



A STUDY ON EVALUATION OF EFFICACY OF TREATMENT OF TYPHOID FEVER WITH CEFTRIAZONE AND CHLORAMPHENICOL IN A TERTIARY CARE CENTRE IN EASTERN BIHAR.

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ABSTRACT

AIMS AND OBJECTIVES: To evaluate and compare the efficacy of ceftriaxone and chloramphenicol in adults.

MATERIALS & METHODS: We assessed a total of 100 patients with enteric fever who reported to the department of Medicine of Jawahar Lal Nehru Medical College and Hospital, Bhagalpur, Bihar from December 2016 to November 2017. Patients with such clinical presentations as blood and/or stool cultures that tested positive for *S. typhi* were included. All the patients were randomly divided into two study groups; group A and group B. Group A included subjects who were treated with ceftriaxone for 7 days, while group B included subjects who were treated with chloramphenicol for 14 days. Complete recording of all the demographic and biochemical parameters of the patients was done regularly. The effects of therapy were assessed both clinically and bacteriologically. All the results were compiled and analysed by SPSS software.

RESULTS: Both the study groups consisted of 50 patients each. Mean age of the subjects of group A and Group B were 19.5 and 22.1 years respectively. Mean duration of fever of subjects of group A and group B were 7 and 8 days respectively. Nonsignificant result was obtained while comparing the efficacy of both the antibiotic therapies (p value > 0.05).

CONCLUSION: For treating enteric fever, ceftriaxone will be useful for patients in whom a shorter course treatment therapy is preferred.

KEYWORDS : Ceftriaxone, Chloramphenicol, Enteric fever.

INTRODUCTION:

Typhoid Fever is a highly prevalent infection in the Indian subcontinent. Due to multidrug resistant strains in these areas, third generation cephalosporins, such as ceftriaxone, are the treatment of choice. However, the latter regimen exhibits a slow response with mean time of 5 to 7 days or even longer to defervescence, which could be attributed to poor penetration capability of the drug into cells, and thus difficulty to eradicate the bacteria from the intracellular niche. Despite advances in public health and hygiene have led to the virtual disappearance of enteric fever (more commonly termed typhoid fever) from much of the developed world, the disease remains endemic in many developing countries.

Enteric fever (typhoid and paratyphoid fevers) is caused by fecal oral transmission of *Salmonella enterica* serotypes Typhi or Paratyphi A. About 27 million people suffer from enteric fever each year, with about 200 000 deaths, almost exclusively in the developing world.[1]The incidence of this neglected illness in some parts of South Asia is as high 1600 per 100 000 population. Because of the ready availability of over-the-counter antibiotics and subsequent resistance to these drugs in areas of endemicity, enteric fever is becoming harder to treat.[2]

Typhoid fever is caused by *Salmonella enterica* serovar Typhi (*S typhi*), a Gram negative bacterium.[3-5 The common mode of infection is by ingestion of an infecting dose of the organism, usually through contaminated water or food. Early diagnosis of typhoid fever and prompt institution of appropriate antibiotic treatment are essential for optimal management, especially in children.[6-8] Trials of ceftriaxone showed that this antibiotic was a credible alternative to chloramphenicol. Ceftriaxone continues to be useful as a back-up choice, and chloramphenicol, despite its history of plasmid-mediated resistance, is making a comeback in developing countries that show their bacteria to be susceptible to it.[9] Although most cases can be managed at home with oral antibiotics and regular follow-up, patients with severe illness, persistent vomiting, severe diarrhoea, and abdominal distension require hospitalisation and parenteral antibiotic treatment.[10,11 The present study was done to evaluate and compare the efficacy of ceftriaxone and chloramphenicol in adults.

