

# A Comparative Study of Cefixime and Chloramphenicol in Children with Typhoid Fever

Pages with reference to book, From 163 To 164

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## Abstract

We compared cefixime with chloramphenicol in a trial for treatment of children with culture positive typhoid fever. Twenty children were given cefixime 10mg/kg/day orally for 14 days and twenty received chloramphenicol 50 mg/kg/day orally for 14 days. On entry the clinical characteristics of the two groups were comparable. Clinical cure was observed in 18(90%) patients treated with cefixime and 9(45%) treated with chloramphenicol. Of 11 patients who did not respond to chloramphenicol, 10 were switched over to cefixime and all were cured. Overall 28 out of 30 cases (93.3%) were cured by cefixime (JPMA 48:163,1998).

## Introduction

WHO has estimated that every year more than 12.5 million cases of typhoid fever occur world wide<sup>1</sup>. Its incidence in developing countries is around 500/10000 annually. Our hospital data over 3 years (1994-96) shows that out of the total admission of 11091 patients in Paediatric unit, 197 cases were of typhoid, thus constituting 1.7% of the total admissions (unpublished data) with maximum cases seen during the summer months. Resistant strains were reported from Mexico in 1972

against chloramphenicol which was drug of choice for the treatment of typhoid fever<sup>2</sup>. Later on in 1990, in UK, 19% of the Salmonella typhi isolates were reported resistant to chloramphenicol<sup>3</sup>. Recently, strains resistant to more than one antibiotic have emerged, which have been labelled as multi-drug resistant (MDR) strains<sup>4-7</sup>.

Different alternatives have been proposed for the treatment of MDR typhoid but none is satisfactory and safe. Fluoroquinolone derivatives are highly active against Salmonella typhi in adults<sup>8</sup> but potential cartilage and bone toxicity limits their use in children<sup>9-10</sup>. Third generation cephalosporins including cefotaxime, ceftriaxone and cefoperazone are reported to have a therapeutic success rate of greater than 90%<sup>11-14</sup> but the need for parenteral administration and high cost are major limitations in their extensive use.

Cefixime is a third generation oral cephalosporin with a spectrum similar to other third generation cephalosporins<sup>15</sup>. A study conducted in Egypt found it useful in paediatric typhoid fever<sup>16</sup>. The drug was also used in MDR typhoid in Pakistan<sup>17</sup>. We, in this study, have evaluated the safety and efficacy of cefixime in comparison to chloramphenicol in culture-positive typhoid fever.

## Patients and Methods

This study was conducted in Department of Paediatric Medicine, Nishtar Hospital, Multan, between August 1994 and February 1995. After informed consent, paediatric patients less than 15 years of age with a diagnosis of typhoid fever confirmed by isolation of Salmonella typhi from blood or bone marrow were recruited for the study. Patients having other concurrent infections, unconscious patients and culture-negative patients were excluded from the study.

Forty patients (20 each group) were randomized to receive either oral cefixime (10 mg/kg/day in two

divided doses) or oral chloramphenicol (50 mg/kg/day in four divided doses). Both the groups were treated for 14 days.

Patients were initially admitted in the paediatric ward for supervision and daily clinical evaluation. Defervescence (in days from start of medication), and any side effects were recorded in all patients. Children with persistent pyrexia after 7 days of appropriate therapy were diagnosed as non-responders and alternate medicine was started. Patients were followed up for four weeks after completion of treatment.

## Results

Patients ranged in age from 2 to 12 years with a mean age of 6.2 years. There were 18 patients in 2-5 years age, 16 in age group 5-9 and 6 patients in >9 years age. There was a striking dominance of male children [males 31 (77.5%) and 9 females (22.5%)]. The mean temperature of patients at the times of admission was 102.4F. On initial examination, 65% of the patients had hepatomegaly and 15% had hepatosplenomegaly. Most of the children were anaemic with average haemoglobin 9.96 gm/dl. The in vitro culture results of the 40 patients showed typhoid bacilli. The sensitivity to cefixime was 100% (40) and to chloramphenicol 92.5% (37).

**Table I. Defervescence of fever in typhoid patients. (n=40)**

Days for defervescence	Medicine used	
	Cefixime	Chloramphenicol
Three	4	0
Four	3	2
Five	2	1
Six	6	5
Seven	3	1
No defervescence till 7 days	2	11
<b>Total</b>	<b>20</b>	<b>20</b>

Table I shows defervescence of fever on an average of 5.05 days in patients responding to cefixime and after an average of 5.5 days in those responding to chloramphenicol.

Table II. Cure rate of cefixime compared with chloramphenicol.

	No.	Cured	Not cured	Efficacy
Cefixime	20	18	2	90%
Chloramphenicol	20	9	11*	45%

\*Of 11 not cured 10 switched over to cefixime. All cured. One being serious (8 years old) put on OFLOXACIN-cured. Overall 28 out of 30 patients - cured=93.3% (P=0.0049).

Table II compares cure rate of cefixime and chloramphenicol. Of the 20 patients who received cefixime, 18 (90%) were cured. Two patients did not respond to cefixime and were given I.V. cephalosporins. Twenty patients were given chloramphenicol and 9 (45%) were cured. Out of 11 non-responders to chloramphenicol, 10 were switched over to cefixime. All of them responded well to the changed treatment and their fever settled on an average of 4th day. Overall 28 cases out of 30 (93.3%) (P=0.0049) were cured by cefixime with fever settling after an average of 4.68 days. No significant adverse effects were noted in either group.

## Discussion

In this comparative study, we have evaluated cefixime in comparison to chloramphenicol, which was an established oral treatment for typhoid fever, before the emergence of resistant *Salmonella typhi* strains. Cefixime was effective clinically in 93.3% of paediatric patients with typhoid fever in our study as compared to chloramphenicol which was effective in 45%. This figure is comparable to other studies conducted previously in Egypt<sup>16</sup> and Pakistan<sup>17</sup>. However, in vitro, sensitivity studies showed that *Salmonella typhi* isolates obtained from the 40 patients were sensitive to cefixime 100% while chloramphenicol was effective in 92.5%.

This study, on a limited scale, confirms that cefixime, in a dose of 10 mg/kg/day, is a safe and cost effective oral option for the treatment of typhoid fever in children.

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