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Randomized Trial Comparing Ceftriaxone with Cefonicid for Treatment of Spontaneous Bacterial Peritonitis in Cirrhotic Patients

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We compared cefonicid (2 g every 12 h) and ceftriaxone (2 g every 24 h) for their efficacy and safety in treating spontaneous bacterial peritonitis in cirrhotic patients in an open randomized clinical trial (30 patients in each group). Clinical, laboratory, and bacteriologic characteristics were similar in both groups. Ceftriaxone-susceptible strains were isolated on 44 occasions (94%), and cefonicid-susceptible strains were isolated on 43 occasions (91.5%). The antibiotic concentration in ascitic fluid/MIC ratio for ceftriaxone was >100 throughout the dose interval (24 h), while it was lower for cefonicid (between 1 and 18). A total of 100% of patients treated with ceftriaxone, and 94% of those treated with cefonicid were cured of their infections (*P* was not significant). Hospitalization mortality was 37% in the cefonicid group and 30% in the ceftriaxone group (*P* was not significant). The time that elapsed between the initiation of treatment and the patient's death was shorter in the cefonicid group patients (5.3 ± 3.90 days) than in the ceftriaxone group patients (11.8 ± 9.15 days) ($P < 0.05$). None of the patients presented with superinfections, and only two patients treated with cefonicid and three patients treated with ceftriaxone developed colonizations with *Enterococcus faecalis* or *Candida albicans*. Ceftriaxone and cefonicid are safe and useful agents for treating cirrhotic spontaneous bacterial peritonitis, although the pharmacokinetic characteristics of ceftriaxone seem to be more advantageous than those of cefonicid.

Spontaneous bacterial peritonitis (SBP) is a frequent and severe complication in cirrhotic patients with ascites (1, 10, 15, 18, 20). Most cases of SBP are caused by enteric gram-negative bacilli, although 25% of cases are produced by other pathogens, particularly gram-positive cocci (1, 10, 15, 18). Various studies have shown that new cephalosporins are more effective than penicillin-aminoglycoside combinations in immunocompromised hosts either with or without associated hepathopathy (6, 9). Broad-spectrum cephalosporins which are active against gram-positive cocci and highly active against gram-negative bacilli have been the most commonly used agents (8). Ceftriaxone has an antibacterial spectrum similar to that of cefotaxime, but it presents a longer elimination half-life in plasma (8 h) and, apparently, some other pharmacokinetic advantages over cefotaxime (5, 12, 13). Expanded-spectrum cephalosporins have never been tested in the treatment of cirrhotic SPB, although their in vitro activities against the predominant causative organisms of SBP are excellent (22). Cefonicid is the expanded-spectrum cephalosporin with the longest elimination half-life in plasma (4 to 5 h) (22). By using drugs with long elimination half-lives, the potential benefit of only a single dose or two daily doses of antibiotic may be obtained, and less variability in the therapeutic concentrations of drug in plasma may be expected. The present study was designed to assess and compare prospectively the efficacy and safety of ceftriaxone versus those of cefonicid in the treatment of SBP in cirrhotics.

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MATERIALS AND METHODS

Following the implementation of a prospective protocol for studying bacterial peritonitis in cirrhotics, 60 patients with SBP admitted to our general hospital between October 1987 and January 1990 were included in an open clinical trial and were randomly assigned to one of two treatment groups. Thirty patients were assigned to receive cefonicid, 2 g every 12 h, and 30 patients were assigned to receive ceftriaxone, 2 g once a day. Both antibiotics were given in 100 ml of 5% glucose administered intravenously over 20 min. All patients received the antibiotics for 10 or 4 days after becoming afebrile, whichever was shortest. Informed consent was obtained from patients or relatives (if the patient had an abnormal mental status) prior to entry into the trial. The reason for exclusion was a history of allergy to beta-lactam antibiotics. All patients fulfilled the clinical, laboratory, or gammagraphic criteria of chronic liver disease, which was confirmed by liver biopsy in 52 patients. The stage of cirrhosis was determined according to the Pugh-Child score (19).

