Assessment of Efficacy of Various Treatment Regimes in Patients with Typhoid Fever: A Prospective Study

Ikram Hussain¹, F.H. Gauri², Anwar Ali Tak³, Nusrat Gauri⁴

ABSTRACT

Background: Typhoid fever is caused by Salmonella enterica serovar Typhi (S typhi), a Gram negative bacterium. Typhoid fever is among the most common febrile illnesses encountered by practitioners in developing countries. Hence, we planned the present study to evaluate the efficacy of various treatment regimes in treating patients with typhoid fever.

Materials & Methods: The present study included assessment of efficacy of different treatment regimes in treating patients with typhoid fever. A total of 40 patients were included in the present study and were broadly divided into two study groups with 20 patients each group. Group 1 included patients who were treated ceftriaxone therapy while group 2 included patients who were treated with chloramphenicol. Bacteriological culturing of the blood, stool and urine samples was done for confirming the diagnosis at the start of the treatment. Repetition of the blood and stool culture was done on day 5 and day 12 after the discharge of the patient. All the results were analyzed by SPSS software.

Results: Complete clinical cure occurred in 17 and 19 patients of group 1 and group 2 respectively. Positive blood culture for S. typhi on day 5 occurred in 0 and 10 days of group 1 and group 2 patients respectively. Conclusion: In treating patients with typhoid fever, Ceftriaxone could be safely used.

Key words: Regimes, Treatment, Typhoid fever

INTRODUCTION

Typhoid fever is caused by Salmonella enterica serovar Typhi (S typhi), a Gram-negative bacterium. Typhoid fever is among the most common febrile illnesses encountered by practitioners in developing countries. The advent of antibiotic treatment has led to a change in the presentation of typhoid, and the classic mode of presentation with a slow and “stepladder” rise in fever and toxicity is rarely seen. However, rising antimicrobial resistance has been associated with increased severity of illness and related complications. This may be related to the increased virulence of multidrug resistant S typhi as well as a higher number of circulating bacteria. Hence, we planned the present study to evaluate the efficacy of various treatment regimes in treating patients with typhoid fever.

METHODS

The present study was planned in the department of general medicine of the Government D.B. General Hospital, Churu, Rajasthan, and included assessment of efficacy of different treatment regimes in treating patients with typhoid fever. Ethical approval was taken from institutional ethical review board. Multidrug resistant typhoid and paratyphoid strains. This is an open access article distributed under the terms of the Creative Commons Attribution-Non-commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.
committee and written consent was obtained after explaining in detail the entire research protocol. A total of 40 patients were included in the present study and were broadly divided into two study groups with 20 patients each groups. Group 1 included patients who were treated ceftriaxone therapy for 7 days while group 2 included patients who were treated with chloramphenicol for 10 days. Complete demographic details of all the patients were obtained and complete physical and medical examination was carried out in all the patients before the start of the treatment therapy. Consistency and frequency of stools were recorded and were re-recorded after every ten hours. Bacteriological culturing of the blood, stool and urine samples was done for confirming the diagnosis at the start of the treatment. Exclusion criteria for the present study included:

- Patients with history of any other systemic illness,
- Patients with any known drug allergy,
- Patients less than 18 years of age,
- Patients with history of any gastrointestinal pathology

After obtaining the stool samples, we streaked the samples in the MacConkey agar for culturing of S. typhi. We also did microscopic examination for the presence of inflammatory cells. Repetition of the blood and stool culture was done on day 5 and day 12 after the discharge of the patient. All the results were analyzed by SPSS software. Chi-square test and student t test were used for evaluation of level of significance. P-value of less than 0.05 was taken as significant.

RESULTS

A total of 40 patients were included in the present study and based on the type of treatment protocol followed, were divided broadly into two study groups: group 1 and group 2. Mean age of the patients of group 1 and group 2 were 29.2 years and 33.1 years respectively. Group 1 included 15 males and 5 females while group 2 included 12 males and 8 females. Mean duration of fever among patients of group 1 and group 2 was 9 and 11 days respectively. Mean duration of diarrhea among patients of group 1 and group 2 was 6 days each. Complete clinical cure occurred in 17 and 19 patients of group 1 and group 2 respectively. Positive blood culture for S.typhi on day 5 occurred in 0 and 10 days of group 1 and group 2 patients respectively.

### Table 1: Comparison of efficacy of antibiotic in both the study groups

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group 1 (n= 20)</th>
<th>Group 2 (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete clinical cure</td>
<td>17</td>
<td>19</td>
</tr>
<tr>
<td>Positive blood culture for S.typhi</td>
<td>Day 5</td>
<td>0</td>
</tr>
<tr>
<td>Positive stool culture for S.typhi</td>
<td>Day 12</td>
<td>0</td>
</tr>
</tbody>
</table>

### Table 2: Comparison of leukocytes in both the study groups

<table>
<thead>
<tr>
<th>Leukocytes 10^9/mm^3</th>
<th>Group 1</th>
<th>Group 2</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Admission</td>
<td>7.9</td>
<td>7.8</td>
<td></td>
</tr>
<tr>
<td>Day 5</td>
<td>8.2</td>
<td>7.9</td>
<td>0.51</td>
</tr>
<tr>
<td>Day 12</td>
<td>8.5</td>
<td>8.1</td>
<td></td>
</tr>
</tbody>
</table>

