episode 2 years ago with diagnosis of aseptic meningitis. Complete blood count, C-reactive protein (CRP), chest X-ray and brain magnetic resonance imaging were without pathological findings. An empiric oral antibiotic treatment with amoxicillin was started in an outpatient setting. Five days after discharge she returned to hospital due to persisting fever, painful bilateral swelling of the cervical lymph nodes and a rash. Laboratory examination revealed anemia, leucopenia, an elevated CRP, an elevated erythrocyte sedimentation rate and an elevated lactate dehydrogenase. The girl was hospitalized for further investigations. Malignancy was highly suspected. Cervical lymph-node biopsy showed extensive necrosis with pronounced proliferation of histiocytes, suggestive of KFD. Fever resolved spontaneously without further treatment and upon a two-week follow-up visit she was completely asymptomatic.

Learning Points/Discussion

Prolonged fever with headache and vomiting might be due to several life-threatening conditions and thus warrants rigorous investigation. Aseptic meningitis accompanied by lymphadenopathy should rise a level of suspicion for KFD. Early diagnosis can help prevent invasive investigations and unnecessary antibiotic treatment. Furthermore, in the rare cases of relapsing disease, early administration of corticosteroid treatment might be considered to shorten the course of the illness.
Impact of moderate vaccination rate against rotavirus during 9 years in the gastroenteritis hospitalization rate

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Background

Rotavirus (RV) vaccines were introduced in Spain between 2006 and 2007, and despite moderate coverage, it showed high effectiveness in the short term. We aim to evaluate the impact of moderate vaccination (22.3-49.3%) during 9 years in all-cause (AC) acute gastroenteritis (AGE) and RV-caused AGE hospitalization rates in Galicia (north-west Spain) in children younger than 5 years.

Methods

In this ecological retrospective study, data have been obtained from Conjunto Mínimo Básico de Datos (CMBD; www.iasist.com) database. The study population considers children younger 5 years old admitted between July 2003 and June 2015. We have considered AGE (ICD-9 code from 001 to 009), and more specifically AGE caused by RV (RV-AGE, code ICD-9 008.6). Population data has been obtained from Instituto Galego de Estatística (www.ige.eu). Yearly hospitalization rates were analyzed excluding year 2007 (when the vaccine was introduced).

Results

A significant decrease in hospitalization rates was observed since RV vaccine introduction when comparing with the pre-vaccination period for children younger than 5 years old for both AGE (from 19.0% in 2014 to 50.3% in 2008) (Figure A) and RV-AGE (from 26.3% in 2014, to 51.1% in 2008) (Figure B). In the last years the magnitude of this decrease is smaller, which could be related to different factors from test sensibility to duration of herd protection or disease seasonality.
Conclusions

Vaccination against RV, even with moderate -but sustained- vaccination coverage, shows a high effectiveness in relation to hospitalization by AGE and RV-AGE. The present study reinforces the convenience of including RV vaccine in the Spanish immunization schedule.

Clinical Trial Registration (Please input N/A if not registered)

N/A
TUBERCULOSIS IN CHILDREN: A STUDY IN A PORTUGUESE TERTIARY HOSPITAL
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Background

Tuberculosis represents a major global health problem. The diagnosis in the child corresponds to a recent transmission in the community. Due to the immaturity of their immune system, about 40% of children with Mycobacterium tuberculosis (Mt) infection develop disease. The aim of this study is to describe the epidemiology and clinical characteristics of hospitalized children with tuberculosis disease in a Portuguese tertiary hospital.

Methods

Retrospective, descriptive study with analysis of epidemiological variables such as age and gender, and clinical variables such as symptomatology and complementary diagnostic tests of children hospitalized with tuberculosis in the last 16 years.

Results

31 children were hospitalized with a diagnosis of tuberculosis, with a median hospitalization time of 13 days (3-57 days). 51.7% were male and the median age at the time of diagnosis was 6 years (0-16 years). In 72.4% of the cases the tuberculin test was positive and all of them performed chest radiography. In those with suspected pulmonary tuberculosis, the study of Mt was positive in only 17.2%; the mycobacteriological examination of the bronchial secretions allowed the diagnosis in 6.9% and Mt was identified in bronchofibroscopy in 4 cases.

Conclusions

Pediatric tuberculosis in Portugal, despite its low incidence, is a reality that persists over the years. Due to the low probability of agent identification and confirmation of the diagnosis, this remains an important challenge in this age group.
CLINICAL OUTCOME OF RESPIRATORY VIRAL INFECTIONS IN CHILDREN UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANT

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Background

There are few data regarding the clinical presentation of respiratory viral infections (RVI) in children undergoing hematopoietic stem cell transplant (HSCT), especially in developing countries. We determine the clinical outcome of RVI in this population.

Methods

Prospective study in children with cancer and HSCT admitted with fever in the Bone Marrow Unit, Hospital Calvo-Mackenna, Chile (April 2016-January 2018). Children were evaluated by clinical examination, laboratory tests, bacterial cultures and nasopharyngeal multiplex-PCR for 20 respiratory pathogens. Clinical outcome variables were collected; children were followed-up in each episode of fever until discharge.

Results

A total of 38 fever episodes were enrolled in 25 children, of whom 25 (66%) were RVI-positive. Twenty-two concluded the study. Median age was 10 years, 68% were male. Most detected viruses were rhinovirus (39%), followed by coronavirus (21%), RSV, adenovirus, parainfluenza (11% each) and influenza(7%). RVI was detected with a median of 146 days after HSCT. 20/22(91%) episodes had respiratory symptoms at admission, 17/22 episodes were single RVI and 5 were co-infections. 4 out of 5 children had ≥1 episode of fever, with the same virus detected (median=79 days). 17/22 (77%) episodes were lower respiratory tract infections(LRTI), 64% required oxygen supplementation and 3 (13%) admission to the PICU. Median days of fever, oxygen and hospitalization were 1, 2 and 13, respectively. No cases of sepsis, mechanical ventilatory support or mortality were reported. In 7 episodes (32%), antimicrobials were withdrawal after knowing the result of the multiplex-PCR.

Conclusions

RVI were frequently detected in fever episodes after HSCT in children. We observed a predominance of LRTI, oxygen requirement and long hospital-stay. Viral persistent-detection was reported in 22% of episodes. RVI detection might help to rationalize the use of antimicrobials in this population (FONDECYT-Grant#1171795).
EVALUATION OF CASES WITH ROTAVIRUS GASTROENTERITIS ACCORDING TO VESIKARI SCORING SYSTEM

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Background

Acute gastroenteritis (AGE) may cause morbidity and mortality in small children and infants. Rotavirus is the most commonly seen cause among viruses. In this study, were viewed the clinical findings of gastroenteritis cases who have been admitted to our clinic for the past three years and how rotavirus positivity affects clinical findings.

Methods

Records of cases which were hospitalized in pediatric clinics with AGE with the age range of 1 month to 18 years between January 2014 and December 2016 were retrospectively reviewed. Cases with any underlying diseases were not included in the study. Rotavirus antigen digital scoring system described by Ruuska and Vesikari.

Results

A total of 241 cases were hospitalized diagnosed with AGE, 33.2% (n = 80) of which were rotavirus gastroenteritis. Age and gender distribution in the rotavirus positive and negative groups were similar, while the application to the hospital in rotavirus negative group was in the summer more frequently, frequency was seen in the spring in rotavirus positive group and the difference was statistically significant (p=0.024). In the rotavirus positive group, restlessness (71.3%), fever (60%) and cough (30%) were the most frequent complaints; 62.5% moderate and 15% severe dehydration were seen. According to Vesikari score of rotavirus GE cases, 71.2% of them had severe and 28.8% of them had moderate disease findings. Any of complication was detected in 82.6% of the cases with moderate Vesikari score and in 57.9% of the severe cases. According to the Vesikari score, more complications were seen in moderate group (p = 0.037).

Conclusions

Rotavirus has been shown to cause various symptoms in the other systems as well as the gastrointestinal system. The Vesikari score was not found to be very effective with the prediction of the complications.
CLINICAL AND MICROBIOLOGIC CHARACTERISTICS OF STENOTROPHOMONAS MALTOPHILIA BLOODSTREAM INFECTION IN CHILDREN--A 10-YEAR ANALYSIS

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Background

S. maltophilia, a multidrug resistant Gram negative and biofilm-forming pathogen, has emerged as an important opportunist, mainly a nosocomial pathogen especially in critically ill or immunocompromised patients. However, there has been little information concerning S. maltophilia bloodstream infection (BSI) in children.

Methods

We retrospectively reviewed microbiological test results for all children (0-18 years old) who were admitted to our pediatric hospital between 1 January 2007-June 2017 and had positive clinical specimen blood and/or catheter cultures for S. maltophilia. Isolates were identified using conventional tests and the BBL Crystal E/NF ID or MALDI-TOF MS systems. Antibiotic susceptibilities were evaluated using the Kirby-Bauer disc diffusion method.

Results

We identified 20 positive cultures from 12 patients with confirmed infections. The median patient age was 28 months (range: 3.1-187.3 months). The female-to-male ratio was 1:1 and all patients had one underlying disease at least. Three patients received chemotherapy and surgery was performed in four patients within 30 days prior to onset of BSI. 83.3% (n=10) patients had medical device. The central line-associated bloodstream infection was the most common (66.6%, n=8). The majority of patients (83.3%, n=10) developed their infections in the hospital. The use of carbapenems rate and the median antibiotic number were 66.7% (n=8) and 3 (range: 0-7) within 30 days prior to onset of BSI respectively. The most active antimicrobial agent was ciprofloxacin (50%, n=6) for S. maltophilia infection, and the mortality rate was 33.3% (n=4). In three (75%) of fatal cases S. Maltophilia was regarded to have direct role in death and one patient received appropriate treatment in the first 24 hour after onset of BSI in this group.

Conclusions

S. maltophilia should also be considered as causative agent for BSI among children who are hospitalized in ≥72 hours, especially in patients with a underlying disease, device, exposure to broad-spectrum antibiotics and it is important to keep in mind the necessity to start an early and effective antimicrobial therapy.
ESP18-1004
E-POSTER VIEWING - MAY 28-JUNE 2 - EXHIBITION HOURS

11C. SCIENCE: SYSTEMIC VIRAL INFECTIONS

HUMAN PARECHOVIRUS INFECTION - IMPORTANT CAUSE OF SEPSIS-LIKE DISEASE IN NEONATES AND YOUNG INFANTS

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Title of Case(s)

HUMAN PARECHOVIRUS INFECTION - IMPORTANT CAUSE OF SEPSIS-LIKE DISEASE IN NEONATES AND YOUNG INFANTS

Background

Human parechoviruses (HPeV) belong to the family of Picornaviridae like the enteroviruses and are an important cause of sepsis-like syndrome and meningitis in neonates and young infants. HPeV3 is currently known to cause more severe disease with highest prevalence in summer and autumn months. Majority present with high fever, tachycardia, poor perfusion, and severe irritability. Diagnostic method is HPeV RT-PCR from different microbiological samples.

Case Presentation Summary

From July 2017 to October 2017 8 patients with suspected late-onset neonatal sepsis were admitted to our department, all of them born at term and previously healthy. Age at admission was 6 to 33 days (median: 18 days), all cases presented within 24h of clinical sign’s onset. The most common clinical presentation was fever (100%), tachycardia (100%), tachypnea (87.5%) signs of poor perfusion (87.5%) and severe irritability (100%). Other features included abdominal distension (50%), rash (12.5%), apnea (25%) and feeding difficulties (37.5%). Laboratory tests showed mildly elevated or normal CRP (median: 10.4 mg/L) and PCT (median: 1.17 μg/L), median WBC count was 6.8 10⁹/L. Blood, urine and CSF bacterial cultures were negative. Lumbar puncture was performed in 5/8, showing no pleocytosis and slightly elevated protein, in 4/5 CSF samples HPeV was detected, 2 of them also had HPeV positive stool samples. In the remaining 4/8 patients HPeV was detected in nasopharyngeal swab. In 7/8 antibiotic therapy was initiated with median duration of 3.5 days. Median hospital stay was 4.8 days with no ICU transfers. All children recovered completely.

Learning Points/Discussion

HPeV should be considered in sepsis-like presentation in patients <6 months of age. Confirmation by HPeV RT-PCR can shorten hospital stay and duration of antibiotic therapy.
ESP18-1005
E-POSTER VIEWING - MAY 28-JUNE 2 - EXHIBITION HOURS

08D. SCIENCE: IMMUNOLOGY AND HOST-PATHOGEN INTERACTIONS

HOT CROSS BABIES: 2 CASES OF KAWASAKI DISEASE IN 6 WEEK-OLD INFANTS
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Title of Case(s)
Infant Kawasaki Disease

Background
Kawasaki disease (KD) is an acute systemic vasculitis. Young infants represent a high risk population.

Case Presentation Summary
We report two geographically and temporally unrelated cases of neonatal KD; two 6 week-old male infants presented with fever, irritability, tachycardia, sterile pyuria, high inflammatory markers and CSF pleocytosis. Each received antibacterial and antiviral cover for suspected meningitis. The microbiologic investigations of infant 1 remained negative. He developed widespread erythematous pleomorphic rash and unilateral cervical lymphadenopathy day 2, conjunctival injection and red lips, Day 3/4. KD was suspected on day 4 of fever. He was treated with intravenous immunoglobulin (IVIG), aspirin, methylprednisolone and cyclosporine. His echocardiography showed progressive coronary artery dilation and valvulitis which stabilized and regressed in response to therapy. He is clinically well at follow up.

Infant 2 tested positive for RSV, had Gram positive cocci later identified as Staphylococcus epidermidis in blood culture and E. coli in his urine. KD wasn’t suspected until day 12 of fever, having developed periungual desquamation. He received IVIG, methylprednisolone, aspirin and cyclosporine but developed large LAD aneurysm, complicated by thrombus requiring ongoing anticoagulation.

Learning Points/Discussion
Infants under 3-months of age account for less than 2% of KD cases and represent a high risk population with up to 35% developing coronary artery abnormalities. The symptoms are frequently incomplete, fever more likely attributed to bacterial or viral sepsis and diagnosis delayed. Our 2 patients, of similar ages and presentation, who received similar treatment albeit at different time points in their illness experienced different outcomes. This underscores the need for early suspicion of KD and an aggressive approach to anti-inflammatory therapies. KD should be considered in any infant with persistent fever and rising inflammatory markers despite seemingly appropriate treatment.
VALUE OF CEREBROSPINAL FLUID ANALYSIS AND SERUM INFLAMMATORY MARKERS FOR DISTINGUISHING BETWEEN VIRAL AND BACTERIAL MENINGITIS IN CHILDREN IN EARLY PHASE OF THE DISEASE

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Background

Regardless of cerebrospinal fluid (CSF) examination there are difficulties distinguishing between bacterial and viral meningitis in early phase of the disease which leads to unnecessary use of antibiotics.

Methods

A retrospective analysis of 175 cases of children with acute meningitis (defined by a leukocyte count >5 per mm³ in the CSF) who were hospitalized in Kaunas Clinical Hospital from 2008 to 2016 and underwent lumbar puncture during the first 48 hours of the disease was performed. CSF parameters (WBC count, absolute neutrophil count (ANC), protein level) and serum inflammatory markers (CRP and WBC count) as potential predictors of bacterial meningitis (BM) were compared.

Results

The age of included patients ranged from 6 months to 18 years. 16 of them were diagnosed with bacterial meningitis and 159 with viral meningitis. Of all evaluated markers, CSF WBC count had the highest area under the ROC curve (AUC) of 0.95 (p<0.001, 95% CI, 0.893-1.00) with 100% sensitivity (52.8% specificity) when CSF WBC count was ≤104 cells/μl. CSF protein ≤0.4 g/l had 100% sensitivity (68.6% specificity) for BM. Serum inflammatory markers (CRP and leukocytosis) were less useful with CRP having an AUC of 0.887 (p<0.001, 95% CI, 0.769-1.00) and leukocytosis of 0.841 (p<0.001, 95% CI, 0.741-0.941). CRP had 100% specificity (64.7% sensitivity) when above 68.5 mg/l.

Conclusions

CSF WBC count, CSF ANC, CSF protein level, serum CRP and serum WBC count were useful biomarkers for distinguishing between bacterial and viral meningitis, based on their AUC values. At early phase of the disease CSF WBC count was the most reliable predictor of BM.
DEEP NECK ABSCESS IN CHILDREN: AN ITALIAN RETROSPECTIVE STUDY

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Background

Retropharyngeal (RPA) and parapharyngeal (PPA) abscesses are rare conditions still associated with high morbidity and risk of life-threatening complications. The treatment includes surgical drainage and/or antibiotic therapy, but the best management is still a theme of debate between clinicians. Aim of the study was to review diagnosis and management of children with RPAs/PPAs and to compare the two types of treatment in four Italian hospitals.

Methods

This observational retrospective study was performed through the review of records of all patients under 15 years of age from 01/01/2008 to 31/12/2016 admitted at the following Italian hospitals: Department for Woman and Child Health of Padua, Pediatric Ward of Ca’ Foncello Hospital of Treviso, Bambino Gesù Pediatric Hospital of Rome and Meyer Pediatric Hospital of Florence.

Results

153 children were included. The median age was 4.4 years. A variety of signs and symptoms were reported (most frequently fever, neck pain, cervical lymphadenopathy and stiff neck). CT (66.7%) and MR (27.5%) were performed to confirm the presence of abscess. CT was the preferred radiological exam for all the centers, but one. 51% of abscesses were > 3 cm. 87 (56.9%) children had surgery while 66 (43.4%) were treated with antibiotics with a huge variability between institutions (table I). Ceftriaxone was the most used antibiotic in every institution. Others frequently prescribed were metronidazole, amikacin, clindamycin and oxacillin. None had severe complications. Multivariate analysis indicated as independent predictive factors of surgery abscess ≥ 3 cm, high WBCs count and,
most of all, the hospital of admission.

Conclusions

An extremely heterogeneous approach was observed in diagnosis and management of children with RPAs and PPAs. Thus, common shared protocols represent an essential tool in order to standardize care and improve patients’ outcomes.
Acute childhood myositis (ACM) is an acute condition which manifests with severe lower-extremity myalgia and reluctance to walk. The syndrome usually occurs during the convalescent phase from a febrile upper respiratory tract infection, most commonly after influenza B and A.

Methods

To evaluate the epidemiology and clinical characteristics of ACM, we conducted a retrospective study of children who were hospitalized at “Aghia Sophia” children’s Hospital, Athens from 2011 to 2017 with the diagnosis of ACM. Clinical, laboratory data, vaccination status, course of illness and complications were retrieved from medical records.

Results

The total number of hospitalizations between 2011 and 2017 was 407 with 2017 being the prevalent year with 115 hospitalizations. Median age of the children investigated was 7 years with a 2:1 male predominance. During 2017, 80.5% (103/115) of patients with ACM demonstrated localized pain and tenderness on the gastrocnemius and soleus muscles. The normal power and reflexes were normal in all but three cases. 66% (76/115) of the ACM were parainfectious vs 39% (39/115) that were infectious and 9 out of 115 cases had recurrent episodes with 1 patient experiencing more than 1 episode. CPK was invariably elevated with leucopenia being the most distinctive finding in the blood tests. 76% showed clinical improvement within 1 day of hospitalization and 80% were treated by hydration only. One case of BACM due to Influenza B was complicated with nephrotic syndrome and two others hospitalized for myositis were finally diagnosed with carnitine palmitoyltransferase II (CPT II) deficiency.

Conclusions

Acute childhood myositis is usual during the course or after viral infections and although acute and alarming, its presentation is usually self-limited. When there are recurrences could be an indication of a metabolic myopathy.
ESP18-1010
E-POSTER VIEWING - MAY 28-JUNE 2 - EXHIBITION HOURS

17F. SCIENCE: VACCINE EFFECTIVENESS AND EFFICACY

IMPACT OF MODERATE ROTAVIRUS VACCINATION RATES DURING 9 YEARS IN THE SEASONALITY OF HOSPITALIZATION BY GASTROENTERITIS
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Background

Apart from its effectiveness, vaccination against Rotavirus (RV) has shown a significant impact in the seasonality of acute gastroenteritis illness (AGE), delaying and reducing the incidence peak and almost removing seasonality. However, the behavior associated to moderate vaccination rates is unknown. We have studied the impact of moderate vaccination rates (22.3-49.3%) over 9 years, in the seasonality of hospitalization rates in Galicia (NW Spain) for children below 5 years admitted by all-cause AGE and AGE caused specifically by RV (RV-AGE).

Methods

Data have been collected from Conjunto Mínimo Básico de Datos (CMBD; www.iasist.com). The study population corresponds to children younger than 5 years old hospitalized between 2003 and 2015. We have counted the number of hospitalizations by GEA (code ICD-9 from 001 to 009), and RV-AGE (code ICD-9 008.6) Monthly hospitalization rates have been computed for different seasons, comparing monthly medians y pre-vaccination and post-vaccination seasons.

Results

Since the introduction of RV vaccines in 2007, changes in seasonality have been observed in regards to hospitalization by AC-AGE and RV-AGE. The data show a delay of 1 month (from February to March) in season peak by AC-GEA, with a decrease of 26.8% in the maximum peak, and 23.8% in the median peak (Figura A). For RV-AGE, the data show a delay of 2 months (from January to March) in the peak, and a decrease of 28.6% for the maximum rate, without significant changes considering the monthly median rates. (Figure B).
Conclusions

Sustained RV vaccination, even with moderate rates, has impacted the seasonality of AC-AGE and RV-AGE, delaying and decreasing the maximum peak of incidence of these pathologies. It seems quite unexplainable that the RV is not part of the Spanish immunization schedule yet.

Clinical Trial Registration (Please input N/A if not registered)

N/A
Title of Case(s)

Outbreak of non-tuberculous mycobacteria due to needle free connectors in a paediatric bone marrow transplant unit

Background

Nontuberculous mycobacteria (NTM) rarely cause infection in the general population but are associated with significant morbidity and mortality in immunocompromised patients, requiring prolonged antimicrobial treatment. Nosocomial infections are an increasing problem. NTM often colonise health care facility water systems. Additionally, needle-free connectors, which attach to central venous catheter (CVC) lumens, have been associated with an increase in the incidence of bloodstream infections. Here we present an outbreak of NTM in a paediatric bone marrow transplant (BMT) unit associated with water contamination of needle-free connectors.

Case Presentation Summary

5 paediatric patients undergoing BMT in our centre in 2010 developed NTM infections with rapidly growing mycobacterial species (Table 1). These patients presented with fever of unknown source with a clear CVC linsertion site. Following first, then second line antibiotic treatment, followed by subsequent CVC removal, all patients recovered on anti-mycobacterial treatment.

Post outbreak the following measures were taken: confirmation of clean hospital water by testing, updated education programme on CVC care for families; repeated education for healthcare staff on CVC management. Furthermore, the type of needle free connector used in the hospital was changed. No further NTM infections were detected following these changes.

Learning Points/Discussion

NTM must be considered as a cause of infection in the immunocompromised patients. Morbidity in these patients can be high and treatment long and costly. Disease prevention must remain the ultimate goal. This can be achieved by increasing awareness about water, intravascular devices and needle-free connectors as sources for infection and review of infection control practices including better patient education about properly covering CVC access site when exposed to water and review of device use.
Background

Nontuberculous mycobacteria (NTM) includes acid-fast bacteria other than Mycobacterium tuberculosis. They can be isolated in water, food or pets. NTM infections are rare and should be considered in children under 5 years of age with unilateral cervical lymphadenitis, non-tender, of subacute onset and unresponsive to antibiotic treatment.

Case Presentation Summary

A 2-year-old girl, seen at the emergency department for left cervical swelling with a week of evolution. No fever. No recent infectious intercurrences. Reference to housing in rural environment with close contact with domestic animals. At the objective examination, the patient had left hard cervical swelling of about 6 cm, with no other changes. She performed an analytical study with elevation of sedimentation velocity, tuberculin test that was positive and cervical ultrasound without signs of abscess and was hospitalized for antibiotic therapy and evolution monitoring. During hospitalization, due to the absence of clinical improvement, a cervical tomography suggestive of granulomatous adenitis with an abscess collection was performed. It was submitted to drainage and material collection for agent identification. After the identification of Mycobacterium avium strain, antibacterial therapy was started and surgical cleaning was performed.

Learning Points/Discussion

Cervical lymphadenitis is common in the pediatric age and its etiology may be due to a variety of infectious and non-infectious agents. NTM infection is an uncommon cause of cervical lymphadenitis. Differential diagnoses should be considered according to age, time of evolution and presence of alarm signals. In this case, the high index of suspicion allowed the speed in diagnosis and initiation of treatment.
Acute peripheral facial nerve palsy (FNP) in children is more common in Borrelia endemic areas. The incidence is 20-60/100.000/year. Children recover fully in 80-100% of cases. Neuroborreliosis (NB) is the most common identifiable cause in children and significantly more common than in adults. Another cause is Bell’s palsy (BP), however less common than in adults. Our aim was to identify the incidence, etiology and prognosis of FNP in children in the Borrelia high endemic region of Stockholm.

Methods

A retrospective study, identifying children 0-18 years of age who visited the Pediatric Emergency Department with a history of FNP during a one-year period 2014-2015. Epidemiological data was collected from medical chart reviews where two different facial grading systems, the House-Brackmann (HB) and Sunnybrook (SB), were used to measure clinical outcome.

Results

We identified 77 children with FNP; an estimated incidence of 40-50/100000 children/year. Forty-five children (58%) were diagnosed with NB and 33 (42%) with BP. Neuroborreliosis was almost only seen in children below 10 years of age and from June till November whereas BP was more evenly spread among age groups and throughout the year. Five patients (6,5%) had remaining symptoms 3 months after onset. Four of them were 10 years or older, all had a SB score ≥80/100 upon their last registered
follow-up visit; three had BP and two NB.

Conclusions

Neuroborreliosis was the major cause of FNP during our study period and dominated in the younger ages. Children heal well from FNP but our data indicates that older children and children with BP may have a risk of slower and incomplete recovery as opposed to younger children with NB. The Sunnybrook grading scale may have a predictive value in children with FNP.
ESP18-1014
E-POSTER VIEWING - MAY 28-JUNE 2 - EXHIBITION HOURS

03A. SCIENCE: SEVERE BACTERIAL INFECTIONS

KINGELLA KINGAE OSTEOARTICULAR INFECTION: CLINICAL EXPERIENCE IN TWO TERTIARY HOSPITALS IN IRELAND.
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Background
Kingella kingae is reported as an emerging cause of osteo-articular infection (OAI) in young children and can cause daycare outbreaks. Molecular testing has improved identification of OAI organisms. We report our experience of K. kingae OAI in children attending two Irish tertiary paediatric centres.

Methods

Retrospective study of children with K. kingae identified by PCR or culture of bone or joint fluid. Patients were identified by interrogation of the microbiologic laboratory systems. Demographics, clinical, laboratory parameters, course and outcome were examined.

