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Research Paper

Clinical Profile of Enteric Fever and Response to Ceftriaxone

Authors

Dr Anjali Kalbhande[1*], Dr Ashwin Meshram[2], Dr Sandeep Manwatkar[3], Dr Shahaji Kure[4]

[1]M. D. Pediatrics, Assistant Professor, Department of Pediatrics, ESIC PGIMSR Hospital, MIDC, Andheri (E), Mumbai

[2,3]M. D. Pediatrics, Senior Resident, Department of Pediatrics, ESIC PGIMSR Hospital, MIDC, Andheri (E), Mumbai

[4]M. B. B. S. Junior Resident, Department of Pediatrics, ESIC PGIMSR Hospital, MIDC, Andheri (E), Mumbai

*Corresponding Author

Dr Anjali Kalbhande

B/101 Ram Kutir, Bhatwadi, Ghatkopar (W), Mumbai, 400084, India

Mob – 9920404016, Email: *anjali.kalbhande2010@gmail.com*

Abstract

Background: *Enteric fever mimics other febrile illnesses. Third generation cephalosporin are increasingly popular in the treatment of typhoid fever because of resistance to previously used first line drugs. Hence, this study was undertaken to evaluate clinical and laboratory profile and determine response to ceftriaxone.*

Method: *Retrospective data of sixty-six enteric fever patients with clinical and laboratory diagnosis was included in the study. Only culture proven or widal positive cases of enteric fever were included in the study. Clinical, laboratory and treatment information were extracted from the medical records on a detailed proforma and analysed.*

Results: *Fever was present in all patients. Vomiting and abdominal pain in 42%,Cough 42%, Coated tongue 41%, Hepatomegaly 58%, splenomegaly 33%, Widal test 91%, Blood culture 29% (salmonella typhi 19% and paratyphi 10%) of patients. Average Total leucocyte count (TLC) was 6934/cu.mm and average platelet count was 2 lacs sixty-five thousand. In the present study, 10 patients had leucopenia while 5 patients had leucocytosis. Ceftriaxone was used in all patients. Response to ceftriaxone was 100% in the present study. Response to fever with ceftriaxone was ranged from third day to tenth day with median of sixth day.*

Discussion and Conclusion: *In the recent years, rising incidence of salmonella paratyphi serotype on blood cultures has been observed, owing to selective immunisation against salmonella typhi. However, salmonella typhi is still the primary causative organism for enteric fever. Ceftriaxone has emerged as effective therapy in the treatment of enteric fever in pediatric patients.*

Keywords: *Fever, Typhoid, Salmonella typhi infection, Ceftriaxone.*

Introduction

Enteric fever is a systemic illness caused by Salmonella enterica, serotypes typhi or paratyphi A/paratyphi B. It predominantly affects children and young adults because of absence of natural immunity and frequent exposure to fecal pathogen [1, 2].

Inspite of being a preventable disease, it is a major burden to public health. In India the disease is endemic with an incidence ranging from 102 to 2219 per 100,000 population[3]. It is a common cause of morbidity in the developing world, particularly in South and South–East Asia. Highest incidence has been documented in impoverished, overcrowded areas with poor access to sanitation such as the urban slum areas of North Jakarta (Indonesia), Kolkata (India) and Karachi (Pakistan) with annual incidence rates of blood culture–confirmed enteric fever ranging from 180–494/100 000 among 5–15 year-olds and 140–573/100 000 among those 2–4 years old[4]. Today due to its changing modes of presentation, as well as the development of multidrug resistance, typhoid fever is becoming increasingly difficult to diagnose and treat.

Despite the high burden of disease, challenges in the diagnosis and management of enteric remain. Clinical diagnosis of enteric fever is nonspecific and mimics other febrile illnesses like malaria and dengue fever and influenza[5,6]. For the diagnosis, culture of several specimens such as blood, bone marrow, urine, rose spot extracts, duodenal aspirates and stool can be done, but blood culture remains the gold standard investigation and provides antibiotic sensitivity pattern for specific therapy[6,7]. However, the Widal test is also used widely after 7 days of fever though it requires expert interpretation. Third generation cephalosporins like ceftriaxone have become popular as first line of treatment for typhoid fever in the past 2 decades after the emerging resistance of salmonella to previously used drugs like chloramphenicol, cotrimoxazole and ampicillin[8]. Recent emergence of multidrug resistant typhoid has conferred the treatment with conventional antibiotics more complex[9]. However, over the last few years there has been increase in the defervescence period in patients treated with 3rd generation cephalosporins. Hence, this study was undertaken to evaluate the clinical and laboratory profile of typhoid fever and the response to ceftriaxone.

Methods

This was a retrospective chart review of all children with enteric fever admitted between January 2013 and December 2016 in the Pediatric Ward of a tertiary care public hospital in Mumbai, India. All children less than 12 years of age were included in study. These records were retrieved from the Medical Records Section of the hospital. Only culture proven or Widal positive cases of enteric fever were included in the study. Clinical, laboratory and treatment information were extracted from the medical records on a detailed proforma and analysed. Defervescence was defined as the number of days required for absence of fever after starting the antibiotics. Patients were deemed to have leucopenia if total white blood cell (WBC) count was less than 4000/cu.mm and leucocytosis was considered if counts more than 11,000/cu.mm. and thrombocytopenia if platelet count was less than 1,50,000 lac/cu mm. Widal test was considered positive when typhoid O antigen was more than 1:80.Blood culture was performed using automated Bact T Alert 3D (Bactialert) method.