The diagnosis of probable bacterial peritonitis or culture-negative neutrocytic ascites was made when the ascitic fluid culture did not grow pathogenic bacteria, the ascitic fluid neutrophil count was >500 cells/μl, there was not evident surgically treatable intra-abdominal source of infection, and there was no antibiotic treatment within 30 days. Other, alternative explanations for an elevated ascitic fluid neutrophil count, such as hemorrhage into ascites, pancreatitis, tuberculous peritonitis, or peritoneal carcinomatosis, were systematically excluded. Spontaneous bacterial peritonitis was defined as the combination of a positive ascitic fluid culture, an ascitic fluid neutrophil count of ≥250 cells/μl,

and no evidence of a surgically treatable intra-abdominal source of infection.

Prior to the institution of the prescribed antibiotic therapy, patients underwent abdominal paracentesis, and 10 ml of blood was drawn for culture (BACTEC NR 600; Becton Dickinson), routine cell counts, and chemistry screening profile. A fraction of the ascitic fluid recovered was used to make neutrophil counts (Coulter S-Plus IV counter and Cytospin cytocentrifuge), a second fraction was sent to the biochemistry laboratory for routine analysis, and a third fraction was inoculated into blood culture bottles (BACTEC NR 600; Becton Dickinson) at the patient's bedside. The fluid was then Gram stained and subcultured when growth was observed. Blood agar and MacConkey agar plates were used for aerobic subcultures, and Schaedler agar with blood, phenylethyl alcohol, and aztreonam was used for anaerobic subcultures. Hemoculture bottles were incubated for 14 days and were discarded if they were negative. The strains that were isolated were identified by conventional methods, and the antibiotic susceptibilities of the strains were determined either by the method of Bauer et al. (4) or with the AUTO BAC system. The MIC and MBC for gram-negative bacilli were determined by using serial microdilutions of the antibiotic in broth (16). Ascitic fluid cultures in which coagulase-negative *Staphylococcus* or *Corynebacterium* species were isolated and those with polymicrobial growth and a neutrophil count of <250 cells/μl were considered contaminated. Ascitic fluid cultures in special media for the growth of fungi and mycobacteria were carried out when indicated. None of the cultures was positive for fungi or mycobacteria. Cultures of urine and stool samples were done prior to antibiotic therapy. A series of clinical, epidemiologic, and laboratory parameters were assessed in both groups before intravenous infusion of antibiotics, after 72 h of treatment, and after the discontinuation of therapy. Cultures of blood, ascitic fluid, urine, and stool samples were made 48 h after the cessation of treatment. At 72 h after the beginning of therapy, blood and ascitic fluid samples were drawn from 9 patients treated with cefonicid and 14 patients treated with ceftriaxone 30 min before the intravenous infusion (trough) and at 60 min after the end of infusion (peak) for ceftriaxone and cefonicid high-pressure liquid chromatography assay.

Patients were considered cured of their infections when all signs and clinical symptoms of peritoneal infection disappeared, sterilization of ascitic fluid and/or blood culture during therapy (bacteriologic cure) occurred, and the neutrophil count in ascitic fluid decreased to <250 cells/μl. Peritonitis-related mortality was defined as death during the scheduled course of treatment with clinical, cytologic, or bacteriologic evidence of active infection. Infection-related deaths after the first 48 h of treatment were considered therapeutic failures. Hospitalization mortality was defined as death from any cause during the hospitalization in which the ascitic fluid infection was detected. Colonization was diagnosed when a nonsusceptible bacterium was isolated in control cultures or when a microorganism resistant to antibiotic therapy predominated in control stool cultures. Superinfection was defined as colonization accompanied by clinical evidence of infection.

Study data were analyzed by the SPSS program by using the chi-square test with Yates' correction for categorical variables and the Student *t* test and the nonparametric Mann-Whitney U test for comparison of the means. Bacteriologic cure was the variable used for the formula of sample size calculations for proportions, with a minimal prespecified difference value of 10%. The null hypothesis was that both antibiotics had the same efficacy. The power of the study to find this prespecified difference was 0.90 (β error, <0.10). Data are presented as means ± standard deviations (normal distributions) or median and range (abnormal distributions). The level of significance was taken at $P < 0.05$.