Results

From Jan 2004 - Dec 2017, inclusive, 15 patients (10 in the last 3 years) had K. Kingae OAI; 10 males, median age 19 (9–72) months. K. kingae were identified in joint fluid (13) or bone (2); by culture (5), PCR (8), or culture & PCR(2). Affected sites included hip(3), knee(7), ankle(2), tibia(1) calcaneus(1) talus(1). Symptoms included limb swelling (13/15), non-weight bearing (8/15), limp (7/15), fever (8/15, 10/15 afebrile at admission, T max 38.5). 87% had a preceding URTI. Median WCC was 11x10^9/l (range 3.8-16.2), CRP 32 mg/dl (range12-92), ESR 55 (range 30-71) mm/hr. Empiric therapy was appropriate in all. Median hospitalisation was 9.5 days(6-15) days, with medians 8 (range 5-21) days parenteral and subsequent 21 (22-28) days oral therapy. 3/4 PCR+/Culture-patients had preadmission antibiotics. All recovered.

Conclusions
Additional PCR testing increases diagnostic sensitivity for Kingella OAI. Reported increases in incidence may in part reflect better diagnostics rather than epidemiologic change. Clinical and laboratory manifestations can be less acute than with other OAI. Consideration of K. kingae in choice of empiric therapy for POI in young children, especially those with preceding URTI, is
01C. SCIENCE: ANTIBIOTIC STEWARDSHIP AND INFECTION CONTROL

TREATMENT AND OUTCOME OF URINARY TRACT INFECTIONS (UTIs) CAUSED BY COMMUNITY-ACQUIRED (CA) EXTENDED SPECTRUM-β LACTAMASE-PRODUCING ENTEROBACTERIACEAE (ESBL+) IN CHILDREN

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Background

A significant increase in ESBL+ has been observed worldwide, including in children. Noncarbapenem antimicrobials have been used with considerable clinical success to treat these UTIs in adults, with few reports from children.

The aim of this study is to analyse the outcome of UTIs caused by ESBL+ in children.

Methods

Retrospective review of all cases of CA-ESBL+ UTIs from 2007-16. The outcome was evaluated with regard to clinical and microbiologic responses and subsequent UITs.

Results

Over 10Y, there were 156 ESBL+ UTIs with 35 (22%) being CA, 15 cystitis and 20 pyelonephritis. The median age was 4.2 years (1M–18Y). It was the first UTI in 86%. 26 (74%) were caused by E. coli, 5 (14%) by K. pneumoniae and 4 (12%) by P. mirabilis. 4 (11%) were resistant to nitrofurantoin, 14 (35%) to ciprofloxacin and 7 (20%) amoxicillin/clavulanate.

Initial treatment was in all cases with cefuroxime (21, 60%) or amoxicillin/clavulanate, according to the local protocol. All but one received oral treatment. Once microbiological results were known, cases were reviewed: 3 had persistent symptoms; 25 children had a repeat urine culture that was negative in 17 (68%). In 6 cases, treatment was modified: 5 based on microbiological results and 1 because of persistent symptoms. On the follow up, 5 children had a repeat UIT within 4W after completion of therapy: 1 had been previously treated with carbapenem, 1 with ciprofloxacin, 2 with amoxicillin/clavulanate and 1 with cefuroxime. Out of these 5, 4 had ESBL infection.

Imaging investigation performed in 60% showed an underlying renal abnormality in 17%.

Conclusions

Although the numbers are small, clinical and microbiological follow-up showed that a considerable proportion of those UITs were successfully treated with noncarbapenem antimicrobials.
FAECAL CARRIAGE OF MULTI-DRUG RESISTANCE MICROORGANISMS IN HEALTHY INFANTS

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Background

There is an alarming increase of multi-drug resistance microorganisms (MDRM) in our environment. Different studies have analyzed the MDRM prevalence on healthy children, obtaining heterogeneous results depending on the regional area and the age.

The aim of our study is to analyze prevalence of MDRM faecal colonization and evaluate associated risk factors in infants up to 12 months old.

Methods

We carried out a prospective follow-up study of a cohort of healthy newborn children. Newborns were recruited recording perinatal and neonatal history. A stool sample and a questionnaire were collected at the age of 1 and 6 months, pending last sample collection (12 months). We analyzed different variables: weight, type of feeding, cohabitants at home, previous antibiotic/antacid’s intake, hospital’s admission and day-care centre assistance.

The study was approved by the Ethics Committee. Written informed consent was obtained.

Results

We recruited 178 patients (51.4% female) analyzing 174 samples at 1⁰ month and 157 samples at 6⁰ month. The analysis at 1⁰ month showed that only one child (0.6%) was colonized by a MDRM. At 6⁰ month, the prevalence observed was 7.6%. The main MDRM isolated was E.coli ESBL (5.3%) followed by K.pneumoniae OXA-48 (1.9%).

There were no significant differences in analyzed variables. Prevalence of MDRM in children whose mothers were colonized by Group B streptococcus at birth (19% vs 5.9%, p=0.06) and children living with their grandparents (15.8 vs 6.6%, p=0.2), was higher although it did not reach statistical significance.

Conclusions

MDRM faecal colonization in healthy children in our hospital (pending of complete sample) seems to be high, similar to those reported in developed countries, underlining the importance of this population as MDRM’s reservoir.
Clinical Trial Registration (Please input N/A if not registered)
Mycobacterium avium complex (MAC) immune reconstitution inflammatory syndrome (IRIS) in HIV-positive adolescent

V. Chechenieva

Title of Case(s)

Mycobacterium avium complex (MAC) immune reconstitution inflammatory syndrome (IRIS) in HIV-positive adolescent

Background

Mycobacterium avium complex (MAC) are developing in HIV-patients with CD 4 cells less than 50. IRIS could occur within 3-12 months of initiating HAART.

Case Presentation Summary

First HIV-diagnosed 13 year old boy was hospitalized in our center with complains: weight loss, fatigue.

Blood test: Hb- 95 g/l, platelets – 143 x10⁹/l, WBC- 10.7x10⁹/l, ERS – 74 mm/h; ALT- 130 U/l, AST - 181 U/l; CD4 – 0.9%-2 cell. viral load - 54667 RNA copy /ml

X-ray: signs of pneumonia.

Antibiotic treatment and ART (TDF/FTC/EFV) were prescribed.

2 weeks later: fever, liver and spleen enlargement appeared. Blood test: Hb- 81 g/l, platelets – 51 x10⁹/l, WBC- 18x10⁹/l; ferritin -2337 µg/l. CD4 – 2%-8 cell, PCR DNA CMV was positive. Thorax and abdominal CT scans: mesenteric and thorax lymph nodes enlargement, hepatosplenomegaly.

HLH and TB /MAC – infections were suspected.

Ethambutol, rifampicin, amikacin, linezolide, levofloxacin, azithromycin, prednisolone, ganciclovir were prescribed. Clinical, laboratorial, radiological improvement were achieved.

On the 9 months of ART treatment: weight loss, abdominal pain and vomiting, mesenteric lymph nodes enlargement appeared. Laboratory data: Hb- 89 g/l, platelets – 136 x10⁹/l, WBC- 6x10⁹/l, ESR-50 mm/h, CRP-92 mkg/l, ferritin -967 µg/l, CD4 – 10%-57 cell, viral load - 60 RNA copy /ml

CT and US image: hepatosplenomegaly, mesenteric lymph nodes enlargement. The biopsy of mesenteric lymph node was made.
Mycobacterium avium complex was diagnosed, worsening of patients condition on 9 months of ART was estimated as a immune reconstitution syndrome (IRIS).

**Learning Points/Discussion**

In our patient the next risk factors for IRIS developing were presented:

- Low CD4 count at initiation of ART;
- High pre-ART HIV viral load;
- Shorter duration of OI treatment prior to starting ART;
- Rapid suppression of HIV viral load.
NINE-YEAR RETROSPECTIVE SURVEY OF CANDIDAEMIA IN A UNIVERSITY HOSPITAL IN TURKEY.

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Background

Despite improvements in diagnosis and treatment, Candida spp. remain a major cause of morbidity and in children particularly with an immunocompromised condition.

Methods

A retrospective observational study was performed between January 2008 and December 2017, to determine the Candida species, demographic and clinical characteristics of the children with Candidemia. The frequency of fungi among agents growing in blood culture was evaluated. In case of the recurrent positive culture from the same patient, only one strain was taken into consideration.

Results

A total of 281 fungal species from 252 patients were evaluated. Candidemia was common in pediatric surgery unit followed by pediatric intensive care, gastroenterology and oncology services. Two hundred seventy five of these strains (97.8%) were Candida species, while six were other fungi. The most common species of Candida was C. parapsilosis. Of the isolates, 32.4 % (91/281) were C. albicans and 65.4% (184/281) were non-albicans Candida; C. parapsilosis (41.6%), C. glabrata (6.4%), C. tropicalis (5.3%), C. krusei (2.8%), C. kefyr (2.1%) and other Candida species (7.2%). In first two years, the most common isolated Candida species was C.albicans and C.parapsilosis was most common between 2010 and 2017. Of the 55 Candidemia due to Candida parapsilosis which caspofungin susceptibility test was performed, caspofungin resistance was observed in 5% of episodes. Of the 59 Candidemia episodes due to C.parapsilosis in which anidulafingin susceptibility test was performed, the rate of resistant strain was %15.2. Overall, attributable mortality was 9.2% and crude mortality was 13.8%.

Conclusions

In conclusion, a rise in frequency of non-albicans Candida species particularly for C.parapsilosis was observed in later part of study.

Taking infection control measures into consideration can reduce the incidence of candidemia due to C. parapsilosis.
ANTIBIOTIC USE AND OVERUSE AMONG PRESCHOOL CHILDREN ATTENDING DAY CARE CENTERS
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Background

Antibiotic resistance has emerged as one of the major global threats to health. Infections caused by antibiotic resistant organisms are associated with significant morbidity, mortality and healthcare costs. Antibiotic use is the major driver of antibiotic resistance. Understanding utilization patterns are necessary in designing interventions. The aim of this study was to examine antibiotic use patterns among preschool children that attend public day care centers (DCCs) in the municipality of Athens.

Methods

All preschool children, aged between 6 months and 5 years that attend public day care centers (DCCs) in the municipality of Athens, Greece were eligible. Nineteen public DCCs were randomly selected to participate in the study among a total of 75 centers throughout the 7 municipal districts. A study investigator (KP) visited participating DCCs during the winter months of the years 2016 and 2017. A preformed questionnaire was distributed to parents and included questions regarding demographic data, antibiotic use within the past month, details about the person that administered therapy, the indication (diagnosis) for which the antibiotic was prescribed and the type of antibiotic.

Results

A total of 1390 questionnaires were distributed and 683 were completed by the parents (response rate 49%). Antibiotics were administered during the previous month to 193/683 children (28.3%). In 135/193 children (69.9%) antibiotic use was found to be inappropriate, based on unjustified physician diagnosis of bacterial infection (54.4%), pharmacist’s advice (3.1%), parental decision (4.2%) or medical advice over the phone (8.1%).

Conclusions

A high rate of inappropriate antibiotic use was recorded in this study among preschool age children. These findings support the urgent need for antibiotic stewardship interventions in the community.
MOTHER’S PERCEPTIONS ON THE COMMUNICATION OF YOUR POSITIVE ZIKV DIAGNOSIS


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Background

Communication of bad news related to the Zika Virus (ZIKV) epidemic during pregnancy and the first months of the baby's life can be considered a new challenge for physicians and other health professionals. The objective is identify the perceptions of mothers when receiving communicating your ZKV positive diagnosis and promoting reflection on the preparation of the medical professional and their impressions when making the statement.

Methods
Exploratory and descriptive research, of a qualitative nature that is part of the macro-project "Vertical infection by the Zika virus and its repercussions in the maternal and child area - Jundiaí Cohort", approved by the Research Ethics Committee of the Medical School of Jundiaí, number 1446577. Participants were 40 women who were diagnosed as having positive ZIKV, even during pregnancy or in the first months after delivery. Five physicians responsible for communicating the diagnosis were also heard.

Results

Three categories were listed for analysis: Pregnancy and ZIKV (1st Category); The moment of communication (2nd Category) and The fact of communicating (3rd Category).

Conclusions

Most mothers reported that they were welcomed by professionals involved in communicating the diagnosis of ZIKV. The evidence-based information available on the Zika Virus Congenital Syndrome is still unclear about possible sequelae in children, mothers of ZIKV-positive mothers acquired during pregnancy, which creates discomfort at the time of communication for both physicians and for patients. Fear and sadness were the most present feelings in the responses of women heard. The creation and adoption of protocols for guidance when communicating bad news is welcomed by professionals. It was observed the importance of the multiprofessional team for therapeutic support of mothers and children.
Infections caused by ESBL+ *Enterobacteriaceae* are an emerging problem worldwide. However, there are very few studies in children and risk factors have been best defined for adults.

We aimed to evaluate these infections in a paediatric population.

**Methods**

Retrospective observational study of all cases of ESBL+ infections, observed in a paediatric tertiary hospital from 2007 to 2016. Clinical, demographic, and epidemiological data and risk factors were analysed. ESBL detection and antimicrobial susceptibility testing were performed with the VITEK 2 automated system and confirmation of ESBL production was done with Etest and combination–disk synergy test. Colonisation was excluded.

**Results**

Over 10Y, 222ESBL-producing bacteria were identified, with a mean of 22 infections/year (3 in 2007 – 42 in 2013). The mean age was 6.3Y (1M-19Y). The most frequent were *Escherichia coli* (137, 62%), *Klebsiella spp* (51, 23%) and *Proteus spp* (16, 7%). Urinary tract infections (UTIs) were largely predominant (156, 70%) (with 35, 22% being community acquired), followed by respiratory infections (10, 4.5%), sepsis (8, 3.6%) and acute appendicitis with peritonitis (7, 3%). Risk factors were present in 184 (83%), mostly antibiotic use in the last 30 days, recent hospitalisation, antimicrobial prophylaxis and the presence of an underlying chronic disease. Of the 38 children with no risk factors, 35 had UTIs, acute appendicitis with peritonitis, bacteremia and pneumonia (1 each).

**Conclusions**

ESBL+ have increased in the last decade in our institution, mainly in UTIs. The majority of these children have risk factors but approximately a quarter of all UTIs happened in healthy children. Of the children with no risk factors only 3 had a diagnosis that was not UTI. It is important to continue monitoring these infections.
09C. SCIENCE: INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS

FREQUENCY OF HSV1/-2 AND VZV VIRAEMIA IN PAEDIATRIC HAEMATO-/ONCOLOGIC PATIENTS AND ITS ASSOCIATION WITH (MUCO-)CUTANEOUS LESIONS


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Background

Herpes simplex viruses (HSV-1/2) as well as varicella zoster virus (VZV) infection or reactivation may lead to relevant complications in immunocompromised patients. While vesicular and aphtheous lesions are well known symptoms, frequency and impact of HSV and VZV viraemia is unclear.

Methods

We retrospectively analysed HSV-1/2 and VZV PCR results from blood specimens, cerebrospinal fluid (CSF), swabs and mouthwash in paediatric haemato-/oncologic patients of the Medical University of Graz between 2001 and 2017 to describe frequency of viraemia and its association with (muco-)cutaneous lesions.

Results

17,262 specimens obtained from 671 patients were analysed. HSV-1 was detected in blood in 53 (1.06%) of 5,014 tested specimens, obtained from 38 (7.3%) positive of 519 tested patients (age 1.0-23.2, median 12.2 years). HSV-1 was detected concurrently in blood and swabs or mouthwashes in 9 (81.8%) of 11 patients. In 17 viraemic patients (muco-)cutaneous lesions were not tested but in 5 (29.4%) of them lesions were documented.

HSV-2 was detected in 2 (0.04%) of 5,015 tested specimens (one each in CSF and blood, age 18.2 and 15.0 years) according to 0.035% of 564 tested patients.

VZV was detected in blood in 15 (0.45%) of 3,348 tested specimens, obtained from 12 (2.1%) positive of 534 tested patients (age 0.8-25.0, median 11.8 years). VZV was concurrently detected in blood and swabs in 2 (50%) of 4 patients. In 10 viraemic patients (muco-)cutaneous lesions were not tested but in 6 (60%) of them lesions were documented.

Conclusions

In paediatric haemato-/oncologic patients, HSV-1 and VZV are far more frequently detected than HSV-2. Viraemia with these viruses were rarely detected and were accompanied by muco-/cutaneous lesions the majority of cases. Thus, routine screening for viraemia cannot be recommended.
07A. EDUCATION: HIV MANAGEMENT DECISIONS

USING NEWBORN SCREENING RESULTS TO EVALUATE FOR ADVERSE EFFECTS OF HIV AND ANTIRETROVIRAL EXPOSURE IN HIV-EXPOSED UNINFECTED INFANTS

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Background

There is a growing population of HIV-exposed uninfected children (HEUs) both globally and in Canada. Increasing evidence suggests multiple excess morbidities in these children including immune abnormalities. Protease inhibitor (PI) exposure in pregnancy/postnatally can affect the infant adrenal axis. We reviewed newborn screening results for congenital adrenal hyperplasia and severe combined immune deficiency to evaluate for adverse effects in HEUs.

Methods

17α-hydroxyprogesterone (17-OH) and T-cell receptor excision circles (TRECs) newborn screening results were obtained for HEUs followed at the Children’s Hospital of Eastern Ontario from 2007-2016 (for 17-OH) and 2013-2016 (for TRECs). T-test comparisons were made between population values and HEUs according to maternal (type of ART, CD4 counts) and infant variables.

Results

96 HEUs with 17-OH results were identified for the period of interest, with complete data on maternal treatment available for 83, of whom 62 (75%) were treated with PIs. Only 4 (5%) of mothers had CD4<200 in pregnancy, and 6 (7%) had detectable viral loads at delivery. 25 HEUs had TRECs results with complete maternal data. Mean (s.d.) 17-OH levels were higher for HEUs compared to the general population [13.6 (16.5) vs 10.1 (6.8) ng/mL] (p<0.001), and specifically for HEUs exposed to maternal PIs [14.6 (18.4) ng/mL] compared to general population (p<0.001) but not for PI-unexposed HEUS [10.5 (9.2) ng/mL] (p=0.80). Mean (s.d.) TRECs values were significantly higher for HEUs versus general population (1513 (1613) vs 921 (516) copy#/3uL] (p<0.001), and specifically for PI-exposed HEUs [1824 (2017) copy#/3uL] (p<0.001) but not for PI-unexposed HEUs [1047 (447) copy#/3uL) (p=0.246).

Conclusions

In this analysis, PI-exposed HEUs demonstrated higher 17-OH and TRECs values than the general population, suggesting newborn screening results may be useful in evaluating for toxicities in HIV/ARV-exposed infants.
A CASE OF R. ORNITHINOLYTICA URINARY TRACT INFECTION IN A PEDIATRIC PATIENT

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Title of Case(s)

A Case of *R. ornithinolytica* Urinary Tract Infection In A Pediatric Patient

Background

Human infections caused by *R. ornithinolytica* are rare. There have been only a few clinical reports on *R. ornithinolytica* urinary tract infection (UTI) and clinical characteristics of pediatric cases have not been determined.

Case Presentation Summary

A 6.5-year-old female child was brought to the emergency department because of fever reaching a maximum of 38.5°C and abdominal pain. She had a medical history of hydronephrosis and recurrent UTI. Minimal abdominal tenderness and pain were noted on physical examination. The laboratory investigations revealed a hemoglobin of 9.4 g/dL, platelet count of 333,000/µL and a white blood cell count of 6000/µL with normal liver enzymes and kidney function tests. C-reactive protein was 16.6 mg/dL (normal: 0 - 0.8 mg/dL). Urinalysis revealed positive nitrite, leukocyte and erythrocyte, and 86 white blood cells/hpf (normal range: 0 - 5), 4 RBC/hpf (normal range: 0 - 3), a large number of bacteria and with the remaining parameters within normal limits. Renal ultrasound showed no radiologic finding concerning acute pyelonephritis. Her urine was sent for culture and sensitivity. Oral empiric treatment was initiated with cefixime (8 mg/kg/day). The urine culture isolate was identified as *R. ornithinolytica*, 100,000 cfu/mL, by MALDI-TOF MS (Matrix-Assisted Laser Desorption/Ionization time of flight, Mass Spectrometry, BioMerieux, France). The *R. ornithinolytica* demonstrated resistant to ampicillin and susceptibility to all other tested antibiotics including cefixime, gentamicin, ertapenem, ciprofloxacin. The patient was treated with a 14-day-course of oral cefixime. The normal urinalysis and negative control urine culture was detected by the 18th day. At the 30th day, left kidney with cortical irregularity compatible with parakical damage in upper pole and lateral upper part was shown in the static renal scintigraphy.

Learning Points/Discussion

The most frequent infection due to *R. ornithinolytica* is bacteremia as well as UTI is not well known in pediatric population. This case of *R. ornithinolytica* urinary infection is reported to raise awareness of it as a potential organism that may cause UTI in children.
Background

Children with meningococcal sepsis are highly at risk for fulminant disease, multi-organ failure and death. Recently, neutrophil extracellular traps (NETs) levels have been indicated as a marker for severity in different kinds of sepsis. Our aim was to study the role of NETosis in meningococcal sepsis in children.

Methods

We measured myeloperoxidase (MPO)-DNA, a marker for NETs, in serum of meningococcal sepsis patients upon admission to PICU, at 24 hours, and at 1 month and studied the association with clinical outcome. Subsequently, we tested whether N. meningitidis, isolated from children with meningococcal sepsis, were able to induce NETosis, using confocal microscopy live imaging.

Results

MPO-DNA levels at admission (n=35, median 0.21 AU/mL, IQR 0.12-0.27) and at 24 hours (n=39, median 0.14 AU/mL, IQR 0.09-0.25) were significantly higher than the MPO-DNA levels after 1 month (controls, n=36, median 0.07 AU/mL, IQR 0.05-0.09, p<0.001). We did not observe a correlation between MPO-DNA levels and mortality, cell-free DNA or other inflammatory markers. In addition, N. meningitidis are fast and strong inducers of NETosis.

Conclusions
Children admitted to PICU for meningococcal sepsis have higher NETs levels at admission and after 24 hours than controls. NETs levels were not associated with outcome, cell-free DNA or other inflammatory markers. These NETs may be induced by *N. meningitidis*, since these are strong NETosis inducers.

**Clinical Trial Registration (Please input N/A if not registered)**

N/A
NEONATAL ENDOCARDITIS AS AN UNUSUAL COMPLICATION OF CATHETER-ASSOCIATED BLOODSTREAM INFECTION IN A PRETERM NEONATE

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Title of Case(s)

NEONATAL ENDOCARDITIS AS AN UNUSUAL COMPLICATION OF CATHETER-ASSOCIATED BLOODSTREAM INFECTION IN A PRETERM NEONATE

Background

Despite not being frequent in the modern era, the incidence of neonatal endocarditis is expected to rise and 31% of its mortality happens in preterms. The higher survival rates of children with congenital heart disease, the increased presence of risk factors such as central vascular catheters and associated bloodstream infections (CABSIs) and prolonged hospitalization at the neonatal intensive care unit account for this.

Case Presentation Summary

We report the case of a female neonate born from a 29-week and 6 days gemellary dizygotic gestation, that had an umbilical vein catheter (UVC) placed at birth. At 4 days old a peripherally inserted central catheter (PICC) replaced the UVC. The echocardiographic evaluation at that time showed no signs of congenital heart disease and revealed the PICC tip located at the right auricle. At 23 days, she presents with late-onset sepsis and initiates empirical antibiotic therapy. The blood cultures reveal an E. faecalis and antibiotic therapy is adjusted according to its drug susceptibility test, with clinical and laboratorial improvement. On day 34, echocardiography demonstrates a hyperechogenic image at the tricuspid valve, suggestive of infective endocarditis. The lesion remains visible and doesn’t diminish for the seven weeks of tailored antibiotic therapy’s duration and thereafter, even though she is always asymptomatic and has serial negative blood cultures. She is discharged at 100 days of life, referred to a pediatric cardiologist.

Learning Points/Discussion

Neonatal endocarditis is to be thought of as a possible complication of CABSIs in the NICU. It might be difficult to observe echocardiographic regression of the lesions despite adequate antibiotic therapy and good clinical response.
Deciding which febrile illness needs antibiotic treatment is challenging particularly in low income countries where laboratory facilities and other resources for proper diagnosis are not readily available.

Methods

Gambian children >1 month to 18 years routinely seen at outpatient with fever (>38°C) or suspected infection, and no history of antibiotic use in the previous 7 days were recruited into the PERFORM study. Based on clinical indication, samples were collected and tested using conventional methods. We describe antibiotic prescription patterns for the study children.

Results

343 children (49.8% males) were recruited into the study [median age 3 years (IQR 1.6-5.4)]. Twenty two (7.2%) of the children were hospitalized and one child died.

Antibiotics were prescribed for 285 (83.1%) children. All 22 children admitted were prescribed antibiotics, except one child. Among those children who received antibiotics, 16 (5.6%), two and one children were prescribed two, three and four antibiotics respectively.

Majority of the antibiotics were given as oral medication 276 (90.8%) and 28 (9.2%) were administered parenterally. All outpatient prescriptions were oral, 267 (100%) compared to 9/37 (24.3%) ward prescriptions, p value < 0.001).

The most common antibiotic prescribed was Amoxicillin 237/304 (78%) followed by Cloxacillin 20/304 (6.6%). Among the ward prescriptions, 15/37 (40.5%) were Ampicillin.

An aetiologic agent was detected in 19 children; ten bacteria [7 urines (5 E.coli, 1 Proteus and 1 Coliform), 2 blood (Salmonella spp and S.pneumoniae), Plasmodium species (8), and E.histolytica (1)].

Conclusions

Although confirmed bacterial aetiology was low, over two thirds of the children presenting to hospital with febrile illness were prescribed antibiotics. Because antibiotic resistance is accelerated by overuse, a robust national action plan, including an antibiotic stewardship system is needed in The Gambia.
SUCCESSFUL TREATMENT OF EXTENSIVELY-DRUG RESISTANT KLEBSIELLA PNEUMONIAE WITH CEFTAZIDIME-AVIBACTTAM.
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Title of Case(s)
SUCCESSFUL OUTCOME OF EXTENSIVELY-DRUG RESISTANT KLEBSIELLA PNEUMONIAE BLOODSTREAM INFECTION

Background
Emergence of extensively drug resistant (XDR) Klebsiella pneumoniae is a major public threat and especially for pediatric patients. Therapeutic treatment options for these bacteria are extremely limited to ≤2 antimicrobial agents (including colistin) for which few or no efficacy/safety data exist. The aim of this study was to describe the successful treatment outcome of an XDR K. pneumoniae bloodstream infection in a 2.5-year-old girl using ceftazidime-avibactam, a newly developed antibiotic with activity against Klebsiella pneumoniae carbapenemase (KPC).

Case Presentation Summary
A 2.5-year-old girl was admitted to PICU for cerebral injury as a result of crushing. She was intubated and had a central venous catheter (CVC) in place. On day 15 of hospitalization she suffered from bacteremia due to Klebsiella pneumoniae resistant to all antimicrobials except colistin, of which MIC of the isolate was, however, high (3 mg/l according to microdilution method). Meropenem and colistin (300,000 IU/kg per day q8h) were initially started and ertapenem, tigecycline and amikacin were subsequently added to the antimicrobial regimen. Blood cultures became negative. However, 22 days later, the patient deteriorated with high fever and CRP (max 313 mg/l). Blood cultures again grew K. pneumoniae, which had the same resistant phenotype. The isolate was susceptible to ceftazidime/avibactam. After special ethics approval, ceftazidime/avibactam was administered to the patient at the dose of 62.5 mg (50/12.5)/kg/dose q8h. Blood cultures became negative after 2 d and the patient improved clinically. Ceftazidime/avibactam was given for a total of 32 days without any related significant adverse event.

