Changing pattern of bloodstream infections and antibiotic resistance in a children hospital of Kabul

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Abstract

Background: Bacteraemia and candidaemia can lead to life-threatening sepsis causing significant mortality and morbidity and require rapid and aggressive antimicrobial treatment. Rational and appropriate use of antibiotics requires understanding of common pathogens and drug resistance patterns in a healthcare setting.
Objective: To analyze the prevalent blood culture isolates and their antimicrobial resistance patterns among in-patients in a pediatrics tertiary care centre in Kabul.
Methods: A cross-sectional study was performed on blood cultures from suspected cases of sepsis admitted at French Medical Institute for Children (FMIC) Kabul. To evaluate the trend of local microbial prevalence and their antibiotic sensitivity pattern, the results of two periods were compared: Period-1 from Jan 2010 to Dec 2012, and Period-2 from Jan to Dec 2013. Blood samples were collected aseptically in culture bottles from BD (Becton Dickinson, USA) and incubated in BACTEC™ 9240 Blood Culture System. The positive growths were examined and isolates were identified to the species level using *Analytical Profile Index (*API) identification strips (bioMerieux, France). Antibiotic susceptibility testing was performed by Kirby-Bauer disk diffusion method and drug resistant strains were studied for extended spectrum beta lactamase (ESBL) production by combination disk method and for methicillin resistant *Staphylococcus aureus* (MRSA) by cefoxitin disk diffusion method.
Results: Out of total 675 cases of culture proven sepsis, 335 (49.63%) were Gram-Negative Bacilli (GNB). Among GNB, we observed a decline in the prevalence of Klebsiella from 32.5% to 21% between periods 1 and 2 respectively. However, there was an increase in the prevalence of both Pseudomonas and *Burkholderia cepacia* from 5.1% to 21% and 1.7% to 16.8% between periods 1 and 2 respectively. Moreover, there were 6 new cases of sepsis caused by *Stenotrophomonas maltophilia* during period 2. A total of 317 (46.96%) Gram-Positive Cocci (GPC) were also isolated during the whole study period. Among GPC, there was an overall 10% rise in the prevalence of Staphylococcus non-aureus during period 2. Regarding antibiotic sensitivity pattern of gram-negative isolates, many were found to be multidrug-resistant and showed high resistance to commonly used antibiotics, namely ampicillin, gentamicin, 3rd generation cephalosporins, fluoroquinolones and co-trimoxazole. However, the frequency of those producing ESBL reduced from 54.2% to 42.1% during period 2. Among gram-positive cocci, the pattern of antibiogram did not show a substantial change.
Conclusion: Klebsiella and Staphylococci remain the most important bacteria responsible for bloodstream infections. However, there has been an increase in the prevalence of Pseudomonas and *Burkholderia cepacia*. Moreover, *Stenotrophomonas maltophilia* is emerging as a new hospital acquired pathogen in a tertiary care settting in Kabul. Rational use of antibiotics with regular antibiotic susceptibility surveillance studies is prudent to maintain high antibiotic therapeutic profile.

Key Words: Antibiogram, Blood Culture, Bloodstream infections, Children, Septicaemia

Factors associated with short-term and long-term suboptimal CD_4 T-lymphocyte recovery in HIV-infected patients

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ABSTRACT

Background: Suboptimal CD_4 T-lymphocyte (CD4) recovery is related to morbidity and mortality in HIV-infected patients. Most studies reported the impact of suboptimal CD4 recovery after the first 6 months of antiretroviral treatment on outcomes. We herein investigated the factors associated with both short-term and long-term suboptimal CD4 recovery in HIV-infected individuals.

Objectives: To investigate the factors contributing to short-term (6 months) and long-term (24 months) suboptimal CD4 recovery in HIV-infected patients who had virological suppression**.**

Methods: A case control study was conducted in adult HIV-infected patients receiving HAART with virological suppression at the Infectious Disease Clinic, Siriraj Hospital. Patients were classified into 4 groups regarding CD4 recovery and duration of HAART; 1.) short-term suboptimal response 2.) short-term optimal response 3.) long-term suboptimal response and 4.) long-term optimal response. Factors associated with these conditions were analyzed.

