MAJOR ARTICLE

Clinical Significance and Outcome of Nosocomial Acquisition of Spontaneous Bacterial Peritonitis in Patients with Liver Cirrhosis

Hae Suk Cheong,[1] Cheol-In Kang,[1] Jeong A. Lee,[1] Soo Youn Moon,[1] Mi Kyong Joung,[1] Doo Ryeon Chung,[1] Kwang Cheol Koh,[2] Nam Yong Lee,[3] Jae-Hoon Song,[1,4] and Kyong Ran Peck[1]

[1]Division of Infectious Diseases, [2]Department of Medicine and Digestive Disease Research Center, and [3]Department of Laboratory Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, and [4]Asian-Pacific Research Foundation for Infectious Diseases, Seoul, Republic of Korea

Background. There have been few reports on the causes and treatment outcomes for nosocomial spontaneous bacterial peritonitis (SBP) in patients with liver cirrhosis.

Methods. We performed a retrospective cohort study to compare the microbiological and clinical characteristics in nosocomial versus community-acquired SBP. All patients with SBP, for whom culture was proven to be positive for SBP at Samsung Medical Center (Seoul, Republic of Korea) from 1 January 2000 through 31 June 2007, were included. Medical records and laboratory data were reviewed. Nosocomial SBP was defined as SBP diagnosed after 72 h of hospitalization.

Results. A total of 236 patients with SBP were enrolled (mean age ± SD age, 56.6 ± 10.7 years); 166 patients were women, and 70 were men. Nosocomial and community-acquired SBP occurred in 126 and 110 patients, respectively. *Escherichia coli* accounted for 102 (43.2%) of 236 isolates, *Klebsiella* species accounted for 33 isolates (14.0%), and *Streptococcus* species accounted for 23 isolates (9.8%). The overall 30-day mortality rate for nosocomial SBP was higher than that for community-acquired SBP (58.7% vs. 37.3%; $P = .001$). Nosocomial isolates of gram-negative organisms were significantly more resistant to third-generation cephalosporins (41% vs. 10.0%; $P < .001$) and quinolones (50.0% vs. 30.9%; $P = .003$), compared with community-acquired isolates. Multivariate analysis revealed that nosocomial infection, concomitant hepatocellular carcinoma, presentation with acute renal failure or shock, and resistance to third-generation cephalosporins were significant risk factors for 30-day mortality associated with SBP.

Conclusions. Nosocomial SBP has a poorer outcome than community-acquired SBP. The resistance to third-generation cephalosporins for gram-negative organisms, which are more common in nosocomial cases of SBP than in community-acquired cases of SBP, adversely affects the outcome of SBP in patients with liver cirrhosis.

Spontaneous bacterial peritonitis (SBP) is a common and severe complication in patients with cirrhosis and ascites [1]. SBP occurs in 10%–25% of patients with liver cirrhosis with ascites, with a mortality rate ranging from 20% to 40% [2–5]. Empirical antibiotic therapy should be initiated immediately after the diagnosis of SBP is made, without prior knowledge of the causative organisms and their in vitro susceptibility. Because gram-negative aerobic bacteria from the Enterobacteriaceae family are the most common causative organisms, the initial empirical antibiotic therapy of SBP should cover these organisms [6, 7]. Cefotaxime has been considered the first choice of empirical antibiotics in SBP treatment, along with other broad-spectrum cephalosporins or amoxicillin-clavulanate [6, 8–10].

Most cirrhotic patients have a high risk of nosocomial infection, because they undergo frequent hospitalization and experience long hospital stays [11]. Previous reports have focused on all types of SBP or only community-acquired infections [12]. Recent studies that included patients with nosocomial SBP have demonstrated that nosocomial pathogens are more resistant

Received 16 September 2008; accepted 22 December 2008; electronically published 20 March 2009.

Presented in part: 18th European Congress of Clinical Microbiology and Infectious Diseases, Barcelona, Spain, 19–22 April 2008 (abstract D-08-00010).

Reprints or correspondence: Dr. Kyong Ran Peck, Div. of Infectious Diseases, Samsung Medical Center, Sungkyunkwan University School of Medicine, 50 Ilwon-dong, Gangnam-gu, Seoul 135-710, Republic of Korea (krpeck@skku.edu).

Clinical Infectious Diseases 2009; 48:1230–6

1058-4838/2009/4809-0012$15.00
DOI: 10.1086/597585

Table 1. Clinical characteristics of patients with spontaneous bacterial peritonitis (SBP).