Learning Points/Discussion
Treatment of bloodstream infections caused by XDR-Enterobacteriaceae in children is challenging. Administration of ceftazidime/avibactam could be efficacious against in vitro susceptible XDR-Enterobacteriaceae without any significant adverse effects.
01C. SCIENCE: ANTIBIOTIC STEWARDSHIP AND INFECTION CONTROL

ANTIBIOTIC USE IN CHILDREN AND RECOMMENDATIONS FOR DECREASING IT
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Background and Objective

Overuse and inappropriate prescribing of antibiotics is driving antibiotic resistance so antimicrobial resistance is a global public health threat and a danger that continues to escalate.

Methods

Various fetal, maternal and NICUs environmental factors contribute toward causing infections in newborns. NICUs environments can be bacteriologically very hostile, containing a wide selection of pathogenic, antibiotic resistant organisms with which the patient becomes colonized. Recent all-cause antibiotic prescribing increased the probability of antimicrobial resistance in pathogenic in children in primary care. Health care-associated infections (HAIs) are a significant public health problem resulting in increased morbidity, mortality and increased hospital stay lengths and health care costs.

On the other hand infection control can improved in kindergartens and schools help to improve children’s and adolescent’s health and reduce illness and antibiotic use. Complex interventions that combine handwashing and hygiene education directed towards children and staff in hospital, kindergarten and primary school, significantly lower the incidence of infections.

Discussion

Children have unique medical needs related to antimicrobials and deserve focused pediatric antimicrobial stewardship programs efforts. The literature regarding pediatric antimicrobial stewardship interventions is limited, but published interventions may serve as paradigms for developing pediatric antimicrobial stewardship programs as demonstrated by the general success of these interventions.
PERITONSILLAR CELLULITIS AND ABSCESS IN CHILDREN: A 8-YEAR REVIEW OF DIAGNOSIS AND MANAGEMENT IN A PORTUGUESE PEDIATRIC WARD

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Background

Peritonsillar cellulitis and abscess are among the most common deep neck infections in children and adolescents. With this study, we proposed to review the management of children admitted to our hospital with this diagnosis in the past 8 years.

Methods

We retrospectively reviewed the records of every children admitted to our hospital with the diagnosis of peritonsillar cellulitis or abscess, from January 2010 to December 2017. Demographic data, clinical manifestations, diagnostic studies, treatment, microbiology and duration of hospital stay were analyzed.

Results

60 cases were identified (55 patients) with a mean age at presentation of 11 years. The mean duration of symptoms before admission was 5 days. The most frequent presenting symptoms were sore throat (98%) and fever (75%). The most common examination findings were bulging of the soft palate (90%) and deviation of the uvula to the opposite side (81%). Laboratory evaluation and imaging studies were carried out in 87% and 36% of cases, respectively. Surgical drainage was performed in 24 cases (40%), mostly in children 10 years old and older. The most common pathogen isolated was Streptococcus pyogenes. Most patients were treated with IV antibiotics, most commonly amoxicillin-clavulanic acid, for a mean duration of 3 days, switching to oral antibiotic for a mean total duration of 10 days. Corticosteroids were administrated in 19 cases (32%); it was not statistically associated with reduced duration of hospital stay. The recurrence rate was 3,6%.

Conclusions

Our results were comparable to previous studies on this subject, except for the recurrence rate which was significantly lower in our study. Regarding the use of corticosteroids, we found no difference in the duration of hospital stay in patients who received corticosteroids.
"Alice in Wonderland" syndrome as a presenting symptom of Epstein-Barr virus infection

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Title of Case(s)

"Alice in Wonderland" syndrome as a presenting symptom of Epstein-Barr virus infection

Background

Alice in Wonderland"(AIW) syndrome to which children seem particularly susceptible due to Epstein-Barr virus(EBV) infection is a rare condition.

Case Presentation Summary

A 11-year-old previously healthy girl was referred to the emergency department with fever, sore throat and respiratory distress. The vital signs included a pulse of 124 bpm, respiratory rate of 30 breaths/min, temperature of 38.2°C and blood pressure of 110/70 mmHg. Bilateral multiple enlarged tender cervical and submandibular lymph nodes, bilateral hyperemic, hypertrophic, membranous tonsils and loss of hyperresonance on Traube's space were noted on physical examination. The laboratory investigations revealed a hemoglobin of 13 g/dL, platelet count of 147,000/µL and a white blood cell count of 8000/µL with normal kidney function tests. The liver enzymes were as follows; ALP: 359 U/L, ALT: 196 U/L, AST: 115 U/L, total bilirubin: 0.58 mg/dL, GGT: 118 U/L. Her erythrocyte sedimentation rate was 18 mm/h (normal: 0-20 mm/h) and C-reactive protein was 3.32 mg/dL (normal: 0-0.8 mg/dL). The neck USG and CT showed no radiological finding concerning a deep-neck infection. EBV infection was suspected and she was hospitalized. IV acyclovir (30 mg/kg/d), ampicillin sulbactam (100 mg/kg/d) and methylprednisolone (2x 30 mg) were started. The blood, throat and urine cultures were negative. Others were as follows: EBV EBNA IgG: negative, EBV VCA IgM: 8.9 (0-1.1), EBV VCA IgG: 85 RU/mL (0-20), EBV EA IgG: negative and EBV DNA 54,499 copy/mL. The fever subsided after 5th day of the treatment. On the 5th day of the treatment, the patient complained about headache with no fever and seeing big-things that no-one else can see like birds and spiders. The neurologic examination and biochemical parameters (electrolytes and glucose) were normal. There was no pathologic finding in cranial MRI and EEG. AIW syndrome was considered. Treatment stopped at the 7th day. The EBV DNA was negative after treatment. The patient discharged with any complication.

Learning Points/Discussion

This case of EBV infection is reported to raise awareness of it as a reason of AIW in children.
COMPUTED TOMOGRAPHY ABNORMALITIES IN HIV PATIENTS WITH NEUROLOGICAL SYMPTOMS: WHEN DO WE NEED TO INVESTIGATE?

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Background

HIV-1 is a neurotropic virus that invades the central nervous system (SNC) early in the course of infection. Children are more vulnerable to neurological and neurodevelopmental complications of HIV.

Our aim was to evaluate the tomographic findings of children and adolescents living with HIV-AIDS that had neurological symptoms and identify risk factors for having an abnormal exam in HIV patients with headache.

Methods

We reviewed the medical records of 86 pediatric patients living with HIV-AIDS followed in a tertiary hospital in São Paulo, Brazil. We selected the patients who had neurological signs or symptoms and had at least one computed tomography scan (CT) of the brain during follow-up.

We collected demographic data (sex, age when the CTs were performed), clinical and immunological classification and information about neurological development.

Results

One third (n=29; 62% females, age 5 months to 17 years) of our patients had neurological symptoms that lead to a CT scan.

Fifteen patients had abnormal CTs (white matter abnormalities n=6; other congenital infections n=4; ischemic injuries n=2; vascular abnormalities n=1; calcifications n=1; neurotoxoplasmosis n=1).

Delay in neurodevelopment was the most common symptom (67.8%). Abnormal CT was present in 57.9% of these patients versus 11% in children with normal neurodevelopment (p=0.039). All patients (n=6) with normal CD4 count and headache as the only neurological symptom had no CT abnormalities.

Conclusions

Neurodevelopmental delay was the most common neurological symptom in our casuistic and was frequently associated with structural abnormalities of the SNC.
Our findings suggest that it is reasonable not to perform CTs in patients with headache as only symptom with normal neurological exam and adequate CD4 count. Further studies are needed to evaluate the indications of CT in children with HIV.
CONTRIBUTION OF SEXUAL INFECTIONS IN NEW HIV DIAGNOSES IN ADOLESCENTS IN SPAIN
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Background

Sexual transmitted diseases present an increasing incidence among adolescents. Data about behaviourally HIV infected adolescents is scarce, especially in Europe. Describing this population will contribute to better approach this problematic situation.

Methods

Description of HIV new infections in patients 12-18 years-old included in CoRISpe Spanish database until December 2016. Demographic, clinical, biological data and way of transmission were analysed.

Results

For 25 adolescents a new diagnosis of HIV was made. Median age at diagnosis was 15.5 years (12.3 – 17.8) and 60% were male. The main way of infection was sexual (18 patients, 72%, 10 heterosexual, 8 homosexual), followed by transfusion/haemophilia (2), possibly vertical (2) and unknown (3). For periods, the average rate of sexual infections was 62.5% until 2013 and increased to 89% in 2014-2016. Contribution of homosexual transmission passed from 14% total diagnosis in 2008-2010 to 67% in 2014-2016. 20% of sexual infections were homosexual in 2008-2010 vs 75% in 2014-2016.

64% of adolescents were born outside of Spain; 61% for sexually infected. From the foreigners, 82% were Latin-American for the sexually infected vs 56% for the global.

Looking to the CD4 rate, late diagnosis (<350/mm³) was made for 12 patients (48%); 8 (32%) of whom were very late (<200/mm³). The proportion of late diagnoses was 56.3% for the foreigners and 33.3%
for those born in Spain. In the sexually infected subgroup, in 5 cases the diagnosis was late (29.4%), of whom 2 (11.8%) were very late.

**Conclusions**

There is an increasing contribution of the sexual way in new HIV infections among adolescents, especially for Latin-American males with homosexual transmission. Almost one third of them were late diagnoses, which emphasizes the vulnerability of this population and the need to develop specific measures.
SUBOPTIMAL VACCINATION COVERAGE OF NURSING AND AUXILIARY STAFF IN A TERTIARY UNIVERSITY HOSPITAL

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Background

Health care workers (HCWs) are exposed to infectious diseases and are considered to be at increased risk for significant morbidity or even mortality for both themselves and susceptible patients. The aim of this study was to record vaccine coverage against vaccine-preventable diseases of the nursing and auxiliary staff working in the only tertiary hospital in Crete, a big prefecture of Greece.

Methods

Data collection took place after a short personal interview with each employee based on selected relevant questions from August to November 2017. The interview was taken by the same person for each study participant.

Results

Data were collected from 823 out of a total of 851 individuals (96.6%). Self-reported vaccination rate for hepatitis B vaccine was 80.4%, for hepatitis A 4.7%, tetanus-diphtheria 56%, with 63.3% among vaccinated staff having received the vaccine more than ten years ago. Vaccine coverage for pertussis was as low as 0.2%, while 19.6% of workers were vaccinated with MMR, and another 38.1% and 46.8% had reported to be naturally immune for mumps and measles, respectively. Influenza vaccine uptake ranged from 13.2% (2012) to 20.3% (2017), with only 8.7% having been vaccinated each year. Younger employees (<40 years) were overall better vaccinated, while no difference was found for HCWs from High-Dependency, Intensive Care Units and Oncology Department, with the exemption of vaccine coverage for MMR which was found to be higher in the above mentioned Hospital Units (p<0.01).

Conclusions

Vaccination rates for vaccine-preventable diseases among the nursing and auxiliary staff of a tertiary hospital are suboptimal, despite vaccine promoting campaigns, implicating the need of more intense vaccination strategies for HCWs.
Background

Since the mid 1980s there has been an increase in incidence of invasive group A streptococcal (GAS) infections causing significant mortality and morbidity. Few data exist concerning the differences between adults and children.

We describe predisposing factors and clinical characteristics specific to age groups and analyze risk factors associated with mortality.

Methods

Retrospective analysis of medical records of all adults and children admitted for an invasive GAS infection in the Cliniques universitaires Saint-Luc between 2011 and 2016. Statistics analysis included chi-square test with Cook’s correction and Cox-Breslow regression.

Results

Eighty-four patients were included, 26 children (median age 1.6 years) old and 58 adults (median age 66.1 years). 90% of adults had 1 to 4 risk factors (RF). In contrast 70% of children had no RF although 19% developed invasive GAS infection following chickenpox. Meningitis represent 12% in children while no adult presented this form of infection ($p=0.0091$). Pleuresia was also typically a pediatric form (23% versus 5%; $p=0.0015$). Frequency of necrotizing fasciitis (17%) was similar among children and adults. Positive blood culture was not different in frequency for children and adults. Survival was evaluated at 10 weeks: 91% for children and 76% for adults. STSS (36%) was associated with mortality, and more frequent among adults ($p=0.037$). Elevated LDH ($p=0.0003$), CPK ($p=0.0004$), GOT ($p=0.0009$), GPT ($p=0.0051$) were all associated with mortality, with no significant difference between children and adults. Thirty-six percent required a surgical treatment for necrotic, osteoarticular, or valvular infection.

Conclusions
Meningitis and pleural infections were specifically pediatric presentations. Chickenpox remains the main risk factor for invasive GAS in children. Increased LDH, CPK, GOT, GPT were associated with mortality.
THE NEWBORN ALSO HAVE FLU

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Background

Children are the population with the highest incidence of influenza and they are the main source of disease spread. However, there are little cases of influenza in neonates reported, so we do not have enough information regarding the management of the disease in this vulnerable population group.

The aim of our study was to describe influenza cases upon neonatal patients admitted in a Neonatology Unit level III, during the last 7 years and to compare the management with other centers, described in the literature.

Methods

We conducted a descriptive, retrospective, longitudinal study, including consecutively admitted neonates with flu diagnosis, between 2009 and 2016, in a referral Division of Neonatology. Inclusion criteria: Term neonate younger than 1 month of life, and preterm neonate with a postconceptional age less than 44 weeks. The influenza diagnosis was defined as a patient with clinical signs and positive PCR for influenza virus.

Epidemiological, clinical, diagnostic, prognostic and therapeutic variables were evaluated.

Statistics: Statistical analysis with SPSS 2.0 program. Kolmogorov – Smirnov test is used to determine distribution of data. The qualitative variables were analyzed using the chi-square test, applying the student's t.

Results
Conclusions

In conclusion, neonatal influenza infection is uncommon but can be a serious illness. The family epidemic environment is a very important risk factor for the transmission. Half of our patients needed ventilation support in NICU, but neither of them received antiviral drugs. Regarding treatment, further studies are necessary.
TIME TO ADMINISTRATION OF FIRST ANTIBIOTICS IS ASSOCIATED WITH HOSPITAL LENGTH OF STAY IN CHILDREN WITH BACTERIAL INFECTIONS

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Background

Delay in antibiotic administration has been associated with increased mortality in adults with sepsis presenting to the emergency department (ED). Data in children are scarce and are skewed towards critically ill children. We assessed the time to first antibiotics (TTFA) in children presenting to the ED with a bacterial infection, and studied the association with outcome.

Methods

Non-academic, single-center, retrospective study in children admitted with a bacterial infection between June 2013 and January 2018, defined as receiving antibiotics within 24 hours after ED registration and a subsequent in-hospital antibiotic therapy duration of at least 4 days. Primary outcome measure was death and/or PICU transfer, and secondary outcome measure was hospital length of stay.

Results

369 patients (202 (55%) male; median age 2.5y, IQR 5m-7y) classified as having a bacterial infection had a median TTFA of 3h20m (IQR 2h-5h). TTFA in children who died and/or were transferred to PICU (n=16, median 5h, IQR 2h-10h) did not differ significantly from children admitted to our hospital (n=353, median 3h, IQR 2h-5h, p=0.23). In the latter group, TTFA was significantly associated with hospital length of stay (n=353, Spearman’s rho 0.14, p<0.01).

Conclusions

Unlike in adults, the time to first antibiotics was not associated with death and/or PICU transfer in this small cohort of children presenting to the ED with a bacterial infection. However, we did find an association between TTFA and hospital length of stay. Future studies in larger cohorts should adjust for pre-existing morbidity and illness severity, and should assess whether implementation of care bundles to reduce TTFA could be beneficial.
01B. EDUCATION: RATIONAL USE OF ANTIBIOTICS


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²Karolinska University Hospital, Division for Pediatric Infectious Diseases, Stockholm, Sweden

Background

A retrospective study of repeated point prevalence surveys of antimicrobial use in a Swedish paediatric hospital 2003–2017 with the aim to evaluate trends in antibiotic use and to identify targets for improving the quality of antimicrobial treatment in our centre.

Methods

Single-day hospital-wide point prevalence survey conducted 8 times between 2003–2017 at Karolinska University Hospital. Children 0-17 year of age, who were paediatric inpatients at 8 am on the day of the survey, were included. Medical records were scrutinized for indications, type of antibiotic agents for prophylaxis, treatment of infections. Existence of guidelines was evaluated in 2017. Patients in the neonatal units were excluded.

Results

1102 patients were included, 384 patients had antimicrobial treatment.

The proportion of patients treated with antimicrobial therapy increased from 30% to over 45% in 2016 and 2017.

Hospital beds for pediatric patients decreased from 142 in 2003 to 91 in 2017 and beds at the pediatric intensive care unit declined from 2.7 to 1.6/100,000 children.

The bed occupancy was 71% in 2003 and 120% in 2017.

The proportion of antimicrobial treatment for CAI gradually decline from 55.5% to 26.5%, prophylactic treatment increased from 11.1 to 42.6% while HAI's has remained at 30%.

The main reason for antibiotic therapy was sepsis or fever without focus followed by intra-abdominal infections and pneumonia. Cephalosporins were the most frequently used antibiotics, constituting over 40% in 2003 to 2008, thereafter decreasing to 20% in 2017.

In 2017 guidelines for antimicrobial therapy were missing in 32.4%

Conclusions

The proportion of antimicrobial treatment increased mainly due to an increase of prophylactic treatment.

The role of an increasing bed occupancy is unknown.

Guidelines for antimicrobial treatment needs to be developed and evaluated.
16A. SCIENCE: TUBERCULOSIS

DRUG-RESISTANT AND MULTIDRUG-RESISTANT TUBERCULOSIS IN CHILDREN- GETTING TO KNOW OUR POPULATION

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¹Hospital Prof. Doutor Fernando Fonseca- EPE, Pediatrics, Amadora, Portugal

Background

Multidrug-resistant tuberculosis (MDR-TB)-resistance to at least both isoniazid and rifampicin- in children has been estimated in 3.2% worldwide and resistance to at least one first-line anti-TB drug (DR-TB) is reported in 17% of pediatric cases. We report data on pediatric DR and MDR-TB in a secondary care centre with a high percentage of immigrants from portuguese-speaking african countries in Amadora, Portugal.

Methods

We retrospectively analised data from children (0-17 years) admitted from 2000 to 2017 diagnosed with M. tuberculosis infection by culture (Lowenstein-Jensen and/or Bactec) in which the drug susceptibility test (DST) revealed drug resistance.

Results

We report 9 cases of DR-TB (15% of pediatric TB cases in our hospital). Five cases were female; median age was 15 (min 1; máx 17). Six children were African descendant, 3 of which born in Portugal. Two cases were MDR-TB and 1 was extensive drug resistant TB (XDR-TB). Four patients had identified source contacts, 1 contact had DR-TB. The clinical presentation was: pulmonary TB in 3 cases; cavitary pulmonar TB in 5 and pleural TB in one. Only one case was HIV+. Median length of hospital stay was 28 days (min 7; max 102). Median treatment duration was 9 months (min 5; max 21), with good adherence and outcome. Adverse effects of anti-TB drugs were mostly observed in MDR-TB/XDR-TB cases (medullary hypoplasia, synovitis, anemia, neutropenia and hypoacusia). One patient (not MDR-TB) had bronchiectasis as sequelae. There was no mortality.

Conclusions

Our results were similar to those found in previous studies. Second-line anti-TB therapy was associated with more adverse effects but also with a good outcome. Although culture and DST are the gold standard, molecular tests allow sooner detection of TB and multidrug-resistance.
E-POSTER VIEWING - MAY 28-JUNE 2 - EXHIBITION HOURS

10A. SCIENCE: FUNGAL INFECTIONS

EVALUATION OF A NEW DOSING REGIMEN OF INTRAVENOUS VORICONAZOLE FOR THE TREATMENT OF INVASIVE ASPERGILLOSIS IN PEDIATRIC IMMUNOCOMPROMISED PATIENTS: THERAPEUTIC DRUG MONITORING AND SAFETY

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²Universidad de Chile, Pediatria y Cirugia Oriente, Santiago, Chile
³Hospital Dr. Luis Calvo Mackenna, Tmo, Santiago, Chile

Background

There are several recommendations for the dosage of voriconazole (VCZ) for the treatment of invasive aspergillosis fractionated in two daily (BID) doses in pediatrics. In immunocompromised children with suspected invasive aspergillosis, achieve early drug levels (DLs) of VCZ ≥ 1 ug/mL, is associated with lower mortality. In this context we proposed that start conventional doses of VCZ IV fractionated three times a day would be related to better DL. With the objective of evaluate and compare the safety and DLs of VCZ, fractionated BID or three times a day (TID)

Methods

Retrospective study in patients with VCZ treatment, between January 2015 and July 2017, in the Oncology and Bone Marrow Transplant Units at Hospital Calvo Mackenna, Santiago, Chile. Were evaluated and compared according to dosage and range of age, considering the optimal DL ≥ 1ug/mL. Pharmacokinetic and safety profile variables were obtained.

Results

118 VCZ treatments were analyzed (53 patients), where 60 were BID (51%) and 58 TID (49%). Average age and weight among groups were: a) BID 7.4 years (SD: 4.6); 25.4kg (SD:16.1) b) TID 9.8 (SD 3.6); 31kg (SD:11.9). The main complication it was a liver function alteration; however, this was not statistically significant between the two groups. Visuals alterations such as photophobia and photo-sensibility were detected in 5/53 patients (9.4%). Drug levels and dosage for BID and TID per age are displayed on the table below.

Conclusions

The dosages TID in patients between 2-12 years achieved better DLs compared to conventional BID regimens, in equal daily doses. On the contrary, patients older than 12 years achieved better levels in conventional dosages of adults. Both regimes presented good security profiles.
LATE-ONSET SEPSIS (LOS) AND COLONISATION BY GRAM-NEGATIVE BACTERIA IN HOSPITALISED NEONATES IN A NEONATAL NETWORK: THE NeoHIEC-STUDY (ON BEHALF OF THE NeoHIEC CONSORTIUM, SOUTH-LONDON, UK)

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Paediatric Infectious Diseases Research Group- Institute for Infection and Immunity, London,
United Kingdom

Background

LOS due to Gram-negative bacteria (GNB) is an important cause of neonatal morbidity and mortality. With the aim of predicting and preventing LOS, neonatal units (NNUs) often conduct routine screening to assess GNB colonisation. To develop strategies to prevent and control LOS the NeoHIEC Study was undertaken in NNUs in the South-London (SL) neonatal network.

Methods

The NeoHIEC-Study is a large observational cohort study conducted in SL NNUs which aimed to describe colonisation with GNB in hospitalised neonates and the association with GNB bacteraemia. During the first 8 months of the study peri-anal swabs were collected, stored and analysed in batches. All identified GNB were subjected to antibiotic susceptibility testing using the BSAC methodology. Participating NNUs submitted details of invasive infection episodes to the neonIN (neonatal infection surveillance) database. A point prevalence survey on antibiotic-prescribing was also conducted monthly in each NNU.

Results

During the study period, 1851 swabs were collected and 1341 GNB isolated (Enterobacteriaceae: 1318). 29 episodes of GNB bacteraemia were reported (incidence 9.9/1000 NNU-admissions). Antibiotic prescribing data as well as pathogen distribution and antibiotic resistance for both
Colonisation and invasive episodes is shown in the Table.

<table>
<thead>
<tr>
<th>Most common Pathogens</th>
<th>Colonisation with GNB</th>
<th>Invasive infections with GNB</th>
<th>Antibiotic prescribing</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>N. Enterobacteriaceae spp n (%)</em></td>
<td>130 (39.5)</td>
<td>10 (34.5)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><em>E. Coli n (%)</em></td>
<td>37 (27.6)</td>
<td>11 (38)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><em>Enterobacter spp n (%)</em></td>
<td>282 (21.0)</td>
<td>5 (20.3)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><em>Citrobacter spp n (%)</em></td>
<td>75 (5.6)</td>
<td>0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><em>Serratia spp n (%)</em></td>
<td>20 (4.5)</td>
<td>0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><em>P. aeruginosa n (%)</em></td>
<td>13 (1.0)</td>
<td>3 (10.3)</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Colonisation with GNB</th>
<th>Invasive infections with GNB</th>
<th>Antibiotic prescribing</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Amoxicillin (%)</em></td>
<td>1123 (94.2%)</td>
<td>26/28 (92.8%)</td>
<td>4/46 (8.7)</td>
<td>n/s</td>
</tr>
<tr>
<td><em>Co-amoxiclav (%)</em></td>
<td>503 (37.5)</td>
<td>16/25 (64)</td>
<td>4/21 (19.0)</td>
<td>n/s</td>
</tr>
<tr>
<td><em>3rd generation Cephalosporins (%)</em></td>
<td>150 (11.2)</td>
<td>9/20 (45)</td>
<td>10/117 (8.5)</td>
<td>0.004</td>
</tr>
<tr>
<td><em>Gentamicin (%)</em></td>
<td>39 (2.9)</td>
<td>1/27 (3.7)</td>
<td>64/119 (53.8)</td>
<td>n/s</td>
</tr>
<tr>
<td><em>Ciprofloxacin (%)</em></td>
<td>100 (7.5)</td>
<td>5/24 (20.8)</td>
<td>Not prescribed</td>
<td>0.092</td>
</tr>
<tr>
<td><em>Tobramycin (%)</em></td>
<td>57 (4.5)</td>
<td>Not reported</td>
<td>Not prescribed</td>
<td>n/a</td>
</tr>
<tr>
<td><em>Aminoglycosides (%)</em></td>
<td>Not tested</td>
<td>0</td>
<td>Not prescribed</td>
<td>n/a</td>
</tr>
<tr>
<td><em>Piperacillin (%)</em></td>
<td>72 (5.4)</td>
<td>3/21 (14.3)</td>
<td>10/67 (14.9)</td>
<td>n/s</td>
</tr>
<tr>
<td><em>Carbenemase (%)</em></td>
<td>62 (4.6)</td>
<td>0</td>
<td>6/79 (7.6)</td>
<td>n/a</td>
</tr>
<tr>
<td><em>Colistin (%)</em></td>
<td>54 (4.1)</td>
<td>Not reported</td>
<td>Not prescribed</td>
<td>n/a</td>
</tr>
<tr>
<td><em>Trimethoprim (%)</em></td>
<td>253 (18.9)</td>
<td>6/12 (50)</td>
<td>Not prescribed</td>
<td>0.015</td>
</tr>
<tr>
<td><em>Chloramphenicol (%)</em></td>
<td>127 (9.5)</td>
<td>Not reported</td>
<td>Not prescribed</td>
<td>n/a</td>
</tr>
<tr>
<td><em>Benzylpenicillin (%)</em></td>
<td>Not tested</td>
<td>Not reported</td>
<td>49/119 (41.2)</td>
<td>n/a</td>
</tr>
<tr>
<td><em>Glycopeptides (%)</em></td>
<td>Not tested</td>
<td>Not reported</td>
<td>27/109 (24.8)</td>
<td>n/a</td>
</tr>
<tr>
<td><em>Metronidazole (%)</em></td>
<td>Not tested</td>
<td>Not reported</td>
<td>5/79 (6.3)</td>
<td>n/a</td>
</tr>
</tbody>
</table>

*p-value test was used to compare resistance to antibiotics between the colonization and bacteremia isolates (where applicable)

n/a: non-significant; n/a: non-applicable

Conclusions

Hospitalised neonates are frequently colonised with GNB while LOS with GNB is infrequent. Although routine swabbing can accurately predict the distribution of pathogens associated with LOS, its ability to reflect their antibiotic susceptibility is variable.

