SHORT COMMUNICATION

Emergence of Multi-Resistant Enteric Infection In A Paediatric Unit Of Karachi, Pakistan

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Abstract

From June 2018, onwards, there has been an upsurge of multi-resistant enteric infections in children admitted from various catchment areas of Abbasi Shaheed Hospital (ASH). This is a serious concern as very few antibiotics are available to treat the children.

Children from June 2018 to September 2018 of age groups 5.7 ± 2.84 (range 1.6 to 11 years), referred to ASH, for admission, with clinical suspicion of enteric fever and having received a third generation injectable cephalosporin by a general practitioner, for 5 days or more, with no response, and continuation of fever, were included.

A total number of 137 patients had culture proven salmonella typhi, of whom 61(44.52%) showed sensitivity only to meropenem, 45 (32.8%) to azithromycin,13(9.4%) to fosfomycin, 11(8.02%) to Amoxicillin/clavulanic acid, 5 patients showed sensitivity to ceftriaxone(3.64%) and one had sensitivity to amikacin. All patients were treated successfully for 10 days and discharged home. There were no reported complications at follow-up.

Multi-Drug Resistance (MDR) enteric fever appears to be a major health concern in Karachi. Mass immunization with oral live attenuated Typhi 21a or injectable unconjugated Vi typhoid vaccine, rational use of antibiotics, improvement in public sanitation facilities, availability of clean drinking water, promotion of safe food handling practices and public health education are vital in the prevention of MDR enteric fever.

Keywords: multi-drug resistant, enteric fever, azithromycin, meropenem.

Introduction

An estimated incidence of enteric fever is 110 cases/100 000 population, in South Asia which is the third highest incidence rate for any region. Pakistan is also included in this part of the globe. In the past few months, Typhoid fever was seen to be caused by Salmonella enterica serovar Typhi (S. Typhi), a Gram-negative bacterium[01]. It continues to be a global public health problem with over 21.6 million cases and at least 250,000 deaths occurring annually [02]. Southeast Asia has the third highest incidence of 110 cases/100 000 population; which includes Pakistan.[03] There is inadequate population-based data from Pakistan however; several hospital-based studies from different parts of the country have consistently shown a very high incidence of typhoid fever, especially in the younger age groups.[04] In the last two decades, multidrug-resistant (MDR) S.Typhi strains have emerged and spread worldwide, resulting in high rates of morbidity and mortality.[05]

In the last few months, from June 2018, onwards, there have been upsurge of multiresistant enteric infections in children admitted from various catchment areas of Abbasi Shaheed Hospital (ASH) to the paediatric ward unit 2, of ASH, with no response to cephalosporins. This is a serious concern especially for paediatricians, who are left with very few antibiotics to treat the children. Majority of the children coming to government hospitals are from low or middle socioeconomic communities, living with poor sanitation and inadequate clean water especially for drinking purposes.[06] This scenario has worsened over the years in our country.

This communication highlights the grave situation where paediatricians are left with very few antibiotics to treat the multi-resistant enteric infections.

Methods

Children of age 5.7 ± 2.84 (range 1.6 to 11 years), referred to ASH, for admission, with clinical suspicion of enteric fever and had already received a third generation injectable cephalosporin, for 5 days or more, with no response, and continuation of fever, were included. The period of the study was from June 2018 to September 2018. The children had been treated by general practitioners or private hospitals and referred to ASH (a tertiary care hospital) due to continuous fever with no response to antibiotic cephalosporin (ceftriaxone). Blood cultures showed multi-resistant salmonella typhi,

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resistant to conventional antibiotics. The children were treated with the respective antibiotic for 10 days and clinical response was achieved.

Result

A total number of patients with culture proven salmonella typhi were 137. Out of these 61(44.52%) showed sensitivity only to meropenem, 45 (32.8%) to azithromycin,13(9.4%) to fosfomycin, 11(8.02%) to Amoxicillin/clavulanic acid and 5 patients showed sensitivity to ceftriaxone(3.64%). One patient had sensitivity to amikacin.(Table) All patients were treated successfully for 10 days and discharged home. There were no reported complications at follow-up.

Table-: Change in sensitivity pattern of antibiotic in patients with enteric fever.

