

Typhoid Fever in Children

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SUMMARY

Typhoid fever remains a common problem of children in Pakistan. We present our experience of 102 cases of culture proven typhoid admitted to the Department of Paediatrics at Shaikh Zayed Hospital, Lahore.

The majority (59=57.8%) were between the ages of 5-12 years with an equal incidence in both sexes. Fever had lasted for 5-15 days in 86.2% and more than 15 days in the rest while 64.7% had a white blood cell count of 5000-15000/mm³. Only 20.5% had leucopenia of less than 5000/mm³. The widal test was positive in 73.5% cases.

Of the total, 22 cases (21.5%) were found resistant to Ampicillin, Chloramphenicol and Trimethoprim-Sulphamethoxazol (TMP-SMP). All these were treated with Cefotaxime (150 mg/kg/day) with good results.

INTRODUCTION

Typhoid fever is still a disease of worldwide distribution. In well developed countries it now occurs in sporadic form or in small localized outbreaks. In the under-developed world, owing to the poor hygienic and sanitary conditions, the disease is highly prevalent and produces significant morbidity and mortality. As many as 4 million cases are seen each year in South Asia alone¹⁻³.

The causative agent is a gram negative, flagellated, noncapsulated, motile and non lactose fermenting bacillus-salmonella typhi or paratyphi. These bacteria enter the bodies of new hosts mostly by ingestion of contaminated food or water. The incubation period is 10-14 days. Via the intestinal lymphatics the organisms reach the liver, spleen and mesenteric lymph nodes and proliferate there. At the end of the incubation period they pass into the blood stream and produce bacteremia and its associated symptoms. Cases usually present as pyrexia of uncertain origin (PUO). Ampicillin, Chloramphenicol and Trimethoprim - Sulphamethoxazole (TMP-SMZ)⁴⁻⁶ have been the primary antibiotics used for treating salmonella infections. In recent years many species of salmonella resistant to ampicillin, chloramphenicol and TMP-SMZ have been reported from many parts of the world including Asia, the

Middle East, Europe, Africa and Canada⁷⁻⁹. In Pakistan also, the emergence of resistant salmonellae has become a serious health problem and has led to many therapeutic failures¹⁰⁻¹³. This situation has stimulated efforts to isolate and test the susceptibility of these organisms to new antimicrobial agents and to initiate clinical trials to evaluate the effectiveness of these drugs.

PATIENTS AND METHODS

A review of 102 cases of proven typhoid fever admitted to the Department of Paediatrics at Shaikh Zayed Hospital from 1st January 1987 to 31st December 1990 is presented in this study. All patients suspected to have typhoid fever were subjected to the following investigations.

Complete Blood Count, Widal test, Blood culture, Stool culture, Urine culture, and CSF analysis (if necessary).

The total leucocyte count was obtained through the coulter counter in all case. Widal test was performed to detect agglutinating antibodies to the somatic (O) and flagellar (H) antigens of salmonella typhi, S. paratyphi A and paratyphi B using "Gamma Biologicals" reagents. The test was performed in doubling dilution starting from 1 in 20 and ending with 1 in 10240. Each batch of tests included positive

and negative controls. Initial screening of each test serum was done by slide method. If antibody was determined to be present in a serum specimen or if prozoning was suspected, the tube test was performed to establish the antibody titre. The titre of the positive widal test serum was expressed as the highest dilution showing 50% agglutination. The test was considered positive in titres of 1:160 or more.

From each suspected case of typhoid fever, 2-8 ml of blood was collected aseptically before starting antibiotics. This was transferred to 2 bottles containing tryptic soya broth and thioglycolate broth respectively. Inoculation was made in the ratio of one part of blood to 10 parts of broth. The culture specimens collected at the bedside were sent to the microbiology lab, to be incubated at 37°C aerobically. Blind subcultures were made into blood agar and MacConkey agar after 48 hrs, 5th day and 10th day of incubation. Most of the isolates were obtained after 48 hrs. Negative samples were discarded after 10 day's subculture. Non-lactose fermenting colonies of salmonella morphology were identified biochemically and serologically. All the isolates were tested for sensitivity against commonly used antibiotics. The sensitivity test was performed using the disc diffusion method recommended by the NCCLS standards 14.