Clinical Trial Registration (Please input N/A if not registered)

N/A
Background

Audit. Respiratory Syncytial Virus (RSV), the most common cause of bronchiolitis in infants results in many hospitalizations, mainly in those with predisposing medical conditions. Administration of palivizumab (monoclonal antibody vaccine) reduces morbidity in this population and during the last 15 years in Israel has been administered routinely between November and March for patients at risk. Albeit, there is conflicting data concerning both efficiency of the vaccination and whom should receive it.

Objective: Characterization of RSV bronchiolitis severity in hospitalized infants in the era of palivizumab vaccination.

Methods

Retrospective chart review of infants hospitalized in a tertiary hospital with RSV confirmed bronchiolitis between 2015 and 2016. Four groups were delineated: 1. Those with an indication for vaccination whom were not vaccinated. 2. Infants with risk factors that are not included in the vaccination indications. 3. Healthy infants. 4. Those with an indication for vaccination that were vaccinated.

Results

During this period 427 infants were admitted. Average hospitalization duration was 6 days. Amongst group 1 the average hospitalization was 9 days versus 6.7 days in group 2 ($p<0.014$). Five percent of the admitted needed intensive care treatment versus 12.5% in group 2 ($p<0.001$). Five of the admissions were prior to the vaccination season and the number of admissions in October was 4-fold more than in March ($p<0.001$).

Conclusions

The morbidity burden in October was significantly greater than in March, similar to the trend observed in recent years, questioning the timing of the initial vaccine dose. Significant morbidity was observed in those infants with risk factors that are not included in the indications for vaccination raising the possible need for expanding indications for this vaccine. Guidelines should be dictated by local epidemiology.
DIAGNOSTIC ACCURACY OF DIGITAL RNA QUANTIFICATION VERSUS REAL-TIME PCR FOR THE DETECTION OF RESPIRATORY Syncytial VIRUS IN NASOPHARYNGEAL ASPIRATES FROM CHILDREN WITH ACUTE RESPIRATORY INFECTION


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3 Ribeirão Preto Medical School, Department of Biochemistry-Immunology- and Cell Biology, Salvador, Brazil
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6 Federal University of Bahia School of Medicine, Department of Pediatrics, Salvador, Brazil

Background

Virus-specific molecular assays such as real-time polymerase chain reaction (RT-PCR) are now considered the gold standard in the diagnosis of viral respiratory tract infections, but simultaneous detection of different pathogens is considered a major limitation. A multiplex digital method of RNA quantification, nCounter (NanoString Technologies), can overcome this disadvantage and identify, in a single reaction, the presence of different respiratory viruses. We aimed to evaluate the accuracy of nCounter to identify and quantify RSV-A and RSV-B in nasopharyngeal aspirates (NPA) of children (6-23-months) with acute respiratory infection (≤7 days).

Methods

NPA was collected at enrolment in a prospective cross-sectional study conducted in an Emergency Department from September 2009 to October 2013, in Salvador, Brazil. A quantitative RT-PCR with a subgroup-specific primer and probeset for RSVA and RSV-B was performed in parallel with a customized nCounter probeset containing viral targets in NPA.

Results

Of 559 NPA tested, RSV was detected by RT-PCR in 139 (24.9%), by nCounter in 122 (21.8%) and by any method in 158 (28.3%) cases. Sensitivity of nCounter was 74.3% (95% CI: 63.3%-82.9%) RSV-A and 77.6% (95% CI: 66.3%-85.9%) RSV-B; specificity was 98.4% (95% CI: 96.8%-99.2%) RSV-A and 97.8% (95% CI: 96.0%-98.8%) RSV-B; positive predictive value was 87.3% (95% CI: 76.9%-93.4%) RSV-A and 82.5% (95% CI: 71.4%-90.0%) RSV-B and negative predictive value was 96.1% (95% CI: 94.1%-97.5%), RSV-A and 96.9% (95% CI: 95.1%-98.2%), respectively, for RSV-A and RSV-B. Accuracy was 95.2% (95% CI: 93.1%-96.7%) for RSV-A and 95.3% (95% CI: 93.3%-96.9%) for RSV-B, while both methods significantly correlated for RSV-A (r=0.44, p=8x10^-5) and RSV-B (r=0.73, p=3x10^-12) quantification.
Conclusions

nCounter is highly accurate in detecting RSV-A/B in NPA. Robustness and high-throughput multiplexing indicate its use in large-scale epidemiological studies.

Clinical Trial Registration (Please input N/A if not registered)
ACUTE HYPOTONIA IN A 51 DAYS OLD INFANT WITH BOTULISM

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¹General Hospital of Kalamata, Pediatric, Kalamata, Greece
²General Hospital of Argolida, Pediatric, Argos, Greece

Title of Case(s)

ACUTE HYPOTONIA IN A 51 DAYS OLD INFANT WITH BOTULISM

Background

Hypotonia, a condition of decreased muscle tone, can be caused by many different reasons, such as neurological conditions, infections, genetic and metabolic disorders. Infant botulism is a rare condition caused by intestinal colonization with Clostridium botulinum and provokes intestinal immobility and progressive descending paralysis. The clinical presentation of a rare disease in the context of the differential diagnosis of acute hypotonia in infants intends to remind us the importance of the right medical history.

Case Presentation Summary

A 51-days-old, exclusively breastfeeding, girl presented in emergency department of a secondary hospital with a 5-day history of constipation, 3 days of poor breastfeeding and was described as being floppy. Her perinatal history was unremarkable. On physical examination, she was afebrile with stable vital signs. Moderate general condition, hypotonia, weak cry and intermittent irritability were observed. Her anterior fontanelle was flat and the rest of the examination was normal. On laboratory investigation hemogram, serum electrolytes, renal and liver function blood tests, CRP and urinary analysis were normal. An abdominal ultrasound was performed, with the suspicion of intussusception, which was excluded. 20 hours after admission she remained hypotonic, denying feeding with generalized and also facial weakness. Therefore she was transferred to a tertiary hospital for further investigation. Her situation was deteriorated within the first 2 days, needing admission in the NICU, where the diagnosis of infant botulism was suspected and subsequently investigated.

Learning Points/Discussion

In Greece during 2004 to 2015, only 1 laboratory-confirmed case of botulism was reported. Despite the relative rarity of infant botulism, this case illustrates the importance of maintaining a high degree of clinical suspicion to make a prompt diagnosis in infants with acute acquired hypotonia.
09C. SCIENCE: INFECTIONS IN IMMUNOCOMPROMISED AND TRANSPLANT RECIPIENTS

SEVERE INFECTIONS DURING THE TREATMENT OF CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Title of Case(s)

SEVERE INFECTIONS DURING THE TREATMENT OF CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

Background

Aim: To describe the incidence and type of severe infections (SIs) during the treatment of children with Acute Lymphoblastic Leukemia (ALL).

Case Presentation Summary

Patients – Methods: We evaluated the charts of 77 children (44 boys, 33 girls, median age 5.4 yo, range 1-16 yo, Standard Risk–SR:7, Intermediate Risk–IR:50, High Risk–HR:20) with ALL treated from 01/2013 to 12/2017 and we recorded the episodes of SIs during their treatment.

Results: Serious infections were seen in 36 patients (median age 5.9 yo). A total number of 54 SIs were recorded (in 11 patients, more than 1 episode). The incidence of at least one SI was found to be 16/44 (36%) among boys and 20/33 among girls (61%), \( p=0.04 \), whereas among SR, IR and HR patients was 2/7 (29%), 24/50 (48%) and 10/20 (50%) respectively, \( p=ns \). Regarding the age, no significant differences were detected. Most of the infection episodes (31) were recorded during the induction treatment. During the consolidation, re-induction and maintenance phase were recorded 2, 8 and 5 episodes respectively whereas during the high-risk protocols 8 cases were detected. Regarding the type of infection, we detected 37 (69%) episodes of Blood Stream Infection (BSI), 7 of severe local infection, influenza:2, fungemia:1, lung aspergillosis:2, herpes zoster:4 and 1 episode of appendicitis. One death attributed to infection (influenza H1N1) was detected in our group of patients.

Learning Points/Discussion

Almost half of ALL patients present at least one episode of SI. Most of the episodes are detected during the induction treatment whereas BSI is the most common type of infection. Girls are more likely to present SIs whereas the risk group and the age are not predictors of SIs.
RISK FACTORS FOR NECROTIZING ENTEROCOLITIS

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¹Serviço de Neonatologia B, Maternidade Bissaya Barreto- Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal

Background

Necrotizing enterocolitis (NEC) in very low birth weight (VLBW) infants has been associated with significant mortality and increased length stay and hospital costs.

Aims: To determine risk or protective factors for the development of necrotizing enterocolitis in VLBW infants.

Methods

Retrospective case-cohort study of VLBW infants hospitalized in a Neonatal Intensive Care Unit during 2005-2017 (13 years). Infants with confirmed diagnosis of NEC were evaluated and compared with a cohort without NEC. Statistical analysis included unadjusted and multivariable analyses. Congenital malformations were excluded. Statistical analysis was performed using the SPSS package.

Results

A total of 592 VLBW infants were admitted; 29 (4.8%) infants developed NEC. In univariate analysis, we identified a difference between two groups (NEC vs without NEC) for: birth weight (892±253g vs 1130±260g; p<0.001), gestational age (26.8±1.8 vs 29.2±2.4; p<0.001), CRIB>5 (p=0.001), patent ductus arteriosus (p<0.001), intubation in the delivery room (p=0.012), bronchopulmonary dysplasia (p=0.001), red cell transfusion (p<0.001), mechanical ventilation > 7 days (p<0.001), antibiotic therapy on day one (p=0.001), hypotension (p<0.001). Protective factors identified were enteral feeding in the first 3 days (p<0.001) and breast milk (p<0.001). After logistic regression, only hypotension (ORa: 3.4; 95% 1.4-8.3; p=0.008) and breast milk (ORa: 3.1; 95% 1.2 -7.8; p=0.017) remained independent factors for NEC.

Conclusions

Breastfeeding should be actively promoted and supported as a key strategy to prevent NEC.
ACUTE BACTERIAL OSTEOMYELITIS: CASES REPORT, 2013-2016, IN A SECONDARY HOSPITAL, VOLOS, GREECE

A. Anastasiou-Katsiardani1, M. Gianniki1, T. Tsikrikas1, D. Papakyritsi1, K. Velali1, A. Stelianidi1, M. Sarigianni1

1"Achilopouleio"- General Hospital of Volos, Pediatric Clinic, Volos, Greece

Title of Case(s)

ACUTE BACTERIAL OSTEOMYELITIS: CASES REPORT, 2013-2016, IN A SECONDARY HOSPITAL, VOLOS, GREECE

Background

Acute bacterial osteomyelitis is the inflammation of the bone of less than two weeks duration which typically spreads heamatogenously, most common affecting the long bones. The major cause of bone infection is Staphylococcus aureus. Not only can osteomyelitis' clinical presentation and imaging be highly variable, but also blood culture can be negative (60%) of histologically proven osteomyelitis cases. It is a potentially limb-and life-threatening condition, requiring prompt diagnosis and treatment.

Case Presentation Summary

Records of 4 male and 1 female paediatric patients (mean age 7.2 years) who underwent medical treatment alone (n=4) or combined with surgery (n=1) for acute bacterial osteomyelitis of ankle, hip and heel were reviewed in our Hospital during 2013-2016. All patients presented with high fever, lameness and topical symptoms and signs, such as pain, tenderness, redness and warmth. Diagnosis was made by blood culture, imaging, and/or clinical presentation. Medical treatment included antibiotics and supportive care. Surgery was indicated, when there was poor response to antibiotics, and ranged from percutaneous drainage to wound debridement and wash out. Resolution of osteomyelitis was based on improvement in clinical signs and inflammatory markers. Of the 5 patients, S aureus was isolated in 2, streptococcus pyogenes in 1, and no organism in 2. Prescribed antibiotics included amoxicillin/clavulanate, clindamycin, ceftriaxone, vancomycin and ampicillin. The mean±SD time from admission to diagnosis was 3±1 days. The mean±SD follow-up period was 12±2 months. No patient had any complications.

Learning Points/Discussion

Acute bacterial osteomyelitis is an entity than should be taken into concideration when fever, lameness and topical symptoms are investigates. Delayed treatment being connected to sepsis, bony deformity, and growth retardation, prompt diagnosis and treatment are of great value.
MENINGOCOCCAL SEPSIS AND SEPTIC SHOCK: A CASE REPORT
A. Reis E Melo¹, I. Medeiros², C. Ferreira², M. Branco², T. Lopes², D. Soares², M. Grilo², T. Cunha da Mota², A. Ribeiro²
¹Hospital Pediátrico Integrado- Centro Hospitalar São João, Pediatrics, Porto, Portugal
²Hospital Pediátrico Integrado- Centro Hospitalar São João, Pediatric Intensive Care, Porto, Portugal

Title of Case(s)

Meningococcal sepsis and septic shock: a case report

Background

*Neisseria meningitidis* is a Gram-negative bacteria that can be highly pathogenic in humans and responsible for life-threatening diseases in pediatric patients. Nowadays, the main serogroup is B, which is not covered by portuguese vaccinal program, but is available for purchase.

Case Presentation Summary
A 5-month old girl presented at emergency department with high fever (T 40ºC), vomiting and nasal congestion. She had no abnormalities on physical exam and was discharged home with diagnosis of a viral infection, after excluding an urinary infection. Ten hours later, she was admitted with prostration and purpuric lesions. The child rapidly progressed to cold shock, starting ventilator, ionotropic support, ceftriaxone and vancomycin. She was admitted in intensive care unit with refractory shock, disseminated intravascular coagulation and hemorrhagic eruption. Volume expansion and transfusion of multiple blood components were needed and inotropic support was adjusted (adrenaline, noradrenaline and milrinone). In the first 24 hours, she presented renal insufficiency with anasarca, initiating hemofiltration. After this, the child started to improve, maintaining hemofiltration for 7 days, ventilatory and inotropic support for 10 days. Thoracic and abdominal hemorrhagic lesions improved, but fingers’ hemorrhagic lesions evolved to necrosis, with risk of amputation. *Neisseria meningitidis* serogroup B was isolated on blood cultures.

**Learning Points/Discussion**

Meningococcal infection has a high mortality and morbidity in children. Aggressive initial shock approach, early antibiotics and precocious referral are potential factors with impact in reducing its mortality. Vaccination with this serogroup may have a role in prevention of this serious illness.
Probable case of CAEBV associated in evolution with a MS-like syndrome in a 12 year old girl

Background

Rare patients infected with EBV (Epstein-Barr virus) develop a life-threatening condition termed Chronic active Epstein-Barr infection (CAEBV). It is a progressive lymphoproliferative disorder with a duration of > 6 months, characterized by markedly elevated levels of antibody to EBV or EBV DNA in the blood, infiltration of tissues with lymphocytes, the absence of any other immunosuppressive condition and elevated EBV-DNA, RNA or protein in affected tissues. The only treatment reported successful in literature is allogeneic HSCT (hematopoietic stem cell transplantation).

Case Presentation Summary

We present a rare case of a 12 year old girl, with acute EBV infection at the age of 6 month that triggered a macrophage activation syndrome with fulminant acute hepatic failure. Since then she has had constantly high titers of EBV antibody titers, hepatosplenomegaly, pancytopenia and a hepatic biopsy showed lymphocyte infiltration probably associated with chronic viral infection. Unfortunately no EBV DNA test from tissue is available in our country. Since the age of 4 until now she started developing atypical neurological signs, corresponding with several episodes of cerebral demyelination including cervical transverse myelitis. The treatment used was corticoids with clinical recovery every time but followed by relapses.

Learning Points/Discussion

In conclusion, in the evolution of an infection with EBV, CAEBV may develop with the possibility of further neurological MS-like syndrome being associated.
Bacteremia is now an uncommon presentation in developed countries due to immunisation against the most common causal bacteria. Local knowledge is important for appropriate empiric antibiotic recommendation.

Methods

A Retrospective analysis of bacteremia in children <16 years of age was conducted at Derbyshire children's hospital between 1 January 2012 and 31 December 2016. Data on etiology, time from incubation to positivity and antimicrobial susceptibility was recorded.

Results

A total of 431 bacteria were isolated by blood culture. Most 337 (78%) were Gram positive bacteria and 94 (22%) were Gram negative bacteria. Amongst the Gram positive bacteria, majority were staphylococcal species; Coagulase negative staphylococcus 102 (30%), Staphylococcus aureus 54 (16%), Staphylococcus epidermidis 36 (11%), other staphylococci 32 (9%) and streptococcal species; Enterococci 24 (7%), Group A streptococci 11 (3%) and other streptococci 49 (15%). There were only 5 cases of Streptococcus pneumoniae. Amongst the Gram negative bacteria, Escherichia coli 23 (24%), Klebsiella spp. 20 (21%), Pseudomonas spp. 16 (17%) accounted for majority of the cases (n=65, 69%).

The median time (IQR) from incubation to positivity for S. pneumoniae was 10 hours (8.8-10.3), for E. coli it was 7.2 hours (5.3-11hrs) and for N. meningitides it was 17 hours (14.9-23.2). There was no resistant pneumococcus or meningococcus.

Conclusions

Vaccine preventable bacteria (pneumococcus and meningococcus) are now rare causes of bacteremia in Derbyshire children. The time from incubation to positivity for these two vaccine preventable bacteria and E. coli was less than 24 hours.

Universal immunisation has changed the etiology of bacteremia in children. Reducing time to incubation could result in earlier identification. Understanding the antibiotic susceptibility of the other bacteria is important in selecting appropriate empiric antibiotics.
INVASIVE STAPHYLOCOCCUS AUREUS INFECTIONS IN CHILDREN IN CRETE

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Background

Invasive infections caused by Staphylococcus aureus are uncommon in children. We review the epidemiology, clinical features and outcomes of children with culture-proven invasive S. aureus infections in a referral paediatric center over a 10-year period.

Methods

Cases of S. aureus septicaemia, osteomyelitis, pneumonia and CNS infection in children aged less than 16 years were reviewed from January 2008 to December 2017. Community and health-care associated isolates were further analyzed looking into clinical characteristics of invasive MRSA and MSSA infections.

Results

A total of 42 invasive infections (22 community-acquired, 14 hospital-acquired and 6 community-onset, healthcare-associated) were identified from 39 patients. No gender predominance was noted, no clustering of cases. Invasive infections were more common among children aged less than 5 years and adolescents. Septicaemia, pneumonia, osteomyelitis and CNS infection were noted in 20, 9, 9, and 2 episodes respectively. Twenty-three percent of patients had underlying comorbidities (14/42, 33%) including previous operations, indwelling catheters and ventriculoperitoneal shunt procedures. Thirty percent of septicaemic patients (6/20) had indwelling catheters or had undergone surgical operations. Pneumonia was more common among children with congenital malformations or cystic fibrosis (6/9). Methicillin-resistant S. aureus (MRSA) was found in 19/42 episodes (45.2%). Incidence was estimated at 7.8 infections per 100,000 hospitalized children. Length of hospital stay did not differ significantly between MRSA and MSSA strains and was similar for community and healthcare acquired infections. There was no mortality associated with invasive S. aureus infections.

Conclusions

The incidence of invasive S. aureus infections is low in children. Clinical characteristics and outcomes in invasive S aureus infection are similar among invasive MRSA and MSSA infections. They often affect children with co-morbidities and are commonly healthcare-associated.
An outbreak of Serratia marcescens in a mixed paediatric and neonatal intensive care unit: risk factors associated with colonization or infection

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Background

S. marcescens is a gram-negative rod of the Enterobacteriaceae family, originally considered to be a non-pathogenic saprophytic water organism. Since several years, it is a well-recognised opportunistic pathogen responsible for endemic nosocomial infections in immuno-compromised hosts especially in neonatal intensive care units. This study aims to identify risk factors for S. marcescens’ acquisition during an outbreak in a mixed paediatric and neonatal intensive care units.

Methods

It was an epidemiological, observational, retrospective, mono-centric, case-control study. Cases (n = 10) were children with at least one positive sample for S. marcescens more than 48 hours after their admission, during the outbreak that occurred in 2016. Controls (n = 40) were patients hospitalized, during the same period, with one or two negative samples for S. marcescens. A multivariate analysis was performed using a logistic regression model for every significant variables in univariate analysis (p<0.05).

Results

Demographic data were comparable in both groups. Low birth weight (OR 0.998 [0.996-1], p =0.048), delivery by caesarean section (OR 9.947 [1.15-86.001], p =0.037), number of central catheters (OR 2.578 [1.179-5.638], p =0.018), use of anti-acid treatment (OR 4.714 [1.069-20.789], p =0.041) and its duration (OR 1.338 [1.028-1.742], p =0.031) appeared as risk factors for acquisition of S. marcescens in univariate analysis. None of these variables were significant in multivariate analysis. Every child infected or colonized with S. marcescens fully recovered.

Conclusions

We didn’t show any risk factor for S. marcescens’ acquisition in multivariate analysis. However, in univariate analysis, low birth weight, central catheter exposure, delivery by caesarean section, use and extended anti-acid treatment appeared as risk factors, and reflect especially severity and vulnerability of neonates. It shows how important it is to evaluate, daily, catheters and anti-acid treatment.
CRITICAL ROLE OF NASAL TISSUE-RESIDENT MEMORY CD4+ TH17 CELLS IN VACCINE-INDUCED PROTECTION AGAINST PNEUMOCOCCAL COLONIZATION

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Background

Because pneumococcal pathogenesis begins with nasopharyngeal colonization, efforts have focused on elucidating the mechanisms of immunity to colonization. In mice, we showed that acquired immunity to colonization following subcutaneous immunization with unencapsulated, killed pneumococci and alum (WCV), is antibody-independent and CD4+ Th17-cell dependent. Surprisingly, we found that transfer of peripheral CD4+ cells from immunized to naïve mice does not confer protection, and systemic Th17 responses do not predict resistance to colonization, raising the hypothesis that protection is conferred by tissue resident effector memory (Trm) Th17 cells rather than systemic T cells.

Methods

To test this hypothesis, we tried to identify and localize Trm in the nasopharynx of immunized mice. We evaluated the impact of administration of FTY720, an S1P1 inhibitor that blocks lymphocyte trafficking out of lymph nodes, on adult and neonatal mice immunized weeks earlier with WCV. We performed immunohistological studies to identify Trm cells, and confirm resistance to FTY720.

Results

Treatment with FTY720 eliminated circulating lymphocytes, but did not interfere with vaccine-mediated protection, whereas systemic anti-CD4+ antibodies completely abrogated protection. We identified these FTY720-resistant CD4+ T cells in the nasal tissues of mice. Studies in neonatal mice showed that a single dose of WCV conferred significant protection against carriage, that was preserved despite FTY720 treatment. Overall, these results strongly suggest that nasal Trm are sufficient for protection.

Conclusions

We propose a highly novel model of protection against pneumococcal colonization by WCV (and likely natural exposure): effector cells generated by immunization migrate to the nose and differentiate into Trm. Upon pneumococcal exposure, these Trm recruit and activate neutrophils to clear the organism. These findings have important implications for the development of novel vaccines against nasal colonization by pneumococcus and other pathogens.

Clinical Trial Registration (Please input N/A if not registered)
N/A
STREPTOCOCCUS PYOGENES IN THE THROAT INFECTIONS IN CHILDREN IN MOROCCO

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Background

Streptococcus pyogenes, or group A streptococcus (GAS), is a human pathogen that causes a wide spectrum of diseases, ranging from relatively benign infections to severe invasive diseases. It can also lead to serious non-suppurative sequelae. In this study we report the prevalence of the throat infections to Streptococcus pyogenes in children in Morocco.

Methods

A prospective study was conducted from February 2017 to January 2018 in a health center in Fez city. One hundred and sixty six patients (145 children and 21 adults) were the object of samplings by throat cotton swab, for researching the group A Streptococcus.

Results

The mean age in children was eight years, there was a masculin predominance (sex ratio:1.1). The mean age in adult was twenty one years, there was a feminin predominance (sex ratio:0.5). One hundred and sixty-six throat swabs were practice: 142 samples for acute tonsillitis and 24 for pharyngitis. No S. pyogenes were identified in cases of pharyngitis. Among the 142 samples of tonsillitis, 11 cases of GAS were identified by the standard microbiological method, 4 cases of Group C Streptococcus and 3 cases of Group G streptococcus. The molecular study identified only 6 cases of GAS with the emm gene and 2 cases of GGS. The prevalence of GAS in children was 4.23%. Of the fifty-six children with exudative pharyngitis, 98.2% are treated with an antibiotic. Children with tonsillitis are also treated with antibiotics (50.9%).

Conclusions

The prevalence of GAS tonsilitis was low compared to the patients proposed for antibiotic treatment. In view of these results, a new treatment strategy for tonsillitis is needed in Morocco. It would be interesting to recommend a Rapid Diagnostic Test before any therapeutic decision.
Spinal epidural abscess as a complication of *Staphylococcus aureus* bacteremia

**Background**

A pyogenic spinal epidural abscess is a bacterial infection in the epidural space that results in the accumulation of purulent fluid or infected granulation tissue. Predisposing factors include immunosuppression, spinal procedures, and local site infections such as vertebral osteomyelitis and paraspinal abscess. Here we present a case with *Staphylococcus aureus* bacteremia complicated by meningitis and spinal abscess.

**Case Presentation Summary**

A 6 month old child presented with a 1 month history of fever and discomfort. Dizziness and lethargy were observed 2 days before admission. He had a history of otitis media and bronchiolitis. A lumbar puncture was performed revealing 850 leukocytes (90% neutrophils), protein 2 g/l, and glucose 5 mmol/l in cerebrospinal fluid (CSF) examination. Vancomycin and ceftriaxone were initiated with a diagnosis of acute bacterial meningitis. *Staphylococcus aureus* was isolated from both blood and CSF cultures. Ceftriaxone was stopped and rifampicin was added to vancomycin. He had mild weakness noted on right hand. Magnetic resonance imaging (MRI) of brain and spinal cord revealed extensive epidural abscess at cervical, thoracal, and lumbosacral spinal regions. Dermal sinus tract or granulomatous otitis were not identified. Blood samples from the father and the patient were studied for dihydrorhodamine test but were not compatible for chronic granulomatous disease (CGD). Serum immunoglobulins and lymphocyte subset analysis were normal. Surgical decompression was performed. Antibiotics were modified as ampicillin-sulbactam since the isolate was found to be methicillin susceptible (MSSA). Clinical condition of the patient improved.

