A Comparative Study of Cefixime and Chioramphenicol in Children with Typhoid Fever

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Abstract

We compared cefixime with chloramphenicol in a randomized trial for treatment of children with culture positive typhoid fever. Twenty children were given cefixime 10 mg/kg/day orally and twenty received chioramphenicol 50 mgfkg/day orally. On entry in the study, the clinical characteristics of the two groups were comparable. Duration of therapy was 14 days. Clinical cure was observed in 18 (90%) patients treated with cefixime and 9 (45%) treated with chioramphenical. Out of the 11 patients who did not respond to chioramphenicol, 10 were switched over to cefixime and all of them were cured. Over all 28 cases out of 30 (93.3%) P=0.0049 were cured by cefixime (JPMA 48:106, 1998).

Introduction

WHO has estimated that ever year more than 12.5 million cases of typhoid fever occur worldwide[1]. The incidence of typhoid fever in developing countries is estimated to be 500/100000 annually. Our hospital data over 3 years (1994-96) shows that out of the total admission of 11,091 patients in Pacdiatric Unit, 197 cases were of typhoid, thus constituting 1.7% of the total admissions. The maximum number of cases were Seen during the summer months (Figure). Resistant strains were reported from Mexico in 1972 against chloramphernicol[2] which was the drug of choice for the treatment of enteric fevet Later on in 1990, in UK, 19% of the .Salmonella typhi isolates were reported resistant to chloramphcnicol[3]. Recently, strains resistant to more than one antibiotic have emerged, which have been labelled as multi-drug resistant (MDR) strains[4-7].

Different alternatives have been proposed for the treatment of MDR typhoid but none is satisfactory as well as safe. Fluroquinolone derivatives are highly active against Salmonella tvphi in adults[8]but potential cartilage and bone toxicity limits their use in children[9,10]. Third generation cephalosporins including cefotaxime, cefiriaxone and cefoperazone, are re?orted to have a therapeutic success rate of greater than 90%[1] 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 the other third generation cephalosporins[15]. A study conducted in Egypt found it useful in paediatric entenc fever[16]. The drug was also used in MDR typhoid in Pakistan[17]..We evaluated the safety and efficacy of cefixime in comparison to chioramphenicol in culture -positive typhoid fever.

Patients, Methods and ResuRs

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 probable diagnosis of typhoid fever (fever forat least 5 days with no localizing signs, with or without splenomegaly) were recruited for the study. Needed investigations were performed to exclude other probable diseases. The diagnosis of typhoid fever was confirmed by isolation of Salmonella typhi from blood orbone marrow. Patients having other concurrent infections, unconscious patients and

culture-negative patients were excluded from the study.
Forty patients successfully conhpleted the study. They were randomized to receive eitheroal cefixiine(10 mg/kg/day in two divided doses) or oral chioramphenicol (50 mg/kg/day in four divided doses). Both groups were treated for 14 days. Study children were initially admitted in the paediatric ward for supervision and daily clinical examination. Defervescence of fever (in days from start of medication), dmg compliance and any side effects were recorded in all patients. Children with persistent pyrexia and toxicity after 7 days of appropriate therapy were designated as antibiotic failures and alternate medicine was startcd. Patients were followed up for four weeks after completion of treatment.
Patient's age ranged from 2 to 12 yeats with a mean of 6.2 years. There was a striking dominance of male children.
The mean temperature at the time of admission was 102.4°F.
On initial examination, 65%of patients had hepatomegaly and 15%hepatosplenomegaly. Most of the children were anaemic.
Average haemoglobin was 9.96 gm/dl.
The in vitro culture and sensitivity results of the 40 patients showed, typhoid bacilli sensitive to cefixime 100% and to chloramphenicol 92.5%.
A defervescence occurred on an average of 5.05 days in patients responding to cefixime and 5.5 days in those responding to 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 switchedovertocefixime. All of them respondedwell to the changcd trealment and their feversettled on an average of4thday. Over all 28 cases out of 30 (93.3%) (N 0.0049) were cured by ccfixime with fever settling after an avenge of 4.68 days. No significant adverse effects were noted in either group.

Comments

In our study despite the fact that many typhoid strains were sensitive to chloramphenicol in vitro (92.5%), yet invivo only (44%) showed a response and defervescence to chloramphenicol within 7 days. However with ccfixime 93.3%, showed defervescence within 7 days. Cefixime being a bactericidal, acts more rapidly. It is also less toxic but more costly. On the other hand chlorainphenicol is bacteriostatic takes more time to act but is economical.
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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