



### Original Research Article

## Efficacy and Safety of Azithromycin and Ofloxacin in Uncomplicated Typhoid Fever, in Tertiary Care Hospital at S.K.M.C.H., Muzaffarpur, Bihar

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### Abstract

**Objective:** Present study was a Comparative Study and undertaken to know the Efficacy and Safety of Azithromycin and Ofloxacin in Uncomplicated Typhoid Fever.

**Materials and Methods:** A total of 120 Patients of either sex, aged between 20 and 55 with positive blood culture and Widal test for salmonella typhi along with clinical picture suggestive of typhoid fever were included in the study. All the patients were randomized in two study Groups. Group A included 60 patients, Group B also contains 60 patients. Group A patients received oral ofloxacin 200 mg twice daily for 7 days and Patients in Group B received oral Azithromycin 1 gm on day one and then 500 mg daily from day 2 to day 6. Written consent was taken from all the patients and all the data regarding age, occupation, clinical illness, past history of treatment were noted. All cases were followed up once weekly for a period of 4 weeks. All the cases came for follow up regularly and were examined for fever clearance time, cure rate and recurrence of symptoms of relapse.

**Results:** Out of 120 patients of typhoid fever 72 patients (60%) were male and 48 patients (40%) were females in the range of 20-55 years. After Ofloxacin treatment in Group A patients, 45(75%) patients showed good or moderate response while a 10 (16.66%) patient showed poor response and 5(8.34%) patients did not responded even after 7 days treatment and was considered treatment failure. Cure rate was found to be 80%. After Azithromycin treatment, all 60 patients (100%) showed good or moderate response and no poor response case was observed.

**Conclusion:** No significant difference in clinical cure rate was observed in two study groups. No relapse was recorded in the present study in a follow up period of 4 weeks in both study groups.

**Keywords:** Enteric fever, Antibiotics, Ofloxacin, Cephalosporins, Azithromycin, Typhoid fever.

### Introduction

Typhoid fever is a systemic disease characterized by fever, severe headache and abdominal pain caused by Salmonella typhi and Salmonella

Paratyphi A, B, C. Relevant and appropriate antibiotic is important for the clinical management of enteric fever. For many decades, antibiotics such as chloramphenicol, ampicillin, and

cotrimoxazole were used for treating enteric fever. The emergence of Multi Drug Resistant (MDR) Salmonella strains, which are resistant to chloramphenicol, ampicillin and cotrimoxazole, has changed treatment options. Second line antibiotics like the fluoroquinolones (ciprofloxacin, ofloxacin), third-generation cephalosporins (ceftriaxone, cefixime), and azithromycin are often now used for treating MDR typhoid fever.

For the treatment of uncomplicated enteric fever caused by fully sensitive and MDR organisms, Fluoroquinolones are commonly used and have been also recommended by the WHO. Ciprofloxacin and ofloxacin were chosen for treating typhoid because of potent bactericidal activity against *S. typhi* and *S. paratyphi* A. In vivo, both drugs have plasma levels considerably in excess of the prevailing MICs and excellent intracellular penetration.

Due to widespread use of fluoroquinolone for the treatment of typhoid fever leads to the emergence of *S. typhi* and *S. paratyphi* A isolates with increase Minimum Inhibitory Concentrations (MIC) to ciprofloxacin and ofloxacin across Asia and in some parts of Africa. These strains are associated with point mutations in the gyr A gene and occasionally the par C gene. Enteric fever caused by *S. Typhi* strains with an elevated MIC to ciprofloxacin and ofloxacin have been coupled with the failure of treatment with these antimicrobials and increased disease severity. There are also reports from the Indian subcontinent of isolates that are fully resistant to fluoroquinolones and the extended spectrum cephalosporins.

Azithromycin, a member of the macrolide group of antibiotics, has been used as an alternative drug for treating typhoid fever. It achieves low intravascular levels, has high intracellular tissue penetration, and a long elimination half life of 72 hours. These properties make for once daily administration and reduction in the duration of therapy. The drug is rapidly absorbed from the gut and is well tolerated when used orally. In vitro

studies have shown that it is more potent than traditional first line drugs and other macrolides against *Salmonella* spp. with an average MIC of 8µg/mL. There are no reports of resistance of *S. Typhi* to azithromycin, and recent studies have shown that it is effective both clinically and bacteriologically in treating enteric fever even in those caused by MDR strains.

So, the present study was conducted to compare the efficacy and safety of azithromycin with ofloxacin in patients with uncomplicated typhoid fever.

### Materials and Methods

Present study was conducted in the Department of Pharmacology, S. K. Medical College, Muzaffarpur, with the help of Department of Medicine, and Microbiology during the period of December 2017 to February 2019. It was a prospective, randomized, open labeled study. A total of 120 Patients of either sex, aged between 20 and 55 with positive blood culture and Widal test for salmonella typhi along with clinical picture suggestive of typhoid fever were included in the study.

