ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Feb. 1982, p. 334–335
0066-4804/82/020334-02$02.00/0

Vol. 21, No. 2

NOTES

Cefamandole Treatment of Salmonella Bacteremia

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Received 7 July 1981/Accepted 9 November 1981

The efficacy of cefamandole in the treatment of 19 patients with salmonella bacteremia was evaluated. Although all of the salmonella strains isolated were highly susceptible to cefamandole in vitro, a therapeutic failure was observed in 7 (36.8%) of the 19 patients.

Salmonellae resistant to several antibiotics have been isolated with increasing frequency, stimulating the study of the drug susceptibility of these organisms to determine therapeutic regimens (1, 3, 4, 11, 12). At low concentrations, cefamandole has been shown to be active in vitro against salmonella strains isolated from different clinical specimens and more potent than other cephalosporins (2, 14).

The present study was undertaken to evaluate the clinical effectiveness of cefamandole in the treatment of patients with salmonella bacteremia.

A total of 19 patients with blood culture-proven salmonella infections were studied. Detailed histories and physical examinations were obtained, and laboratory evaluations (including complete blood cell counts, urinalyses, and testing for creatinine, serum glutamic oxalacetic transaminase, serum glutamic pyruvic transaminase, alkaline phosphatase, and bilirubin levels) were performed before and, whenever possible, at the completion of therapy. The presence of associated disease was recorded. Blood cultures were obtained before, during, and after the completion of the antibiotic therapy. Blood was cultured in tryptic soy broth and bile broth (Difco Laboratories); the organisms were isolated, identified, and serotyped; and the minimum inhibitory concentrations were determined by tube dilution.

The mean dose of cefamandole naftate was 120 mg/kg daily (60 to 240 mg/kg daily), with a total dose ranging from 1.0 to 8.0 g daily. The intravenous route was most frequently used although the intramuscular route was used in the initial treatment for three patients and after clinical improvement for another four patients. The mean duration of therapy was 12 days, although for four patients with persistently positive blood cultures, antibiotic treatments were discontinued earlier.

The group of patients consisted of 14 males and 5 females of ages from 5 to 38 years (mean, 14.5). In 5 patients, there were clinical and bacteriological features of typhoid fever; 14 individuals had salmonella bacteremia associated with hepatosplenic schistosomiasis.

The bacteriological data and the therapeutic responses are shown in Table 1. Of the 19 types of salmonellae isolated, 8 were *Salmonella typhi*, 2 were *Salmonella* group A, 3 were *Salmonella* group B, 2 were *Salmonella* group C, and 4 were non-*S. typhi* group D. All of the isolated bacteria were highly susceptible to cefamandole in vitro. Most (73%) were susceptible to concentrations of 0.19 μg/ml, and all were inhibited at a concentration of 1.5 μg/ml.

The response to therapy was considered good in 12 of 19 patients, as determined by clinical improvement and the disappearance of salmonellae from blood culture samples taken during and at the end of treatment. Therapeutic failure was documented in seven patients. In six of them, no or slight improvement was documented during the course of therapy, and salmonellae were isolated during week 2 of treatment with cefamandole. In the other patient, despite a good clinical response, the blood culture remained positive after 10 days of therapy. Patients who failed to respond to cefamandole therapy were treated with chloramphenicol or ampicillin, and all were cured.

Despite its effectiveness in the majority of the patients we tested and in a single case reported in the literature (8), the observed failure rate (36.8%) in the treatment of salmonella bacteremia with cefamandole was too high for us to

TABLE 1. Susceptibility and therapeutic responses of salmonellae recovered from the blood of patients treated with cefamandole

Type of salmonella	No. of cases	Susceptibility (MIC[a] [μg/ml])	Therapeutic responses	
			Good	Failure
S. typhi	8	0.19–0.75	5	3
Salmonella group A	2	0.19	1	1[b]
Salmonella group B	3	0.19–1.5	2	1
Salmonella group C	2	0.19	2	
Salmonella group D (non-*S. typhi*)	4	0.19	2	2

[a] MIC, Minimal inhibitory concentration.

[b] Patient had a good clinical response; however, the blood culture at the end of therapy was positive. Without any therapy, subsequent blood cultures were negative, and the patient had no symptoms or signs of the disease when discharged from the hospital.

recommend cefamandole for regular use even as an alternative. The reason for the failure of cefamandole in this study is not clear. The salmonellae isolated from the seven patients who did not respond to therapy were susceptible in vitro to cefamandole at concentrations of ≥0.75 μg/ml, a level much lower than that readily achievable with therapeutic doses of the drug (10). On the other hand, infections caused by less susceptible strains of salmonellae were well controlled with the same therapeutic regimen. A discrepancy between in vitro susceptibility and in vivo responses to therapy in salmonella infection is, however, not surprising; such a discrepancy has also been described for kanamycin and tetracycline (13, 16).

Although the non-*S. typhi* group seems to be more resistant to most antibiotics than the *S. typhi* group (2), in three of the seven patients who failed to respond to therapy, the isolated salmonella was *S. typhi*. A relationship between the salmonella group and the response to antibiotic therapy could not be shown. Patients with salmonella bacteremia and hepatosplenic schistosomiasis have been shown to have a high relapse rate after antibiotic therapy (7). However, only four of the seven patients who failed to respond to cefamandole had this syndrome, whereas the others had classic typhoid fever.

Among the cephalosporins, cefazolin has been reported to be an effective antibiotic in the treatment of salmonella bacteremia (15) although more extensive studies are needed before a definite conclusion can be drawn. Even though cefamandole is more effective in vitro than other cephalosporins (14), this antibiotic does not seem to be a reliable alternative for the treatment of salmonella bacteremia since the failure rate is higher than that reported for treatment with ampicillin, amoxicillin, or sulfamethoxazole-trimethoprim (5, 6, 9).

This work was supported by the Center of the Study of Regional Disease.

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