The Korean Journal of Internal Medicine
Vol. 2, No. 1, January, 1987

Successful Treatment of Typhoid Fever with a Single Dose of Ceftriaxone for One or Two Days*

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The therapeutic efficacy of ceftriaxone was evaluated in variable dose and duration schedules in twenty patients with bacteriologically proven typhoid fever. The results were satisfactory in the cases that were given a single dose of 3 g for two days (12/12) or 4 g for one day (3/4). Some untoward reactions were observed in 8 cases, but it was not clinically significant.

Ceftriaxone appears to be safe and effective in the treatment of typhoid fever when administered in a single dose of 4 g for one day or 3 g for two days on an outpatients basis.

Key Words: *Ceftriaxone, Typhoid fever*

INTRODUCTION

Chloramphenicol has been the antibiotic of choice for patients with typhoid fever for more than 30 years. although ampicillin and cotrimoxazole have been introduced as alternatives, they have side effects, and disadvantages of frequent administration and long duration of treatment similar to chloramphenicol therapy.

Reports on the usefulness of cephalosporin antibiotics (cefazolin, cefamandole, cefotaxime, etc.) in the treatment of salmonella bacteremia have been inconclusive[1~3]. The purpose of this study was to determine whether the treatment of typhoid fever with a single dose of ceftriaxone, given for one or two days, is effective.

MATERIALS AND METHODS

During a one-year period from February, 1984, to February, 1985, twenty patients, 9 males and 11 females, ranging from 20 to 61 years of age were studied. In every case, the clinical features were compatible with typhoid fever and the diagnosis was confirmed by isolating salmonella typhi from blood. None of the patients had any specific underlying diseases or abnormal renal function. Ceftriaxone (F. Hoffmann-La Roche Inc.) was administered by bolus injection to all patients as shown in Table 1. Blood cultrues were repeated every other day until the patients were discharged from the hospital. Tests for monitoring possible drug toxicity included the white blood cell count and differential, creatinine, bilirubin, liver function enzymes, and urinalysis. Laboratory tests were performed before the beginning of therapy and after discontinuation of therapy.

Table 1. Days of Defervescence after Treatment with Ceftriaxone

Dose	Duration (days)	Number evaluated	Days of defervescence				
			3	4	5	6	failed
2 g qd	3	2		2			
2 g qd	2	1					1
3 g qd	2	12	4	5	2	1	
3 g qd	1	1		1			
4 g qd	1	4	2	1			1
		20	6	9	2	1	2

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**This work was presented in part at the 14th International Congress of Chemotherapy, held in Kyoto, Japan, 23-28 June 1985*

RESULTS

Table 1 shows the different dose and duration schedules of ceftriaxone which was administered on a graduated varying basis, and the days of defervescence.

The results were satisfactory except in two cases, the ones who had a single dose of 4 g for one day administered. Bacteremia cleared within one day after treatment in all patients. In seventeen cases, stool cultures became negative within 7 days, however, in three, within 14 days.

Untoward reactions were mild. The elevation of SGOT developed in three cases, however, the authors were not able to determine whether this was directly related to ceftriaxone or not. Nausea during injection was noticed in two cases.

Pruritus, diarrhea, or flushing of face were observed in each one case respectively.

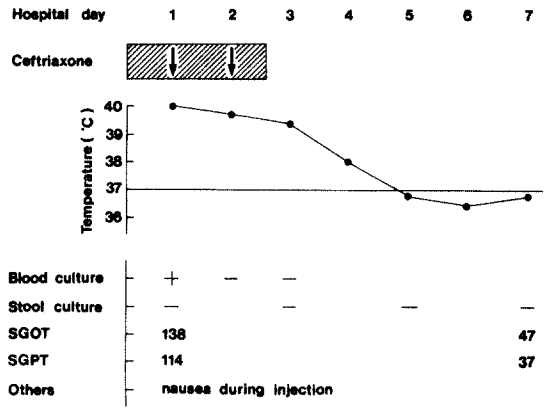

Fig. 1. *The effect of ceftriaxone in a patient who was given a single dose of 3g for two days.*

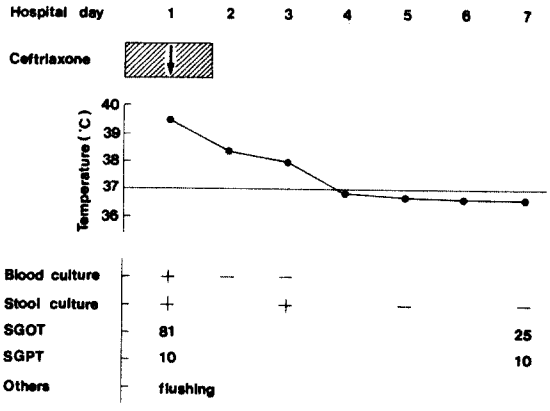

Fig. 2. *The effect of ceftriaxone in a patient who was given a single dose of 4g for one day.*

DISCUSSION

Ceftriaxone, a new parenteral cepalosporin, has some properties which may make it particularly useful in the treatment of typhoid fever.

