

Treatment of Severe *Salmonella typhimurium* Infection with Ciprofloxacin

P. Dutta
M.R. Saha
U. Mitra
R. Rasaily
S.K. Bhattacharya
M.K. Bhattacharya
B. Kundu
A. Gupta

Enteric bacterial infections caused by non-typhoidal *Salmonella* species are still common throughout the world(1,2). The treatment of non-typhoidal salmonellosis with antimicrobials is still controversial. Antimicrobial treatment of salmonellosis has largely been discouraged because of common belief that antimicrobials do not significantly decrease the duration or severity of diarrhea, length of fever and excretion of organism(3,4). However, several other workers opine that antimicrobials are necessary when there is colonic

involvement(1,5). Dysenteric clinical presentation of salmonellosis patients with high fecal leucocyte counts is indicative of colonic involvement(6). A current problem of non-typhoidal *Salmonella* is the acquisition of resistance to most of the commonly used antimicrobials. These resistant strains are now widespread throughout the world(1,2,5).

Ciprofloxacin and related fluorinated 4-quinolones are active *in vitro* against isolates of *Salmonella*(7) and have been used successfully to treat non-typhoidal salmonellosis in adults(8,9). However, there has been no study evaluating the usefulness of ciprofloxacin in treating non-typhoidal salmonellosis in children. We report here our experience of treating 23 children with severe colonic infection of multi-drug resistant *Salmonella typhimurium* with ciprofloxacin.

Patients and Methods

Children of both sexes up to the age of 5 years, suffering from acute watery diarrhea or dysentery of less than 3 days duration, irrespective of severity, admitted at the Dr. B.C. Roy Memorial Hospital of Children between 9 a.m. and 1 p.m. during the first four days of the week were surveyed. They did not receive any antibiotic before admission or did not have any other systemic illness. On admission, a detailed clinical history was obtained from parents and a thorough physical examination was performed. Patients were weighted to the nearest 100 g. Investigators followed up the patients daily and recorded the following parameters: number of stool; consistency; presence of blood and

From the National Institute of Cholera and Enteric Diseases P-33, C.I.T. Road, Scheme XM, Beliaghata, Calcutta 700 010, and Dr. B.C. Roy Memorial Hospital for Children, 111 Narkeldanga Main Road, Calcutta 700 054.

Reprint requests: Dr. P. Dutta, Assistant Director, National Institute of Cholera and Enteric Diseases, P-33, C.I.T. Road, Scheme XM, Beliaghata, Calcutta 700 010.

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mucus in stool; temperature; tenesmus and vomiting. Patients were also carefully observed for possible complication like, toxic megacolon, paralytic ileus, hemolytic uremic syndrome and any systemic illness. The WHO guidelines were followed for management of diarrhea/dysentery in this hospital. Fresh stool sample was obtained from each patient before initiation of therapy and transported to the laboratory immediately for detection of established enteropathogens using standard techniques. Stool sample was also examined microscopically for presence of ova, cysts and parasites. All the *Salmonella* isolates were tested for susceptibility to various antimicrobials by the Kirby-Bauer disc diffusion technique using commercially available discs. Minimum inhibitory concentration (MIC) of the *Salmonella* isolates for nalidixic acid and norfloxacin was determined by Agar dilution method.

Results

A total of 387 children were investigated during the period between January 1988 and December 1989. Of these, 207 had watery diarrhea and 180 had dysentery. *Salmonella typhimurium* were recovered from 30 (14.5%) cases in the first category and 25 (13.9%) cases in the second category. All the patients with watery diarrhea and two patients with dysentery infected with *Salmonella typhimurium* recovered with standard hospital treatment. However, 23 children who were clinically diagnosed as severe dysentery on admission and received nalidixic acid in standard doses (55 mg/kg/day in 4 divided doses) did not respond to therapy even at 72 hours (frequency of stool was same on admis-

