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Assessment of Efficacy of Various Antibiotics Therapy in Treating Typhoid: A Prospective Study.

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ABSTRACT

Background: Typhoid (cloudy) fever is a systemic infection, caused mainly by Salmonella typhi found only in man. It is characterized by a continuous fever for 3-4 weeks, relative bradycardia, with involvement of lymphoid tissue and considerable constitutional symptoms. Hence; we planned the present study to assess the efficacy of two different antibiotic regimes in treating patients with typhoid fever. **Methods:** We planned the present study on a total of 20 patients who were confirmed with diagnosis of typhoid fever and were broadly divided into two study groups as follows: Group 1- Patients who were treated with Ceftriaxone for 5 Days and Group 2- Patients who were treated with Chloramphenicol for 14 Days. Stool samples and venous blood samples were sent to laboratory for further investigation by bacteriologically culturing for confirming the presence of S. typhi. Stool specimens were examined microscopically for the presence of leukocytes, ova, parasites, and occult blood. Repeating of the blood cultures was done on days 3 and 14, and culturing of the stool specimens was done on days 5 and 14 and 1 week after the patient's discharge from the hospital. All the results were analyzed by SPSS software **Results** Clinical cure was seen in 8 and 9 patients of group 1 and group 2 respectively. Positive blood culture for S. typhi was seen in 4 patients of group 2 on third day whereas none of the patient of group1 exhibited positive blood culture. **Conclusion:** Ceftriaxone has equal efficacy in comparison to chloramphenicol in treating typhoid patients.

Keywords: Ceftriaxone, Chloramphenicol, Tyhphoid.

INTRODUCTION

Typhoid (cloudy) fever is a systemic infection, caused mainly by Salmonella typhi found only in man. It is characterized by a continuous fever for 3-4 weeks, relative bradycardia, with involvement of lymphoid tissue and considerable constitutional symptoms. In western countries, the disease has been brought very close to eradication levels.[1-3] In the UK, there is approximately one case per 100,000 population per year. Each year, the world over, there are at least 13-17 million cases of typhoid fever, resulting in 600,000 deaths. 80% of these cases and deaths occur in Asia alone. In South East Asian nations, 5% or more of the strains of the bacteria may already be resistant to several antibiotics. Antibiotics resistance, particularly emergence of multidrug resistant (MDR) strains among Salmonellae is also a rising concern and has recently been linked to antibiotic use in livestock.[4-6] Many S typhi strains contain plasmids encoding resistance to chloramphenicol, ampicillin and co-trimoxazole, the antibiotics that have long been used to treat enteric fever. In addition, resistance to ciprofloxacin also called nalidixic-acid-resistant S typhi (NARST) strain either chromosomally or plasmids encoded, has been observed in Asia. A significant number of strains from Africa and the Indian subcontinent are MDR type. A small percentage of strains from Vietnam and the Indian subcontinent are NARST strains.[7-9] Hence; we planned the present study to assess the efficacy of two different antibiotic regimes in treating patients with typhoid fever.

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MATERIALS AND METHODS

We planned the present study in the department of general medicine of R.B.M. Hospital, Bharatpur, Rajasthan. A total of 20 patients with confirmed diagnosis of typhoid fever were included in the present study and were broadly divided into two study groups as follows:

Group 1- Patients who were treated with Ceftriaxone for 5 Days, and

Group 2- Patients who were treated with Chloramphenicol for 14 Days

Both the groups consisted of 10 patients in each group. Ethical approval was taken from institutional ethical committee and written consent was obtained after explaining in detail the entire research protocol. Inclusion criteria for the present study included:

- Patients within the age group of 18 years to 50 years,
- Patients with history of fever for more than 4 days,
- Patients with history of diarrhea as characterized by presence of three or more liquid stools in 24 hours,
- Patients with somatic 0 agglutinin titer of >80 for S. typhi, as determined by the Widal test
- Patients who showed positivity for the presence of typhoid fever as demonstrated with positive stool cultures.

Complete demographic details of all the patients were obtained along with their clinical and past medical history. Recording of the body temperature, pulse rate, blood pressure and respiratory rate was done after 8 hours of starting of the study. We also recorded the frequency and consistency of stools every 8 hours. Stool samples and venous blood samples were sent to laboratory for further investigation by bacteriologically culturing for confirming the presence of S. typhi. Streaking of the stool swabs was done onto MacConkey agar and salmonella-shigella agar. Stool specimens were examined microscopically for the presence of leukocytes, ova, parasites, and occult blood. Repeating of the blood cultures was done on days 3 and 14, and culturing of the stool specimens was done on days 5 and 14 and 1 week after the patient's discharge from the hospital. All the results were analyzed by SPSS software. Chi- square test was used for assessment of level of significance. P- value of less than 0.05 was taken as significant.