First, it has excellent in-vitro activity against most clinical isolates of *Salmonella* spp.[4], and also superiority over ampicillin and other cephalosporin in experimental *Salmonella typhimurium* infection.

Second, it has a high level of biliary excretion. Increased biliary excretion is desirable in the treatment of typhoid fever, because the gallbladder contains a large number of bacilli and excretes them even in the acute stage. The gallbladder also becomes a source of the organisms in chronic carriers. In addition, it possesses a long serum halflife which permits single dose therapy in an inpatient or outpatient setting.

Initially, the authors evaluated a single dose of 2 g for three days in two cases: the results were excellent. However, a single dose of 2 g for two days failed in one case. So, the single dose of 3 g for two days was evaluated in twelve cases. The fever subsided within four days in nine cases and within six days in three cases (Fig. 1). Although the single dose of 3 g for one day was successful in one case, the dose was increased to 4 g in four cases, with satisfactory responses being achieved in three cases (Fig. 2). It has been suggested that endogenous pyrogens released by local inflammatory effects of *Salmonella typhi* endotoxin may sustain the pyrexia in typhoid fever. It dosen't seem likely that persistent high fever should be always related to the organisms in the blood.

According to our previous study, bacteremia cleared within one day after intravenous injection of ampicillin or chloramphenicol in almost all cases.

In this study, also bacteremia cleared within one day after treatment in all cases.

It is interesting the results were excellent inspite of the withdrawal of antibiotics during the persistent fever.

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Stool cultures became negative within 14 days

in all cases, but follow-up cultures for the evaluation of chronic carriers could not be obtained.

There was no clinical evidence of relapse within eight weeks.

In conclusion, this study gives support for the clinical efficacy of ceftriaxone as a single dose of 3-4 g for one or two days, although these regimen might be suitable for the treatment of patients with typhoid fever on an outpatient basis, especially in developing countries where there may be difficulties in admission.

It would be reasonable to carry out clinical trials to assess the optimal duration of treatment in other bacterial infectious diseases in normal host.

REFERENCES

1. Uwaydah E: *Cefazolin in the treatment of acute enteric fever. Antimicrob Agents Chemother 10: 52, 1976*
2. Uwaydah M, Nassar NT, Harakeh H, Vartivarian S, Talhouk A, Kantrajian H: *Treatment of typhoid fever with cefamandole. Antimicrob Agents Chemother 26:426, 1984*
3. Park SC, Lee CH, Seok SE, Kim TW, Park CH, Chung SK, Kim SY, Choi HS, Choi HR, Lee MA: *Clinical trial of cefotaxime in patients with typhoid fevcer. Korean J Infect Dis 16:8, 1981*
4. Chau PY, Ng WS, Ling J, Arnold K: *In vitro susceptibility of Salmonella to various antimicrobial agents, including a new cephalosporin, Ro 13-9904. Anbtimicrob Agents Chemother 19:8, 1981*
5. Patel IH, Kaplan SA: *Pharmacokinetic profile of ceftriaxone in man. Am J Med 77:17, 1984*
6. Hornick RB, Greisman Se, Woodward TE, Dupont HL, Dawkins AT, Snyder MJ: *Typhoid fever: pathogenesis and immunologic control (first of two parts). N Engl J Med 283:686, 1970*
7. Zhou HH, Chan YPB, Arnold K, Sun M: *Single-dose pharmacokinetics of ceftriaxone in healthy chinese adults. Antimicro Agents Chemother 27: 192, 1985*
8. Hoffman TA, Ruiz CJ, Counts GW, Sachs JM, Nitzkin JL: *Waterborne typhoid fever in Dade County, Florida. Clinical and therapeutic evaluation of 105 bacteremia patients. Am J Med 59:481, 1975*
9. Kim YM, Chung HY: *Disappearance of Salmonella typhi in peripheral blood of typhoid fever after administration of ampicllin or chloramphenicol. Journal of Catholic Medical College (Seoul) 34: 474, 1981*