The diagnosis was considered confirmed when the blood culture was positive for salmonella typhi. The diagnosed cases were then carefully analysed for age/sex distribution, symptomatology, physical signs and lab. investigations. Ampicillin (200 mg/kg/day in 4 doses) or chloramphenicol (75 mg/kg/day in 4 doses) were used as the primary drugs for treatment. Cefotaxime (150 mg/kg/day in 4 doses) was employed where the isolated organism showed resistance to Ampicillin and Chloramphenicol.

RESULTS

Among the 102 cases, 85 (55%) were boys and 46 (45%) were girls. Eleven (10.7%) were below one year of age, 31 (31.3%) were between one to five years, whereas the majority i.e. 59 (57.8%) were between the age of five to twelve years.

The historical data obtained from these 102 patients showed that fever was the commonest feature among all of them. Fever had lasted for 7-15 days in 88 (86.2%) and for more than 15 days in the rest. The details of symptomatology and physical signs are given in Table 1 and Table 2 respectively.

Table 1: Clinical symptoms.

| Symptoms | Number (Total-102) | Percentage |
|----------------|--------------------|------------|
| Fever | 100 | 98.0 |
| Vomiting | 40 | 39.2 |
| Diarrhea | 38 | 37.2 |
| Cough | 18 | 17.6 |
| Anorexia | 22 | 21.5 |
| Abdominal pain | 22 | 21.5 |
| Constipation | 3 | 2.9 |
| Fits | 2 | 1.9 |
| Drowsiness | 1 | 0.9 |

Table 2: Physical signs.

| Physical signs | Number (Total-102) | Percentage |
|----------------------|--------------------|------------|
| Pallor | 18 | 17.6 |
| Hepatomegaly | 56 | 54.9 |
| Splenomegaly | 13 | 12.7 |
| Dehydration | 12 | 11.7 |
| Throat congestion | 10 | 9.8 |
| Abdominal tenderness | 20 | 19.6 |
| Neck stiffness | 3 | 2.9 |
| Hypothermia | 2 | 1.9 |

Laboratory findings

The total leukocyte count was between 5,000 to 10,000/mm³ in 66 (64.7%) cases. It was more than 10,000/mm³ in 21 (20.5%) cases whereas it was less than 5000/mm³ only in 15 (14.7%) cases. Widal test was positive in 75 (73.5%) of the cases. Urine cultures were positive in only 5 (4.9%) whereas only 12 (11.7%) showed *S. typhi* in stool culture. CSF analysis was performed in 3 cases. Two (1.9%) had a cytology suggestive of meningitis whereas none had a positive culture.

Out of the 102 cases, 22 (21.5%) were found resistant to Ampicillin, Chloramphenicol and TMP-SMZ. These cases were given Cefotaxime (150 mg/kg/day) in 4 divided doses intravenously for ten days. All showed good response, although in the majority (55=53.9%) it took another five days for the temperature to settle to normal.

DISCUSSION

In a developing country like Pakistan, typhoid

fever continues to be an important clinical problem and seems to be one of the principle causes of PUO. We have made an attempt to present our clinical experience with typhoid fever over a 4 year period. The disease seems to be commoner in older children with an almost equal incidence in both sexes. In this series of 102 cases, 57.8% were between the ages of 5-12 years. As far as the clinical presentation is concerned there was no distinct clinical picture and presentation was quite variable in different cases. Persistent fever may or may not be associated with gastrointestinal/respiratory/central nervous system symptoms. The physical examination may also be unrewarding. The cutaneous manifestations, the temperature/pulse dissociation and splenomegaly which are classically associated with typhoid fever were not seen in the majority of our patients. Leucopenia was found in 20.5% and its importance in the recognition of the disease should not be overemphasized.

Another alarming point in this study is the identification of strains resistant to multiple antibiotics. These strains are now widespread throughout most of South Asia and Middle East¹⁵⁻¹⁷ and have caused many out-breaks and are also capable of epidemic spread. At the same time a search for additional alternative antibiotics is going on throughout the world. Among the cephalosporins, cefotaxime, ceftriaxone and cefoperazone have been found effective in the therapy of resistant typhoid, although the relapse rate may be as high as 7%. The problem however is with the necessity to use these drugs parenterally and with the high cost¹⁸⁻²⁰. As reported in other studies^{19,21} we have also found cefotaxime very useful and effective. Quinolones are newer agents. Although limited clinical information is available about these drugs, their activity in bone²² CSF²³⁻²⁴ and intestinal tract²⁵ suggests their usefulness in the treatment of salmonella species. Their use in children is however restricted because they are known to cause damage to the cartilage in joints of juvenile animals and degeneration of the growth plates in puppies²⁶⁻²⁸.

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