Since this was a retrospective study involving extraction of data from the records, waiver of consent was granted by the Institutional Ethics Committee.

Results

A total of 66 patients of typhoid fever satisfied the inclusion criteria and were included in the study. Out of these 33(50%) were males and 33(50%) were females. Average age of presentation was 7.25 years. Average duration of hospital stay was found to be 8 days.

Fever was present in all patients. Other findings such as cough, vomiting, abdominal pain, jaundice and other clinical manifestation were recorded. Vomiting and abdominal pain was present in 42% of patients. Cough was present in 42% of patients. Coated tongue was present in 41% of patients. Hepatomegaly was present in 58% while splenomegaly was found in 33%of patients.

Widal test was positive in 91% of patients. Blood culture was positive in 29% (salmonella typhi 19% and paratyphi 10%) of patients. All culture positive patients were sensitive to ceftriaxone. Average Total leucocyte count (TLC) was 6934/cu.mm and average platelet count was 2 lacs sixty-five thousand. In the present study, 10 patients had leucopenia 5 patients had leucocytosis. Ceftriaxone was used in all patients. Response to ceftriaxone was 100% in the present study. Response to ceftriaxone was ranged from third day to tenth day with median of sixth days. No mortality was reported in the present study. Appropriate antibiotic as indicated by sensitivity tests should be employed to prevent the development of resistant strains of *S. typhi.*

Table 1 Age and sex wise distribution of patients

Age in years	Sex	No	Percentages
0 – 1	Male	2	3
	Female	0	0
>1 – 5	Male	12	18
	Female	6	9
>5 – 12	Male	19	29
	Female	27	41

Table 2 Clinical features of patients

Clinical features	No. of patients	Percentage
Fever	66	100
Cough	28	42
Coated tongue	27	41
Vomiting/Abdominal pain	28	42
Hepatomegaly	38	57
Splenomegaly	22	33

Table 3 Laboratory features of patients

Laboratory features	No. of patients	Percentage
Leukocytosis	5	7.5
Leukopenia	10	15
Widal Positive	64	91
Positive Blood Culture	19	29
S. typhi positive	13	19
S. paratyphi positive	6	10

Discussion

Our study was conducted on 66 patients of typhoid fever in a tertiary health care hospital in a metropolitan city. The sex ratio was 1:1 with average age of presentation was 7.25 years. This demographic profile was comparable to a study by Ganesh R et al in 2010, where male:female ratio was 1.29:1 and majority of cases were clustered in the age group of 5 to 12 years[9]. The preponderance of this age group can be attributed to the faulty habits like roadside food consumption, lack of concern for hygiene, poor vaccination coverage etc[15]. Children between age 1 – 3 years are prone for typhoid infection because of meagre immunity transferred through mother's milk or unsafe drinking water[16].

In our study, all patients (100%) presented with fever. Hepatomegaly (57%) was the next common presenting clinical feature in these patients. Cough, vomiting, abdominal pain, jaundice and other clinical manifestations were documented in around half of the total cases. In a similar study by Ranganatha et al in 2017, the most common symptom was fever (100%), followed by anorexia (61%), vomiting (44%), pain abdomen (18%), diarrhea (16%), headache (12%), and cough (10%), whereas the most common physical finding was toxic look in 68% of the cases followed by coated tongue in 49%, hepatomegaly (44%), splenomegaly (21%) and pallor in 10% of cases[10].

Laboratory studies showed 91% of patients positive for widal test, which was in concordance (89.9%) with a study by Sudarshan et al in 2014 [11]. Blood culture was positive in 29% of our patients, which grew salmonella typhi in 19% and salmonella paratyphiin 10% of all cases. Fifteen percent patients had leucopenia while 7.5% patients had leucocytosis. In the aforementioned study, the culture positivity was 35.4% and majority of the children had WBC count in the range 5000-10000/cu mm (70.9%). No resistance was found to injection ceftriaxone in both the studies[11]. Another study by Sheikh M et al in 2017 found that the blood culture was positive in

27.9%, where Salmonella typhi isolates accounted for 15.5% and Salmonella paratyphi A for 12.4% out of the cohort[12]. On contrary, Jog S et al in their study in 2008, 40% isolates were S paratyphi in blood culture which was reported to be higher than the literature. This was attributed to the increasing awareness and use of vaccines against Vi polysaccharide antigen that have no protective action against S.paratyphi[13].

In the present study, response to injection ceftriaxone was 100%. All patients responded and demonstrated defervescence by around 6th day of injection ceftriaxone therapy. Hannan A et all, have studied response of ceftriaxone in the treatment of fever in 2015 in Peshawar, Pakistan, in which fever in all the patients was resolved by 7 days of injection ceftriaxone. Mean time to defervescence after injection ceftriaxone therapy was 3.89 days as recorded in their study[14]. Mortality was not reported in our study, so was not in all the above studies under discussion.

This study has determined the clinical profile of typhoid in the children who responded to injection ceftriaxone within a week, as consistent with most of the recent studies. Neverthless, more studies are needed to discern uncommon presentations in children with typhoid and estimate the efficacy of other antibiotics which may cut down the hospital stay of such patients.

Conclusion

Typhoid fever has varied clinical presentation in children. In the recent years, rising incidence of salmonella *paratyphi* serotype on blood cultures has been observed, owing to selective immunisation against salmonella *typhi*. However, salmonella typhi is still the primary causative organism for enteric fever.Third generation cephalosporins such as intravenous ceftriaxone, have emerged as effective therapy in the treatment of enteric fever in pediatric patients.

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