Results: Of 187 patients enrolled, 149 had 6-month data for analysis and 23 of those were classified as short-term suboptimal response group, whereas 43 out of 145 patients were classified as long-term suboptimal response group. Among 121 patients who had optimal CD4 rise at 6 months, 30 of those (24.8%) turned to be suboptimal at 24 months. In contrast, among 23 patients with short-term suboptimal CD4 response, 10 (43.5%) turn into optimal response at 24 months. History of previous opportunistic infections, including tuberculosis and cryptococcosis, were associated with short-term suboptimal CD4 response in multivariate analysis with odds ratio of 3.32 (p=0.02) and 5.41 (p=0.01), respectively. Factors associated with long-term suboptimal CD4 response in multivariate analysis included male gender (OR=3.26; p=0.02), initial CD_4 cell count less than 50 cells/mm^3 (OR=2.77; p=0.03). Interestingly, use of TDF/3TC/EFV regimen was associated with suboptimal CD4 recovery at 24 months (OR=3.14; p=0.03).

Conclusions: Short-term CD4 recovery at 6 months does not predict CD4 response at 24 months after HAART. History of tuberculosis and cryptococcosis were associated with short-term CD_4 suboptimal response, whereas male sex and low initial CD4 counts less than 50 cells/mm^3 were associated with long-term suboptimal CD4 response. We observed that, compared to other regimens, use of TDF/3TC/EFV was associated with long-term suboptimal CD4 recovery.

Title:

Association of Newly Emerging RSV-A ON1 genotype with PediatricARI Hospitalization and Lower Respiratory Tract Infection in Central Vietnam

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Abstract

Background

Human Respiratory Syncytial Virus (RSV) is a major viral etiology of Lower Respiratory Tract Infection (LRTI) among children. Since 2010, RSV-A ON1 genotype had been reported in several countries, yet there is limited information about its clinical severity. Through our prospective Acute Respiratory Infection (ARI) surveillance in Central Vietnam, we investigated the emergence and clinical impact of RSV-A ON-1 in Vietnam.

Methods

ARI cases enrolled to our population based prospective pediatric ARI surveillance at KhanhHoa General Hospital, Central Vietnam from January 2010 to December 2012 were studied. Clinical information was collected and multiplex RT-PCR assays were performed to screen for RSV and other respiratory viruses. RSV positive samples were further genotyped for subgroup and genotype by sequencing of G glycoprotein. Statistical analysis was performed to compare clinical severity among RSV subgroups and genotypes.

Results

During the study period, 1852 cases were enrolled of which 424 (22.89%) were positive for RSV. Both RSV-A and RSV-B were detected among hospitalized ARI in 2010 and 2011 however the proportion of RSV-A subgroup increased after the emergence of RSV-A ON1 genotype in May 2012. Moreover RSV-A

ON1 infection increased LRTI 3.75 (95%CI: 1.79-7.87) times and chest X-ray abnormality 2.47 (95%CI: 1.16-5.26) times compared to Non-ON1 RSV-A infection among hospitalized pediatric ARI cases.

Conclusions

RSV played a major role among pediatric ARI. The emergence of new RSV-A ON1 genotype was associated with increased clinical severity among pediatric ARI cases in central Vietnam.

Discovery of Novel Series of FabI Inhibitors Active againstDrug Resistant S.*aureus*& *S. epidermidis*strains

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Background: Antibiotic resistance in Gram-positive bacteria especially in *Staphylococcus aureus* has created an urgent clinical need to develop novel anti-staphylococcal agents.However, very few drugs with novel mechanism of action have been introduced for past several years. We have initiated a research program to identify a novel series of FabI inhibitors active against drug resistant *S. aureus*&*S. epidermidis* strains.

Methods: Initial compounds have been designed based on available SAR and structure guided approach to identify a novel chemical series of compoundswith moderate activity against*S.aureus*FabI. The binding modeof hit compounds bound to FabIhas beendetermined using X-ray crystallographyto aid the optimization of chemical series.Subsequent SARonthese hit compounds produced lead molecules with potent FabIinhibitionand activity against multi drug resistant *S. aureus*strains.*S. aureus*FabI enzyme expressed and purified was used to determine the IC_{50}. In vitro minimum inhibitory concentrations (MICs)by broth micro-dilution method against standard and clinical isolates were performed as per clinical laboratory standards (CLSI) guidelines. Respective quality control strains were incorporated. In vivo efficacy study was carried out in Swiss albino mice of age 4-6 weeks with weight between 18-22 gms.Mice were infected by intraperitoneal route with methicillin sensitive (MSSA)&resistant *S. aureus*(MRSA) *strains*, and the treatment was given one and five hour post infection by oral or intravenous route. Animals were observed for survival/mortality for seven days and ED_{50} value calculated.This poster describes the in vitro, ADME, pharmacokinetic profile and in vivo efficacy of lead compounds.