MATERIALS AND METHODS:

In the present study, we assessed a total of 100 patients with enteric fever who reported to the department of Medicine of Jawahar Lal Nehru Medical College and Hospital, Bhagalpur, Bihar from December 2016 to November 2017. Ethical approval was taken from institutional ethical committee and written consent was obtained after explaining in detail about the entire research protocol. Presence of

enteric fever in all the patients was confirmed by Widal test. Patients with such clinical presentations as blood and/or stool cultures that tested positive for *S. Typhi* were included. All the patients were randomly divided in to two study groups; group A and group B. Group A included subjects who were treated with ceftriaxone for 7 days, while group B included subjects who were treated with chloramphenicol for 14 days.

Complete recording of all the demographic and biochemical parameters of the patients was done regularly. The frequency and consistency of stools were also recorded every 8 hours. Venous blood, stool, and urine samples of patients were bacteriologically cultured for *S. Typhi* and other bacteria at the time of admission. The effects of therapy were assessed both clinically and bacteriologically on the basis of criteria as described previously in the literature.[12] All the results were compiled and analysed by SPSS software. Chi-square test and one way ANOVA were used for assessment of level of significance. P-value of less than 0.05 was taken as significant.

Table 1: Demographic and clinical details of the subjects

Parameter	Group A	Group B
Number of Subjects	50	50
Mean Age (Years)	19.5	22.1
Duration of Fever (Days)	7	8
Duration of Diarrhoea (Days)	5	6

Table 2: Response of the patients to the treatment

Parameter	Group A (N= 50)	Group B (N= 50)	p- value
Cure (Clinically)	44	46	0.25
Relapse	2	2	0.55
Blood culture positive for <i>S.typhi</i> at 14 days	0	0	0.55
Stool culture positive for <i>S.typhi</i> at 14 days	0	0	0.55

RESULTS:

In the present study table 1 shows the demographic and clinical details of the subjects included in this study. Both the study groups consisted of 50 patients each. Mean age of the subjects of group A and Group B were 19.5 and 22.1 years respectively. Mean duration of fever of subjects of group A and group B were 7 and 8 days respectively. Table 2 shows the response of the patients to the treatment. Non-significant result while obtained while comparing the efficacy of both the antibiotic therapies (p value > 0.05).

DISCUSSION:

In the present study, we observed nonsignificant difference in the efficacy of both the treatment therapies in treating patients with enteric fever. Gidvani C et al analysed one hundred cases of enteric fever in the age group of 6 months to 12 years, with respect to culture sensitivity pattern and treatment outcome. Patients were divided into 5 treatment groups – chloramphenicol, amoxycillin, trimethoprim-sulfamethoxazole + furazolidine, gentamicin + cephalixin and ciprofloxacin. Out of 91 culture positive cases, 100% were sensitive to ciprofloxacin followed by gentamicin (84.9%), cephalixin (83.6%), furazolidine (36.6%), trimethoprim-sulfamethoxazole (34.1%), chloramphenicol (34.0%) and amoxycillin (23.8%). In 60 cases resistant to chloramphenicol, resistance to other drugs varied from 20 to 88.3%. The treatment response was 100% to ciprofloxacin, 72.7% to chloramphenicol, 50% to gentamicin + cephalixin, 38.5% to trimethoprim-sulfamethoxazole + furazolidine and 12.5% to amoxycillin. Out of 48 cases who did not respond to initial regimen, 33 were treated successfully with ciprofloxacin and remaining with other drug regimens. Time taken for defervescence was shortest with gentamicin + cephalixin (4.6±2.0 days) followed by ciprofloxacin (6.1±2.5 days) and chloramphenicol (6.4±3.5 days).[13] Maheshwari VD et al assessed drug Sensitivity of Salmonella typhi isolated from 30 blood culture positive cases of typhoid fever, to determine their in vitro susceptibility to various antimicrobials. 56.6% showed resistance to chloramphenicol, 70% to amoxycillin, 50% to amikacin, 43.3% to gentamycin, 40% to ampicillin, 33.3% to cotrimoxazole, 30% to cephalixin and very low resistance (6.6% each) to ceftriaxone and cefotaxime. All the 30 cases were sensitive to ciprofloxacin and ofloxacin. chloramphenicol resistant typhoid cases in whom chloramphenicol was initially started failed to respond to this drug even after 4-5 days therapy, indicating that in vivo response matched with the in vitro sensitivity. Clinical response to ciprofloxacin, whether given initially or following chloramphenicol failure was prompt and satisfactory. Ciprofloxacin thus appears to be a good choice in such cases.[14] Madan A et al reported a sudden and marked increase in the occurrence, in a captive population, of typhoid fever cases showing multiple drug resistance. Shared resistance to chloramphenicol, ampicillin, amoxycillin and sensitivity to gentamicin, kanamycin, sisomicin, cephalixin, norfloxacin and ciprofloxacin in most of our cases suggest infection by a common strain with R-factor, mediated resistance. The illness was prolonged and associated with serious complications. Therapy with combination of quinolone derivatives and aminoglycoside antibiotics seemed justified on the basis of the in-vitro tests and clinical response. Efforts to identify the strain and stern public health measures to prevent further development of drug resistant S typhi are urgently indicated.

