CLINICAL PROFILE AND OUTCOME IN ENTERIC FEVER

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ABSTRACT

Sixty five blood culture positive cases of S. typhi were studied for clinical profile. A total of 64.6% were multidrug resistant and 35.4% were chloramphenicol sensitive. In patients with multidrug resistant S. typhi the age was higher ($p<0.01$), and incidence of complications such as shock (35.7%), encephalopathy (42.9%), myocarditis (14.3%) and gastric hemorrhage (4.7%) were more frequent, compared to chloramphenicol sensitive group. Cases with multidrug resistant S. typhi (MDRST) were treated with oral ciprofloxacin; the period of defervescence of fever was significantly less ($p<0.05$) compared to the chloramphenicol group. Our study suggests the use of ciprofloxacin in the treatment of MDRST without any side effects.

Key words: *Enteric fever, Chloramphenicol sensitive, Multidrug resistant.*

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The incidence of multidrug resistant *Salmonella typhi* (MDRST) is rapidly increasing in India and is ranging between 10-83%(1-5). With the emergence of MDRST strains, treatment of typhoid fever in children has become an increasingly difficult problem and it would appear that conventional antibiotics cannot be recommended as first line therapy in a patient suspected to have typhoid fever. This is all the more important in developing countries like India, where culture facilities are not available at most of the primary health care centres. This report highlights the clinical profile of multidrug resistant enteric fever and use of ciprofloxacin in its management.

Material and Methods

Sixty five blood culture-proven cases of typhoid fever were studied. A detailed clinical history and physical examination was done in all cases. Besides blood culture and widal reaction, other investigations included complete hemogram, *X*-ray chest, blood urea, serum electrolytes and stool examination.

On the basis of strong clinical suspicion all the cases were initially treated with oral chloramphenicol (75 mg/kg/day). After the blood culture report was available, chloramphenicol was continued in only those cases who showed chloramphenicol sensitivity. The patients who showed multiple drug resistant *S. typhi* were treated with oral ciprofloxacin (10 mg/kg/day).

Results

Of 65 children, 14 (21.5%) were less than 5 years, 21 (32.3%) were between 6 and 10 years, and 30 (46.3%) were between 11 and 14 years of age.

Forty two (64.6%) cases, showed multidrug resistant *S. typhi* (Group A),

while in 23 (35.4%) patients the organism was sensitive to chloramphenicol (Group B). In MDRST group organism was resistant to chloramphenicol, cotrimoxazole, ampicillin; sensitive to gentamicin and norfloxacin and sensitivity to cephalosporine was not done. Antibiogram did not include furazolidine because of resistance of *S. typhi* to this drug.

The mean age (*Table I*) in Group A pateints (9.8 ± 3.3 years) was significantly higher as compared to Group B patients (6.8 ± 3.5 years) ($p<0.01$). All the cases presented with high grade continuous fever, associated with chills and rigors (45%), toxic look and a coated tongue (80%). The incidence of hepatomegaly and splenomegaly was 35.5 and 25.8%, respectively. There was no difference in the clinical features at the onset between the two groups. The other clinical features are shown in *Table II*. The incidence of various complications was higher in MDRST patients (*Table III*). One case each in Group A and Group B died due to persistent shock.

Discussion

In this study 64.6% of blood culture positive patients with enteric fever were resistant to chloramphenicol, cotrimoxazole and ampicillin but sensitive to norfloxacin and gentamycin. Other workers have also reported similar results(1-5). We did not use gentamicin because of its limited *in vivo* efficacy against the organism(6,7).

Drug resistance to *S. typhi* against

TABLE I—*Clinical Features of Enteric Fever*

Feature	Group A (n = 42)	Group B (n = 23)	Significance*
Age (yr)	9.8 ± 3.3	6.84 ± 3.5	$p < 0.01$
Duration of fever (days)	15.8 ± 8.2	13.1 ± 9.0	$p > 0.05$
Defervescence (days)	5.4 ± 2.5	6.60 ± 2.3	$p < 0.05$

* Student 't' test

TABLE II—*Clinical Features of Enteric Fever*

Feature	Total patients (n = 65)		Group A (n = 42)		Group B (n = 23)	
	n	%	n	%	n	%
Vomiting	19	(29.2)	16	(38.1)	3	(13.1)
Bronchitis	19	(29.2)	11	(26.2)	8	(34.8)
Diarrhea	6	(9.2)	6	(14.3)	--	
Constipation	1	(1.5)	--	--	1	(4.3)
Burningmicturition	2	(3.1)	2	(4.7)	--	

TABLE III –*Complications of Enteric Fever*

Complication	Total patients (n = 65)		Group A (n = 42)		Group B (n = 23)	
	n	%	n	%	n	%
Shock	17	(26.1)	15	(35.7)	2	(8.7)
Encephalopathy	24	(36.9)	18	(42.9)	6	(26.1)
Myocarditis	6	(9.2)	6	(14.3)	-	-
Gastric hemorrhage	2	(3.1)	2	(4.7)	-	-
Mortality	2	(3.1)	1	(2.4)	1	(4.3)

chloramphenicol and other antibiotics is through plasmid mediated R factors derived from non-pathogenic entero-bacteria like *E. coli*(2,7,8). In India, relatively high incidence of enteric fever and misuse of antibiotics singly or in irrational combinations (Chloramphenicol and streptomycin) for the treatment of diarrheal diseases and other infections may be responsible for inducing multidrug resistance(9). It has been postulated that a pool of microorganisms, *e.g., E. Coli* bearing transposons coded for multidrug resistance to *S. typhi* has come into existence(10).

The significantly higher age in cases with multidrug resistant *S. typhi* (*Table I*) compared to chloramphenicol sensitive cases may be due to higher exposure to indiscriminate antimicrobials and thus higher incidence of MDRST strains. Observation from areas where antibiotics have not been used suggests that the increase in the resistance plasmids are because of excessive and inappropriate usage of antibiotics(11,12).

The higher incidence of some of the clinical features and complications in MDRST group may be due to: (*a*) much greater bacterial load in tissues due to resistance to conventional agents, or (*b*) virulence of bacteria as a consequence of genes present on R-plasmid(13). Other workers have also mentioned a higher incidence of complications in multidrug resistant cases (5,6). However, a few other reports have indicated a lower incidence of complications in cases with infection with MDRST strains(2,3).

The clinical response to ciprofloxacin as indicated by the period of defervescence was satisfactory (*Table I*) thus requiring shorter hospital stay, compared to chloramphenicol group. Although the clinical safety of ciprofloxacin in children is controversial, careful use of the drug in life threatening cases with MDRST may be justified(6,14). Morevoer, the arthopathic side effects are seen with high dose when used for a prolonged period and are species specific(15). Most of the studies done so far in children have not documented skeletal toxicity(16-18).

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