RESULTS

Table 1: Pre-treatment details of the patients of the present study

Parameter	Group 1	Group 2
No. of patients	10	10
Mean age (years)	19.5	20
Fever duration (days)	9	8
Diarrhea duration	6	5

Table 2: Responded of the patients to the treatment

Parameter		Group 1 (N=10)	Group 2 (N=10)	P-value
Cure clinically*		8	9	0.55
Relapse		1	1	-
Positive blood culture for S. typhi	Day 3	0	4	0.00**
	Day 14	0	0	-
Positive stool culture for S. typhi	Day 3	2	1	.85
	Day 14	1	0	-

*: As characterized by returning of the body temperature within physiologic range
**: Significant

A total of 20 patients were included in the present study and were broadly divided into two study groups; group 1 and group 2. Mean age of the patients of the group 1 and group 2 was 19.5 years and 20 years respectively. Mean duration of fever among patients of group 1 and group 2 were 9 and 8 days respectively. Mean duration of diarrhea among patients of group 1 and group 2 were 6 and 5 days respectively. Clinical cure was seen in 8 and 9 patients of group 1 and group 2 respectively. Positive blood culture for S. typhi was seen in 4 patients of group 2 on third day whereas none of the patient of group1 exhibited positive blood culture. Significant results were obtained while comparing the positivity of blood culture on third day of treatment.

DISCUSSION

In the present study, we observed approximately equal efficacy of both the treatment regimes in treating patients with typhoid fever. Alam MN et al compared the efficacy of two regimens of ciprofloxacin in a randomized study conducted on 69 patients with enteric fever, 52.2% of whom had infection with multidrug-resistant (MDR) strains of Salmonella typhi or S. paratyphi. Patients were randomly assigned to two regimens (10 days versus 14 days) of ciprofloxacin (500 mg twice a day). The mean +/- SD time required for defervescence was similar for both regimens (4.2 +/- 1.9 days in the 10-day group and 4.9 +/- 2.6 days in the 14-day group). A 100% cure was observed in each treatment group and no serious side effects were observed. Relapse occurred in two patients (14-day regimen). Only one patient (14-day regimen) had growth of S. typhi in stool culture at the time of the first follow-up three days after completion of therapy. Follow-up studies on available patients on two, six, and 12 months after completion of therapy revealed that all patients had negative stool cultures for S. typhi and S. paratyphi. This study indicated that ciprofloxacin may be recommended as an initial therapy for enteric fever for adult men and nonpregnant and nonlactating women in areas where MDR strains of S. typhi and S. paratyphi are prevalent, and that 500 mg twice a day of the drug given for 10 days is as effective as 14 days at the same dosage.9 Begum B et al carried out an intervention study to compare the clinical efficacy of Azithromycin in the treatment of childhood typhoid fever with that of cefixime for a period of one year from January 2011 to December 2011. A total of 60 cases of typhoid fever were enrolled in to a randomized clinical trial and was divided into two groups. The inclusion criteria of the cases were: Documented fever for more than 4 days plus two or more of the following clinical features: toxic physical appearance, intestinal complaints, coated tongue, ceacal gurgling, hepatomegaly and splenomegaly, diarrhoea and constipation plus positive Widal test and/or blood culture positivity. Patients who had complication like GIT heamorrhage; intestinal perforaion and/or shock were excluded from the study. Data were collected in a structured questionnaire. Azithromycin was given at a dose of 10mg/kg/day for a period of 07

days Cefixime was given at a dose of 20mg/kg/day in two divided dose for 14 days. The mean time of defervesence was 4.05+1.14 days with azithromycin and 3.41+0.95 with cefixime respectively. The minimum defervesence time was 02 days and maximum defervesence time was 07 days. Clinical cure rate was 87% in azithromycin group and 93% in cefixime group. No serious adverse effect was noted related to azithromycin and cefixime therapy except nausea, vomiting, diarrhoea and jaundice. It was found that azithromycin is almost as effective as cefixime in the treatment of typhoid fever.[10] Tatli 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.[11]

CONCLUSION

From the above results, the authors concluded that Ceftriaxone has equal efficacy in comparison to chloramphenicol in treating typhoid patients. However; we recommend future studies.

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