Characteristic	Total (n = 236)	Nosocomial SBP (n = 126)	Community-acquired SBP (n = 110)	P
Age, mean years ± SD	56.6 ± 10.7	57.2 ± 11.0	55.9 ± 10.4	.336
Sex				.335
Male	166	92 (73.0)	74 (67.3)	
Female	70	34 (27.0)	36 (42.7	
Cause of liver cirrhosis				
HBV infection	164 (69.5)	86 (68.3)	78 (70.9)	
HCV infection	24 (10.2)	14 (11.1)	10 (9.1)	
Alcohol use	15 (6.4)	11 (8.7)	4 (3.6)	
Other	33 (14.0)	15 (11.9)	18 (16.4)	
Child-Pugh classification				
Mean score ± SD	10.6 ± 1.8	11.2 ± 1.5	10.0 ± 1.9	<.001
Class B	48 (20.3)	14 (11.1)	34 (30.9)	
Class C	187 (79.2)	112 (88.9)	75 (68.2)	<.001
Concomitant hepatocellular carcinoma	103 (43.6)	61 (48.4)	42 (38.2)	.114
Initial presenting symptoms				
Fever	118 (50.0)	78 (61.9)	40 (36.4)	<.001
Abdominal pain	120 (50.8)	41 (32.5)	79 (71.8)	<.001
Hepatic encephalopathy	37 (15.7)	21 (16.7)	16 (14.5)	.655
Diarrhea	9 (3.8)	3 (2.4)	6 (5.5)	.310
Gastrointestinal bleeding ⩽7 days after illness onset	48 (20.6)	33 (26.2)	15 (13.6)	.013
Presentation with septic shock	48 (20.6)	26 (20.6)	22 (20.0)	.904
Laboratory finding				
Ascites PMN leukocyte count, mean cells/μL ± SD	5621 ± 9804	4159 ± 5417	7294 ± 12972	.020
Serum creatinine, mean mg/dL ± SD	1.70 ± 1.32	1.68 ± 1.40	1.73 ± 1.21	.742
Previous history of SBP	62 (26.3)	35 (27.8)	27 (24.5)	.574
Receipt of inappropriate antibiotics	61 (25.8)	51 (40.5)	10 (9.1)	<.001

NOTE. Data are no. (%) of patients, unless otherwise indicated. HBV, hepatitis B virus; HCV, hepatitis C virus; PMN, polymorphonuclear.

to antibiotics, compared with pathogens acquired in the community [13, 14]. However, few data are available regarding clinical and microbiological characteristics of nosocomial versus community-acquired SBP during this era of increasing rates of antimicrobial resistance. Furthermore, a previous study regarding the influence of nosocomial acquisition on the clinical outcomes of patients with SBP did not show a significant difference between outcomes for community-acquired SBP and those for nosocomial SBP [14].

In the present study, we delineated the differences in clinical and microbiological characteristics between nosocomial and community-acquired SBP. This study was performed to identify the risk factors for mortality and evaluate the impact of nosocomial acquisition on outcome in cirrhotic patients with SBP.

MATERIALS AND METHODS

Study design and population. A retrospective, observational cohort study was conducted to evaluate the outcomes of cirrhotic patients with SBP and to determine the impact of nosocomial acquisition on clinical outcome. We compared data from patients with nosocomial infection with data from those with community-acquired infection. Microbiology laboratory files were reviewed to identify all cases with a positive result of an ascitic fluid culture among patients hospitalized at the Samsung Medical Center (Seoul, Republic of Korea) during the period from 1 January 2000 through 31 June 2007. Only patients aged >15 years with liver cirrhosis were included, and only 1 episode for each patient was included in the analysis.

Patients with a culture positive for skin contaminants (i.e., coagulase-negative staphylococci or *Corynebacterium, Propionibacterium,* or *Bacillus* species) and those with secondary peritonitis were excluded from the study. Secondary peritonitis was considered in cases of polymicrobial infection. We reviewed the medical records of the patients, and the following information was collected from patients: age, sex, cause of cirrhosis, Child-Pugh score, concomitant hepatocellular carcinoma, initial symptoms at the time of presentation, gastrointestinal bleeding, presentation with septic shock, laboratory results, previous SBP history, and empirical antibiotic regimen. The primary outcome measure was 30-day mortality rate.

Table 2. Comparison of microbial isolates in nosocomial and community-acquired spontaneous bacterial peritonitis (SBP).

