

Ceftriaxone: Use in Multidrug Resistant Typhoid Fever

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Multidrug resistance in *Salmonella typhi* is well known. There are recent reports of outbreak of multidrug resistant typhoid fever from various parts of the country(1-4.). The quinolone group of drugs especially ciprofloxacin have been found to be effective in the treatment of such cases in adults(3,5). However, safety of these drugs in children has not been established as yet. Ceftriaxone, a 3rd generation cephalosporin is a useful alternative for the treatment of multiresistant typhoid fever(8). Experiences with this drug are being communicated in this report.

Material and Methods

The study was conducted in the Intensive Care Unit of Kalawati Saran Children's Hospital, New Delhi. Patients with a

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clinical diagnosis of typhoid fever were treated with one of the first line antibiotics, viz., chloramphenicol or cotrimoxazole. Complete blood counts, blood culture, Widal test, peripheral smear and X-ray chest were done routinely. Other investigations, viz., lumbar puncture, ECG, serum biochemistry were done as and when indicated. Children proved to be cases of multidrug resistant typhoid fever by blood culture and sensitivity tests were ultimately included. Ceftriaxone was used in the doses of 100 mg/kg/day in two divided doses by intravenous route. Daily clinical monitoring was done in all cases. Observations were recorded on a pre-designed and pretested proforma.

Results

The average age of 15 children was 51.67 ± 34.67 months with 73.3% children being above 24 months of age. Males outnumbered the females (2 : 1). The mean duration of fever before hospitalization was 13.93 ± 5.46 days. The fever was high grade continuous in all cases and was associated with chills and rigors in 5/15 (33.3%) cases. Hepatomegaly was seen in 12/15 (80%) cases and splenomegaly in 10/15 (66.6%) cases.

Six children (40%) had encephalopathy. One of these was associated with hepatitis. Hepatitis was seen in another child who was fully conscious. Pneumonitis (20%) and myocarditis (13.3%) were the other complications seen. All the cases were sick enough to require intravenous drugs and fluids. The relevant details of individual children are shown in Table I. Widal test was positive in 9 (60%) patients and 5 (33.3%) had hemoglobin less than 10 g/dl. Leucopenia (<4000 cells/cu mm) was

TABLE—*Complications, Sensitivity Pattern of S. Typhi and Period of Defervescence of Fever*

S. No.	Age/Sex (mo)	Duration of fever before hospita- lization (days)	Compli- cations	Resis- tance pattern	Sensiti- vity	Ist afe- brile day afte ceftria- xone
1.	48 M	10	—	A,C,Co,T	G,F,Ceph,Ct, Ctx, Of	5
2.	14 M	10	Hepatitis	A,C,Co,T, G	F,Ceph,Ct,Ctx, Of	4
3.	84 M	12	—	A,C,Co,T	G,F,Ceph,Ct, Ctx,Of	5
4.	60 F	22	Encephalo- pathy	C,Co,T,G	A,F,Ceph,Ct, Ctx, Of	7
5.	35 F	7	Myocarditis	A,C,Co, T,G	F,Ceph,Ct,Ctx Of	8
6.	31 M	24	—	A,C,Co,T	G,F,Ceph,Ct, Ctx,Of	4
7.	48 M	14	Encephalo- pathy	A,C,Co,T	A,G,P,Ceph,Ct, Ctx,Of	
8.	78 M	15	Hepatitis with encephalo- pathy	A,C,Co,T, G	F,Ceph,Ct,Ctx, Of	8
9.	25 M	8	Encephalopathy	A,C,Co,T	G,Ct,Ctx,Of	7
10.	23 F	10	Pneumonitis	A,C,Co	G,Ct,Ctx,Of	4
11.	36 M	15	Encephalopathy	A,C,Co,T	G,Ceph,Ct,Ctx, Of	6
12.	120 F	20	Pneumonitis	A,C,Co,T,G	Ceph,Ct,Ctx,Of	6
13.	120 M	9	Myocarditis	A,C,Co, T,G	Ceph,F,Ct, Ctx,Of	—
14.	42 F	12	Pneumonitis	A,C,Co,T	G,Ct,Ctx,Of	7
15.	11 M	21	Encephalopathy	A,C,Co,T	G,Ct,Ctx,Of	9

Abbreviations used : A—Ampicillin, C—Chloramphenicol, Co—Cotrimoxazole, T—Tetracycline, G—Gentamicin, Ceph—Cephaloridine, Ct—Cefotaxime, Ctx—Ceftriaxone, Of—Ofloxacin.

seen in 3 (20%) patients only. One child developed bradycardia and hypotension and died of suspected myocarditis on day

two of starting the treatment. Three children developed rigors after administration of ceftriaxone which improved with conser-

vative management and did not require discontinuation of the drug.