CONCLUSION:

From the present study we concluded that for treating enteric fever, ceftriaxone will be useful for patients in whom a shorter course treatment therapy is preferred. As this study is hospital based, the findings of this study cannot be generalised for the whole population.

REFERENCES

1. Crump JA, Luby SP, Mintz ED. The global burden of typhoid fever. *Bull World Health Org* 2004;82: 346-53 [PMC free article] [PubMed]
2. Maskey AP, Day JN, Tuan PQ, et al. Salmonella enterica Typhi and Paratyphi A cause indistinguishable clinical syndromes in Kathmandu, Nepal. *Clin Infect Dis* 2006;42: 1247-1253 [PubMed]
3. Alonzo TA, Pepe MS. Using a combination of reference tests to assess the accuracy of a new diagnostic test. *Stat. Med.* 1999; 18:2987-3003.
4. Baker S, Favorov M, Dougan G. Searching for the elusive typhoid diagnostic. *BMC Infect. Dis.* 2010; 10:45.
5. Banoo S, et al. Evaluation of diagnostic tests for infectious diseases: general principles. *Nat. Rev. Microbiol.* 2006; 4:S21-S31.
6. Chaudhry R, et al. Rapid diagnosis of typhoid fever by an in-house flagellin PCR. *J. Med. Microbiol.* 2010; 59:1391-1393.
7. Chandra J, Marwaha RK, Sachdeva S. Chloramphenicol resistant Salmonella typhi : Therapeutic consideration. *Indian J Pediatr.* 1984;51:567-570.
8. Hill CFL, Armstrong JV, Mcdonald CK, Allott EN. Treatment of typhoid fever with chloramphenicol. *Lancet.* 1950;2:802-804.
9. Butler T. Treatment of typhoid fever in the 21st century: promises and shortcomings. *Clinical Microbiology and Infection* 2011;17(7):959-963.
10. Pais N, Ravindranath S. Kesavamurthy. Drug resistant typhoid in Bangalore. *J Assoc Physicians India.* 1991;39:654.
11. Scragg JN. Further experience with amoxycillin in typhoid fever in children. *BMJ.* 1976;2:1031-1033.
12. Sen S, Goyal RS, Dev R. Ciprofloxacin in the management of multiple drug resistant typhoid fever. *Indian Pediatr.* 1991;28:417-419.
13. Gidvani C, Chandar V, Raghunath D, Puri R, Wilson C, Nagendra A. Enteric fever – culture and sensitivity pattern and treatment outcome. *Medical Journal, Armed Forces India.* 1995;51(2):83-86. Maheshwari VD1, Agarwal SK. Present status of drug resistance in cases of enteric fever in Rajasthan. *J Assoc Physicians India.* 1996 Sep;44(9):618-9.
14. Madan A1, Dhar A, Kulshrestha PP, Laghate VD, Dhar P. Preliminary observation on drug resistant cases of typhoid fever. *J Assoc Physicians India.* 1991 Jun;39(6):449-51.