Isolates	No. (%) of patients		
	Total (n = 236)	Nosocomial SBP (n = 126)	Community-acquired SBP (n = 110)
Gram-negative organisms			
All	172 (72.9)	82 (65.1)	90 (81.8)
Escherichia coli	102 (43.2)	51 (40.5)	51 (46.4)
Klebsiella species	33 (14.0)	16 (12.7)	17 (15.4)
Aeromonas species	11 (4.6)	3 (2.4)	8 (7.3)
Enterobacter species	4 (1.7)	2 (1.6)	2 (1.8)
Acinetobacter species	3 (1.3)	2 (1.6)	1 (0.9)
Stenotrophomonas maltophilia	3 (1.3)	2 (1.6)	1 (0.9)
Serracia marcescens	3 (1.3)	1 (0.8)	2 (1.8)
Other	13 (5.5)	5 (3.9)	8 (7.3)
Gram-positive organisms			
All	54 (22.9)	37 (29.3)	17 (15.5)
Streptococcus species	23 (9.8)	14 (11.1)	9 (8.2)
Enterococcus species	10 (4.2)	8 (6.3)	2 (1.8)
Staphylococcus aureus	12 (5.1)	11 (8.7)	1 (0.9)
Streptococcus pneumoniae	8 (3.4)	4 (3.2)	4 (3.7)
Other	1 (0.4)	0 (0.0)	1 (0.9)
Anaerobes	7 (2.9)	4 (3.2)	3 (2.7)
Fungi	3 (1.3)	3 (2.4)	0 (0.0)

Definitions. SBP was defined by an ascitic fluid polymorphonuclear leukocyte count $\geqslant$250 cells/mm^3 and a positive culture result. Nosocomial infection was defined as an infection that occurred >72 h after admission to the hospital, and the infections diagnosed within the first 72 h of hospitalization were classified as community-acquired infection. Septic shock was defined as sepsis associated with evidence of organ hypoperfusion and a systolic blood pressure <90 mm Hg or >30 mm Hg less than the baseline or a requirement for the use of a vasopressor to maintain the blood pressure. The initial empirical antimicrobial therapy was considered appropriate if the initial antibiotics, which were administered within 24 h of acquisition of ascitic fluid samples, included at least 1 antibiotic that was active in vitro against the isolated pathogen and if the dosage and route of administration conformed to current medical standards. We considered antimicrobial therapy to be inappropriate if the drugs used did not have in vitro activity against the isolate or if the patient did not receive antimicrobial therapy.

Laboratory testing. During the study period, ascitic fluid specimens were obtained aseptically by paracentesis and inoculated into blood culture bottles at the bedside. Ascitic fluid samples were also sent to the microbiology laboratory for polymorphonuclear leukocyte counting and Gram staining. The recovery of isolates from ascitic fluid was performed with the BACTEC model 9240 system (BD Diagnostic Instrument Systems) or the BacT/ALERT 3D system (bioMérieux). Identification of isolates was performed using a standard identification card. Antibiotic susceptibility testing of isolates was performed on the VITEK II automated system (bioMérieux) using the modified broth microdilution method. MIC breakpoints and quality-control protocols were used according to standards established by the Clinical and Laboratory Standards Institute [15].

Statistical analysis. Student's t test was used to compare continuous variables, and the χ^2 test or Fisher's exact test was used to compare categorical variables. In identifying the risk factors for mortality, proportional hazards Cox regression model was used to control for the effects of confounding variables. Variables with $P < .05$ in the univariate analyses were candidates for multivariate analysis. In addition, in identifying the risk factors for resistance to third-generation cephalosporins, stepwise logistic regression was used. We used backward elimination of any variable that did not contribute to the model on the grounds of the likelihood ratio test, using a statistical significance cutoff of .05. All P values were 2-tailed, and P values <.05 were considered to be statistically significant. SPSS for Windows, version 11.5 (SPSS), was used for these analyses.

Table 3. Risk factors for 30-day mortality in patients with spontaneous bacterial peritonitis.