Results: Lead compounds displayed potent IC_{50} against *S. aureus*FabI enzyme in the range of ≤ 0.7µMand exhibitedpromising MIC in the range of 0.25-1.0µg/mL against methicillin sensitive&resistant strainsof*S. aureus*,and *S. epidermidis*.Lead compounds exhibitedexcellent ADME and pharmacokinetic profile suitable for i.v. and oral dosing. Efficacy in MSSA &MRSA systemic infection model by i.v. and oral administration of the lead compoundshowed a dose proportional efficacy across the doses tested.

Conclusion:A novel series of potentFabI inhibitors active against multi drug resistant Staphylococcal infection is identified. Further preclinical evaluation of lead compoundis ongoing.

Delayed Serological Response Against *Treponema pallidum* : Are we Missing the Infectious Syphilis Window of Opportunity?

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Background: Detection of syphilis spirochetes through dark field microscopy has been known to have limitations due to the lack of sensitivity in microscopy and the subjectivity of the morphological state of the spirochete to the technologist. Conversely, PCR has been known to have great specificity and sensitivity and can detect down to single spirochete.

Methods: As microscopy and PCR vary vastly in sensitivity, we evaluated the performance of dark field microscopy and PCR techniques by comparing the results to our own established "gold standard." This "gold standard" was defined by comparing the cumulative results of two or more test platforms (dark field microscopy, PCR, real-time PCR, and RPR). 630 samples were evaluated which encompassed samples over a nine year period.

Results: When dark field was compared to our established gold standard, the sensitivity and specificity were 58.1% and 98.5% respectively. The observed low sensitivity is expected due to the limitations of microscopy. When comparing PCR methods to the established gold standard, the sensitivity and specificity are 98.8% and 98.7%. The seemingly lower specificity of PCR compared to the gold standard could be due to the fact that the definition of the gold standards are based on test platforms that are intrinsically lower in sensitivity than compared to PCR.

The higher sensitivity observed in PCR, has led to the finding of multiple cases of syphilis infection in which PCR could reliably detect the presence of infection before dark field microscopy as well as standard serological tests.

Conclusion: As expected, PCR provided greater sensitivity and specificity than traditional dark field microscopy. This advantage may prompt physicians to start treatment before serological detection.

Identification of Rotavirus Strain Causing Diarrhea In Children Under Five Years Old in Yogyakarta, Indonesia

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Background. Rotavirus is the major cause of severe diarrhea in children under five years old in both developed and developing countries. Since improvements in sanitation and hygiene have a limited impact in reducing the incidence of rotavirus diarrhea, implementation of a vaccine will be a better strategy. Before implementing a vaccine, a strategy should be developed. The strategy of vaccine development would be enhanced by knowledge of circulating virus genotypes. The aim of this study was to identify the circulation of the rotavirus strains causing diarrhea in children under five years old in Yogyakarta.
Methods. Clinical data and stool samples were collected from children under five years old hospitalized in Kodya Yogyakarta General Hospital. Rotavirus was detected in stool samples using enzyme immunoassay, followed by G and P-genotyping using RT-PCR. Electhopherotyping was performed to the positive rotavirus samples.
Results. During February – August 2009, 104 stool samples were collected and 57 samples (54.81%) were rotavirus positive. Of the 56 samples subjected to G-typing, 80.36%, 16.07% and 3.57% were classified as G1, G2 and G3, respectively. For P-typing, the strains were classified as P[8] (69.64%), P[4] (17.86%), P[6] (7.14%) and untypeable (5.36%). The G and P-type combination were G1P[8] (74%), G2P[4] (17%), G1P[6] (8%) and G1P[4] (2%). Of the 54 samples subjected to electropherotyping, 49 of G1 isolates and 1 of G3 isolate have a long pattern, whereas 3 of G2 isolates and 1 of G1 isolate have a short pattern.
Conclusion. Since the majority of the strains circulating in Yogyakarta are similar to the global rotavirus strains' circulation, we suggest that the currently developed rotavirus vaccines could be effective in decreasing rotavirus diarrhea in children in Yogyakarta.

Keywords: rotavirus, acute diarrhea, *G-type, P-type, electropherotyping*