**Learning Points/Discussion**

Community-acquired MSSA meningitis is a serious infection, occurring in patients without risk factors. Hematogenous dissemination may lead to multiple tissue infection. A long course of antibiotics is needed to treat meningitis but also extraneurological localizations.
MANAGEMENT OF FEBRILE NEUTROPENIA IN HEALTHY PATIENTS

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Background

Febrile neutropenia in the oncological patient is a widely studied entity. However, when it is presented in a healthy patient, the management is not so defined. This patients are often hospitalized and treated with antibiotics without an evidence of infection. We investigate the infectious causes and clinical features of febrile neutropenia in healthy children.

Methods

This is a observational, retrospective study of a tertiary children’s hospital. We study patients 0-14 years with severe or moderate neutropenia (absolute neutrophil count <1,000 cells/µL) diagnosed in Pediatric Emergencies from January 2015 to January 2016.

Results

We found 60 patients. 81.7 % with moderate neutropenia. Median age was 16 months (IQR 8.25-41.5). Respiratory symptoms were the most frequent (71%).

Infectious agent was identified in 43%; 88% were viruses and 12% bacterial agents. The most frequent virus was influenza A (41%), followed by herpes 6 (19%) and influenza B (14%).

25% of the patients were admitted; 66.5% with a broad-spectrum antibiotic.

The hospitalization and antibiotic prescription was higher in patients with severe neutropenia with statistically significant difference (10% vs 72% p: 0.05 and 16% vs 63.3% p: 0.013). Median hospitalization was 4 days. Only 2 patients were diagnosed with potentially serious bacterial infection (SBI).

Follow-up was performed in 63.3%, with resolution of neutropenia in 98% with a median of 12.5 days (RIC 6.25-20.25). Only one patient was diagnosed with chronic autoimmune neutropenia.

Conclusions

Our study support the mild clinical course of febrile neutropenia in a previously immunocompetent infant, with a low prevalence of SBI. We mainly found moderate transient neutropenia associated to mild viral illness. A conservative treatment is possible in most healthy patients with neutropenia although larger studies are necessary to optimize the management.
LUCKY ON HOLIDAY? - A TEENAGER WITH KAWASAKI DISEASE

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**Title of Case(s)**

Kawasaki Disease

**Background**

Kawasaki disease (KD) is the second most common vasculitis of childhood, particularly affecting the coronary arteries. Diagnosis is based on characteristic clinical signs and affects primarily children younger than 5-years-of-age. Nevertheless, adolescents/young adults involved present higher risk for immunoglobulin (IVIG) resistance. Treatment with IVIG markedly reduces the incidence of coronary aneurism formation.

**Case Presentation Summary**

A healthy 15-year-old male from Venezuela, in Portugal on holiday, presented with high fever, odynophagia and maculopapular exanthema and was treated with benzylpenicillin for presumed scarlet fever. At D5 returned with persistent symptoms, vomiting and diarrhea, without cough, rhinorrhea or Koplik’s spots. He received proper measles vaccination. Laboratory tests showed normal leukocyte and platelet counts, CRP 363 mg/L, elevated transaminases, mild leukocyturia and negative urine culture. Due to ill appearance he was admitted for suspected bacteremia/toxic shock syndrome and treated with ceftriaxone and clindamycin. Coprocultures, blood cultures, serologic tests for EBV and CMV, PCR in urine and nasopharyngeal secretions for measles and ASO titre were negative. Later, bilateral conjunctivitis and extremity changes appeared, which together with pharyngeal erythema, persistent fever and rash constituted criteria for KD diagnosis. With 7 days of fever he received IVIG and aspirin but after 48h of apyrexia became febrile again. A second dose of IVIG achieved complete response. Cardiac ultrasound and EKG were unremarkable. He was discharged with low-dose aspirin returning to Venezuela 2 weeks later, losing follow-up.

**Learning Points/Discussion**

A high index of suspicion is necessary to identify KD cases in adolescents, especially since this age group has a higher risk for adverse outcomes. In countries where IVIG is unavailable, such as Venezuela nowadays, treating KD and reducing cardiac complications is a challenge, as there are currently no other proven treatments.
Background and Objective

Acute Otitis Media (AOM) is a leading cause of healthcare resource and antibiotic use, surgical intervention and hearing loss in children under 5. While Pneumococcal Conjugate Vaccines (PCV) effectively reduce AOM incidence, PCV cost-effectiveness analyses (CEA) may not consider the full AOM impact, including caregiver burden. We therefore reviewed the literature on burden and impaired quality of life (QoL) for caregiver's of children with AOM and their consideration in PCV CEAs.

Methods

Structured searches of Medline, Embase and the Cochrane Library (29.10.2007 to 29.10.2017) and 3 conference websites (past 2 years) identified published AOM articles and abstracts. Caregiver burden and/or QoL studies, together with CEAs for the 10- and 13-valent pneumococcal vaccines, were identified. QoL themes were grouped into high, moderate or low impact on caregiver QoL and ranked according to mean impact score.

Learning Points Discussion

3,298 articles were identified and screened. Of those reporting caregiver burden, 9 were included. 18 CEAs reported sufficient information on inputs for inclusion.

Caregiver burden was categorised into 4 main groups (Table). Caregiver QoL was most reported, although scales used varied between studies precluding direct comparisons. Lack of/disturbed sleep and its consequences had the greatest impact on QoL scores. Economic burden such as absenteeism from work (15.9–20.9 mean hours/recent episode), loss of earnings (mean USD96–114/recent episode) and productivity loss (mean 3.6 hours/recent episode) were reported.

Few PCV CEAs considered caregiver burden, and those doing so only considered absenteeism (7/18).

Although limited studies have evaluated caregiver burden in AOM, this review highlights that the impact of AOM on caregivers is potentially substantial. CEAs evaluating impact of PCVs did not fully account for societal costs of AOM, likely significantly underestimating the overall value of pneumococcal vaccination programmes.
<table>
<thead>
<tr>
<th>Caregiver burden outcomes reported</th>
<th>Studies reporting outcomes (n)</th>
<th>QoL categories impact on overall QoL</th>
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<tr>
<td></td>
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<td>High Impact† (n)</td>
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<tr>
<td>Absenteeism from work</td>
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<tr>
<td>Disruption of family life</td>
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†High/moderate/low impact on caregiver QoL was defined for individual scales used. Due to differences in style of reporting, not all themes could be classified as high/moderate/low impact for all studies reporting caregiver QoL.
THE EFFECT OF SEASONAL INFLUENZA IMMUNISATION ON HIV-1 RESERVOIR IN PERINATALLY HIV-INFECTED CHILDREN

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Background

HIV-infected children are at increased risk for complicated influenza infections, and therefore vaccination with the inactivated seasonal Influenza Vaccine (IIV) is an important priority. However, transient increases in HIV viral load (VL) and decreases of reservoir markers such as HIV-DNA seen post-immunisation in recent studies have caused concerns regarding vaccine safety in this population.

Objectives: We aimed to determine the impact of IIV on the HIV-reservoir in the Greek cohort of perinatally-infected children. To this end we enumerated HIV-DNA before and 1 month post-immunisation.

Methods

15 vertically HIV-infected children on suppressive ART were enrolled. All patients have received ART since birth and 14/15 had undetectable VL at the time of the study. All patients received 1 dose of the trivalent IIV 2015/2016 between November 2015 and January 2016. Blood samples were drawn before and 1 month post-immunisation. PBMCs were isolated and frozen before transfer to UCL, London for quantification of HIV-DNA.

Results

Plasma VL remained at baseline levels post-immunisation with IIV. HIV-DNA was lower at 1 month post-vaccination than at baseline (mean difference: -234.5, 95% CI: -549 – 79.97 c/10⁶ PBMCs); however this difference was not statistically significant (p=0.078, Wilcoxon matched-pairs signed rank test). There were no local or systemic adverse events post-immunisation.

Conclusions

Immunisation with IIV did not affect plasma HIV VL in this cohort of vertically HIV-infected children. The moderate decrease in HIV-DNA seen in this small cohort, though not statistically significant, is in accordance with previous reports of HIV-reservoir mobilisation by routine immunisations. Large randomised controlled studies are necessary in order to evaluate the effect of immunisations on the latent reservoir of HIV in vertically-infected children on ART.

Clinical Trial Registration (Please input N/A if not registered)

N/A
Title of Case(s)

Acute Mastoiditis and the Importance of Pathogen Identification: Two Case Reports

Background

Acute mastoiditis (AM) is a complication of acute otitis media. Clinical spectrum of AM ranges from absence of symptoms with spontaneous resolution to progressive disease with life-threatening complications.

Case Presentation Summary

Two cases of bilateral mastoiditis in 8 months-old children were diagnosed at two weeks interval in a secondary Hospital in Brussels. Both patients were treated by intravenous 3rd generation cephalosporin.

In our first case, no ear pus sample was taken in order to isolate infecting pathogen and antibiotherapy was started immediately. However, the patient presented an adequate treatment response, becoming afebrile and presenting a decrease of the retroauricular swelling within the first 24 hours following antibiotherapy.

On the second patient, we performed a tympanocentesis before starting antibiotherapy. This patient didn’t show adequate treatment response within 48 hours post antibiotic administration and continued with high fever, toxic aspect and the apparition of a macular rash with redness, tenderness and heat of the upper and lower limbs.

The ear puss culture returned positive for Group A Streptococcus. We considered the macular rash and swelling as suggestive for a Streptococcal-toxic-shock-syndrome with diffuse capillary leak and added Clindamycin to the treatment. The response to the bitherapy was favorable with rapid apyrexia as well as decrease of the rash and biological inflammation.

Learning Points/Discussion

This case report highlights the importance of isolating the pathogen in AM in order to guide appropriate antibiotherapy. Given the variety of organisms causing AM and the potential for antibiotic resistance, the importance of isolating the germ cannot be overemphasized.
Specimens should be obtained from the middle ear by tympanocentesis through an intact eardrum or by aspiration through a tympanostomy tube or perforation.
CASE PRESENTATION OF A MALE TEENAGER WITH BACTERIAL-MENINGITIS AS A RESULT OF EXTENSION OF A SUBDURAL EMPYEMA CAUSED BY CHRONIC SINUSITIS

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Title of Case(s)

CASE PRESENTATION OF A MALE TEENAGER WITH BACTERIAL-MENINGITIS AS A RESULT OF EXTENSION OF A SUBDURAL EMPYEMA CAUSED BY CHRONIC SINUSITIS

Background

The complications of acute and chronic sinus infection are defined as any extension of local disease into adjacent structures. Some complications are orbital cellulitis, meningitis, subdural empyema, intracerebral and epidural abscesses, cavernous or superior sagittal sinus thrombosis and subperi orbital abscesses and osteomyelitis. The most common bacteria implicated in complicated bacterial sinusitis are Staphylococcus aureus and Streptococcus anginosus.

Case Presentation Summary

13-year-old male teenager presented with fever, frontal-headache, right-eye redness and photophobia. Close questioning reveals a history of nasal congestion with clear-nasal discharge for 3 months. During clinical examination, slight neck stiffness, red throat with halitosis, green postnasal discharge and tenderness to pressure on the forehead. Blood tests revealed WBC:13200/μl, Neut:85,1%, CRP:148,44mg/lt. We started treating with IV amoxicillin-clavulanate. Due to continuation of severe frontal-headache and vomiting, brain CT was performed:right frontal sinusitis, with a suspect of fluid collection nearby right frontal-lobe. The antibiotic therapy was switched to IV ceftriaxone and vancomycin. Brain MRI confirmed the diagnosis of subdural empyema and meningitis. CSF analysis revealed WBC:220c/mm3, Neut:90%, Leu:75,46mg/dl, Glu:85mg/dl, D(x):137mg/dl. Blood culture grew Streptococcus intermedius (an aerotolerant anaerobic commensal bacterium, member of the Streptococcus anginosus group). The patient was transferred to the nearest third-grade-hospital's neurosurgical clinic, craniotomy and empyema drainage was performed, he was intubated and stayed in Childrens' ICU for further treatment.

Learning Points/Discussion

Bacteria responsible for complications of chronic sinusitis are usually virulent and can cause clinical situations with very high mortality rate, such as meningitis. Therefore, rapid and appropriate differential diagnosis, in combination to appropriate and rapid laboratory examinations too, and onset of proper antibiotic therapy are crucial for our patients' lives.
Two Cases of Sternal Kingella Kingae Osteomyelitis

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Title of Case(s)

Two Cases of Sternal Kingella Kingae Osteomyelitis

Background

Kingella kingae has increasingly been associated with osteoarticular infections in preschool children. Often it is regarded as a subacute infection with less inflammatory reaction than Gram-positive infections like S. aureus. Sternal osteomyelitis is rarely reported in the literature. We here report two cases with sternal osteomyelitis due to K. kingae.

Case Presentation Summary
Case 1. A 21 months old boy was admitted due to parasternal swelling since 10 days. No fever was reported and CRP peaked at 21 mg/L. Total WBC were $12 \times 10^9$/L. Ultrasound and MRI was performed (Figure 1). Fine needle aspirate was negative in cultures but 16S rRNA Gene Sequencing detected *K. kingae*. He was treated with intravenous cefotaxime for four days and amoxicillin/clavulanate for a total of four weeks. Follow-up ultrasound showed regression of the infection.

Case 2. An 8 months old girl presented to the paediatric ER with fever and a swelling at the lower part of the sternum. CRP peaked at 156 mg/L and total WBCs were $20 \times 10^9$/L. Ultrasound showed an abscess directly adjacent to the sternum. Culture from the aspirate was negative but 16S rRNA Gene Sequencing detected *K. kingae*. She was treated with intravenous cefotaxime for six days and
amoxicillin/clavulanate for an additional four weeks. CRP normalised in a week and follow-up ultrasound showed partial resolution of the abscess.

Learning Points/Discussion

Sternal *K. kingae* osteomyelitis is rare. The cases presented here show that *K. kingae* sternal osteomyelitis may present with mild symptoms and low-grade inflammation (Case 1) as well as with fever and intense inflammation. PCR is needed for the detection of *K. kingae.*
The need for greater promotion of immunization, which has proven to be a sovereign method for eradicating childhood infectious diseases around the world and opposing anti-vaccine propaganda by pediatricians. The impact of immunization over the reduction and eradication of infectious diseases and reducing the negative impact of the anti-vaccine media campaign.

Methods

Data from infectious diseases reports and immunization reports of the patients in our office for the period of 2 years (2016-2017) have been used. An analytical, descriptive and comparative method is used for processing.

Results

In accordance with the immunization program in Macedonia, out of a total of 438 children (2016-2017), aged 0 to 6 years, 95% of the children were successfully vaccinated. For the period of 2 years we have registered 3 cases of Morbili, 1 case of Rubella, 3 of Parotitis and 180 cases of Varicella.

The results clearly show a significant number of Varicella for which no immunization is carried out, while infant fever is registered only sporadically. Other childhood diseases such as Poliomyelitis, Tetanus and Perthusis are considered to be eradicated in Macedonia. No child with Tuberculosis has not been registered.

Due to the overwhelming media anti-vaccination campaign, there is also a slight decrease in the percentage of regularly vaccinated children. In 2010 the percentage of vaccinations in our clinic was 98%, and in 2015 it was 96%.

Conclusions

Pediatricians are regularly educating parents about the benefits of regular immunization. Regular pediatricians’ representation in electronic and written media giving advice on the importance of immunization in preventing the occurrence of infectious diseases is really beneficial. The results clearly show the benefit of the successful immunization, which has saved a lot of money both for treating the diseases and for dealing with its consequences.
ANTI-N-METHYL-D-ASPARTATE RECEPTOR (NMDAR) ENCEPHALITIS ASSOCIATED WITH OVARIAN TERATOMA

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Background

Anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis is an autoimmune disease characterized by the presence of anti-NMDAR antibodies in the cerebrospinal fluid (CSF) and serum. It is often presented with a prodrome of neuropsychiatric symptoms and there is a more frequent association with tumors in adults. The ovarian tumors are the most commonly found tumors associated with anti NMDAR encephalitis.

Case Presentation Summary

A 14-year-old girl, who suffered a left oophorectomy due to an ovarian teratoma, presented with audiovisual hallucinations and initial insomnia in post D1 surgery, complaints that were attributed to manifestations of anxiety and medication effect after anesthesia, and started, one week later, to have dyskinetic movements (orofacials and of the upper limbs). At admission to the hospital, she was firstly evaluated by child psychiatry and pediatric neurology (Glasgow coma scale 15, slow speech and persistent dyskinetic movements). Cerebrospinal fluid (CSF) had 8 white blood cells [WBC]/mm³ (mononuclear) and a slightly slow background activity in electroencephalogram (EEG) with a normal brain magnetic resonance imaging (MRI). She was empirically diagnosed with anti-NMDAR encephalitis and immunoglobulin IV (IgIV) therapy (1g/kg/d for 2 days) was promptly instituted, with progressive improvement of symptoms and being asymptomatic on discharge date. The immunoglobulin G (IgG) anti-NMDAR antibodies in CSF, based on semiquantitative indirect fluorescent antibody methodology, were still positive after a second cycle of immunoglobulin. Because the patient remained asymptomatic, the IgIV therapy was not continued.

Learning Points/Discussion

In this case, the presentation was in D1 after oophorectomy, which leads to a comment and the association with a tumor have a different prognosis by eliminating the trigger and this may justify the good evolution of this patient, in association with the early diagnosis and treatment.
PROLONGED FEBRILE ILLNESS CAUSED BY SICILIAN VIRUS INFECTION IN PORTUGAL

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Title of Case(s)

PROLONGED FEBRILE ILLNESS CAUSED BY SICILIAN VIRUS INFECTION IN PORTUGAL

Background

Sandfly Fever Sicilian Virus (SFSV) is usually seen in summer months, especially in the Mediterranean area, and causes a self-limited benign disease. The only reference to this virus presence in our country was made in 1974 and was regarding antibody detection in a seroprevalence study. Since then, there are no other reports.

Case Presentation Summary

An 8-years-old boy was admitted with fever (39°-38°), malaise, mild headache and weight loss (6%). He owns a dog and one week earlier he reported traveling to Ribatejo. Besides skin pallor and hepatosplenomegaly (4cm), oral mucosa aphotic ulcers were noted from D3 to D7 and scaling of hands and feet from D15 to D20. Blood screening revealed microcytic and normochromic anemia (Hb 9.2 x 10g/L, HTc 26.8%, MCV 74.7fL), leucocytes 6.8x10⁹/L, C-reactive protein 65.3mg/L, erythrocyte sedimentation rate 84 mm/h and hypergammaglobulinemia. The cardiologic evaluation was normal. HSV1 were isolated from the mouth ulcers and the antistreptolysin O titer was high (664 to 1120 UI/mL). IgM and IgG antibodies for Sicilian virus were positive and diagnosis was confirmed by seroconversion. The blood SFSV molecular amplification was negative. Sandfly vector collection was performed at Ribatejo, but the two trapped specimens were negative for Phlebovirus RNA. Other causes for prolonged fever were excluded. After hospital discharge he maintained asthenia and intermittent vespertine fever for one month, being clinically improved afterwards.

Learning Points/Discussion

Although in Portugal sandflies virus infections were earlier identified, SFSV has never been linked to symptomatic infections. Sandfly fever known as the three days fever may cause prolonged fever and asthenia and complete recovery may last up to 30 days. However, in our case we cannot exclude that other co-infections might have had a role.
Background

The gradual decline in immunization coverage reported in many Italian regions in recent years is related to parents' dissent given misinformation on unjustified vaccine-related risks. Understanding parental attitudes is essential for identifying the best opportunities to transmit evidence-based information and increase immunization adhesion. We aimed to assess parents’ attitude to vaccinations, the main sources of information used by parents and ways they prefer to receive information on vaccinations.

Methods

We carried out a longitudinal questionnaire-based study including a convenience sample of mothers of newborn babies between March and May 2017. A first questionnaire was administered while mothers were admitted at the maternity ward and a second one after 3-4 months (time of first immunization round).

Results

131 mothers completed the first questionnaire and 85 (65%) completed the second one. Despite the high level of education, their perceived knowledge about immunizations was just sufficient (median of 6 on a 1 to 10 scale, IQR 5-7). 19% (25/131) reported they had never received information about vaccinations and 10% (13/131) stated they were against or uncertain about vaccinating their child (median reported perceived knowledge 6.25, IQR 5-8). Internet was the most used source of information (64%), followed by family pediatricians (48%). At both time points mothers rated as very useful potential opportunities of information that could be provided by healthcare professionals during antenatal classes (median 9, IQR 7-10) or during admission at the maternity ward (median 9, IQR 8-10).

Conclusions

Mothers’ perceived knowledge about immunizations is far from being optimal and a non-negligible percentage are against or uncertain about vaccinating their children. Opportunities for providing information on vaccinations during antenatal classes or on the maternity ward should be implemented.
Title of Case(s)

Erythema multiform

Background

Erythema multiform (EM) is an acute, immune-mediated disorder, that affects the skin and mucous membranes. The major form (EM major, EMM) is a more severe, rare, potentially life-threatening disorder.

Case Presentation Summary

A 25-month-old healthy boy presented with an acute rash with erythematous papules, initially diagnosed as varicella. There was no recent immunization or any drug. He developed conjunctival hyperemia, mucosal involvement, fever, great discomfort and poor oral and fluid intake, leading to the suspected diagnosis of Stevens-Johnson Syndrome and referral to our hospital. At admission, the patient showed target-like lesions on his extremities with centripetal distribution affecting a body surface area of twenty-five percent, bullae with negative nikolsky sign and oral mucosa ulcers, with no other significant findings on physical examination. Laboratory tests showed leukocytosis and increased C-reactive protein without other abnormalities. After observation by Dermatology, the diagnosis of EMM was proposed. The boy was hospitalized with supportive care, methylprednisolone, ceftriaxone, azithromycin and acyclovir. Exams showed doubt Ig M for HSV-1, negative Ig G and positive viral load; serologies were negative for VZV, HHV-6/7, HSV-2, CMV, EBV, Chlamydia pneumonia and Mycoplasma pneumonia. Skin lesions resolved within two weeks leaving hyperpigmented areas at discharge.

Learning Points/Discussion

With this case report, the authors highlight the difficulty in diagnosis of some cases without classical presentation and where no obvious trigger is found. It is important to recognize EMM in order to avoid patient misdiagnosis and mismanagement.
Background

Cytomegalovirus (CMV) infection causes significant morbidity and mortality in immunocompromised children. Our aim is to describe the impact of CMV infection in pre-hematopoietic cell transplantation (HCT) for combined immunodeficiencies.

Methods


Results

41 children were treated for CID / SCID; 10 with CMV infection pre-HCT (24%); mortality 60% in patients with CMV and 32% in the rest. The age at diagnosis of CMV was 4.1 months (IQR, 3.1-8.4) and CID/SCID 5.6 months (IQR 2.8-14.5). Persistent CMV infection was the debut of the CID / SCID in 80% of cases. The initial symptomatology of CMV was respiratory (9/10). Further, seven cases were associated with fever, six with elevations of transaminases, five with gastrointestinal symptoms and four with neurological symptoms. They received ganciclovir (10 patients), a combination therapy with foscarnet (3), two of them have also received cidofovir, leflunomide, infusions of anti-CMV T lymphocytes and specific gamma globulin. In six patients, ganciclovir was changed for valganciclovir prophylaxis, reaching four cases to HCT with negative CV. The three children who required polytherapy against CMV died pre-transplantation due to respiratory failure. Another three patients died post-HCT, two due to un-controlled VL (respiratory failure and liver failure) and one case due to causes other than CMV. None of the patients have died with undetectable VL pre-HCT.

Conclusions

Uncontrolled CMV infection pre-HCT in children with IDC / IDCS is associated with high mortality. It is essential to control CMV infection pre- HCT to improve the survival of these patients.
RENAL DYSFUNCTION IN A SMALL COHORT OF PERINATALLY INFECTED HIV-1 PATIENTS
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Background

Chronic kidney disease is an important health concern in HIV-positive patients. Renal affection can be due to HIV infection itself and or effects of some antiretroviral medications mainly tenofovir (TDF). Among renal abnormalities in HIV patients, microalbuminuria is an important marker that is used as screening tool for kidney injury in HIV pediatric patients.

Methods

A retrospective analysis was performed on a cohort of HIV positive children from 2007 to 2015 at an urban pediatric HIV clinic. Patients were included if they acquired HIV perinatally, had at least 2 microalbumin: creatinine ratio (MC) measurements separated by at least 1 month during the study period, and had complete demographic, clinical and laboratory data.

Results

Among 77 perinatally HIV-infected patients, 69 met the rest of the inclusion criteria for the study. 16/69 patients (23%) met a preset definition for microalbuminuria which is: 2 or more MC measurements separated by at least 1 month period that are above 30 mg/g). Demographics and laboratory outcomes and TDF exposure data for the microalbuminuria group (16 patients) were compared to those of the 53 patients who did not meet the definition of microalbuminuria.
Conclusions

Our study shows significant prevalence of microalbuminuria (23%) in our cohort of pediatric HIV patients. The microalbuminuria group exhibits marked activation of CD8+, higher cumulative VL and lower CD4% nadir during the study period. In this cohort, TDF exposure did not seem to be a contributing factor to microalbuminuria indicating a likely multi-factorial mechanism of microalbuminuria in this patient population.
IMPACT OF ANTIMICROBIAL STEWARDSHIP PROGRAMS IN A PEDIATRIC CENTER

Background

Antibiotic resistance is an increasingly worldwide problem, with particularly in the context of impact in hospital infections. As serious infections can be caused by multi-resistant microorganisms and new antibiotics are lacking, antimicrobial stewardship programs are necessary to ensure the judicious use of antibiotics.

Methods

We performed a retrospective study which included antibiotic consumption in a tertiary pediatric center with patients admitted in general pediatric care, pediatric and neonatal intensive care and pediatric surgery. The aim was to evaluate trends of antibiotics use with implementation of a restrictive policy for prescription of restricted antibiotics. Since 2014, this policy included a formal review by local antimicrobial stewardship team including an infectious diseases pediatrician, of prescribers’ justification for prescription of restricted antibiotics, made in a maximum of 72 hours after prescription.

Results

In 2014, the consumption of antibiotics was 94 DDSs per 100 bed days, with carbapenems use of 6.69 DDDs per 100 bed days and quinolones use of 3.05 DDDs per 100 bed days. Three years later, the consume of antibiotics was 102.82 DDDs per 100 bed days. There was a reduction of approximately 37% in the use of carbapenems and a reduction of approximately 63% in the use of quinolones. The incidence of multi-resistant’s microorganisms has been increasing from 1.77 to 3.09 DDDs per 1000 bed days.

Conclusions

In general and along these 3 years, antibiotics consumption had a small increase. This can be explained in part by the use of antibiotics with a higher weight in terms of DDDs calculation, like penicillins. With the implementation of this policy, a reduction of the use of carbapenems and quinolones was achieved in the context of increasing drug resistance, highlighting the importance of interventions targeted to restricted antimicrobials. However, this interventions should be combined with strategies to improve antimicrobial prescription in order to achieve sustainability.
01A. EDUCATION: PAEDIATRIC ANTIBIOTIC STEWARDSHIP

ANTIMICROBIAL CONSUMPTION IN NEONATAL INTENSIVE CARE UNIT OF BRAZIL.

