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ORIGINAL RESEARCH ARTICLE

Efficacy of Cefixime in the Treatment of Typhoid Fever

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ABSTRACT:

Typhoid fever is defined by fever (greater then 38.5°C for more than three days) and isolation of *Salmonella typhi* from blood or bone marrow culture. The causative agent *Salmonella typhi* is developing resistance against the various lines of antibiotics. So this is becoming more and more serious problem gradually. The aim of this study was to determine the efficacy of Cefixime in typhoid fever in different hospitals of Rupandehi and Palpa districts of Nepal. An open-labeled, non-comparative, study was conducted in 112 subjects to evaluate the efficacy and safety of Cefixime (5mg/kg or 200mg twice daily for 7 days) for the treatment of typhoid fever. Of the patients enrolled based on symptoms of typhoid fever, 106 (94.6%) completed the study. Clinical cure was seen in 98 (92.5%) subjects. The efficacy was measured as absence of symptoms in 10th day of treatment. No serious adverse event was observed. Cefixime was found to be safe and efficacious for the treatment of typhoid fever.

Key words: Cefixime, *Salmonella typhi*, Typhoid fever, Resistance.

INTRODICTION

Typhoid fever (TF), also known as enteric fever, is caused by the Gram-negative bacterium *Salmonella enteric* serovar Typhi. The disease is mainly associated with low socio-economic status and poor hygiene, with human beings the only known natural hosts and reservoir of infection [1]. *Salmonella enterica serotype typhi* is the aetiological agent of typhoid fever, a multi-systemic disease with protean manifestations and initial lesions in the bowel. *Salmonella typhi* is a gram negative non spore bearing organism that is motile by means of flagellae. They can survive long periods in hot, humid environment and withstand freezing. Infective dose is about 105-109 organism, with an incubation period ranging from 4-14 days [2].

Typhoid Fever is only found in human. It is characterized by a continuous fever for 3-4 weeks, relative bradycardia, with involvement of lymphoid tissue and considerable constitutional symptoms [3]. Early in 20th century the advent of chloramphenical treatment changed the perceptions of typhoid fever from a severe, fatal disease to common, readily manageable infection but the occurrence of chloramphenicol resistant typhoid were reported in 1972 and also in the late 1980s and 1990s, occurrence of cotrimoxazole, ampicillin, amoxicillin were reported [4].

Widespread emergence of multidrug-resistant *S. typhi* has necessitated the search for therapeutic options for TF. Fluoroquinolones have proven effective, but to date they are not recommended for use in children, and quinolone resistant strains of *S. typhi* have been reported [5]. Azalides are another class of antibiotics which have shown promise in the treatment of typhoid fever. Studies comparing the efficacy of Azithromycin with cefixime in adults and in children with typhoid fever have reported it to be safe and efficacious [6].

In the search for alternative antibiotics for the treatment of TF, the third generation Cephalosporins has shown good activity against *S. typhi* [7]. Cephalosporins exert bactericidal activity by interfering with bacterial peptidoglycon synthesis after binding to the β-lactam-binding proteins. The Cephalosporins are also thought to play a role in the activation of bacterical cell autolysins which may contribute to bacterial cell lysis [8]. However, only cefixime and Cefpodoxime proxetil allow oral administration for use in ambulatory patients. Cefixime is a third generation cephalosporin, for oral use in children

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and adults, administered once or twice daily with good antimicrobial activity against *S. typhi*. Due to emergence of multi-drug resistance (MDR) *S. typhi* alternative drugs for the treatment of TF are required. We conducted this study to assess the efficacy of Cefixime in the treatment of TF.

METHODS

We perform an open-label and non-randomized study to assess the efficacy of Cefixime in the treatment of TF. The study was carried out at different hospitals in the Lumbini zone, Neapl from August 2012 to November 2012. This multicenter study was conducted with prior approval of the study protocol from the Institutional Ethics committee form all participating institutions. We enrolled adult and pediatric out patients, both sexes and without intestinal complications or extra-intestinal complications like arthritis, multifocal osteomyelitis, brain abscesses, pneumonia or sepsis. Subjects with history of hypersensitivity to Penicillins or Cephalosporins were rejected. Typhoid fever was defined by fever > 38.5°C for longer than three days and the isolation of *S. typhi* from blood culture. Patients were included after medical history and cultures were taken (day 0). Written informed consent was taken from all subjects prior to enrolment. All pediatric patients received doses of 5 mg/kg of Cefixime po, twice-daily. Adult patients received a dose of 200 mg po, twice-daily. Subjects were evaluated on day 0, day 5, and day 10. A window period of ±2 days was admissible for each visit. If the temperature increased or the clinical conditions of the patient worsen or there was a serious drug reaction, patient was take off from the study and managed according to the conditions. All follow ups were carried out in the out-patient department of the hospital.

