

## Original Article

# Comparative Study of Effectiveness Between Azithromycin and Levofloxacin in the Treatment of Childhood Typhoid Fever

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## Abstract

**Background:** Typhoid fever is an important cause of morbidity and mortality in patients especially in developing country. Therapy with conventional drugs is associated with increasing resistance, non-compliance to therapy and toxicity.

**Objective:** The aim of this study was to compare the effectiveness of Azithromycin and levofloxacin in the treatment of childhood typhoid fever.

**Methods:** This comparative study was carried out among 120 patients presenting with symptoms, signs and laboratory investigations diagnostic of typhoid fever in IPD and OPD of Paediatric Department, Dhaka National Medical College Hospital, Dhaka, from April to October 2013. Patients received Levofloxacin (n=60) consider as group I and Azithromycin (n=60) consider as group II. Widal test positive was included for the study & specific antibiotic (Levofloxacin or Azithromycin) treatment was started by randomization using lottery method. Statistical analysis of the results were obtained by using window based computer software devised with Statistical Packages for Social Sciences (SPSS-20.1).

**Results:** Majority of the patients time of afebrile after taking antibiotic was 6 days in group I (n=21, 35.0%) whereas it was 4 days in group II (n=23, 38.3%). The difference was not statistically significant ( $p>0.05$ ) between two groups. Almost two third 68.33% of the patients in group I and 100.0% in group II patients were receiving treatment for 7 days. Regarding the side effects, it was observed that nearly three fourth (73.3%) of the patients in group I and 45(75.0%) in group II patients had nausea. Vomiting was found 8(13.3%) and 4(6.7%) in group I and group II respectively. Diarrhoea was 2(3.3%) in group I and 13(21.7%) in group II. Abdominal discomfort was 17(28.3%) in group I and 13(21.7%) in group II. The difference was not statistically significant ( $p>0.05$ ) between two groups.

**Conclusion:** Both drugs are equally effective in the treatment of childhood typhoid fever. Considering duration of treatment Azithromycin is better than levofloxacin.

**Keywords:** Levofloxacin, Azithromycin, Typhoid fever

## Introduction:

Typhoid fever (typhoid or paratyphoid fever) caused by *Salmonella* serotype Typhi (S Typhi) or *Salmonella* serotype Paratyphi (S Paratyphi) remains endemic in many areas of the developing world, causing over 26 million infections and over 200,000 deaths annually.<sup>1</sup> The incidence is highest in south-central Asia and South East Asia over

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Received: 05.04.2023 Accepted: 18.07.2023

100/100,000 cases/year, with the highest burden of disease in children aged 2-15 years.<sup>2, 3</sup> S Typhi represents the commonest cause of bacteraemia in this age group.<sup>4</sup> Early recognition and management of typhoid fever is needed to avoid the severe complications and possible fatality.<sup>6</sup> If not treated properly, enteric fever carries a mortality rate of 30%, whilst appropriate antimicrobial treatment reduces the mortality rate to as low as 0.5%.<sup>7</sup> Levofloxacin is a third generation fluoroquinolone drugs. The role of levofloxacin on intestinal bacteria and Enterobacteriaceae are strong, such as *Shigella*, *Salmonella*, *E. coli*, etc. Fluoroquinolones are the drug of

choice for the treatment of typhoid fever.<sup>8</sup> Application of levofloxacin in the pediatric field have different controversy. In recent years, levofloxacin has been widely used in pediatrics, yet no serious reactions, including cartilage involvement reported.<sup>9</sup> Azithromycin is the first of a new class of broad-spectrum antibiotics called azalides, which contain a nitrogen atom in the macrolide aglycone ring.<sup>10</sup> Azithromycin has an MIC of 4–16 mg/L against isolates of *S. typhi*.<sup>11</sup> Rapid movement of azithromycin from blood into tissue results in significantly higher azithromycin concentrations in tissue than in plasma (up to 50–100 times the maximum observed concentration in plasma). The prolonged concentration of azithromycin in cells is advantageous in the treatment of experimental *Salmonella* spp. infection in mice, which is intracellular, and may explain the good results obtained with azithromycin in children and adults with typhoid fever in Chile and Egypt.<sup>12</sup>

#### Materials & Methods:

This comparative study was carried out on children age belonged to 1 – 12 years presenting with symptoms, signs and laboratory investigations diagnostic of typhoid fever in IPD and OPD of Paediatric, Dhaka National Medical College Hospital, Dhaka, Bangladesh during the period from April 2013 to October 2013. The diagnosis of typhoid fever was based on fever for more than 7 days; positive Widal test and exclusion of other febrile illnesses were enrolled in this study. Typhoid fever associated with other disease and patient who were already receiving antibiotics were excluded from the study. Patients receiving Levofloxacin consider as group I and Patients receiving Azithromycin consider as group II by using lottery method. The results were compared statistically between two groups. The collected data were entered into the computer and analyzed by using SPSS (version 20.1) to assess the comparative effectiveness of Azithromycin and Levofloxacin in the treatment of childhood typhoid fever. The study was approved by the Institutional Ethical Committee.