TABLE 1. Characteristics of patients[a]

Characteristic	Cefonicid-treated patients (n = 30)	Ceftriaxone-treated patients (n = 30)
Sex (no. of males/no. of female)	26/4	21/9
Age (yr)	59.9 ± 10.74	57.6 ± 10.73
Origin of cirrhosis (no. [%])		
Alcoholic	17 (57)	19 (63)
Nonalcoholic	13 (43)	11 (37)
Evolution of hepatopathy since diagnosis (mo [range])	24 (1–145)	48 (1–198)
Previous decompensations (no. [%])	23 (77)	26 (87)
Stage (Child-Pugh) (no. [%])		
A	2 (6)	1 (3)
B	7 (23)	9 (30)
C	21 (70)	20 (67)
In-hospital onset (no. [%])	10 (33)	12 (40)
Previous maneuvers (no. [%])	8 (27)	10 (33)
Duration of symptoms (h [range])	30 (2–72)	36 (2–56)

[a] There were no statistically significant differences between groups with respect to any data. Data are means ± standard deviations or median (range).

RESULTS

Fourty-seven men and 13 women were included in the study. The mean age of the patients was 58.6 ± 10.7 years. At the time of inclusion, there were 41 patients (68%) with Pugh-Child class C, and 49 (82%) had experienced complications of progressive liver disease on previous occasions. In 22 cases (37%), SBP developed in hospitalized patients (>72 h); diagnostic therapeutic maneuvers were performed before the development of peritonitis in 18 patients (endoscopy or sclerosing therapy of varices in 14 patients and therapeutic paracentesis in 4 patients) (Table 1).

The duration of symptoms before the diagnosis of peritoneal infection varied between 2 h and 3 days (median, 34 h). Most patients had fever (80%), abdominal pain (67%), and jaundice (63%), although the most frequent sign was an increase in ascites (83% of cases). Eleven patients in the cefonicid group and 12 patients in the ceftriaxone group had leukocyte counts of >10,000/μl. At the time of diagnosis, a serum creatinine concentration of >2 mg/dl was found in six patients treated with cefonicid and eight patients treated with ceftriaxone. Analysis of the ascitic fluid revealed neutrophil counts of >1,000 cells/μl in 27 patients in the cefonicid group and 26 patients in the ceftriaxone group and of >5,000 cells/μl in 15 and 12 patients in the two groups, respectively. Comparison between the two groups did not show statistically significant differences with regard to clinical or laboratory data at the time of diagnosis.

Ascitic fluid cultures were positive for 47 patients (78%), blood cultures were positive for 25 patients (42%), and urine cultures were positive for 7 patients (12%). In two patients with culture-negative neutrocytic ascites, the blood culture was positive. A single pathogen in ascitic fluid cultures was isolated in 46 cases (97%) and was a gram-negative aerobe in 40 cases. The microbiologic results for patients in both

TABLE 2. Microbiological results for patients in both groups[a]

Characteristic	Cefonicid-treated patients (n = 30)	Ceftriaxone-treated patients (n = 30)
Culture-negative neutrocytic ascites	7 (23)	6 (20)
Spontaneous bacterial peritonitis	23 (77)	24 (80)
Positive blood culture	12 (40)	13 (43)
Positive urine culture	4 (13)	3 (10)
Microorganisms		
Escherichia coli	16 (53)	18 (60)
Klebsiella spp.	1 (3)	2 (6)
Enterobacter cloacae	0 (0)	1 (3)
Citrobacter freundii	1 (3)	0 (0)
Aeromonas sobria	0 (0)	1 (3)
Streptococcus pneumoniae	1 (3)	0 (0)
Enterococcus faecalis	1 (3)	0 (0)
Streptococcus spp	2 (6)	1 (3)
Bacteroides distasonis	1 (3)	0 (0)
Polymocrobial infection	0 (0)	1 (3)