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Background

Broad-spectrum antibiotic consumption in intensive care is common due to possibility of life-threatening infections and occurrence of multi-drug resistance agents. Judicious use of antibiotics in this setting is a challenge to all paediatricians.

Aim: To describe antimicrobial use in NICUs.

Methods

We did a prospective audit surveillance of antimicrobial consumption in a NICU level III of Rio de Janeiro state, Brazil using the tool days of antibiotic therapy per 1000 patient-days (DoT/1000 PD), during one year. Neonates were included if stay longer than 24h.

Results

Between January and December of 2017, the unit admitted 657 neonates, totaling 5280 patient-days. In this period, we registered 47 healthcare-associated infections (rate of 7.2%). Gentamycin was the most common antimicrobial consumed in eight of twelve months (range from 117,9 to 379,1 DoT), ampicillin in three months (range from 67 to 334 DoT) and cefazolin in the remaining month (range from 0 to 149,3 DoT). Consumption of broad-spectrum antibiotic was also measured: vancomycin (40,8-128,8 DoT), meropenem (0-110,4 DoT), teicoplanin (0-27,1 DoT), ciprofloxacin (0-24,9 DoT), cefepime (0-28,6 DoT), piperacillin-tazobactam (0-77,9 DoT).

Conclusions

Days of antibiotic therapy (DoT) is an interesting tool to follow antimicrobial consumption within NICU and should be a component of paediatric antimicrobial stewardship program. In our experience, even in a NICU level III, consumption of broad-spectrum antibiotic was lower.
A CASE WITH OPISTHOTONUS: A RARE ETIOLOGY FOR A WELL-KNOWN FINDING

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Title of Case(s)

A Case with Opisthotonus: Is it tetanus or not?

Background

Opisthotonus is a type of abnormal posture due to muscle spasms. The condition is usually a sign of serious brain conditions, such as meningitis, tetanus, and trauma.

Case Presentation Summary

A 15-year-old Syrian boy from a border city of Syria (Cerablus), was brought to our emergency service with acute severe headache and hyperextension posture of head (Figure1). One month ago, he had fallen from the motorcycle, a wound on the forehead was sutured in Cerablus without any tetanus prophylaxis. He had no fever or other recent illnesses. On examination, tonus of other muscles were normal. There wasn’t trismus, he had a normal gag reflex response but he couldn’t speak properly. Instead of high creatinine kinase levels, other laboratory tests and cranial CT were normal. Because of not having a history of proper vaccination, tetanus immune globulin and vaccine was administered. A mild sedation relieved the patient’s symptoms and continued for seven days in ICU. In the second week, significant improvement was seen. By further radiologic studies, we found an extensive spinal arteriovenous fistula in cervical and thoracic regions. After first findings had resolved, patient developed bilateral lower extremity flask paralysis. EMG showed peripheral neuropathy which was resolved spontaneously in two weeks. That was attributed to tetanus immune globulin. At the end of
the forth week, the case was discharged without any neurological abnormality.
Learning Points/Discussion

Opisthotonus is a very dramatic sign typically for tetanus. But, it is also necessary to consider other factors such as meningitis, subarachnoid bleeding, tumors and trauma. The lack of abnormal gag reflex response (positive spatula test) or trismus sign, requires investigation of other etiologies.
HEPATITIS A CASES IN A PERIPHERAL HOSPITAL: AN IDEAL PREVENTION WITH HYGIENIC MEASURES AND THE VACCINATION

Background

Hepatitis-A has noticeably decreased due to health policy improvement, Spain being a country of low endemicity.

The clinical course is usually benign and self-limited, but may rarely progress to fulminant hepatitis.

Prevention is based on hygienic measures and vaccination.

Case Presentation Summary


There were 7 hepatitis-A cases, 71.4% female, mean age 101 ± 22 months. An increase was observed during the 2016-2017 period in children (4 cases) as well as in adults (12 cases in 2016-2017 vs. 3 during the 2011-2015 period).

Moroccan origin was noted in 71.4% and 57.1% have recently travelled to Morocco.

Cases identified were 71.4% sporadic and 28.6% family, all without previous hepatitis A vaccination (85.7%).

Symptoms were vomiting (57.1%), choluria (57.1%), abdominal pain (42.9%), anorexia (42.9%), jaundice (42.9%), tiredness (28.6%) and fever (14.3%).
Hypertransaminasemia and conjugated hyperbilirubinemia were observed in all cases, and a modest coagulopathy (71.4%) that required vitamin K (42.8%).

85.7% were admitted to the hospital due to moderate anorexia (66%), with a mean hospitalization stay of 3 ± 1.4 days, with good progress (100%).

**Learning Points/Discussion**

Incidence of hepatitis-A in children remains low, however an increase has been noticed due to the outbreak in adults during 2016-2017.

Hepatitis-A transmission is associated with travelling to areas of moderate or high endemicity.

It is essential to recommend vaccination to the children of immigrants as well as to travellers to areas of high or moderate endemicity.
EFFICACY AND HEMATOLOGICAL TOXICITY OF A REDUCED 2 WEEKS POST-EXPOSURE PROPHYLAXIS WITH ZIDOVUDINE FOR HIV-1 EXPOSED INFANTS WITH LOW TRANSMISSION RISK

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Background

In recent years introduction and optimization of combination antiretroviral therapy for HIV-1 infected pregnant women reduced the risk of mother-to-child transmission significantly. In the low transmission risk setting with suppressed maternal viral load the optimal duration of neonatal post-exposure prophylaxis (PEP) with zidovudine (AZT) is unknown. Considering the haematological toxicity of AZT we compared effectiveness and safety of a risk-adapted 2 weeks versus 4 weeks PEP in infants born to mothers on stable cART.

Methods

In a retrospective study we analysed data of all HIV-1 exposed infants born between 2010 and 2016 that were followed at two German Paediatric Infectious Disease Centres. Only infants with low transmission risk, most with complete maternal HIV-1 suppression at birth, were included, while those carrying risk factors associated with an increased transmission risk were excluded. We compared haemoglobin levels classified according to toxicity grades established by the Division of Acquired Immunodeficiency Syndrome (DAIDS) between participants receiving risk-adapted AZT for either 2 or for 4 weeks (plus) according to national guidelines.

Results

A total of 382 HIV-1 exposed infants were screened for inclusion and 322 (84.3%) with a low transmission risk were included. Of these 138 (43%) were treated with 2-weeks AZT and 184 (57%) with 4-weeks (plus few days). We observed a single transmission corresponding to an overall transmission risk of 0.3%. Children receiving 4 weeks (plus) AZT had a significant higher incidence anaemia (97/157 (62%) and 55/152 (36%)) as compared to the 2-weeks group (43/114 (38%) and 17/111 (15%)) at one and three months of age, respectively (p<0.05).

Conclusions

Two weeks AZT-PEP is effective in HIV-1 exposed infants with low transmission risk and resulted in less haematological toxicity compared to 4 weeks (plus).

Clinical Trial Registration (Please input N/A if not registered)
N/A
INTERNATIONAL SURVEY ABOUT PROPHYLACTIC ANTIBIOTICS AND VACCINATION IN SICKLE CELL DISEASE CHILDREN. DO WE DO SO DIFFERENT?


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Background

Vaccination and prophylactic antibiotic are the cornerstone of Sickle Cell Disease (SCD) children infections’ prevention. Conditions to stop antibioprophylaxis remain controversial. Our aim is to describe current practice in preventive measures in SCD children.

Methods

An online survey was conducted in January 2018 among members of the Sickle cell disease Pediatric Research about Infections Group (SPRING). SPRING is a group that assembles physicians all over the world interested in infectious diseases in SCD children.

Results
From 23 centres contacted, 19 (83%) completed the survey. Centres are in Europe (12), Africa (3), Asia (3) and South America (1). These centres treat in total more than 5000 SCD patients. 13 (68%) centres follow national guidelines concerning antibiotic prophylaxis and so, their information concerns more than 2,400,000 SCD children. 14 (74%) centres give penicillin as prophylaxis, 3 (16%) amoxicillin. Differences are large concerning the moment to stop prophylaxis, being 5 years-old for 9 centres (47%) (5 European, 3 African, 1 Asian), 10-12 years-old for 3 (16%) (2 European, 1 South-American) and until adulthood for 5 (26%), all European centres. Conditions as splenectomy or previous sepsis would prolong antibiotics in centres who stop them during childhood.

Concerning vaccination, 17 centres (89%) give any Pneumococcal conjugated vaccine (2 African centres do not), 15 centres (79%) Pneumococcal 23-valent polysaccharide vaccine and 14 (74%) yearly flu vaccine. Any Meningococcal vaccine is given in 14 centres (74%) (3 African and 2 Asian centres do not); 9 European centres (47%) vaccinate for all serotypes (A-B-C-W135-Y).

Conclusions

Although there is consensus to give penicillin as prophylaxis to SCD children, age to stop remains a dilemma, with different attitudes even among centres from the same continent. SCD vaccination programs differ greatly depending on continents.
Introduction to vertical transmission of HIV infection and response to vaccines.

Methods

We conducted a retrospective, observational study. All participants had HIV congenital infection and had been vaccinated according to the Italian National Immunisation Schedule (diphtheria, tetanus, pertussis, polio, hepatitis B, measles, mumps, rubella and varicella), including all recommended booster doses. For each patient, we evaluated the first available serology after completing immunization schedule, at around 6 years of age (1991-2011), and the most recent serology, after at least ten years (2014-2016). Multivariate logistic regression models were used to compare serologies with medical history and clinical data, such as infections, CD4 count, HIV load, duration and ongoing antiretroviral therapy, were also collected.

Results

Compared to the general population, the 68 patients enrolled showed an inferior seroconversion rate. Multivariate analysis showed a direct correlation between a low CD4 level and the presence of HBsAg. Moreover, the development of anti-HBsAg antibodies was observed in young children that were never treated with AZT monotherapy. In the second serology, an adequate CD4 level appeared to be linked to a good antibody titre.

Conclusions

As reported in literature, our HIV-infected patients developed lower antibody titres after vaccinations compared to the general population. It is important to monitor closely children susceptible to vaccine-preventable diseases, identifying those who would require earlier booster doses. Anyways, the higher titres reported in children that were never exposed to AZT monotherapy is an encouraging perspective for patients that were immediately treated with combined therapy.
INFECTION AS A THROMBOTIC RISK FACTOR: A CASE SERIES

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Title of Case(s)
INFECTION AS A THROMBOTIC RISK FACTOR: A CASE SERIES

Background

Amid risk factors (RF) of venous thromboembolism (VTE), infection is among the most important. Our objective was to analyze the diagnosis, treatment and evolution of VTE associated with complicated infections, unrelated to the use of central venous catheter (CVC).

Case Presentation Summary

We reviewed the medical records of patients diagnosed with VTE and followed up in the thrombosis unit of a tertiary hospital between October 2016 and December 2017. 37 patients were diagnosed with VTE. 32 patients (86.5%) presented TEV secondary to the use of CVC and five (13.5%) secondary to the infectious process. In two patients, VTE was secondary to mastoiditis: a 3-year-old patient with subperiosteal abscess and sigmoid sinus thrombosis and a 12-year-old adolescent with venous sinus thrombosis. Two other cases were secondary to deep cervical abscesses. The first case was an abscessed cervical adenitis with thrombosis of the internal jugular vein, in a 15-year-old patient with Lemierre’s syndrome. The second case was a 3-year-old patient with right retropharyngeal abscess, left retropharyngeal phlegmon and thrombosis of the right internal jugular vein. The last case was a 22-month patient with left popliteal vein thrombosis in the context of S. pyogenes myositis. This patient is also being investigated for primary immunodeficiency due to subsequent invasive infection by S. pneumoniae and H. Influenzae b. All patients were treated with low molecular weight heparin between 3 and 6 months and have presented with complete resolution of the thrombosis.

Learning Points/Discussion

Infections are a risk factor for the development of VTE on adjacent vascular territories, with mastoiditis and cervical abscesses being the main RF. The combination of antibiotic and anticoagulant treatment allows a complete clinical resolution.
DETECTION OF VIRAL PATHOGENS OTHER THAN MEASLES DURING INVESTIGATION OF SUSPECTED PAEDIATRIC MEASLES CASES IN IRELAND: A RETROSPECTIVE ANALYSIS

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Background

Crevicular fluid is the specimen of choice for laboratory investigation of viral exanthem in children. A non-invasive sample, it can be used for the molecular detection of Measles, Human Herpes Virus 6 (HHV-6), Rubella, Parvovirus B19, Enterovirus and Human Parechovirus. We describe the utility of testing for an expanded panel of pathogens in cases of viral exanthem during a two-year period when sporadic outbreaks of Measles were occurring in Ireland.

Methods

Crevicular fluid samples, submitted to the National Virus Reference Laboratory, Ireland for investigation of viral exanthem were identified by review of NVRL IT records. Data from those aged ≤ 18 years were extracted for analysis (Excel) by review of NVRL IT records (Clinisys)

Results

635 samples were tested, and measles RNA was detected in 46 (7.2%). In two cases HHV-6 was co detected. Alternative diagnoses were established in 312 cases (49%) (Table 1). Age stratification of the samples in which HHV-6 DNA demonstrated that 97.5% (n=197) were from patients aged less than 6 years.

<table>
<thead>
<tr>
<th>Target</th>
<th>Total tested</th>
<th>Number positive (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HHV-6</td>
<td>375</td>
<td>202 (53.9%)</td>
</tr>
<tr>
<td>Enterovirus</td>
<td>551</td>
<td>94 (17.1%)</td>
</tr>
<tr>
<td>Human Parechovirus</td>
<td>321</td>
<td>5 (1.6%)</td>
</tr>
<tr>
<td>Parvovirus B19</td>
<td>368</td>
<td>11 (3%)</td>
</tr>
<tr>
<td>Rubella</td>
<td>34</td>
<td>0</td>
</tr>
</tbody>
</table>
Conclusions

Establishing an alternative diagnosis in a child presenting with suspected Measles is of significance for Public Health and to allay parental concern. HHV-6 may be a significant confounding pathogen in outbreak scenarios. Distinguishing between recent infection and integration with HHV-6 was not performed routinely, as subsequent samples were not available for all children. Nevertheless, our study demonstrates that in a child with suspected measles infection, testing for HHV-6 DNA and EV RNA by PCR should be considered in those testing negative for measles RNA, particularly in those aged less than 6 years.
Title of Case(s)
“Rhombencephalitis” - Enterovirus infection is not benign after all!

Background
Rhombencephalitis (RE) is an acute and rare neurological complication in children with Enterovirus 71 infection. Enterovirus 71 is the second most common infective cause of Rhombencephalitis. Enteroviral meningo-encephalitis generally has a good prognosis. However, in 9.6% patients, when the cause is Enterovirus 71, there is a substantial mortality, especially when associated with cardiac failure with and without hypertension or with acute neurological disease. Radiological features are generally non specific in most viral encephalitis, but Enterovirus 71 rhombencephalitis has characteristic lesion locations in the posterior portions of the brain stem, substantia nigra, dentate nucleus and anterior horns of the spinal cord.

Case Presentation Summary
An eight month old child, previously fit and well, presented with 48 hour history of fever and coryzal symptoms. Clinical assessment showed features of encephalitis, hypertension and inappropriately normal heart rate despite pyrexia. Neurological involvement started with mono-paresis and progressed to truncal ataxia and bulbar palsy. MRI head showed increased T2 signal intensity in medulla and anterior horns of spinal cords C2-C6. CSF PCR for 16S ribosomal RNA of bacterial and viral RNA and DNA were negative. Stool PCR was positive for Enterovirus and further serotyping confirmed Enterovirus 71. Over the next 2 week period, the encephalopathy resolved, but the child has residual mono-paresis and bulbar palsy.

Learning Points/Discussion
Early recognition of Enterovirus 71 rhombencephalitis is critically important, as it is potentially epidemic and fatal. In a child with significant cardiovascular or neurological involvement, it is vital to extend the diagnostic tests to ensure isolation of the organism from blood, CSF, urine and stool. Early detection of cardiovascular or neurological manifestations may result in aggressive monitoring and treatment, hence reducing morbidity and mortality.
MANAGEMENT OF ASYMPTOMATIC CHILDREN WITH TST(+) BUT IGRA(-) RESULTS IN A LOW PREVALENCE SETTING; A 10-YEAR FOLLOW-UP EXPERIENCE

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Background

Evidence of TB infection is routinely examined with the use of Tuberculin Skin Test (TST). Interferon-γ release assays (IGRAs), with their greater specificity over TST, have improved the accuracy of testing for TB infection. There is lack of data on children TST(+) but IGRA(-) results and this discordance is very common in paediatric clinical settings. Withholding anti-TB treatment among older children with close follow-up is the current practice in our TB clinic. This study aims at examining the incident TB disease and LTBI cases among TST(+)IGRA(-) children and assessing the level of reproducibility of IGRAs in a low prevalence setting.

Methods

This is a prospective, longitudinal study of 123 asymptomatic children [mean age 9y (range 1-16y)] with TST(+)IGRA(-) results referred to our clinic between 2008-2017. The majority (106) was detected through routine screening and 17 through contact tracing. At baseline visit all had normal CXR and 111/123 (96%) were BCG vaccinated. None of the participants received anti-TB treatment and were followed with repeat CXR and QFT-GIT.

Results

Overall, 76 children (37 from high risk countries and 6 with history of contact) returned for follow-up. All subjects were asymptomatic, had normal CXR, negative QFT-GIT, except one child who converted QFT-GIT. No incident TB cases were detected. Forty seven failed to attend the visit, but were contacted through telephone interview and reported no symptoms that could be related to TB.

Conclusions

This study indicates that withholding anti-TB treatment for TST(+)IGRA(-) older children is a safe practice and this discordance is most likely due to higher IGRA specificity. There is need to confirm these findings in a larger number of subjects at high risk for TB infection and also at younger ages.

Clinical Trial Registration (Please input N/A if not registered)
MICROORGANISMS WITHOUT BORDERS

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³Hospital Pediátrico Integrado- Centro Hospitalar São João, Pediatric Infectious Diseases, Porto, Portugal

Title of Case(s)

MICROORGANISMS WITHOUT BORDERS

Background

Portugal has an important relationship with ancient colonies. We report 5 cases of exposure/infection due to tropical microorganisms.

Case Presentation Summary

An asymptomatic 10-month boy in clinical surveillance since birth in Portugal, because his mother was diagnosed with zika virus infection in 1st trimester in Brazil with positive IgM and IgG and no circulating virus. During pregnancy, seroconversion was observed.

A newborn, clinically well, is being followed up due to perinatal exposure to *Tripanosoma cruzi*. His mother from Brasil had Chagas disease and died 7 days after delivery.

A 17-years-old adolescent natural from Guiné presented at the emergency department with right ocular pain, hyperemia and hypovision. Ophthalmologic evaluation showed granulomatous iritis, vitritis, and chorioretinitis. Etiologic study showed positive IgG to toxoplasma. Ocular toxoplasmosis was assumed, he was treated with trimethoprim-sulfamethoxazole and prednisolone, with clinical improvement.

A 15-years-old Portuguese girl presented with a small hypopigmented lesion in the right forearm with 2 years of evolution. After delayed diagnosis of multibacillary lepromatous leprosy in her mother from Brazil and living in Portugal since several years, the girl underwent a skin biopsy which revealed paucibacillary Hansen's disease. She was treated with dapsone and rifampicin.

A 7-years-old girl from Guiné, was evaluated due to nodular cutaneous lesions and chronic osteomyelitis since 2 years old. The suspicion was confirmed when *Histoplasma duboisii* was observed in bone and ganglionar tissues. She started treatment with amphotericin B with slightly improvement. At the same time pulmonar tuberculosis was diagnosed.

Learning Points/Discussion

Currently, with increasing migration of people, diseases considered tropical can be seen in industrialized countries. Pediatricians must be aware of them in order to better diagnose and treat. Also a proper surveillance in cases of exposure must be guaranteed.
PREVENTION OF INFECTIOUS DISEASE IN NATURAL DISASTERS
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²PHI D-r Angelovska and D-r Timovski, Paediatrician, Skopje, FYR Macedonia
³HMS, Paediatrician, Bitola, FYR Macedonia

Background
As a result of natural disaster-flood the most documented and commonly occurring diseases are water-borne diseases with the children.

Methods
The study involves 1 rural regions in the Republic of Macedonia hit by flood in February 2016. It includes 230 children age 1 to 14 years. 120 are female children while 110 are male ones. Analytic and descriptive methods have been used for data processing.

Results
When Macedonia was struck by the flood in February 2016 in one rural region the health of 230 children had been jeopardized. With symptoms of vomiting and diarrhea where 27 children got. Later, 4 children got hepatitis of type A. Due to the timely take measures from the competent authorities, outburst of epidemic was prevented. Drinking water from taps in the flooded regions was banned, and the inhabitants were given bottled water. Also, the inhabitants of the regions were trained about some hygienic and epidemiological measures and the flooded houses were disinfected.

Conclusions
Assuring access to safe water and primary healthcare services is crucial, as are surveillance and early warning to detect epidemic-prone diseases known to occur in the disaster-affected area. Practically, prompt and adequate prevention and control measures, and appropriate case management and surveillance systems are essential for minimizing infectious disease burdens.

Systematic Review Registration (Please input N/A if not registered)
N/A
GLOBAL ANTIMICROBIAL RESISTANCE, PRESCRIBING AND EFFICACY AMONG NEONATES AND CHILDREN (GARPEC PROJECT): RESULTS OF ANTIMICROBIAL PRESCRIBING IN PICU-BRAZIL

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²Prontobaby, Infection Control Committee, Rio de Janeiro, Brazil
³St. George’s University of London, Paediatric Infectious Diseases Research Group, London, United Kingdom

Background

One of most important key-point of antimicrobial stewardship program is knowledge about use of antimicrobials in hospitals, including paediatric intensive care units (PICUs)

Aim: To describe antimicrobial use in PICU.

Methods

The GARPEC project aims to implement standardized web-based surveillance methods for antimicrobial use in hospitalised children and neonates worldwide. This study was a part of the GARPEC project to measure antimicrobials use in a PICU of Rio de Janeiro state, Brazil, through successive one-day cross-sectional point prevalence surveys (PPS).

Results

We followed 59 children during 2016 year, totalizing 135 prescriptions in a single PICU. Twenty-two (37.3%) were female, 12 (20.3%) received invasive ventilation and 34 (57.6%) had at least one or more previous disease. Community acquired infections were the indication for antibiotic use in 39/59 (66%) patients and healthcare-associated infections in 10/59 (17%) of the patients. Proven or probable bacterial lower tract respiratory infection was the most common diagnosis and present in 30/59 (50.8%). The most common antibiotics prescribed were Clarithromycin (22/136- 16.2%), Oseltamivir (15/136- 11%) and Vancomycin (11/136- 8.1%). The rate of other broad-spectrum antibiotics was: meropenem (8/136- 5.9%), cefepime (6/136- 4.4%) and ceftriaxone (3/136- 2.2%).

Conclusions

This study demonstrates that PPS is a useful tool to monitor antimicrobial use in PICU. Even in a critical unit as PICU, use of broad-spectrum antibiotics was not common in our unit.
Valganciclovir in congenital cytomegalovirus infection. Who and when to treat?

Background

Congenital cytomegalovirus (CMV) is one of the major causes of sensorineural hearing loss and neurodevelopmental abnormalities in developed countries. Antiviral therapy of children reduces the risk of long-term disabilities. However, absence of guidelines regarding prevention, diagnostic methods and therapeutic strategies may difficult this approach. Also, the large variable genetic background of CMV genotypes, may hamper its comprehension and vaccine prevention.

Case Presentation Summary

We present three cases of congenital CMV, with different severity, that underwent treatment with valganciclovir 15mg/kg/dose for 6 months.

A 39-week female neonate, 2930g, with first-trimester CMV seroconversion, confirmed with amniocentesis. Postnatal neurosonography revealed ventriculomegaly, calcifications and thalamostriate vasculopathy. Thrombocytopenia and bilateral moderate sensorineural hearing loss were detected. Follow-up evidenced normal neurodevelopment with profound right hearing loss and normal left hearing.

A 37-week female neonate, 1765g, with growth restriction detected after third-trimester CMV seroconversion. After birth, hepatitis was detected with progressive transaminases normalization. Neuroimaging with MRI was normal. Follow-up revealed normal neurodevelopment with no sensory deficit.

A 39-week female neonate, 2865g, with second-trimester CMV seroconversion, confirmed with amniocentesis. Postnatal neurosonography demonstrated mild thalamostriate vasculopathy with rare calcifications. No clinical or analytical manifestation were detected at birth. However, follow-up revealed postnatal hearing deficit.

All cases showed good response to valganciclovir with progressive decrease in serum and urine CMV titers. No adverse reaction was recorded.

Learning Points/Discussion

Recent expert consensus recommends therapy with valganciclovir in neonates with moderate to severe manifestations of congenital CMV. However, literature is unclear whether mild to asymptomatic cases should undergo the same treatment, making this an off-label approach.
Increasing knowledge on defined CMV genotypes, may define viral markers for prediction of clinical severity, possibly affecting future decision on pregnancy interruption or valganciclovir therapy.
RECURRENT PNEUMONIA. WHEN TO SUSPECT AN IMMUNODEFICIENCY?

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1Hospital La Paz, Pediatric Infectious Diseases, Madrid, Spain

Title of Case(s)

RECURRENT PNEUMONIA. WHEN TO SUSPECT AN IMMUNODEFICIENCY?

Background

Recurrent pneumonia is defined as ≥ 2 episodes / year or three episodes throughout life. Many children have recurrent respiratory infections and it is challenging to select those patients that would require extensive studies of predisposing factors.

Case Presentation Summary

A 4-year-old Moroccan boy, referred for cough and fever that does not respond to Amoxicillin-clavulanic acid. Adenovirus positivity was determined in his aspirate. He was born in the rural area of consanguineous parents, with a neonatal history of meconium aspiration and sequela of hemiparesis, tendency to bronchoaspiration and failure to thrive. Since his arrival in Spain 7 months ago he had 3 episodes of bronchopneumonia and gastroenteritis due to Campylobacter. CRA: bilateral subcrepitations, without hypoxemia. Mild hemiparesis. Nail dystrophy and oral leukoplakia. Chest XR: infiltrate in right lower lobe without condensation. Analytical: 3220 leukocytes (lymphocytes 1320, neutrophils 1450), platelets 86,000. PCR 40 mg / L. CD3 95%, CD 19 0.4%, CD4 40%, CD8 40%, NK 3%. Immunoglobulins IgG 975; Ig A 44; Ig M 338; Ig D 13. Positive burst-test. In bronchoalveolar lavage, P.jirovecii, CMV and Adenovirus were isolated, with 1,000,000 copies of CMV in blood. Myelogram: hypoplastic marrow compatible with congenital dyskeratosis (DC).