#### Results:

In group I, majority 21(35.0%) patients time of afebrile after taking antibiotic was 6 days and in group II 23(38.3%) patient's time of afebrile after taking antibiotic was 4 days. The difference was not statistically significant ( $p>0.05$ ) between two groups. (Table I)

**Table I: Distribution of the study patients by time of afebrile after taking antibiotic (n=120)**

Time of afebrile after taking antibiotic	Group I (n=60)		Group II (n=60)		P-value
	n	%	n	%	
3 days	7	11.7	4	6.7	0.239 <sup>ns</sup>
4 days	14	23.3	23	38.3	
5 days	18	30.0	12	20.0	
6 days	21	35.0	21	35.0	

Ns =not significant

p value reached from chi square test

Almost three fourth (73.3%) patients in group I and 45(75.0%) in group II patients had nausea. Vomiting was found in 8(13.3%) patients of group I and 4(6.7%) patients of group II. Diarrhoea was found in 2(3.3%) patients of group I and 13(21.7%) patients of group II. Abdominal discomfort was observed in 17(28.3%) patients of group I and 13(21.7%) patients of group II. Skin rash was 2(3.3%) patients in group I and 4(6.7%) patients in group II. The difference was not statistically significant ( $p>0.05$ ) between two groups (Table II)

**Table II: Distribution of the study patients by side effects after taking antibiotic (n=120)**

Side effects	Group I (n=60)		Group II (n=60)		P-value
	n	%	n	%	
Nausea	44	73.3	45	75.0	0.834 <sup>ns</sup>
Vomiting	8	13.3	4	6.7	0.223 <sup>ns</sup>
Diarrhoea	2	3.3	5	8.3	0.219 <sup>ns</sup>
Abdominal discomfort	17	28.3	13	21.7	0.399 <sup>ns</sup>
Skin rash	2	3.3	4	6.7	0.339 <sup>ns</sup>

ns=not significant

p value reached from chi square test

Almost two third, 39(65.0%) patients in group I and 56(93.0%) in group II patients were receiving treatment for 7 days. Duration of treatment was statistically significant ( $p<0.05$ ) between two groups (Table III).

**Table III: Distribution of the study patients by treatment duration (n=120)**

Time of afebrile after taking antibiotic	Group I (n=60*)		Group II (n=60**)	
	n	%	n	%
10 Days	19	31.7	0	0.0
7 Days	41	68.33	60	100

**Discussion:**

In this current study it was observed that time of afebrile after taking antibiotic 6 days in 35.0% patients in group I and 4 days 38.3% in group II. The difference was not statistically significant ( $p>0.05$ ) between two groups. This finding is consistent to the finding of Frenk et al.<sup>13</sup> who observed the mean afebrile period was  $3.9\pm1.0$  days and  $4.1\pm1.1$  days in case of Levofloxacin and Azithromycin respectively<sup>13</sup>. Another study conducted in our country with azithromycin showed a mean afebrile period of  $3.82\pm1.49$  days.<sup>14</sup> Levofloxacin and Azithromycin are generally well tolerated. Side effects include nausea, vomiting, dyspepsia, abdominal pain, diarrhoea, headache, dizziness and asthenia; rarely tremor, anxiety, tachycardia, hypotension, hypoglycaemia, pneumonitis, rhabdomyolysis etc. Sheng<sup>15</sup> mentioned in his study that Gastrointestinal symptoms (nausea, vomiting, diarrhea, abdominal pain etc.) observed 60.53%, respiratory symptoms (cough, sore throat, etc.) observed 31.58% and headache observed 26.32%. In our study we observed that nearly three fourth (73.3%) of the patients in group I and 45(75.0%) in group II patients had nausea. Vomiting was found 8(13.3%) and 4(6.7%) in group I and group II respectively. Diarrhoea was 2(3.3%) in group I and 13(21.7%) in group II. Abdominal discomfort was 17(28.3%) in group I and 13(21.7%) in group II. The difference was not statistically significant ( $p>0.05$ ) between two groups.

**Conclusion:**

Time of afebrile after taking antibiotic 3–6 days in both groups. Duration of treatment was prolonged in Levofloxacin group with compared to Azithromycin. Nausea and abdominal discomfort were the more common side effects in both groups. Diarrhoea and skin rash occurred in some cases in both groups. Both drugs are equally effective in the treatment of childhood typhoid fever. Considering duration of treatment Azithromycin is better than levofloxacin

**Acknowledgement:**

The authors are grateful to the entire staff of Pediatric department of the Dhaka National Medical College and Hospital for their cooperation and support during the study period.

**Conflict of Interest:**

Authors declare no conflict of Interest.

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Posted: 2010-03-02 07:06:31.