All the cases improved on ceftriaxone with the exception of one. The mean duration for defervescence of fever was 6.07 ± 1.64 days after starting ceftriaxone. Two of the six children with encephalopathy were fully conscious on day 3 and remaining four on day 4. Jaundice in two cases having hepatitis, disappeared on day 6 and 7 and children with pneumonitis had no evidence of respiratory distress on second day of starting ceftriaxone therapy.

Only 9/14 children could be followed up for 3 months. None of these had relapse during this period. Two never turned up after discharge and the rest 3 had no relapse in a follow-up of 6-8 weeks.

Discussion

In the recent past, there has been a tremendous interest, in the management of multidrug resistant cases of typhoid (2-4). In the present study—ceftriaxone was successfully used for the management of serious cases of multidrug resistant enteric fever.

Since this study was done in cases requiring hospitalisation in intensive care unit, a very high incidence of complications is seen. Other features were similar to what have been observed by other workers (9-11). The mean duration of defervescence of fever was 6.07 ± 1.64 days as compared to 4 days by Farid *et al.* (8) and 3.8 days by Meloni *et al.* (7). Only one child, in their study, became afebrile in 6 days (8). This may be because of more seriously ill children in present series. Except for rigors, which were seen in 20% cases, no other side effect was seen. Even rigors did not require discontinuation of the drug.

It can be concluded that ceftriaxone is a reasonably safe drug. Fourteen of the 15

cases improved on ceftriaxone. Similar have been the observations of other workers (8,12) from other parts of the world. It shows that this drug can be used for the treatment of complicated hospitalized cases, where cost of treatment is not a major factor.

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Antiphospholipid Antibodies (APA) and Cerebral Stroke

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Antiphospholipid antibodies (APA) are a group of complexly related autoantibodies directed against phospholipids found in cell membranes. Association of APA and thrombotic events had been

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demonstrated in 1946 by Aggeler *et al.*(1) who documented thrombotic episode with circulating anticoagulant and thrombocytopenia. Appan *et al.*(2) reported a 5-year-old child having anticardiolipin antibodies (ACA) with multiple thrombosis; Pereira *et al.*(3) reported a neonate with spontaneous aortic thrombosis due to passive transfer of maternal lupus anticoagulant; and

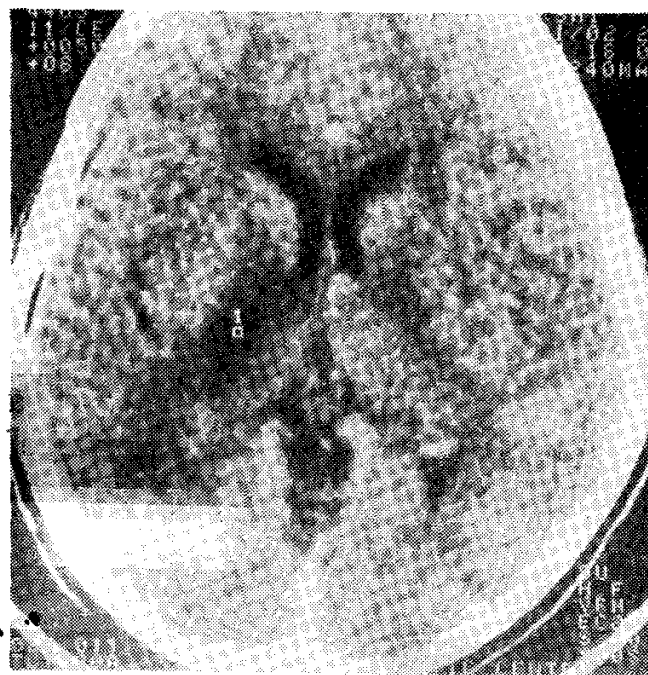


Fig. CT scan of brain showing infarct in the left thalamus, basal ganglia and posterior limb of internal capsule.

Roddy *et al.*(4) reported the first infant with APA and stroke. Since there is no report in the Indian literature, we are reporting a child with ischemic cerebral stroke and raised ACA.

Case Report

A 9-year-old female was referred in February, 1991 with complaints of right sided hemiplegia and right facial asymmetry for one month and inability to talk for 4 days. One month prior to her admission, she developed sudden weakness on the