[a] Data are numbers of patients (percentage of total). There were no statistically significant differences between groups with respect to any data.

treatment groups were not significantly different (Table 2). Forty-four (94%) of the isolated pathogens were susceptible to ceftriaxone and 43 (91.5%) were susceptible to cefonicid. The MIC for gram-negative bacilli in the cefonicid group ranged from 0.5 to 16 μg/ml, with an MIC for 50% of isolates tested of ≤2 μg/ml and an MIC for 90% of isolates tested of ≤32 μg/ml. The MBC/MIC ratio was always less than 16. In the ceftriaxone-treated group, the MIC for all gram-negative bacilli was ≤0.03 μg/ml. The MBC/MIC ratio was always less than 3. With regard to the ceftriaxone susceptibility of cefonicid-resistant pathogens isolated from ascitic fluid cultures, only an *Escherichia coli* strain was susceptible to ceftriaxone. Ascitic fluid cultures carried out 72 h after the initiation of treatment were positive on two occasions, yielding growth of resistant *Citrobacter freundii* and *E. coli*. These two episodes had a fatal outcome and the patients died at days 3 and 4, respectively, with signs of active infection, despite substitution of the scheduled agent (cefonicid) with an alternative antibiotic.

Pharmacokinetic data were assessed for 23 patients and are depicted in Fig. 1. The mean elimination half-lives of cefonicid and ceftriaxone from plasma were 8.9 ± 6.0 and 11.6 ± 4.4 h, respectively. The ascitic fluid/peak concentration in serum ratio was equal for both antibiotics (0.34 ± 0.21), whereas the ascitic fluid/trough concentration in serum ratio was higher for cefonicid (0.74 ± 0.30) than for ceftriaxone (0.56 ± 0.12). The trough antibiotic concentration in ascitic fluid/MIC ratio was always >100 for ceftriaxone and ranged from 1 to 18 for cefonicid.

The mean duration of antibiotic therapy was 8.4 ± 4.17 days in cefonicid-treated patients and 9.1 ± 3.45 days in ceftriaxone-treated patients (P = 0.86). In patients who responded to antibiotic treatment, the mean duration of therapy was 10.6 ± 4.11 days in the cefonicid group and 10.1 ± 2.55 days in the ceftriaxone group. The time that elapsed between the initiation of treatment and patient death was shorter for cefonicid (5.3 ± 3.90 days) than for ceftriaxone (11.8 ± 9.15 days) (P < 0.05).

In cefonicid-treated patients, colonization of the gastrointestinal tract by *Candida albicans* was documented in one case, and *Enterococcus faecalis* was isolated in the control urine culture for another. In ceftriaxone-treated patients, *E. faecalis* grew from the stool culture for one patient and from the stool culture and control pharyngeal swab for another patient; *C. albicans* was isolated in the urine culture from a third patient. None of these patients developed clinically significant manifestations. In all cases control cultures became negative spontaneously, without specific antibiotic therapy.

No difference in clinical outcome was found between either treatment group (Table 3). The mean duration of fever was 3 days in patients treated with cefonicid and 2 days in patients treated with ceftriaxone (P = 0.35). At 72 h of therapy, most patients were asymptomatic, and 50% of patient in both groups fulfilled the ascitic fluid cytologic criteria used to define cure (Table 3). Two cefonicid-treated patients with renal failure at the time of diagnosis showed improved renal function during therapy, whereas six patients demonstrated a decrease in kidney function during therapy. Four patients treated with ceftriaxone showed improved