The primary criteria of efficacy were clinical cure (defined as absence of symptoms and signs of infection at day 10 of treatment) and bacteriological cure (defined as a negative culture to *S. typhi* at day 10 of treatment). This study was performed according to the guidelines of Santillan RM et al study [9].

RESULTS

A total of 112 pediatric and adult patients were enrolled, but 6 were lost to follow up and 106 (94.64%) completed the study. Out of 106 patients 45 were males and 61 were females, this is shown in figure below. Mean (SD) age was 20.72 (15.47) years. All patients showed improvement of symptoms and signs, particularly fever abatement, which was observed on the average at day 4 after start of treatment.

Fig 1: Gender wise distribution of patients

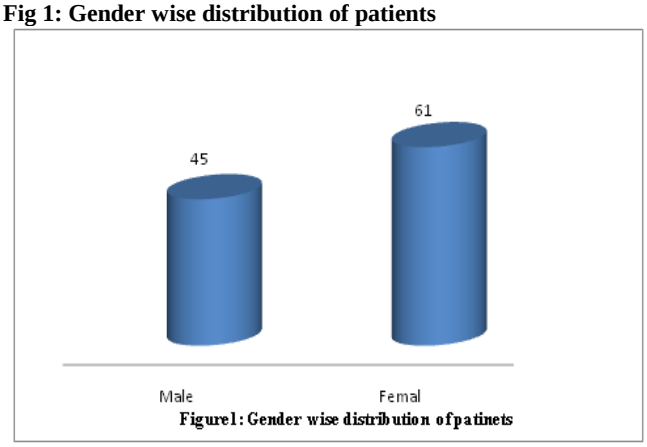
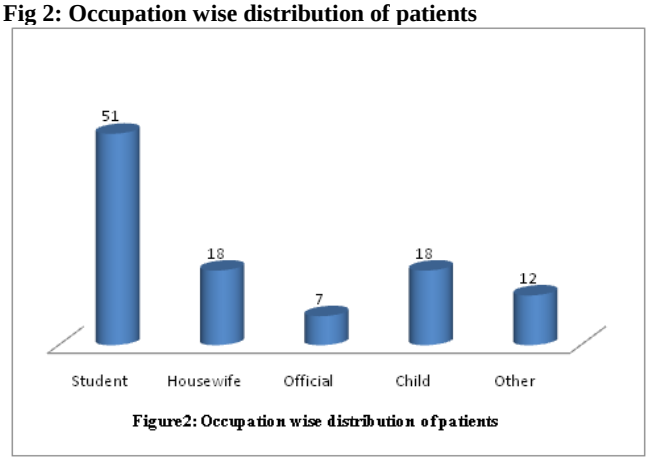


Fig 2: Occupation wise distribution of patients



The Widal test report of the typhoid fever patients before treatment is shown in (**Table 1**).

Table 1: Laboratory information of Widal test

Widal test	Frequency	Percent
Widal test O+	53	50.0
Widal test H+	10	9.4
Widal test AH+	32	30.2
Widal test BH+	10	9.4
Widal test H,BH+	1	0.9
Total	106	100

At the end of the study, 98 (92.5%) patients, showed clinical cure. No serious adverse effects were observed (**Table2**).

Table 2: Side effects of Cefixime

Side Effect	Frequency	Percentage
Nausea	2	1.9
Diarrhea	6	5.7
Stomatitis	4	3.8
Rashes	2	1.9
Drowsiness	1	0.9
No Complication	91	85.8

DISCUSSSION

Usually, chloramphenicol has been the drug of choice for the treatment of typhoid fever particularly in developing countries. Due to a high rate of relapses, the unacceptable risk for inducing aplastic anemia of chloramphenicol and the emergence of multi-drug resistance, its necessary

to search drugs that, prevent relapses and chronic carrier state, produce quick remission of the fever and can be administered orally with the smallest number of daily doses.

To date, the Fluoroquinolones are the agents of choice for the treatment of TF. However, the role of these agents in the pediatric patient is controversial, as they can cause damage to the articular cartilage [10]. In this study, cefexime accomplishes the desired characteristics of antibiotics and may be the treatment of TF, particularly in children and all age groups. In our study Cefixime showed clinical efficacy around 92.5%. No treatment failure rate has been obtained in earlier study, Cefixime showed clinical efficacy around 100%, with low rate of relapses and all strains isolated were sensitive to Cefixime [9]. This justifies the importance of Cefixime in TF.

This study was not a randomized controlled trial or a comparative trial which is one of the limitations of the study.

CONCLUSION

Thus after research the efficacy of Cefixime was 92.5% (cured 98 patients completely out of 106 patients). Hence, Cefixime is highly effective and safe drug for treatment of typhoid.

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