	Mean ± SD
Age	5.7 ± 2.84
Characteristic	**Number (%)**
Male	84 (61.3)
Female	53 (38.6)
Ceftriaxone sensitive	5 (3.64)
Meropenum sensitive	61 (44.52)
Amikacin	1 (0.01)
Azithromycin	45 (32.8)
Fosfomycin	13 (9.4)
Amoxicillin/clavulanic acid	11 (8.02)

Discussion

In Pakistan, for the last ten years, Salomenlla Typhi infection is a serious concern.[07] Initially in 1948 salmonella typhi could be easily treated with chloramphenicol, Ampicillin or co-trimoxazole[08] .First resistance was observed in 1987.[09] Thus, fluoroquinolones became the drug of choice for the treatment of Multi-Drug Resistant Typhoid Fever (MDRTF) worldwide.[10] However, this was soon followed by reports of isolates of S. Typhi showing resistance to fluoroquinolones, with the first case being reported in 1992.[11] After that, the enteric infection had to be treated by ceftriaxone[12] injectable , third generation cephalosporin. Children who could take oral medication, were given cefixime with an equally good response[12], but sporadic reports of resistance to them also followed.[13] Over the years, hardly any complications have been seen secondary to salmonella infection other than anorexia in children which resolved in 48 to 72 hours after starting treatment.

Overuse, misuse, and inappropriate antibiotic prescribing practices have significantly contributed in developing multi-drug resistance.[14] Diagnostic uncertainties and time pressures are some of the main forces behind irrational prescription of antimicrobial combinations.[15] Moreover, in some countries such as Pakistan, local production of many different antimicrobial drugs with questionable quality and potency control, coupled with poor compliance of patients to costly antimicrobials adds to the threat of resistance. Antibiotics are unnecessarily prescribed for infections such as the common cold, cough and diarrhoea, which are usually of viral etiology and can be resolved by the immune system. This leads to patients being prescribed broad spectrum antibiotics, which results in the emergence of MDR organisms.[15] However, due to parental and time pressure or lack of knowledge, physicians change different antibiotics unnecessarily during the treatment of typhoid fever, which leads to the emergence of resistant strains. All these risk factors were evident in our group of patients also. All of them had taken multiple antibiotics which were either under-dose or over-dose with non-compliance.

The children with MDRTF are more sick-looking and more toxic at admission[16]. Maximum cases of MDRTF are seen in children under five years of age.[17] This could be due to the association of typhoid fever outbreaks with malnutrition, commonly seen in children under the age of five in developing countries. However, in our case most of the children were above five years. The reason can be their unhygienic habits and dependence for food on adults, who may be carriers of MDR strains.

The overall mortality reported during MDRTF epidemics is 7% to 16%, and is much higher than the figure of 2% seen in susceptible typhoid fever.[05] Gastrointestinal complications such as bleeding, intestinal perforation, paralytic ileus, hepatitis, cholecystitis and peritonitis have been described. Respiratory system complications include bronchopneumonia and pleural effusion. Central nervous system complications described are encephalopathy, meningitis, chorea, intracranial haemorrhage, cerebellar ataxia and seizures. Renal complications include hypernatraemia, hypokalaemia, acute renal failure and glomerulonephritis. Cardiovascular complications are seen as myocarditis and peripheral circulatory failure. Haematological complications include disseminated intravascular coagulation and bone marrow suppression.[05] Luckily, none of our patients developed any of these complications.

Blood cultures are the primary diagnostic method for MDRTF.[18] During the first week of illness, approximately 90% of patients have a positive blood culture, which decreases to 75% in the second week, 60% in the third week, and 25 % in the fourth and subsequent weeks until

the subsidence of pyrexia. The World Health Organization (WHO) recommends that between 10mL and15 mL of blood be taken from school children and 2mL to 4 mL from toddlers and preschool children to achieve an optimal isolation rate. Bone marrow aspirate culture is particularly valuable for patients who have been previously treated, who have a long history of illness, and for whom there has been a negative blood culture with the recommended volume of blood.[19] All of our patients were blood culture proven.

There are no systematic studies which have measured the frequency of relapses and recurrences of typhoid fever in a community. However, an attack of typhoid fever does not provide long-lasting immunity from a future episode of the same illness. An episode of typhoid fever usually means that the child lives in an environment in which further exposure to infection is likely. The general recommendation is to administer the typhoid vaccine at least four weeks after full recovery from the illness.

Conclusion

MDR enteric fever is a major health concern in Pakistan.. Mass immunization in endemic areas with either the oral live attenuated Typhi 21a or the injectable unconjugated Vi typhoid vaccine, rational use of antibiotics, improvement in public sanitation facilities, availability of clean drinking water, promotion of safe food handling practices and public health education are vital in the prevention of MDR enteric fever.

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