Patients with refused consent, evidence of progressive or complicated disease, inability to swallow oral medication, history of significant underlying disease, hypersensitivity to either of the trial drugs or were pregnant or lactating, patients who gave a history of treatment with a fluoroquinolone, a third generation cephalosporin or a macrolide within one week of hospital admission were excluded from the study.

All the 120 patients were divided in two treatment study Groups 60 of each. Patients in Group A received oral ofloxacin 200 mg twice daily for 7 days and Patients in Group B received oral Azithromycin 1 gm on day one and then 500 mg daily from day 2 to day 6.

The progress of the cases was recorded with special reference to period of defervescence of fever and general condition. All cases were followed up once weekly for a period of 4 weeks. All the cases came for follow up regularly and

were examined for fever clearance time, cure rate and recurrence of symptoms of relapse.

### Results

Out of 120 patients of typhoid fever 72 patients (60%) were male and 48 patients (40%) were females in the range of 20-55 years. The maximum incidence was between the age group of 18-38 years.

Patient was declared clinically cured when fever does not repeat within seven days of antibiotic therapy and without any clinical relapse during four weeks follow up period.

After Ofloxacin treatment in Group A patients, 45(75%) patients showed good or moderate response while a 10(16.66%) patient showed poor response and 5(8.34%) patients did not responded even after 7 days treatment and was considered treatment failure. Cure rate was found to be 80%. After Azithromycin treatment, all 60 patients (100%) showed good or moderate response and no poor response case was observed. Treatment failure was not noted in any case in this group. Cure rate was found to be 100%. There is no significant difference in clinical cure rate was observed in two study groups. No relapse was recorded in the present study in a follow up period of 4 weeks in both study groups.

### Discussion

Typhoid fever caused by *Salmonella* sp is one of the most common causes of systemic infections in India and is one of the common causes of travel associated illnesses. Several developing countries recently reported the emergence and spread of drug resistant *Salmonella typhi* that resulted in significant increase in morbidity of typhoid fever and a frantic search for inexpensive but effective alternative drug. MDR strains of *S. Typhi* have been reported from all parts of the world. Second-line antibiotics like the fluoroquinolones (ciprofloxacin, ofloxacin, Levofloxacin), third-generation cephalosporins (ceftriaxone, cefixime), and azithromycin are often now used for treating MDR typhoid fever. Infections with isolates

susceptible to nalidixic acid respond extremely well to fluoroquinolones. Lately, there have been several reports of fluoroquinolone-resistant *S. Typhi*. Quinolone resistant strains are reportedly also MDR and infection with resistant *S. Typhi* is associated with increased morbidity and mortality. There are also reports from the Indian subcontinent of isolates that are fully resistant to fluoroquinolones and the extended spectrum cephalosporins. These reports further support the need for alternative antibiotics such as azithromycin for treating enteric fever.

In the present study both groups were compared in term duration of fever, fever clearance time, cure rate and relapse rate, age and fever duration prior to treatment. Similarly, no significant difference in fever clearance time and cure rate was observed between Azithromycin and ofloxacin treated group. Treatment was well tolerated with ofloxacin and azithromycin with only minor side effects. No major adverse effect was noted with these antibiotics.

Drug resistance in *Salmonella* has been on the rise in India especially in North Bihar with emergence of Nalidixic Acid-Resistant (NAR) *Salmonella* and an increasing clinical non-response to fluoroquinolones. Treatment options are getting limited with emergence of resistance to fluoroquinolones. The Western studies have favored azithromycin as the potential drug that produces good clinical response. However, due to the lack of breakpoint concentrations in various international guidelines, it's in vitro interpretation has often been difficult for *Salmonella*. In the Western literature, treatment has heavily banked upon the use of azithromycin due to its high intracellular concentration and good clinical response. Clinical trials suggest the use of 20 mg/kg per day with a maximum dose of 1000 mg/day for 5 to 7 days for complete cure. Randomized trials have suggested similar efficacy of azithromycin and ciprofloxacin, both clinically and in vitro studies, against enteric fever caused by sensitive as well as MDR. A trial conducted by Girgis et al., in Egypt compared the effectiveness

and safety of azithromycin and ciprofloxacin in uncomplicated typhoid fever. This study promotes the effectiveness of azithromycin in uncomplicated typhoid fever. However there was lack of substantial data in Indian population. This prompted us to compare the efficacy and safety of azithromycin with ofloxacin in patients with uncomplicated typhoid fever. Our study also suggests effectiveness of azithromycin in uncomplicated typhoid fever.

### Conclusion

Both ofloxacin and azithromycin are equally efficacious and safe in treatment of typhoid fever. Azithromycin is an effective option where ofloxacin is contraindicated like children, pregnant women and quinolone resistant patients of typhoid fever.

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