sion, no remission of fever, no improvement in other parameter like tenesmus). Ultimately on day 4 of admission, the therapy was changed to ciprofloxacin at the dose of 10 mg/kg body weight per day in two divided doses for 5 days. Finally, the bacteriological report confirmed that these patients were infected by multi-drug resistant *Salmonella typhimurium*. *Salmonella typhimurium* strains isolated from these patients were resistant to commonly used antimicrobials like chloramphenicol, furazolidone, ampicillin, gentamicin, nalidixic acid, co-trimoxazole, tetracycline, streptomycin and amikacin. However, they were susceptible to norfloxacin and ciprofloxacin. The MIC of ciprofloxacin was 0.5 mg/ml and nalidixic acid was >16 mg/ml. These twenty three patients are the subjects of our discussion.

Table I shows the clinical characteristics of 23 salmonellosis patients at the time of initiation of ciprofloxacin. Clinical presentations indicated that all the patients were severely ill.

Table II shows the clinical response of the salmonellosis patients after initiation of ciprofloxacin therapy. Cure (no fever, no blood in stool, stool semisolid with frequency less than 3 for last 24 hours or no stool for last 18 hours) was achieved in all 23 (100.0%) patients after receiving ciprofloxacin. No treatment failure (no change or deterioration of clinical condition inspite of 3 days of therapy and or development of signs of complications, e.g., toxic megacolon, paralytic ileus, hemolytic uremic syndrome or any systemic illness) was observed after receiving ciprofloxacin. Stool samples of these 23 children were reexamined at the time of discharge but

TABLE I—Clinical Characteristics of 23 Patients with Salmonellosis at the Time of Initiation of Ciprofloxacin

Characteristics	Observed value	Range
Age (mo) [mean±SD]	40.3 ± 9.0	26-58
Body weight (Kg) [mean ± SD]	10.8 ± 2.5	6.4-15.5
Duration of diarrhea before initiation of ciprofloxacin. (days) [mean ± SD]	5.4 ± 0.6	4-6
Stool frequency per day [mean±SD]	20.5 ± 2	16-24
Fever (>39.5°C) [%]	100.0	
Tenesmus [%]	100.0	

TABLE II—Clinical Response in Salmonellosis Patients

Parameters	Duration (mean ± SD) in days after receiving ciprofloxacin	
	Observed value	Range
Blood in stool	1.9 ± 0.3	1.5-2.5
Diarrhea	2.6 ± 0.4	2-3
Fever (≥38.0°C)	1.4 ± 0.3	1-2
Tenesmus	1.7 ± 0.3	1.2-2.3

none was positive for any known enteropathogen including *Salmonella typhimurium*. All the children were discharged from hospital after completion of 5 days ciprofloxacin therapy. No adverse effects related to the drug were noticed in the patients and no complaints were received from the patients or their parents during treatment.

Discussion

The results of the present study

indicate that ciprofloxacin is beneficial in patients with severe colonic infection of *Salmonella typhimurium* and the cure rate was*100%. It had also been documented in placebo controlled, double-blind studies that ciprofloxacin significantly shortened the duration of fever and diarrhea in adult salmonellosis patients(8,9). In contrast, earlier reports(3,4) of poor clinical efficacy of other antimicrobials, probably resulted from failure of antimicrobials to achieve good levels at the intracellular sites of bacterial replication. However, ciprofloxacin achieves high levels within the bowel mucosa and also penetrates well into macrophages, a site of *Salmonella* replication(10).

We agree with the widespread belief that antimicrobial is not beneficial for the treatment of simple *Salmonella* infection without colonic involvement. In this present observation all the salmonellosis patients who had watery diarrhea were cured by standard hospi-

tal treatment without any antimicrobial therapy. Two salmonellosis cases who had mild dysentery were recovered with furazolidone therapy though isolated *Salmonella typhimurium* strains were resistant to that drug.

On the basis of the results of this non comparative study, ciprofloxacin in one of the drugs that can be used to treat multiply resistant, severe *Salmonella typhimurium* infections in children.

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