Learning Points/Discussion

In our case, the history of neurological involvement due to neonatal meconium aspiration could justify bronchoaspiration as a cause of recurrent pneumonia and failure to thrive. In addition, DC can associate esophageal involvement with a tendency to stenosis and bronchoaspiration. Among the causes are primary immunodeficiencies which require early diagnosis to improve survival. We should suspect such disorders in consanguinity, failure of therapy, bilateral pneumonias, pneumococcal pneumonia due to vaccine serotypes in immunized children, or infants with severe viral pneumonias.
Background

Bacterial antibiotic resistance is an emerging problem with major impact in health care. Several mechanisms of bacterial resistance to antimicrobials, including enzyme-mediated hydrolysis, have been described. We highlight the production of *Klebsiella pneumoniae* carbapenemases (KPC). In Portugal, several outbreaks have occurred recently in adults and have been implemented a program for prevention and control of infections and resistance to antimicrobials that established criteria for the research of these microorganisms. The objective of this study was to analyze the patients hospitalized in a Paediatric Intensive Care Unit who underwent KPC screening at admission.

Methods

Retrospective and descriptive study based on the clinical files of patients admitted to the PICU between February 1, 2016 and August 31, 2017 and laboratory registries. Data regarding age, sex, criteria established by PPCIRA for KPC screening (rectal swab) were collected. The established criteria were: 1. Transfer from other hospital units; 2. Previous stay in institutional care units/nursing homes; 3. Hospital admission in the previous 6 months. The KPC screening was done by molecular biology.

Results

During the 19 months study, 273 patients were admitted to the PICU; 48 (17.6%) were screened. There was a male predominance (68.8%), the age range varied from 21 days to 17 years, with an average of 4.8 years old. The transfer from another hospital unit was the screening criterion found in the majority of patients (39), followed by hospitalization in the previous six months (29), of whom 23 had had previous antibiotic treatment. 58.3% had more than one criterion for screening. Two positive cases (2/48 - 4.2%) were identified, one with urinary tract infection and the other with gastrointestinal colonisation.

Conclusions

Identification of patients at risk of transmission of problem microorganisms is a basic principle of infection control, along with hand hygiene, use of personal protective equipment and cleaning. In this study we document the emergence of KPC-producing bacteria also in paediatric age, which reinforces the importance of systematic screening on admission of the patients at risk.
EPIDEMIOLOGICAL STUDY ABOUT INFECTIONS ASSOCIATED WITH FEBRILE SEIZURES AMONG CHILDREN HOSPITALIZED IN OUR GENERAL PEDIATRIC CLINIC, DURING ONE YEAR.
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¹"Achilopouleio"- General Hospital of Volos, Pediatric Clinic, Volos, Greece

Background
Febrile seizures (FSs) are the most common type of seizures seen in children. The purpose of this study was to find the incidence and investigate the risk factors connected with FSs, especially infectious agents, among children that were hospitalized during 2015 in our department.

Methods
53 cases hospitalized with seizures, aged 2 months to 14 years old, were collected in our department. 29 of them had febrile seizures (8 months-6 years old), during 2015.

Results
There were 13 females(f) and 16 males(m) with febrile seizures (m/f:1,2) and the age spectrum was 8 months-6 years. 23 (79,3%) of them were simple FSs and the rest of them (6 cases-20,6%) were complex. The cause of fever was an upper respiratory tract infection in 15 patients, lower respiratory tract infection in 4 cases, HHV-6 in 6 cases, 2 cases with acute otitis media and 2 with unknown reason. The mean hospitalization duration was 3 days. Most of the children were admitted into the hospital with a fist seizure attack and had positive family history of FSs. The distribution through the year was: Autumn(27,5%), Winter (34,4%), Spring (13,7%) and Summer (24,1%).

Conclusions
The frequency and epidemiology of the FSs recorded in our department is according to the ones measured the previous years and according to the international bibliography. Common virus infections, especially HHV-6, were found as the risk factors associated with FSs in our study.
Title of Case(s)

Kawasaki disease shock syndrome associated with severe gastrointestinal manifestations

Background

Kawasaki disease shock syndrome (KDSS) is a rare complication characterized by hemodynamic instability. The presence of shock syndrome and gastrointestinal symptoms predicts KD refractory to immunoglobulin (Ig) treatment. We present a case of a child with KDSS and gastrointestinal manifestations.

Case Presentation Summary

A 4-year-old girl was admitted with a 4-day history of fever associated with mucositis, conjunctival hyperemia, cervical adenopathy, rash, abdominal pain and diarrhea. Laboratory examination revealed anaemia, neutrophilia, hyponatremia, hypoalbuminaemia (2.6 g/dL), hypertransaminasemia, elevated C-reactive protein (17 mg/dL) and elevated sedimentation rate (91 mm/h). On day 5, the patient received Ig treatment and intravenous (I.V.) fluids due to tachycardia and hypotension. There was worsening of the abdominal pain associated with signs of peritoneal irritation and respiratory insufficiency. Computed tomography scan revealed hepatomegaly, colic oedema, gallbladder hydrops (with no lithiasis), ascites and bilateral pleural effusion. Ig treatment was repeated on day 7. There was progressive clinical worsening and on day 9, valvular regurgitation and pericardial effusion were evidenced. Abnormalities of the coronary arteries were excluded. At this stage, the girl also had anasarca with worsened hypoalbuminaemia (1.7 g/dL) and anaemia (Hb 6.7 g/dL). The patient initiated methylprednisolone and received I.V. albumin and red blood cell transfusion. After 48 hours, the patient remained without fever. Apart from an episode of lipase elevation (up to 99 U/L) and arthritis of the coxofemoral joint, there was clinical and analytical improvement.

Learning Points/Discussion

We present a case of KDSS associated with severe gastrointestinal manifestations. The patient had several risk factors on admission, including gastrointestinal involvement, which increases the likelihood of refractory KD. The initial stratification of patients with KD is key to consider the early initiation of corticotherapy.
CONGENITAL CYTOMEGALOVIRUS INFECTION: ABOUT A CASE
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¹Serviço de Pediatria, Centro Hospitalar de Leiria, Leiria, Portugal

Title of Case(s)
CONGENITAL CYTOMEGALOVIRUS INFECTION: ABOUT A CASE

Background
Cytomegalovirus (CMV) is the most common, yet under-recognised, congenital viral infection in the developed world, with an overall birth prevalence of 0.2-2%. Early treatment with antiviral therapy has shown protection against sensorineural hearing loss and long-term neurodevelopmental disabilities.

Case Presentation Summary
As part of our active surveillance for CMV congenital infection in small for gestational age newborns (SGA), which birth weight, length and head circumference are under the 10th percentile for gestational age (Fenton Charts 2013), we identified an 1 month-old breastfed, considered as a fetal growth restriction during pregnancy, with positive CMV deoxyribonucleic acid (118×10⁶ ADN/mL) in urine polymerase chain reaction. During the follow-up consultations hearing loss and chorioretinitis were excluded and a global developmental delay was diagnosed. Blood workup including blood count, transaminases and bilirubin, was normal. Magnetic resonance imaging at 12 months showed multiple white matter lesions attributed to the congenital CMV infection. Attending to the late acknowledge of neuroimaging findings treatment was not performed.

Learning Points/Discussion
Screening for CMV should be considered as a standard procedure in SGA newborns to facilitate an early detection and intervention for sensorineural hearing loss and developmental delay. In the present case the late acknowledge of symptomatic congenital CMV infection lead to a point where the treatment seemed unappropriated. Would it be legitimate to institute antiviral therapy with valganciclovir in this case?
A RETROSPECTIVE COHORT STUDY EXPLORING THE MANAGEMENT OF PAEDIATRIC PATIENTS WITH SUSPECTED SEPSIS COMPARED TO THOSE WITH LESS SERIOUS INFECTIONS

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Background

Sepsis is a rare, life-threatening complication of infection. Early treatment and implementation of sepsis bundles of care have been shown to improve outcomes. However increased vigilance for sepsis, risks increasing unnecessary investigations and antibiotic treatment.

Methods

This was a single centre retrospective cohort study. Inclusion criteria included patients discharged between October 2016 - May 2017, aged 28 days - 18 years with a discharge diagnosis indicating bacterial infection. Bacterial infection was identified using a list of 95 ICD-10 codes devised by consensus amongst regional infectious disease, intensive care and general paediatric consultants. Case notes and electronic records were interrogated and data on delivery of paediatric sepsis 6 criteria extracted. The patients were coded as either sepsis or infection following notes review by experienced clinical researchers.

Results

306 episodes were recorded, 36 patients with clinically suspected sepsis cases and 270 with infection. In the first hour 55% of sepsis group/10% of infection group received antibiotics, 42%/9% blood cultures, 42%/6% blood gas, 38%/2% fluid resuscitation, 44%/35% senior review, and 35%/26% high-flow oxygen respectively. A further 55%/11% had additional tests (e.g. FBC, CRP). See figure for monthly rates.
Conclusions

Overall the trend reflected a moderate improvement of timely treatment of sepsis throughout all performance indicators. Limitations of the study are small numbers of septic patients in keeping with national figures. Our findings indicate that despite the vigilance for sepsis, this does not appear to have resulted in the over-investigation and treatment of less severe cases. Further work should investigate what barriers lead to delays in treatment for sepsis being promptly delivered.
CONFIRMED MENINGITIS. DESCRIPTIVE STUDY IN A THIRD LEVEL HOSPITAL IN SPAIN
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²Hospital de Poniente, Pediatric Infectious Diseases, El Ejido, Spain

Background

The early diagnostic in patients with clinical findings of meningitis is still challenging. Our aim is to determine the epidemiological characteristics in a series of children diagnosed with meningitis in a tertiary hospital in southern Spain.

Methods

Retrospective descriptive study of children treated in the Emergency Department during the years 2014-2017, with diagnosis of meningitis confirmed by biochemistry, culture or PCR in CSF.

Results

A total sample of 62 cases is presented. According to sex: males 66%; 34% women; By age: median in 6 years. Laboratory data: Pleocitosis: positive in 96% of the cases; in the remaining 4% no pleocitosis was found, resulting this latest ones positive for enterovirus. Predominant cells: in enterovirus meningitis, mononuclear cells predominated in 66% of the cases, while polymorphonuclear cells predominated in the remaining 33%. In contrast, in bacteria caused, polymorphonuclear predominated in 100%. The median of the glucose and proteins in the CSF in the group caused by enterovirus was 64 and 35 mg / dl, while in the group caused by bacteria was 54 and 109 mg / dl respectively. Germs were confirmed only by biochemistry 13%, enterovirus 79%, meningococcus B 3%, meningococcus C 3%, pneumococcus 2%.

Conclusions

Most of the meningitis in the pediatric age are caused by enteroviruses, generally occurring in the spring, as reflected in our series. The median age and the predominance of the male sex also coincide with what is described in the literature. In 33% of the cases caused by enteroviral infection, a polymorphonuclear predominance can be observed in the biochemical analysis of the CSF which probably leads to an increasing use of antibiotic therapy. Furthermore, we highlight cases produced by meningococcus C all occurring in unvaccinated patients.
Title of Case(s)

Diabetes mellitus (DM) type 1, a hole in the palate and its several infections

Background

Infectious diseases are more prevalent in patients with DM. The hyperglycaemic environment, associated with the reduced chemotaxis and phagocytic activity and the low interleukins levels explain this predisposition.

Case Presentation Summary

An 11-years-old girl, born and living in Angola, with type 1 DM diagnosed the year before, was admitted for a huge, nodular, vegetative ulcerated lesion on the palate for 6 month. On admission she was obnubilated, acidotic and had multiple necrotic crusts on the nasal septum and palate. A tumoral infiltrating lesion on the nasal cavity, destroying the harsh palate, nasal septum, the left pterygopalatine fossa and the internal wall of the maxillary sinus was noted on CT, together with multiple 1-2 cm cavitated pulmonary nodules. The Mantoux and IGRA tests were negative and HIV infection was excluded.

The nasal tumor histopathological exam showed nonseptate hyphae compatible with zygomycosis and on cultures Candida glabrata and krusei, Actinomyces, Mycobacterium tuberculosis, Kodamaea ohmeri, Providencia stuartii, Klebsiella pneumoniae, were isolated.

She was submitted to two surgical cleanings and debridements, and treated with penicillin, clindamycin, isoniazid, rifampicin, ethambutol, pyrazinamide and amphotericin B. At 5 months of evolution she maintains amoxicillin, posaconazole, isoniazid and rifampicin with notorious improvement of the palate and lung lesions.

Learning Points/Discussion

Polimicrobian severe infections can affect badly controlled DM patients. Rapid diagnosis and early treatment are fundamental for disease prognosis. In this patient we suspect that both zygomycosis and actinomycosis could have had a preponderant role in the patient disease.
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Background

Acute gastrenteritis (AGE) is one of the main public health issues worldwide. We aimed to study the epidemiology of paediatric AGE cases in South Athens Greece, in view of their clinical characteristics, etiology, antibiotic use and rotavirus vaccination.

Methods

Retrospective analysis over a two year period 2016-2017 of A&E records and inpatient files of all AGE paediatric cases from an NHS District General Hospital in South Athens Greece.

Results

A total of 530 paediatric AGE cases were analysed, 49.8% boys, 48.7% girls, Greek ethnicity 70.9%, mean age=60 months (r: 9 days-16 y). Maximum admission A&E rate was recorded on December (15.09%) and minimum on April (2.64%). Main reason for A&E admission was vomiting 72.9%, diarrhoea 50.2%, vomiting and diarrhoea 23%, fever 37%. Hospitalization rate 19.6%, maximum rate recorded on January (15.09%) and minimum on October (2.9%) and mean hospitalization days=2. Boys 48.1%, girls 51.9%, greek ethnicity 69.2%, mean age 72 months (r: 5 months-16 years), mean vomiting episodes/day=5, mean diarrhea episodes/day=3, fever 48.1%, bloody stools 5.8%, mean siblings=2. Borderline leucopenia or leukocytosis <6000 or >10,000 had 76%. Rotavirus detection 23.1%, adenovirus 2.9%, salmonella 4.8%. From the 6 cases with bloody stools salmonella identified in only one. One case only treated with antibiotics. Rotavirus vaccination data were available in 15/104 hospitalized cases of which only 4/15 were vaccinated (26.7%). In the 24 rotavirus cases age spectrum was 5 months-15 years old, vaccination data were available in 5/24 of which 4/5 (aged 4 months-7 years) were not vaccinated.

Conclusions

AGE paediatric cases presented mainly on December with a fifth being hospitalized mainly on January. Rotavirus vaccination rate is low, although rotavirus remain the main detected agent with another 69.2% being identified.
PERINATAL HIV-1 INFECTION IN AN EXTREMELY PREMATURE INFANT.
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¹University of Texas- McGovern Medical School, Pediatrics, Houston, USA

Title of Case(s)
Perinatal HIV-1 infection in an extremely premature infant

Background
Prematurity is associated with a higher risk of perinatal HIV transmission mainly in vaginal deliveries and higher mortality rates in HIV-infected infants. While more upcoming data are supporting the benefits of treatment of perinatal HIV infants soon after birth, there is lack of guidance regarding how to treat extremely premature newborns.

Case Presentation Summary
An infant was born at 24 weeks of gestation (birth weight: 665 grams) via emergent C-section to a mother living with HIV for the previous five years. Mother was non adherent to combined antiretroviral therapy (cART), did not have prenatal care and had a viral load at 1240 copies/ml on the day of delivery. The first HIV testing was obtained on day of life (DOL) 13 and it was positive (qualitative HIV DNA PCR). It was unclear if the baby was infected in-utero or intrapartum. Due to lack of guidance for dosing of most antiretroviral medications in extremely premature infants, cART was not initiated until DOL 75. Hospital course was complicated by pulmonary hypertension (treated with sildenafil), pancreatic enzyme deficiency, potential drugs interactions between sildenafil and cART and multiple culture-negative sepsis evaluations. The patient had a relatively slow slow viral clearance, possibly related to pharmacokinetics of cART in young infants, malabsorption and immature neonatal immune system that is incapable of controlling HIV replication. The patient did not have significant infections.
Learning Points/Discussion

We describe viral dynamics and clinical outcomes of an extremely low birth weight infant with perinatal HIV-1 infection.

We highlights the importance of more studies needed to establish recommended dosing of cART in these newborns. This allows early cART initiation and provide a potential opportunity to limit the size HIV reservoir.
ANTIRETROVIRAL POST-EXPOSURE PROPHYLAXIS (PEP) AFTER SEXUAL EXPOSURE: 7-YEAR REVIEW

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Title of Case(s)

Antiretroviral Post-Exposure Prophylaxis (PEP) After Sexual Exposure: 7-year review

Background

Possible sexual exposure to HIV represents an emergency and post-exposure prophylaxis is currently under discussion. A 28-day course of antiretroviral therapy after sexual exposure is used to prevent HIV infection. The authors proposed to review all cases of sexual exposure over 7 years in a tertiary hospital in northern Portugal where there is an institutional protocol of action, after non-occupational exposure to HIV in children and adolescents, which determines the use of antiretroviral prophylaxis within the first 72 hours.

Case Presentation Summary

50 cases of sexual exposure were identified, with an average of 7 cases/year and a higher number of cases in the last 2 years. 43 cases were female; the cases were aged between 2-17 years (median 14). In one case there was sexual contact with an HIV positive source. In all cases HIV serology, prior to prophylaxis, was negative. 31 cases were eligible for HIV infection prophylaxis. The most commonly used combination was Zidovudine+Lamivudine+Tenofovir. From 2015 the protocol indicates as preferable Emtricitabine/Tenofovir+Raltegravir. The prescription were made for 5 days, and the physician's telephone contact and scheduled appointment were provided. All cases were followed up by a pediatrician. In 2 cases antiretroviral therapy was interrupted after confirming the negative source. All the others completed 28 days with good tolerance and were discharged 16 weeks later, with confirmation of negative serology. There was no case of HIV infection.

Learning Points/Discussion

The prophylaxis schemes used, in constant updating according to scientific evidence, have been shown to be effective and it's important to highlight their early onset and adherence. Despite the dissemination of information on HIV transmission, in our study we identified increasing numbers of sexual exposure with an inherent risk of infection.
LUMBAR PUNCTURE SIMULATION HELPS PAEDIATRIC TRAINEES GAIN EXPOSURE IN PRACTICAL TECHNIQUE, IMPROVES CONFIDENCE AND INCREASES CSF INTERPRETABILITY.

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Background

The RCPCH provides a comprehensive curriculum for paediatric trainees. Level 1-training includes lumbar puncture (LP) as a core practical procedure but lack of opportunity, experience and low procedural confidence can make it difficult to achieve this competency. Traumatic lumbar punctures causing blood stained CSF can lead to difficulties with interpretation. The objective of this quality improvement project was to increase CSF interpretability by 50% in a 5-month period. An LP simulator was used to enhance trainee technique.

Methods

Prospective data was collected during August 2017 to December 2018 for the acute general paediatric admissions looking at patient demographic, location of LP, trainee grade, CSF microscopy results and interpretability. Three half-day simulated procedural training days practicing LP technique, discussing appropriate sedation and case based teaching occurred during this time and trainees were surveyed about experiences and confidence levels.

Results

58 lumbar punctures were performed during the study period, most occurred in patients aged between 7days and 3months old. Participation of junior trainees increased from 8% to 40% in the first 4months but then decreased in 15% in December possibly reflecting winter pressures. Encouragingly after the second LP course CSF interpretability increased from 47% to 92%, this fell to 69% by the end of the study period.

24 trainees were surveyed, 12 (50%) described their LP skills as satisfactory pre-intervention. 23 (96%) felt significantly more confident after the course.

Conclusions
Simulation-based training for procedural skills has been shown to be effective for trainees. This project shows that when juniors are given the opportunity to gain hands-on experience using high-fidelity models it can lead to enhanced user confidence, willingness to participate in the clinical setting and increased procedural competence therefore benefitting the patients.
PAEDIATRIC TUBERCULOSIS SCREENING - CURRENT PRACTICE AND A LONDON DISTRICT GENERAL HOSPITAL REALITY

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Background

With changing demographics, some boroughs of London have been shown to have tuberculosis rates comparable to less economically developed countries. Systematic screening can control transmission and reduce incidence, however in a paediatric population there remain many challenges including indeterminate diagnostic/screening tools. We sought to capture and evaluate current practice and its impact at a busy London hospital against latest NICE guidelines.

Methods

We identified 88 patients referred to respiratory clinic from Dec 2016-Nov 2017 for suspected active TB and TB contact. A retrospective review of casenotes surveyed several processes including time from referral to investigations and diagnosis by a trained paediatrician. We also assessed the diagnostic value of each component of the pathway including chest x-ray, Mantoux tuberculin skin test (TST), Elispot Interferon-γ release assays (IGRA) in the context of benefit and burden to both patients and services.

Results

Of 88 patients referred, 93% had TST as first line test in a nurse-led clinic at median average time of 16 days following referral.

64 patients were referred for TB contact - 60 had CXRs, 98.3% of which were normal. Only one patient referred in this group had an abnormal CXR but had positive TST and Elispot diagnosing active TB. There was variable practice in interpreting TST/Elispot for 13 patients diagnosed with latent TB.

Conclusions

Patients referred for TB screening were seen on average around 2 weeks later and while no guidelines stipulate expected times, this falls in line with most waiting times targets for serious illness. In our assessment chest X-ray added no diagnostic value for children referred for TB contact, risking unnecessary radiation exposure and cost to services. We found current screening practice to be variable, confounded by recent changes in NICE guidelines.
PERTUSSIS INCIDENCE IN A TERTIARY HOSPITAL IN SPAIN IN A FIVE YEAR PERIOD
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Background

Whooping cough is a disease that has blunted its incidence in recent years. The importance of early diagnosis is essential, especially in the emergency services (ES), where cough is one of the main reasons for consultation.

Methods

All the samples sent to the Microbiology service of a tertiary hospital in the province of Granada (Spain) in the last five years were analyzed.

Results
We analyzed a total of 650 samples in the years 2013-2017 sent from our area of influence in the province with the following results: Age of request: Under one year: 377. Total 58%; Greater than one year: 202. Total 31%; Adults: 71. Total 11%. Provenance: Out-of-hospital: 385 (59%). Intra-hospital: 265 (41%): 214 in the ES (81% of all intrahospital requests). Incidence per years in intra-hospital requests: (table above)

**Conclusions**

The incidence in our province highlights an increase in possible relationship with the rise of anti-vaccine groups in certain population areas. Therefore, it is a disease to be taken into account due to its high morbidity and mortality, especially in children under one year of age. Emphasis should be placed on emergency services on the importance of primary vaccination as well as revaccination in young adults as the main reservoir.
TRAVEL RELATED INFECTIONS IN CHILDREN – A SINGLE CENTRE OBSERVATIONAL STUDY

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Background

Recent surveillance shows a 50% increase in travel over the last decade.¹ The Health Protection Agency (HPA) recommends health precautions prior to travel that are effective in preventing the acquisition of infections prevalent in the tropical regions.

Methods

A retrospective observational study analysing the presentation of children returning from travel outside the United Kingdom over a 4-year period (2014-2017).

Results

342 children presented unwell with a travel history to the health service in the Birmingham catchment area over the 4 year period. Of them, 176 (51%) children presented to the General Practitioners and 166 (49%) children presented to the Heart of England Hospital.

Of the 166 children who presented to the Hospital, the median age at presentation was 4 years (Range- 6 months- 16 years). 93% (n=155) presented with a fever, 77% (n=128) with gastro-intestinal symptoms, 27% (n=45) with respiratory symptoms. 78% (n=129) returned from South Asia (Pakistan-84, India-29, Afghanistan-6, Sri-lanka-5, Bangladesh- 4 Vietnam -1) and 15% (n=25) from Africa. Chemoprophylaxis was taken by 4% (n=7). Only five had travel vaccines prior to travel.

9% (30/342) were confirmed to have tropical infections; 14 had Malaria (8 -P.falciparum, 4 -P.vivax, 1 -P.ovale, 1- Malarial antigen +ve), 9- enteric fever, 3- Hepatitis-A, 3- Cryptosporidium, 1 – Giardia. All were treated according to the local protocol. No deaths were noted in this cohort.

Conclusions

<10% of the children presented with tropically acquired infections post-travel. This study highlights the lack of compliance in the use of travel vaccines and chemoprophylaxis.
Severe diphtheria in a partially immunised UK 4 year old

Background

Diphtheria is a serious and life-threatening infection. Since 2015, two unvaccinated children have died of diphtheria in Europe. Due to the rarity of this infection in the UK, delay in diagnosis and recognising complications, can lead to delay in effective patient care. Severe disease can also occur in partially immunised children.

Case Presentation Summary

A 4 year old Slovak boy, presented with a croup-like illness; adenovirus, Moraxella and Haemophilus were isolated from respiratory secretions. He developed upper airway obstruction requiring intubation and ventilation; on extubation a grey pharyngeal membrane was discovered. Toxigenic C. diptheriae was later confirmed microbiologically. He had received vaccine at 2 and 12 months. A clinical decision was made to treat. As he was afebrile and clinically improving, he received 40,000 units of antitoxin. Five days later he developed further respiratory compromise with a pulmonary haemorrhage, myocarditis and prolonged QT. A further 60,000 units were administered with no adverse reaction. He required a tracheostomy and was discharged to the ward. He developed persistent fever; investigations including imaging and CSF did not identify other causes. A repeat echocardiogram showed evidence of coronary artery dilatation. After discussion with experts nationally IVIG was not given due to concern about exacerbation of an immune complex process. His fever settled spontaneously. He developed diphtheritic polyneuropathy which was biphasic and required readmission to PICU with bulbar and diaphragmatic palsies. He was discharged after 3 months, with significant but improving polyneuropathy.

Learning Points/Discussion

Severe diphtheria may occur in partially immunised children in low incidence countries. Neurological involvement may be insidious and diagnosis may be delayed in countries with little experience. Diphtheria associated coronary artery dilatation is not well documented.
Kawasaki disease with Hemophagocytic Lymphohistiocytosis in a child with STXBP2 monoallelic mutation

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Title of Case(s)

Kawasaki disease with Hemophagocytic Lymphohistiocytosis in a child with STXBP2 monoallelic mutation

Background

Hemophagocytic Lymphohistiocytosis (HLH) is a rare and potentially life-threatening complication of Kawasaki disease (KD). This entity resembles primary HLH, a group of immune dysregulation syndromes, inherited in an autosomal recessive fashion. Genetic polymorphisms may play a central role in secondary HLH.

Case Presentation Summary

A 4-year-old male with a 6-day history of fever, diffuse erythema, odynophagia and right foot pain. Physical examination revealed cheilitis, strawberry tongue, perineal rash with desquamation, conjunctival hyperaemia and feet oedema. Echocardiogram was normal. Treatment for KD was initiated with intravenous immunoglobulin (IVIG) and acetylsalicylic acid. Nevertheless, fever persisted, whereby IVIG was repeated with subsequent clinical improvement.

On day 6, right ankle swelling exacerbated, and a MRI suggested distal tibia osteomyelitis. Cefuroxime and clindamycin were initiated and surgical bone drainage isolated methicillin-sensitive Staphylococcus aureus.

On day 20, patient developed fever, exanthema and splenomegaly. Laboratory test revealed haemoglobin 7.8g/dL; leucocytes 2320/uL; neutrophils 80/uL; platelets 135000/uL; ALT 221U/L; ferritin 36036ng/mL; CRP 1.04mg/dL; fibrinogen 247mg/dL; sCD25 3346U/ml. Hemophagocytic syndrome was suspected and the patient was transferred to a reference unit. Bone marrow biopsy was negative for hemophagocytosis, and a conservative approach was assumed, with gradual clinical and analytical normalization.