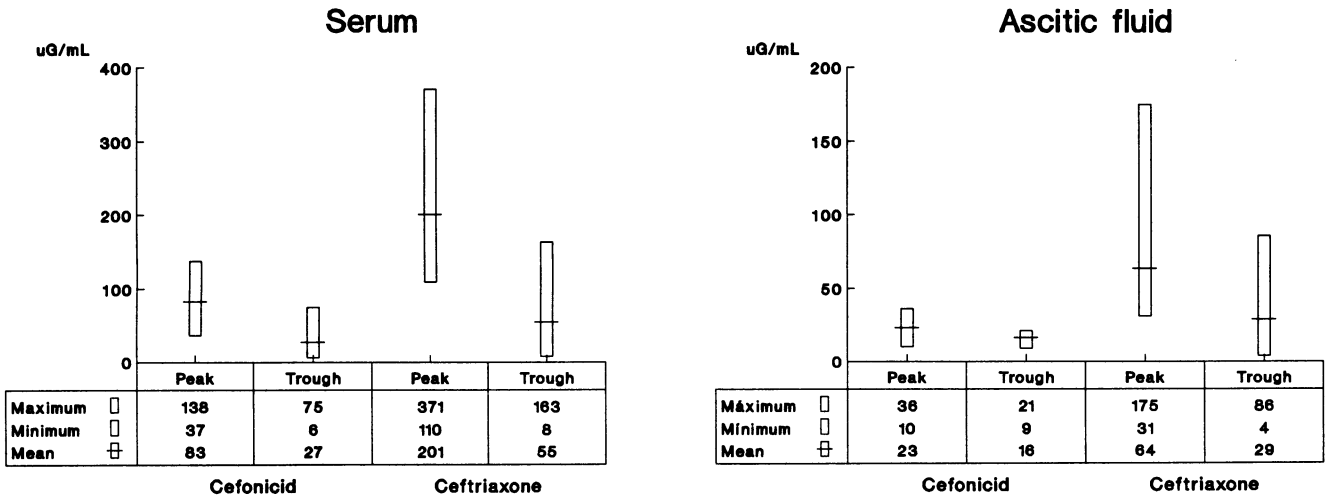

FIG. 1. Concentrations of cefonicid and ceftriaxone in the sera and ascitic fluid of patients with cirrhosis and SBP.

TABLE 3. Clinical outcomes for patients who survived peritonitis[a]

Parameter	Cefonicid-treated patients (n = 25)	Ceftriaxone-treated patients (n = 27)
Afebrile in 72 h	22 (88)	24 (89)
Pain-free in 72 h	17 (68)	19 (70)
Encephalopathy-free in 72 h	19 (76)	22 (81)
Worsened renal function	6 (24)	4 (15)
Ascitic fluid neutrophil count of <250/μl in 72 h	12 (48)	16 (59)
Colonization	2 (6)	3 (10)
Superinfection	0 (0)	0 (0)
Adverse effects	2 (6)	2 (6)
Bacteriologic cure	28 (94)	30 (100)
Therapeutic failure	3 (10)	0 (0)
Death during therapy	9 (30)	4 (13)
Death caused by infection	3 (10)	2 (6)
Hospitalization mortality	11 (37)	9 (30)

[a] Data are numbers of patients (percentage of total). There were no statistically significant differences between groups with respect to any parameter.

kidney function, and the renal functions of four other patients worsened.

There were no statistically significant differences with regard to causes of death between the two treatment groups. Overall, 20 patients died: 11 patients treated with cefonicid (9 [30%] during therapy [2 within the first 48 h of treatment and 2 after the end of treatment]) and 9 patients treated with ceftriaxone (4 [13%] during therapy [2 within the first 48 h of treatment and 5 after the end of treatment]). The causes of death were hepatic encephalopathy in 6 patients (30%), hepatorenal syndrome in 1 patient, gastrointestinal bleeding in 5 patients (25%), multiorgan failure in 5 patients (25%), septic shock in 2 patients (10%), and anaphylactic shock in 1 patient (after the first dose of cefonicid).

Except for the patient who had a cefonicid-associated anaphylactic reaction, there were no major adverse effects. One patient in each group developed a cutaneous rash. Another patient treated with cefonicid had fever, but it subsided at the end of treatment.

