Typhoid encephalopathy with normal CSF was noted in 27.5% of cases while convulsion as CNS manifestation was seen in only one case. This finding is contrary to the findings of Scragg *et* c/.(8) who found convulsion to be the most common neurological manifestation.

Nearly 87% cases in our series were resistant to chloramphenicol and 66% were resistant to all the three commonly used drugs, *viz.,* chloramphenicol, amoxycillin and cotrimoxazole. A total of 98.5% cases were sensitive to ciprofioxacin. Similar findings were observed by others(9,10).

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Cefotaxime in Multi Drug Resistant Typhoid Fever

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The recent emergence of multi-drug resistant *Salmonella typhi* (MDRST) strains has caused a great concern amongst physicians(l-3). 4-flouroquinolones are increasingly being used in these cases(4). Unfortunately, they have not been approved in children because of their strong arthropathic potential(5,6). We report our experience with

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a third generation cephalosporin, cefotaxime in such cases.

Material and Methods

A group of 21 cases of enteric fever, of which 8 were bacteriologically confirmed, 7 showing a 4 fold or more rise in the Widal titres and 6 showing significant fall of the high Widal titres > 1/160 to l/4th or less when their sera were treated with 2 mercapto-ethanol (modified Widal positive) (7) were studied. All the culture positive cases had showed *in vitro* resistance to chloramphenicol, cotrimoxazole, amoxycillin and ampicillin but were sensitive to ciprofloxacin and cephalexin. All patients except 2 were initially treated with parenteral chloramphenicol or ampicillin in a dosage of 100 mg/kg/day and 200mg/kg/day, respectively both divided in four equal doses. Failure to respond for a period of one week or deterioration while on this therapy, the antibiotic was changed to cefotaxime. Two patients were treated with cefotaxime on admission as both had already received other antibiotics adequately in a peripheral hospital.

Cefotaxime was administered in the dosage of 100-150 mg/kg/day intravenously in 4 divided doses till the patient was afebrile for seven days. Renal functions were monitored using blood urea and serum creatinine. All the patients were followed for a period of 4-5 months.

Results

There were 12 girls and 9 boys; their age ranged from 1.5 to 7 years (mean 4.4 years). All patients presented with remittent moderate to high grade fever ranging from 6-21 days (mean 10.2 days) prior to admission. Sixteen patients had received one or more antimicrobials before admission. Thirteen patients had splenomegaly and bronchitis occurred in 3.15 patients had or more complications at the time of starting cefotaxime, including intestinal hemorrhage in 5 patients, abdominal pain, tenderness and distension in 5 patients, enteric encephalopathy in 6 and myocarditis in 3 patients. All 3 cases with myocarditis had muffling of heart sounds with gallop rhythm and cardiomegaly proved radiologically; 2 had evidence of congestive cardiac failure. The electrocardiogram showed low voltage pat terns in 1 and T wave inversion in one case. Hepatitis was observed in one case, who showed tender hepatomegaly and icterus. All the patients with these complications were managed conservatively and all recovered.

All the patients responded to cefotaxime. The period of defervescence ranged from 4 to 10 days (mean 6.2 days) and the drug was continued for 7 afebrile days. Cefotaxime was administered for a total duration of 11-17 days (mean 13.2 days). None of the cases showed evidence of renal dysfunction, either clinically or on blood urea and serum creatinine estimation. All except one patient could be followed up for 4 to 5 months after discharge and none relapsed.

Discussion

The recent emergence of MDRST has perplexed many physicians dealing with them. Hence, many unconventional antimicrobias which include quinolones, aminoglycosides and cephalosporins are being used in such cases(8). Prospective studies of clinical experience with these drugs are not available; therefore there are no clear cut therapeutic guidelines available. Despite its well known arthropathic potential, ciprofloxacin is very commonly being used for MDRST, primarily because of its ease in administration. However, sudden deaths have been

reported because of administration of intravenous ciprofloxacin(9), and the drug is still not recommended in the pediatric age group(5,6).

A combination of cephalexin with gentamycin has also been successfully used for treating MDRST(10). Cefamandole has also been used(11), but the most widely used cephalosporins have been the third generation ones. In a clinical trial moxalactum was effective initially in all the 25 patients(12). Further, they observed that none of the 11 cases relapsed when the duration of therapy was 10 to 11 days but with 3 to 5 days of therapy, they observed a very high relapse rate. Finally, the authors advocated its use only as a reserve antibiotic as it carries the risk of bleeding diathesis. Cefotaxime and ceftriaxone are the third generation cephalosporins which are widely used in pediatric practice and safely recommended even in newborn period(13). Ceftriaxone was first reported to be successful in treating MDRST in adults and thereby subsequently advocated in the dose of 75 mg/kg/day for a short duration of 5 days(6). Now it has been accepted as an alternative for MDRST in children too(14,15). Gulati and co-workers reported it to be effective in 5 children, of which one relapsed(8). Cefotaxime has been used in MDRST and found to be an effective therapeutic alternative(4,13). Although in earlier trials it has been used for a minimum of 10 days or for 3 days after defervescence(14), we continued it for 7 days after defervescence as majority of patients had complications or were extremely toxic at the time of starting therapy. All our cases stabilized within 48 hours of starting cefotaxime and finally all recovered. The mean duration of defervescence and therapy were 6.2 days and 13.2 days, respectively. All but one could be followed for 4 to 5 months after discharge and none relapsed. We did not observe even a single case of relapse in the 20 cases followed, probably because of the longer duration of therapy given. This observation is similar to the observation made by Uwaydah and his co-workers in a clinical trial with moxalactum in typhoid fever(12).

The emergence of MDRST demands an urgent call for therapeutic reappraisal especially in the circumstances where one cannot wait for culture reports. Cefotaxime offers an excellent and safe therapeutic option in such cases.

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Clinical Profile and Therapy in Enteric Fever

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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.

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