



COMPARISON BETWEEN CEFTRIAXONE AND AZITHROMYCIN IN PATIENTS OF ENTERIC FEVER.

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ABSTRACT

A total number of 60 patients aged 18 years onwards, with history of fever for not less than 7 days and clinical features suggestive of typhoid fever with blood culture positive for *S. typhi* were divided into two groups and started treatment for first group with Azithromycin 500mg OD orally and the second group with Ceftriaxone 1gm OD through intravenous route. The clinical efficacy regarding clinical cure, microbiological cure and relapse were denoted for the two groups. It was found that for the first group i.e. Azithromycin group, clinical cure rate and microbiological cure rate were more than the second one. But relapse rate was more for the second group i.e. Ceftriaxone group than the first one. So it can be concluded that Azithromycin (oral) is better than Ceftriaxone (intravenous).

KEYWORDS: Azithromycin, Ceftriaxone.

INTRODUCTION

Typhoid fever is a systemic infection caused by salmonella typhi and salmonella paratyphi. It is a common and sometimes fatal in this developing country like India. For decades, chloramphenicol has been highly effective against *S. typhi* and *S. paratyphi*, and it often remains the antibiotic of choice for the treatment of typhoid fever.^[1, 2] But the multidrug resistance has emerged day by day. Due to this, it is necessary to search any other therapeutic alternative for the treatment point of view.

Fluoroquinolones have proved to be the alternative, but quinolone-resistant strains of *S. typhi* have began to be reported.^[3,4] Ceftriaxone, a third generation cephalosporin, is highly effective against *S. typhi* and has become the standard of care for the treatment of typhoid fever in many parts of the world.^[5] However, because parenteral administration of ceftriaxone is required, the antibiotic is a less-than-ideal treatment alternative.

The recent availability of the azalide class of antibiotics has provided another potential option for the treatment of typhoid fever. Azithromycin, the first azalide evaluated, has in vitro activity against many enteric intracellular pathogens, including *S. typhi*.^[6-8]

Animal models have demonstrated that azithromycin is highly effective against both *Salmonella enteritidis* and *Salmonella typhimurium*, with drug efficacy related to the tissue concentration, rather than the serum

concentration, of the antibiotic.^[9,10] Studies of human volunteers have shown that neutrophil concentrations of azithromycin are >100 times the serum concentration of the antibiotic.^[11] Five days after a 3-day course of azithromycin was completed, neutrophil concentrations of the drug still exceeded the typical MIC for *S. typhi* by 120 times, whereas the drug was unmeasurable in the serum.^[11] Due to this and also the oral route & OD dose treatment led us to perform the study.

MATERIALS AND METHODS

After taking IEC Approval, this study was done at Medical Out Patient Department (MOPD) and Medical Indoor of Kalinga Institute of Medical Sciences, Bhubaneswar, Odisha.

Study Population

Inclusion Criteria

Patients (≥ 18 years old) coming to the MOPD with the history of fever (≥ 38.5⁰ C) for at least 7 days or more associated with the clinical suspicions of typhoid fever (abdominal tenderness, hepatomegally, splenomegally and / or rose spots)

Exclusion Criteria

Allergy to ceftriaxone and / or azithromycin, Major complications of typhoid fever like pneumonia, intestinal haemorrhage, inability to swallow oral medication. After admission, blood samples of all of the patients were sent for culture. A total number of 60 patients whose blood culture were positive for *S. typhi* were taken for this

study in 12 months duration from January 2014 to December 2014. From the beginning they were divided into two groups and they put in these two groups nearly equal distribution from January 2014 onwards.

The first group was prescribed Azithromycin 500 mg per oral per day for 7 days; and the second group was prescribed Ceftriaxone 1gm. intravenous injection per day for 7 days.

During the period of staying at hospital, clinical signs like body temperature (8 hourly), general conditions of the patient as well as presence of coated tongue, abdominal tenderness, splenomegally, hepatomegally all noted.

Response to treatment were classified as clinical cure (resolution of typhoid related features by the end of 7 days of therapy) or clinical failure (persistence of ≥ 1 typhoid related features) or the development of typhoid complications by the end of 7 days of therapy. Remission of fever, Microbiological cure (Sterile blood culture on day 10 of therapy) and Relapse (recurrence of fever with features of typhoid fever within 4 weeks of completion of therapy along with isolation of *S.typhi* from the blood) are three other parameters (response to treatment).

After 10 days of treatment the patients of each group who were microbio-logically cured were discharged with the advice to attend MOPD after 2 weeks and thereafter 4 weeks i.e. 2 weeks after first review with repeat blood culture report.

RESULTS

Table:1

	Azithromycin	Ceftriaxone
Clinical Cure by day 7	27(90%)	21(70%)
Clinical Failure by day 7	3(10%)	9(30%)
Remission day of fever	4.4 \pm 0.86	4.6 \pm 0.86
Microbiological Cure	29(96.7%)	22(73.3%)
Relapse	0	3(10%)

Responses to treatment were excellent in both groups (table1). Patients responded nicely to therapy; the mean time to defervescence \pm SD was 4.4 \pm 0.86 days and 4.6 \pm 0.86 days for azithromycin recipients and ceftriaxone recipients, respectively. Clinical cure occurred in 27 (90%) of 30 patients treated with azithromycin, compared with 21 (70%) of 30 patients treated with ceftriaxone. Of these, 3 patients with clinical failure in the azithromycin group and 9 patients with clinical failure in the ceftriaxone group. Microbiological cure was achieved in 29 (96.7%) patients of Azithromycin group; whereas that of in Ceftriaxone group was 22(73.3%). Most interestingly it was noticed that there was not a single case of relapse in Azithromycin, but that was 3 (10%) in Ceftriaxone group.

DISCUSSIONS

In this comparative, randomized trial, we demonstrated that azithromycin is highly effective for the treatment of typhoid fever. In the present study, findings of clinical cure rates 90% and microbiological cure rates 96.7% for subjects receiving azithromycin which is in consistent with the previous findings^[1,4] and those of for ceftriaxone were 70% & 73.3% respectively. In this present study, the relapse rate is 10% in case of Ceftriaxone treated patients. These data was consistent with relapse rates of 5%–15% in other trials of ceftriaxone for the treatment of typhoid fever.^[1,5] Although our sample size was small, no subject who was treated with azithromycin had a relapse; this finding may be attributable to the long half-life of azithromycin within the intracellular compartment, with eradication of residual organisms after completion of therapy, as well as to its elevated concentration within the biliary system.^[12]

In conclusion, azithromycin given for 7 days at a dosage of 500 mg/day appears to be highly effective for the treatment of enteric fever with clinical cure rates comparable to those for ceftriaxone. Once-daily administration of oral azithromycin may offer a simple treatment regimen for typhoid fever caused by susceptible strains of *S. typhi* and may be suitable for use in areas where medical resources are limited.

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