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Clinical Profile and Therapy in Enteric Fever

T.S. Raghu Raman
L. Krishnamurthy
P.K. Menon
Daljit Singh
D.G. Jayaprakash

Till recently, most of the patients of enteric fever could be effectively managed by administration of either chloramphenicol, amoxycillin, ampicillin, or cotrimoxazole. The emergence of multi-drug resistant *Salmonella typhi* (MDRST) infection in children has posed many problems relating to diagnosis and therapy. As alternate therapy in resistant enteric fever, various drugs singly, or in combination, such as cotrimoxazole and cephalosporins, or cephalexin and gentamicin, third generation cephalosporins and newer quinolones have been tried with varying results. This communication describes our observations on the clinical profile of children with enteric fever due to MDRST infection and, compare different drug regimes in the treatment of resistant enteric fever.

From the Department of Pediatrics and Pathology, Command Hospital, (A.F.), Agaram, Bangalore.

Reprint requests: Dr. T.S. Raghu Raman, Department of Pediatrics, Command Hospital (A.F.), Bangalore 560 007.

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Material and Methods

In this prospective study, ninety consecutive culture positive cases of enteric fever admitted to the Pediatric ward were studied. A detailed history, clinical profile, complications encountered at the time of admission and during the course of stay in hospital were recorded. A complete hemogram, X-ray chest, Widal reaction were part of diagnostic work up. Other relevant investigations were carried out depending on the clinical presentation. Disc susceptibility testing was done by the Stokes methods using Muller Hinton agar against thirteen antibiotics(1).

Patients with infection caused by the strains of *S. typhi* sensitive to chloramphenicol and other antibiotics were treated with chloramphenicol. Those presenting with MDRST infection were put either on single drug therapy with ciprofloxacin (n = 25) or a combination of cephalexin and gentamicin (n = 25). Alternate cases of MDRST infection were treated with ciprofloxacin. The efficacy of these regimes was evaluated on the basis of the time taken for defervescence, regression of organomegaly, duration of hospitalization and cost effectiveness.

Analysis of significance was done in case of clinical features by Chi square test. The efficacy of therapeutic regimes was compared in the two groups of MDRST infection.

Results

The average age of patients was 5.6 years with the youngest being two months old. The male : female ratio was 3 : 2. The age and duration of fever at the time of admission was not significantly different between those with chloramphenicol sensitive *S. typhi* and MDRST infection.

Presence of fever greater than 104°F, minimal toxemia, hepatomegaly ranging from 4 to 8 cm, abdominal distension were seen in a higher percentage of cases with MDRST infection as compared to cases caused by chloramphenicol sensitive strains of *S. typhi (Table I)*. The complications encountred during the period of study are shown in

TABLE I-*Comparative Clinical Profile in Enteric Fever*

Features	Sensitive *Salmonella typhi* group (n=40) No. (%)	MDRST (n=50) No. (%)	P value
Fever 104°F	18 (45)	44 (88)	<0.01
Toxemia	32 (80)	15 (30)	<0.01
Hepatomegaly	16 (40)	44 (88)	<0.01
Splenomegaly	26 (65)	22 (45)	<0.2
Abdominal distension	16 (40)	45 (90)	<0.01
Complications			
Hepatitis	2	3	
Pneumonia	2	1	
Encephalopathy	2	-	

TABLE II-*Comparative Clinical Response [Mean (SD)] to Therapeutic Regimes*

Criteria	Chloramphenicol (n=40)	Gentamicin (n=25)	Ciprofloxacin (n=25)
Days for defervescence	7.2(1.18)	6.5(1.85)	4.6(1.08)
Regression of organomegaly	5.5(0.9)	5.0(1.0)	4.0(1.2)
Duration of hospitalization	10.5(1.4)	8.4(1.1)	6.2(1.49)
Average Cost (Rs.) of therapy (10 kg)	75.0	115.0	60.0

Table I. The five cases of enteric hepatitis were diagnosed on the basis of hepatomegaly with icterus, marked elevation of serum transaminases, conjugated hyperbilirubinemia, and HBsAg negative parameters. Pneumonia was diagnosed on the basis of clinical and radiological features in cases of enteric fever. Encephalopathy in two cases presented with fever, unconsciouness, and seizures. The CSF study was normal in both cases.

Time taken for defervescence of fever, regression of organomegaly, period of hospitalization in children treated with ciprofloxacin differed significantly from those children treated with Cephalexin and gentamicin as shown in *Table II.* Similarly, the therapy with ciprofloxacin was cost effective as compared to therapy with Cephalexin and gentamicin (Rs. 60/- *vs* Rs. 115/- in a child of 10 kg).

Discussion

The epidemic proportion of enteric fever resistant to multiple antibiotics is a relatively recent phenomenon. Since 1989, this centre has been isolating MDRST with increasing frequency. The incidence of resistant enteric fever is rapidly increasing in India and is currently ranging between 10-50%(2,3). In the present study, 55.5% of cases were resistant to multiple antibiotics including chloramphenicol, ampicillin, amoxycillin and trimethoprim.

Age and duration of fever at the time of admission was not significantly different among the sensitive *S. typhi* strains and MDRST groups. Pyrexial peaks greater than 104°F associated with rigors were seen in a higher percentage of MDRST infection. At the same time the degree of toxemia was minimal, an observation recorded by other workers(3,4). Dominant hepatomegaly, relative absence of splenomegaly, persistant abdominal distension as seen in MDRST infection have also been observed in another study (5).

Life threatening complications including shock, myocarditis, gastrointestinal hemorrhage were not seen in this study. Among the rarer complications of enteric fever, we encountered five cases of hepatitis. A brief report of enteric hepatitis has been documented earlier(6). Typhoid encephalopathy, another interesting complication seen in two of our patients is being reported as a rising trend.

The clinical efficacy of cephalexin or gentamicin when used alonge is not satisfactory (2). The combination of these two drugs has been found effective(S). Similar results have been observed in this study. However, when compared to the cases of MDRST treated

with ciprofloxacin, the response by way of time taken for defervescence of fever, regression of organomegaly, period of hospitalization was significantly longer. And taking the cost of drugs only, the cost of therapy also is much less in those treated with ciprofloxacin. The newer quinolones have been shown in adults to have very favorable results in treatment of resistant typhoid(7). Though as yet not recommended for use in Pediatric use, ciprofloxacin has been used in MDRST infection by many others with good results(8,9). The study confirms the efficacy of ciprofloxacin in 25 cases of MDRST enteric fever. The drug is safe, easier to administer, reduces the period of hospitalization, and an effective alternative. However, the safety of this drug *vis-a-vis* damage to growing cartilage requires to be established by conducting long term and multicentric epidemiological studies.

The characteristic clinical features in MDRST infections as seen in this study should be a pointer to the clinician to suspect and choose appropriate therapy to avoid undue delay and prolonged morbidity. The benefits of ciprofloxacin in cases of resistant enteric fever are many and the overall cost of treatment is less.

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