DISCUSSION

Many challenges remain for the effective control and management of typhoid in endemic countries. Although these include establishing rapid clinical diagnosis and confirmation, the fact that both S. typhi and S. paratyphi are rapidly becoming resistant to commonly used antibiotics is of great concern. [6-8]

In the present study we observed that in comparison to chloramphenicol, Ceftriaxone could be safely used. Tati MM et al compared ceftriaxone with chloramphenicol for treatment of 72 children who had bacteriologically confirmed typhoid fever. Ceftriaxone was given at a dose of 75 mg/kg per day (maximally 2 g/day) intravenously, in two doses until defervescence and continued 5 days after that time. Chloramphenicol was given at a dose of 75 mg/kg per day (maximally 2 g/day) in four doses for 14 days. Mean defervescence time was in 5.4 days in the ceftriaxone group and 4.2 days in the chloramphenicol group (P=0.04). Clinical cure without complications was achieved in all patients in both groups. No patient relapsed in the ceftriaxone group, and four patients relapsed in the chloramphenicol group (P=0.048). The overall results of this study suggest that a flexible-duration of ceftriaxone therapy given until defervescence time, followed by an additional 5 days of therapy is a reasonable alternative to conventional 14-day chloramphenicol treatment in children with typhoid fever. [9]

Khan MA et al successfully treated 25 patients with typhoid fever, who were resistant to amoxicillin and chloramphenicol, with ofloxacin. Ofloxacin was administered at a dosage of 200 mg three times daily for 7 to 10 days. In a few seriously ill patients, a dosage of 400 mg three times daily for 3 days, followed by 200 mg three times daily for 4 to 7 days, was administered. This study confirmed the presence of resistant strains of Salmonella typhi. These strains were resistant to the commonly used drugs, chloramphenicol and amoxicillin. Ofloxacin was found to be well tolerated and effective in treating typhoid fever. [10]

Acharya G et al compared the efficacy of a short course of ceftriaxone with a standard course of chloramphenicol for typhoid fever, a randomized trial was conducted in 46 patients (30 adults and 16 children) who were blood culture-positive for Salmonella typhi or S. paratyphi. Ceftriaxone was given intravenously once a day for three days to 15 adults at a dose of 2 g/day and to eight children at a dose of 50 mg/kg/day. Chloramphenicol was given orally four times a day to an equal number of patients at a dose of 60 mg/kg/day until defervescence, followed by 40 mg/kg/day for a total of 14 days. Clinical cure without complications or relapse occurred in 19 patients (83%) treated with ceftriaxone and in 20 patients (87%) treated with chloramphenicol (P > 0.05). Four patients with clinical failures in the ceftriaxone group included two with fever lasting six days or more, one with altered sensorium, and one with relapse; three patients treated with chloramphenicol developed leukopenia and thrombocytopenia and were switched to amoxicillin therapy. Bacteriologically, blood cultures of all 46 patients were sterile three days after the start of treatment and remained so through day 15 of follow-up. These results extend previous observations on the efficacy of ceftriaxone in short courses for both adults and children with typhoid fever. [11]

Islam A et al compared the therapeutic efficacy of ceftriaxone given once daily for 5 days and chloramphenicol given four times daily for 14 days, a controlled trial was carried out with 59 patients who were culture positive for Salmonella typhi.
Ceftriaxone was given to 28 patients in once-daily intravenous doses of 75 mg/kg of body weight to children and 4 g to adults for 5 days; chloramphenicol was given to 31 patients at a dosage of 60 mg/kg/day until defervescence and then at 40 mg/kg/day to complete 14 days of treatment. All Salmonella isolates were susceptible to both antibiotics. Clinical cures (defervescence without complications, no relapse, and no need for further treatment) occurred in 79% of the patients treated with ceftriaxone and 90% of those treated with chloramphenicol (P = 0.37). On the third day of treatment, blood cultures were positive for S. typhi in 60% of the patients in the chloramphenicol group and 0% of the ceftriaxone group (P = 0.001). Defervescence occurred in half the patients in both groups during the first 7 days, but on days 9 to 13 after the start of treatment, nine patients in the ceftriaxone group, compared with six patients in the chloramphenicol group, remained febrile (P = 0.4). The median hematocrit and total leukocyte counts at day 14 were significantly lower for the chloramphenicol group than those for the ceftriaxone group (P = 0.01 and P = 0.02, respectively). These results indicate that the effects of therapy with ceftriaxone for typhoid fever differed from those of chloramphenicol therapy in that blood cultures became negative earlier, prolonged fever persisted in some patients, and bone marrow suppression was reduced. We conclude that a short, 5-day course of ceftriaxone is a useful alternative to conventional 14-day chloramphenicol therapy in the treatment of typhoid fever.

**CONCLUSION**

From the above results, the authors concluded that in treating patients with typhoid fever, Ceftriaxone could be safely used; specifically, in patients in which shorter course of therapy is required. However; we recommend, future studies.

**REFERENCES**