DISCUSSION

Until the end of the 1980s, few prospective therapeutic trials had been carried out on patients with SBP. Two studies described the treatment of severe infections in cirrhotics (7, 9), and another analyzed the use of aztreonam in the treatment of SBP caused by gram-negative bacilli, although with little success (2). Even though the study of Cabrera and associates (7) seemed to show a high sensitivity to nephrotoxicity caused by aminoglycosides in cirrhotic patients and that of Felisart and colleagues (9) indicated that cefotaxime has greater efficacy and safety in the treatment of severe infections than the conventional ampicillin-aminoglycoside combination, the latter regimen continued to be recommended (26) and is still listed as the treatment of choice in some reference texts (23).

A few studies have dealt specifically with the treatment of SBP in cirrhotics (14). Although some studies suggest that treatment with ceftriaxone results in higher concentrations than ceftriaxone in peritoneal fluid and has pharmacokinetic characteristics superior to those of cefotaxime, the concentrations of both agents in tissue and peritoneal fluid are greater than the minimum level necessary to inhibit the growth of peritoneal pathogens (5, 12). In theory, the only disadvantage of using these cephalosporins in the treatment of peritoneal infection is their low activity against *E. faecalis* and *Bacteroides fragilis*. Recent studies, however, show that SBP is only rarely caused by these microorganisms (1, 10, 25, 26). In the present study, the incidence of peritoneal infections caused by these pathogens was only 3%, and in our opinion, there is no need to take them into consideration when establishing empirical treatment for SBP in cirrhotics.

Most studies that have specifically assessed the use of antibiotics for treating SPB were not comparative trials of antibiotic regimens, so that different series must be compared when reviewing the antibiotics that should be used to treat SPB. One of the main problems that arises when assessing the efficacy of two antibiotic regimens tested in different studies lies in the appropriate definition of variables, such as the prognostic group to which the patients included in the study belonged and the criteria used to consider a patient's infection cured.

In the study of Felisart and colleagues (9), prognostic groups were not clearly determined and poorly specified bacteriologic, clinical, and biologic criteria were used to define cure. A total of 78% of the patients that received cefotaxime (2 g every 4 h) were considered to be cured of their peritoneal infections, although hospital-related mortality was not mentioned. In the first report by Ariza and associates (2) which studied the efficacy of aztreonam (1 g every 8 h) in the treatment of SBP in cirrhotics, only 57% of the patients were considered to be cured; hospital-related mortality occurred in 62% of cases, and the incidence of superinfection was high. Prognostic categories were established by the Pugh-Child methods in the study of Grange and coworkers (11), which analyzed the efficacy of amoxicillin-clavulanic acid (1 g and 200 mg, respectively, every 6 h); in the most recent study by Ariza et al. (3), which compared cefotaxime (1 h every 6 h) with aztreonam (0.5 g every 8 h) for the treatment of SBP caused by gram-negative bacilli; and in the present study. Grange and coworkers (11) used bacteriologic criteria together with the normalization of ascitic fluid neutrophil count to define cure in patients with SBP; they reported that 85% of patients were cured, although only 63% of patients could be discharged from the hospital. In patients with SBP caused by gram-negative bacilli, Ariza et al. (3) reported a mortality rate of 58% in the group treated with cefotaxime, whereas the mortality rate was 43% in the group treated with aztreonam (P = 0.265). Streptococcal superinfections occurred in 14% of the group treated with aztreonam. The authors concluded that both antibiotics were effective and well tolerated, although the use of another agent that was active against gram-positive cocci and the possibility of the appearance of streptococcal superinfections in patients who received aztreonam would seem to indicate that cephalosporins should be used in the initial empirical treatment of these patients.