Repeated outpatient bone marrow examinations were performed. Hemophagocytic cells were detected nine months after discharge, although with no other hemophagocytic criteria. Primary HLH-related genes study revealed a monoallelic STXBP2 mutation.

Learning Points/Discussion

Type 5 Familial HLH is caused by biallelic STXBP2 mutation. However, heterozygosity may grant hemophagocytosis susceptibility, when triggered by conditions, such as KD or infections.
Optimal approach guidelines and specific HLH criteria for KD are necessary. We highlight the importance of genetic study in these patients, in order to prevent possible future recurrence.
05B. EDUCATION: POST - NEONATAL VIRAL AND OTHER CULTURE NEGATIVE INFECTIONS

DIRECT ACTING ANTIVIRAL TREATMENT FOR CHRONIC HEPATITIS C VIRUS INFECTION. REAL WORLD EXPERIENCE IN AN IRISH PAEDIATRIC COHORT

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Title of Case(s)

Real world experience of direct acting antiviral (DAA) treatment of chronic hepatitis c virus infection in an Irish paediatric cohort

Background

DAA treatments are now considered the gold standard for treatment of chronic hepatitis c virus (HCV) infection. All oral, short-course, interferon-free regimens are well tolerated, associated with few adverse effects and eradication rates far exceed previous interferon-based regimens. To date, cost of DAA medication has largely precluded their use in the paediatric population in Ireland and elsewhere. In 2017, the National HCV Treatment Programme agreed to extend access to DAA to our paediatric HCV-infected cohort. We report our preliminary experience with DAA treatment of an adolescent HCV-infected cohort in a real world setting.

Case Presentation Summary

To date, 7 genotype-1 chronic HCV-infected adolescents (4 male) (age range, 14-18 years) have received DAA treatment (Ledipsavir 90/Sofosbuvir 400). Patients are reviewed after weeks 1, 2, 4, 8 and 12 on treatment and weeks 12, 24 and 48 post-treatment. Week-one median HCV viral load decrease, 4 log. Week-four HCV viral load -, 3; positive < limit of detection, 2; viral load +, 1.3-1.6, 2. DAA was well tolerated with few adverse effects: fatigue, 2; headache 1; GI upset, 1. No discontinuation due to adverse effects. No abnormalities on monitoring laboratory tests. Problems encountered during treatment included: inadvertent self-medication with antacid, 1; missed doses due to lack of parental supervision, 2; failure to redose within permitted timeframe, 1; or double dosing after missing a dose, 1.

Learning Points/Discussion

Early virologic responses to DAA treatment in our paediatric HCV-infected cohort are encouraging. Treatment was uniformly well tolerated. Despite careful patient selection and extensive education 5 of 7 patients deviated from protocol suggesting that their frequent regular follow-up is justified and essential.
04A. EDUCATION: SEVERE PNEUMONIA IN CHILDREN

COMPARISON OF CULTURE AND MOLECULAR TECHNIQUES TO IDENTIFY THE MICROBIOLOGICAL ETIOLOGY OF SEVERE PNEUMONIA IN CHILDREN: IMPACT ON NEW VACCINE DEVELOPMENT
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Background
Severe pneumonia remains the leading cause or mortality beyond the neonatal period in children < 5 years old worldwide, particularly severe pneumococcus pneumonia. Pneumococcus conjugate vaccine has been identified as one of the effective strategies to reduce mortality in this population. Thorough understanding of the microbiologic etiology of severe pneumonia in children will allow for design of new and improved vaccines.

Methods
We conducted a prospective surveillance (2013 – 2016) of all cases of community acquired pneumonia complicated by empyema, as a surrogate of severe pneumonia, in children (0 – 18 years old) treated at a large children’s hospital in Orange County, California, and evaluated the microbiologic diagnosis sensitivity by routine culture as well as by molecular methods. When available, pneumococcal serotype was determined.

Results
During the study period 60 cases of empyema were identified, the microbiologic diagnosis was improved from 19 (31.7%) to 39 (65%) cases. Pneumococcus was identified in 27 (69.2%) cases, of which 17 (63%) were identified by molecular techniques. During the study time there were 38 additional cases of invasive pneumococcal disease. Among the 10 pneumococci identified by culture in subjects with empyema, 7 (70%) were current vaccine serotypes (0 in 2016) all the while only 6 (15.8%) of non-respiratory invasive pneumococcal isolates were vaccine serotype.

Conclusions
Culture is not an appropriate modality to identify pneumococcus in children with severe pneumonia. Pneumococcal serotypes identified in non-respiratory disease do not accurately reflect those responsible for severe pneumonia. Molecular techniques are going to be necessary to identified the proportion of pneumococci and there serotype in children with severe pneumonia to improve the composition and evaluate the efficacy of new vaccines.
LEMIERRE SYNDROME IN ADOLESCENT POPULATION: THE IMPORTANCE OF DIFFERENTIAL DIAGNOSIS OF OROPHARYNGEAL INFECTIONS WITH UNFAVORABLE EVOLUTION

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Title of Case(s)

Lemierre Syndrome in adolescent population: the importance of differential diagnosis of oropharyngeal infections with unfavorable evolution

Background

Lemierre syndrome (LS) is an uncommon but potentially dangerous disease in children; its incidence was drastically reduced with the introduction of penicillin. It is a severe disorder characterized by pharyngitis, septic trombosis of the internal jugular vein and distant septic metastasis mainly caused by Fusobacterium necrophorum

Case Presentation Summary

A 15-year-old boy had been suffering from lateral-cervical pain for about 1 week, in association with intermittent fever of up to 39ºC. Initially it was diagnosed as muscle contracture. Due to the persistence of cervical pain, without fever, and the appearance of cervical swelling, he visited the ER for the third time. Blood test: CRP 186 mg/L, 17590 leukocytes (65.3% N). Ultrasound (US) showed right-sided cervical adenopathy conglomerates. Empirical treatment with amoxicillin-clavulanic acid was initiated, combined with corticosteroids for four days. A significant reduction of the swelling was observed however the pain persisted. US demonstrated a growth in size of the conglomerates with presence of cystic areas. A puncture was made with the extraction of a large quantity of pus. Clindamycin was started. CT scan showed a latero-cervical abscess and jugular vein thrombosis. The abscess was drained and the patient was treated with meropenem and heparin with clinical improvement. F. necrophorum was detected by PCR and culture.

Learning Points/Discussion

The exceptionality and diverse clinical picture of LS can have an impact on the difficulty of its initial diagnosis since it is not suspected in the context of oropharyngeal infections with torpid unfavorable evolution. It presents a high morbidity and mortality in the absence of treatment, but with a good prognosis and early infection control complications derived from thrombosis can be avoided.
CHRONIC OSTEOMYELITIS IN A PATIENT FROM GAMBIA

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Title of Case(s)

Chronic osteomyelitis in a patient from Gambia

Background

Chronic osteomyelitis is a pathology characterized by a long-standing and recurrent clinical course; especially significant in developing countries. Its management usually requires both antibiotic and surgical treatment.

Case Presentation Summary

17-year-old patient from Gambia with a 7-year history of bone pain in left lower limb (LLL) associated with abscessed lesions. Two surgical interventions were performed and a 6-month course of parenteral antibiotics was administered in his country. Subsequently, he presented exacerbations with discharge of purulent material along multiple fistulous paths treated with oral antibiotics. No BCG vaccination, no other symptoms, no significant previous history.

Complementary tests: CRP 12.5mg/l, ESR 58mm, fibrinogen 569mg/dl. Normal CBC, coagulation and other biochemistry tests. Mantoux 0mm, negative Quantiferon. Negative thick blood smear and PCR for Plasmodium. Negative blood, urine, stool cultures, and parasites tests. Negative HIV, Syphilis, Schistosoma, Strongyloides and Toxocara canis serological testing. Normal chest Xray. LLL Xray showed increased fibular radiolucency without corticomedullary differentiation and irregular contours. MRI findings were suggestive of chronic osteomyelitis with diffuse affection of the fibula and formation of bone sequestration and sewers with extension of inflammation to soft tissues and collections in muscular compartment. Bone scintigraphy didn’t show other foci.

Given the high suspicion of chronic osteomyelitis, surgery was performed with resection of the peroneal diaphysis, fistulectomy and debridement of LLL. Anatomopathological findings were compatible with chronic osteomyelitis, and Methicillin-sensitive Staphylococcus aureus was isolated. PCR Mycobacterium and other cultures were negative. Parenteral antibiotic treatment with rifampicin and cefazolin was administered for 14days, continued with oral cloxacillin and rifampicin for 6-9months.

Learning Points/Discussion

Chronic osteomyelitis is a complex pathology, which requires a multidisciplinary approach; both surgical treatment and microbiological diagnosis are fundamental to optimize the treatment.
Perianal dermitis in a 3.5 year old toddler presented as query sexual abuse

Background

Sexual abuse is a problem with epidemic characteristics in our society with 15% of men and 25% of women in their adulthood confirming a sexual abuse episode in their childhood. Thus is crucial for physicians to be able to recognise a possible sexual abuse case in order to protect the child as well as other children for repetitive episode. Several medical conditions can be mistaken as sexual abuse and lead innocents in the court, separating children from their families.

Case Presentation Summary

A 3.5 year old toddler presented to the A&E department with an extensive perianal dermitis, with pain, redness, itching and clear borders. He was given an history of a male who did this in his father house at Christmas Holidays. From the family-social history parents were divorced. father was a drug user with good relationship with his ex wife and his parents. Following query sexual abuse protocol we took cultures form the lesion including sexually transmitted diseases and we started oral Augmentin with the possible diagnosis of Group A streptococcal perianal dermititis. Cultures were positive for GAS and the child improved within 24 hours. Nevertheless from Developmental examination he had hyperactivity disorder but he was giving the same story of this man who did this.

Learning Points/Discussion

GAS perianal dermitis is commonly mistaken with sexual abuse as well as worm or fungal infection, constipation or inflammatory bowel disease. In our case despite the definite diagnosis of GAS perianal dermitis the fact that the child present the same story of sexual abuse we informed legal authorities for further investigation.
ETIOLOGY OF ACUTE DIARRHEA IN CHILDREN ATTENDING THE EMERGENCY SERVICE IN SERGIPE/NORTHEAST, BRAZIL

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Background

Diarrhea still represents 8% of deaths in children under 5 years of age worldwide and an important cause of infant consultation and hospital admission. This study aims to verify the presence of three etiological agents (Rotavirus, Norovirus and Cryptosporidium spp.) associated with acute gastroenteritis in children aged 0 to 11 years old in the reference Emergency Hospital of Sergipe.

Methods

An observational cross-sectional study was conducted in 92 children with acute diarrhea from January to July in 2014. The samples were tested by ELISA for the detection of Cryptosporidium spp. and Rotavirus and subsequently tests were performed for the detection of Norovirus by the RT-PCR technique.

Results

It was observed that 57 (62%) of the samples presented infection by one of the pathogens studied. The average age of the children affected by one of the three pathogens was 22.24 months (95% CI, 15.26 - 29.21), 64% of males and 36% of females. In addition, 2 (3%) presented Norovirus and Cryptosporidium spp. co-infection. Rotavirus and Norovirus were present in all months of the studied period, but Cryptosporidium spp. was only observed in two months (April and May) during the fall. In relation to the vaccination against Rotavirus of those infected by one of the three pathogens, 66% (n = 38) received the two doses, 5% (n = 3) were not vaccinated and 29% (n = 17) could not inform.

Conclusions

Norovirus is currently the most frequent agent (49%) associated with acute diarrhea, followed by Rotavirus (10%) and Cryptosporidium spp. (4%) in children admitted to a pediatric reference center, and most of cases were infected by one of the three investigated agents.
Background

Fever in infants younger than 3 months can reflect a serious bacterial infection, so routine behaviors are blood cultures samples.

OBJECTIVE: To describe type and positivity time of isolated bacteria in blood cultures of infants under 90 days hospitalized for fever.

Methods

Retrospective descriptive study. Positive blood cultures taken in children under 90 days of age during the period from 2014 to 2016 were reviewed. The identification and time of positivity of each bacteria data, demographic and laboratory variables were obtained. We excluded patients who were not hospitalized, those who did not have a fever and those with comorbidity.

Results

There were 172 young infants with positive blood cultures. Only 51 patients met inclusion criteria. 21 pathogenic microorganisms were identified and 30 were considered contamination, mainly S. coagulase negative. The median time of positivity was 10 hrs. After 24 hrs of culture, bacterial growth was detected in 48 samples (94%), the remaining 3 corresponded to bacteria considered to be contamination. Regarding pathogens, E. coli was identified in 20% of the samples with a median time of positivity of 6.7 hrs, S. agalactiae was isolated in 5% with a median of 5 hrs and S. pyogenes was identified in 5% with a median of 10 hrs.

Conclusions

Isolated pathogenic bacteria correspond mainly to gram-negative bacilli and streptococci. All the isolated pathogens were detected before 24 hrs of incubation. There is not yet enough available evidence regarding the recommended observation time for febrile infants without a source, but with the current automated bacterial growth detection systems it seems that 24 hrs is an adequate period to rule out hidden bacteremia.
Title of Case(s)

Chronic Strongyloidiasis in a transplant recipient

Background

Strongyloidiasis is a parasitic infection caused by a nematode, endemic in tropical and subtropical countries. Recently, autochthonous cases have been described in Spain's east coast. It can occur asymptomatically or cause skin, gastrointestinal or pulmonary involvement, and immunosuppressed subjects are at risk of hyperinfestation and disseminated disease. Nowadays, it is not included in the systematic screening for patients before initiation of immunosuppression and there are not guidelines for its treatment and prophylaxis in high-risk subjects.

Case Presentation Summary

7-year-old boy with a deficiency of the mitochondrial chain with a multivisceral transplant and a splenectomy at 3 years, under treatment with Tacrolimus and Methylprednisolone. At 4 years old he presents recurrent urticaria with eosinophilia (2490/mm3) and IgE (3200 mg/dL). Positive Strongyloides stercoralis serological testing.

Treatment with Ivermectin was started with clinical improvement, initial decrease of eosinophilia (1190/mm3) and serological titers. Subsequent reactivation (Eosinophilia 2000/mm3, IgE > 5000 mg/dL, higher serological titers) led to a new treatment cycle that was not completed due to drug interaction. 14 months after the first cycle, combined treatment with Ivermectin-Albendazole was administered for 10 days. 4 months later, a new cycle of combined treatment, accompanied with a delayed hypersensitivity reaction to Albendazole.

Due to persistence of clinical and analytical alterations, he received again Ivermectin for 7 days and desensitization against Albendazol was performed. He received a new cycle Albendazol-Ivermectina, with improvement of serological titres and eosinophilia. Subsequently, he has continued with prophylactic Ivermectin (monthly).

Learning Points/Discussion

Strongyloidiasis should be included in the systematic screening prior to immunosuppression, given the potential severity of the condition and the difficulties in treatment.
Pulmonary Nocardiosis in Cystic Fibrosis: colonizer or pathogen?

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Title of Case(s)

Pulmonary Nocardiosis in Cystic Fibrosis: colonizer or pathogen?

Background

The clinical significance of *Nocardia* spp. isolated from the respiratory tract in cystic fibrosis (CF) patients is unknown. While its role as a pathogen is highly debated, it is an exceedingly uncommon finding in pediatric CF patients. Here we report a case of an immunocompetent CF patient who developed progressive clinical worsening attributed to pulmonary nocardiosis in the setting of clinical features not typically associated with CF pulmonary exacerbations (e.g. high fevers and pleuritic chest pain).

Case Presentation Summary

A 17-year-old male with CF presented with weight loss (>2kg) and decreased PFTS (FEV1 58% down from a baseline of 80%). CXR was concerning for multifocal pneumonia. He was initially treated with 3-weeks of tobramycin and piperacillin/tazobactam but failed to improve. He subsequently developed pleuritic chest pain and fever to 40.5°C. Vancomycin was added to his regimen and chest CT identified diffuse scattered tree-in-bud opacities with focal areas of consolidation, most prominent in the right middle and lower lobes, and a small cavitary lesion in the left upper lobe. Sputum cultures resulted positive for *Nocardia* species. In the setting of clinical deterioration over a 1.5-month period, he was empirically treated for nocardia with imipenem and amikacin. When cultures speciated to *Nocardia transvalensis*, he was narrowed to trimethoprim-sulfamethoxazole (TMP/SMX) based on sensitivities. He was subsequently treated for 12 months with improvement in chest CT and PFTs.

Learning Points/Discussion

- High fevers are usually not associated with pulmonary exacerbations in CF
- *Nocardia* can be associated with significant lung disease in CF. Aggressive multi-drug therapy should be instituted early when there is such deterioration.
- TMP-SMX is not reliably effective for *Nocardia transvalensis*. Therefore, antibiotics should only be narrowed based on sensitivities.
A 3-YEAR PROSPECTIVE DESCRIPTIVE STUDY OF THE EPIDEMIOLOGY, CLINICAL PRESENTATION AND MANAGEMENT OF KAWASAKI DISEASE (KD) IN COSTA RICAN (CR) INFANTS <6 MONTHS OF AGE

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Background

KD is the leading cause of pediatric acquired cardiac disease. In developed countries, KD in infants <6m is associated with higher rates of incomplete KD, coronary artery lesions (CALs), and late diagnosis. We describe the first prospective descriptive analysis of KD in CR infants <6m.

Methods

We analyzed pts <6m who met AHA’s clinical criteria for classic and incomplete KD, and were discharged from the only national pediatric tertiary referral academic hospital of CR from June-1-2014 to May-31-2017.

Results

Among 101 KD pts enrolled during the study period, 9 (8.9%) were <6 months of age. 7 (77.8%) were female pts. All pts were hospitalized. Mean length of fever at admission was 4 (2-7) days, and in 5 (55.6%) pts, KD was not considered among the admission diagnoses. Prior to final KD diagnosis, 8 (88.9%) pts received >1 antibiotics for other clinical presumptions. 5(55.6%) pts had acute BCG scar skin reactions. All pts received IVIG and ASA, but none steroids or a second dose of IVIG. All pts had a baseline echocardiogram performed, of which coronary artery dilations and/or aneurysms were detected in 4/9 (44.4%) pts. Incomplete KD was diagnosed in 3 (33.3%) pts on discharge. No deaths occurred.

Conclusions

The high rate of previous recent antibiotic use suggests that KD in CR infants <6m is misdiagnosed with common bacterial infections. In our study, the percentage of pts with incomplete KD was higher than other age groups, highlighting the importance of an early clinical diagnostic suspicion in this age group, for whom BCG scar changes can be helpful. To our knowledge, the rate of CALs found in this age group is the highest reported among Central America and Caribbean countries.

Clinical Trial Registration (Please input N/A if not registered)

N/A
THE EFFECTS OF NATIONAL VACCINATION PROGRAM AND MASSIVE MIGRATION ON THE EPIDEMIOLOGY OF HEPATITIS A INFECTION IN CHILDREN OVER THE PAST 5 YEARS

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Background

Acute hepatitis A infection is a common public health problem in undeveloped and developing countries. The hepatitis A vaccine has been implemented as part of the National Immunization Program in Turkey in November 2012. The aim of the present study was to investigate effects of the national vaccination program and massive migration on epidemiology and clinical burden of Hepatitis A infection.

Methods

This was a single center, retrospective chart review study among children diagnosed with viral hepatitis A infection between 0 and 18 years of age from January 2013 to February 2018 in Gaziantep, Turkey. In addition to the admission time, age, nationality and gender information of all cases, the length of stay and direct medical cost of hospitalization were also evaluated in hospitalized cases.

Results
During study period total of 1039 cases were diagnosed with hepatitis A infection. Of these cases, 53% were males, 14% were Syrian refugees and median age was 7.9 years. Number of cases per year (2013 through 2017) was 321, 360, 157, 119 and 73 respectively. The majority of the cases were detected in the November and December. While total number of cases were declining, we saw the number of Syrian children was increasing. Percentage of Syrian children in total cases in 2013 and 2017 was 6.5% and 52.1% respectively. Mean hospitalization rate was 49%, mean LOS was 4.84 days and mean medical cost of hospitalization per case was 262$.

**Conclusions**

After implementing of the vaccine in the national program, case numbers are declining. But the number of susceptible individuals in population is still adversely affecting the epidemiology of the disease. We think, monitoring epidemiological datas continuously and try to increase coverage of vaccination is neccessary for controlling infection.
SYPHILIS: COINFECTION OR CO-ADJUVANT OF THE CLINICAL PROBLEMS PRESENTED BY ZIKA VIRUS INFECTION

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Background

The World Health Organization (WHO) estimates 12 million new cases of syphilis worldwide each year. In the world, the incidence rate of congenital syphilis and the rates of its detection in pregnant women was increased by 3 times, ranging from 3.5 to 12.4 cases per thousand live births. In Brazil, according to WHO, 937,000 new cases of syphilis occur every year. The prevalence in the pregnant woman is 2.6%. PURPOSE: To evaluate the Syphilis and Zika Virus interaction with clinical worsening of coinfections.

Methods

A retrospective study evaluating the medical records of the Zika-Jundiai Cohort, São Paulo-Brazil, was performed from February 2016 to December 2017. A total of 752 pregnant women data of the ZiKa-Jundiai Cohort were reviewed and serological tests for Syphilis and qPCR in urine for Zika Virus were analysed.

Results

Of the 752 pregnant women, 572 (76%) patients had VDRL present on the Pre-natal Card. It was observed that 17/572 (2.9%) patients with positive VDRL, varying positivity from 1/32 to 1/512. The qPCR positivity for Zika virus was 6.7% (51/572) of these patients. Only one mother was positive for Syphilis and for Zika Virus, and she was adequately treated for syphilis during pregnancy. Concerning this mother, there were not any perinatal complications, and the newborn was negative for both tests.

Conclusions

In this study, the preliminary data shows that prenatal evaluation was important and effective in combating syphilis during pregnancy. It was not observed any association between Zika virus and syphilis in the present study, however further studies should be carried out to clarify whether there is any correlation between those infections.
STAPHYLOCOCCAL OSTEOMYELITIS IN CHILDREN: CAN IT BE TREATED WITH ORAL ANTIBIOTICS?

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Title of Case(s)

Staphylococcal osteomyelitis started on oral antibiotics

Background

Acute osteomyelitis in children has an increased incidence of about eight cases per 100,000 children per year. It occurs mainly in males possibly due to microtrauma and increased physical activity. Traditional treatment is based on prolonged intravenous antibiotics, although recent reports suggest shorter intravenous courses with subsequent switch to oral. We present two cases of staphylococcal osteomyelitis in order to discuss in certain cases optional treatment with oral antibiotics only.

Case Presentation Summary

Case 1: A 15 year old male teenager presented with right hip pain and limp. In 48 hours he deteriorated with pyrexia 37.8°C and increased hip pain. Lab tests revealed elevated neutrophile count, CRP=189 mg/L, ESR=52. Patient refused admission for intravenous antibiotics. Blood culture on D3 was MSSA positive and thus patient was called back to hospital. He was afebrile, in good condition and he was receiving oral amoxycillin-clavoulanic acid. Right hip MRI showed periosteal oedema.

Case 2: A 81/2 year old boy admitted with a 48 hours history of fever 38.5°C, right groin pain and limp. There was a recent history of abdominal trauma. Initial orthopaedic examination diagnosed transient hip synovitis and he was treated with bed rest. CRP was 52.3 mg/L, ESR=50mmHg and D3 blood cultures MSSA positive. MRI showed periosteal oedema.

Learning Points/Discussion

Although patients had been improved on initial treatment with oral antibiotics (case1) or no antibiotics and bed rest (case2) because of positive MSSA cultures intravenous antibiotics for a sort course started later before switched to oral. In both cases course of the disease was unremarkable despite the delayed onset of intravenous antibiotics. Literature data support the use of oral antibiotics in benign cases of pediatric osteomyelitis.
STREPTOCOCCI PNEUMONIA EMPYEMA IN A FULLY IMMUNISED INFANT WITH THE 13-VALENT PNEUMONOCOCCAL VACCINE

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Title of Case(s)

Empyema in a 26 months old infant fully vaccinated with Streptococci Pneumonia vaccine

Background

Streptococcus Pneumoniae is one of the main pathogens in community acquired pneumonia complicated with parapneumonic effusion and/or empyema. We present a case of pleural empyema in a fully vaccinated infant in order to discuss new serotypes of streptococci pneumonia that are not included in available pneumonococcal vaccines and raise a public health issue.

Case Presentation Summary

A 26 months old infant presented with an eight day history of hyperpyrexia 40°C, coughing and difficulty with feeding. He was in poor general condition with grunting, respiratory distress, tachypnea and left sided reduced air entry. Chest x-Ray and chest ultrasound showed left sided pleural effusion. CRP was 117mg/l. He was on treatment with oral amoxycillin-clavulanic acid (60mg/kg/d). He was started on intravenous antibiotics with Ceftriaxone and Vancomycin. On D2 he deteriorated further and repeated chest ultrasonography showed increased pleural effusion >1/2 of the left hemithorax. He was transferred in a peadiatric surgical unit for chest drainage and fibrinolysis. Pleural fluid PCR was Str.Pneumoniae positive, with a serotype not present in the 13-valent pneumonococcal vaccine. Infant was fully immunized with the 13-valent pneumonococcal vaccine.

Learning Points/Discussion

Although the 13-valent pneumonococcal vaccine thought to diminish the increased incidence of pneumonococcal effusions after the use of the 7-valent vaccine it seems that new or old serotypes, not included in the 13-valent vaccine, continue to complicate community acquired pneumonia with serious conditions, such as parapneumonic effusion and empyema.
Background

The most common cause of pediatric patients’ presentation in the ER are infectious diseases. In order to achieve better disease prevention and public health, it is mandatory that infectious diseases, such as food-borne infections and CNS infections, are being recorded to «ΚΕΕΛΠΝΟ» (Greek Center of Control and Prevention of Diseases). Recording of these cases contributes to better planning of convenient prevention programs.

Methods

Between 1/1/2013 and 14/12/2016, a retrospective epidemiological study was carried out in our Pediatric Clinic, in the county of Magnesia, in Central Greece. 84 printed cases were collected and written down, using Excel System. Data have been edited and analyzed based on demographic and other criteria, type of infectious disease, clinical status of patient when presented in ER and duration of hospitalization.

Results

During 2013-2016, 84 cases (1.8%), of a total hospitalized children in our Clinic, 40 girls and 44 boys, aged 14-day-old to 16-year-old, suffered from an infectious disease of these recorded to “ΚΕΕΛΠΝΟ” = “DCAPGC”. 0.2% of them (especially meningitis) were transferred to a third-grade hospital. Salmonellosis seems to be the most frequent of the infectious diseases and meningitis (aseptic or bacterial) is second. Also, a decrease of infectious diseases is noted since 2014. Neither cases of hepatitis A nor of pertussis have been recorded during the last two years and no case of singlellosis was recorded during 2016.

Conclusions

Vaccination coverage and epidemiological recording of infectious diseases contributes to prevention of life-threatening diseases and, generally, to public health. Immunization against Meningitococcus (especially against group B) is proven to be a necessity for all children. Immunization against hepatitis A and pertussis is necessary for gypsies. Also, due to high frequency of foodborne infectious diseases, preventing measures against them seems to be an issue of great importance.