Our results suggest that both ceftriaxone and cefonicid are effective in the initial empirical treatment of SBP in cirrhotics. Both groups of patients showed similar characteristics with regard to the severity of chronic liver disease and the clinical manifestations of peritonitis. There was no difference in the number of bacteriologically confirmed cases of peritonitis or the bacteriologic characteristics of infectious episodes in either group. The isolated pathogens were susceptible in vitro to cefonicid and ceftriaxone in 86.6 and 90% of cases, respectively. In our study, a 94% bacteriologic cure rate was obtained after 48 h of antibiotic therapy in the cefonicid-treated group and a 100% bacteriologic cure rate

was obtained in the ceftriaxone-treated group. Thirty percent of the patients who received cefonicid died during treatment. However, if the two patients who died within the first 48 h of antibiotic therapy are not included in this figure, the mortality rate during treatment would be 23%. For patients treated with ceftriaxone, the mortality rate during treatment was 13%. Half of the patients died within the first 48 h of treatment. In only 6% of cases could death be directly related to peritonitis. Survival at the end of hospitalization was 63% in the cefonicid-treated group and 70% in the ceftriaxone-treated group. Although these differences were not statistically significant, ceftriaxone would seem to be a more effective agent than cefonicid. This assumption is based, on the one hand, on the fact that the mean survival of ceftriaxone-treated patients who died was 11 days, while that of cefonicid-treated patients who died was 5 days and, on the other, a more advantageous relationship between the MIC and peak concentrations of antibiotic in plasma for ceftriaxone than for cefonicid. Although it is easy to establish when peritonitis is cured in those cases in which, despite the absence of symptoms of active infection, the patient dies after a more or less prolonged period of hospitalization, this is not so when death occurs during the first days of antibiotic therapy, when the patient's general condition is apparently improving and death occurs as a result of some acute complication of the underlying disease. For this reason, a time-related evolution of peritonitis has been established by some authors, in which early death is more closely related to the infection and later death is more closely related to the underlying illness (15). Although the diffusion of both drugs in ascitic fluid is similar, the concentrations for ceftriaxone in serum and ascitic fluid were higher than those of cefonicid. The ratio of the concentrations of antibiotic in ascitic fluid/serum was greater for both drugs at the end of each dose interval. The concentration of antibiotic in ascitic fluid/MIC ratio for ceftriaxone was >100 throughout the dose interval (24 h), while it was lower for cefonicid (between 1 and 18). For the majority of the organisms isolated, the mean levels of cefonicid in ascitic fluid came within the MIC range. The high concentrations of ceftriaxone in serum and ascitic fluid and the low MIC for the causative organisms of SBP afford the possibility of reducing ceftriaxone doses in the treatment of SBP.

No significant differences in the disappearance of clinical manifestations, worsened renal function, or time course of biologic and bacteriologic data were observed between either group. Both cefonicid and ceftriaxone have been shown to be safe antibiotics with a low incidence of adverse effects, and in terms of nephrotoxicity, their use would appear to be preferable to that of the beta-lactam and aminoglycoside combination. Ceftriaxone-associated biliary pseudolithiasis (17) was not assessed, since this phenomenon was unknown at the time when the present study was undertaken. Nevertheless, pseudolithiasis was not detected in any of the 16 patients treated with ceftriaxone whose gall bladders were examined sonographically. Although some authors recommend that doses of ceftriaxone should be lower in patients with chronic liver disease (24) because of the biliary excretion of the drug, the doses of ceftriaxone given to this group of patients have been shown to be safe, particularly if we bear in mind the fact that 2 g every 24 h is half the recommended dose for treating meningitis (13). The index of colonization by pathogens against which both antibiotics present little or no activity (*E. faecalis* and *C. albicans*) does not constitute a problem for its clinical use either.

In conclusion, both cefonicid and ceftriaxone were demonstrated to be safe antibiotics that are useful in the treatment of SBP in patients with cirrhosis. Ceftriaxone, however, shows greater bactericidal activity against the causative organisms of SBP and possesses certain pharmacokinetic advantages over cefonicid. The high concentrations of ceftriaxone in plasma and ascitic fluid and the low MIC for the causative microorganisms of SBP suggest the possibility of reducing the dose to 1 g per day for the treatment of SBP. The use of antibiotics with a long elimination half-life in plasma, which permits the administration of one or two doses daily, and the tendency to shorten the duration of treatment (21) will no doubt contribute greatly to advances in the treatment of SBP in patients with cirrhosis over the next decade.

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