Risk factor	Survivors (n = 121)	Nonsurvivors (n = 115)	Unadjusted analysis		Adjusted analysis	
			HR (95% CI)	P	HR (95% CI)	P
Age, mean years ± SD	55.6 ± 11.7	57.6 ± 9.5	1.01 (1.00–1.03)	.099	…	
Sex						
Male	78	88	0.68 (0.44–1.04)	.074	…	
Female	43	27	…		…	
Child-Pugh classification						
Class B	33 (27.3)	15 (13.0)	1		…	
Class C	87 (72.7)	100 (87.0)	2.14 (1.24–3.69)	.006	…	
Concomitant hepatocellular carcinoma	41 (33.9)	62 (53.9)	1.81 (1.26–2.62)	.001	1.58 (1.08–2.30)	.019
Previous antibiotics use within 90 days	46 (38.0)	60 (52.2)	1.53 (1.06–2.21)	.022	…	
Nosocomial infection	52 (43.0)	74 (64.3)	1.97 (1.34–2.89)	.001	2.18 (1.47–3.23)	<.001
Gastrointestinal bleeding ⩽7 days after illness onset	19 (15.7)	29 (25.2)	1.48 (0.97–2.25)	.070	…	
Presentation with acute renal failure	26 (21.5)	67 (58.3)	3.19 (2.20–4.64)	<.001	3.14 (2.11–4.68)	<.001
Presentation with septic shock	14 (11.6)	34 (29.6)	2.37 (1.59–3.55)	<.001	1.71 (1.11–2.62)	.014
Receipt of inappropriate antibiotics	15 (12.4)	46 (40.0)	2.46 (1.69–3.58)	<.001	…	

NOTE. Data are no. (%) of patients, unless otherwise indicated. HR, hazard ratio.

RESULTS

Clinical characteristics of patients with nosocomial versus community-acquired SBP. During the study period, 359 patients with a positive ascitic fluid culture result were identified. Among them, 123 patients (34.3%), including 79 with an ascitic fluid polymorphonuclear leukocyte count <250 cells/mm^3, 25 with suspicious secondary peritonitis, and 20 with a culture positive for common skin contaminants, were excluded in the analysis. Therefore, a total of 236 consecutive patients with SBP were enrolled in the study. The demographic and clinical features of the study population are given in table 1. One hundred twenty-six patients (53.4%) had nosocomial infections. The most frequent causes of cirrhosis were hepatitis B virus (164 patients [69.5%]), hepatitis C virus (24 patients [10.2%]), and alcohol (15 patients [6.4%]). No statistically significant differences were found in age, sex, cause of liver cirrhosis, or concomitant hepatocellular carcinoma between patients with nosocomial infection and those with community-acquired infection (table 1). However, the Child-Pugh score was statistically significantly higher in patients with nosocomial SBP than in those with community-acquired SBP, and the receipt of inappropriate initial antibiotics and prior gastrointestinal bleeding history ⩽7 days after illness onset were statistically significantly more common among patients with nosocomial SBP than among those with community-acquired SBP.

Microbiological characteristics of nosocomial versus community-acquired SBP. The organisms isolated from the ascitic fluid of patients with SBP are listed in table 2. *Escherichia coli* was the most common isolate (102 isolates [43.2%]), followed by *Klebsiella pneumoniae* (33 isolates [14.0%]). No statistically significant differences were found between types of isolates of nosocomial SBP and those of community-acquired SBP.

Clinical outcome and predictors of mortality. The overall 30-day mortality rate for SBP was 48.7% (115 of 236 cases), and the mortality rate of nosocomial SBP was significantly higher than that of community-acquired SBP (58.7% [74 of 126 cases] vs. 37.3% [41 of 110 cases]; $P = .001$). Of 236 patients, 234 received empirical antimicrobial therapy: 186 (79.5%) received third-generation cephalosporins, 20 (8.5%) received fluoroquinolones, 18 (7.7%) received carbapenems, and 6 (2.6%) received β-lactam/β-lactamase inhibitors. Multivariate analysis using a proportional hazards Cox regression model, including the variables associated with mortality by univariate analysis, showed that the significant independent risk factors for mortality were concomitant hepatocellular carcinoma, nosocomial infection, presentation with acute renal failure or septic shock, and inappropriate initial antimicrobial therapy (table 3).

Predictors of mortality in patients with SBP caused by gram-negative organisms. Gram-negative bacilli accounted for 72% of isolated pathogens in SBP, and we thus tried to identify the predictors of mortality in SBP caused by gram-negative bacilli. Factors associated with 30-day mortality rate are given in table 4. In the multivariate analysis, Child-Pugh class C, concomitant hepatocellular carcinoma, presentation with acute renal failure or septic shock, and inappropriate initial therapy were found to be independent factors associated with 30-day mortality ($P < .05$) (model 1 in table 4). When inappropriate antimicrobial therapy was excluded in the propor-

Table 4. Risk factors associated with 30-day mortality in patients with spontaneous bacterial peritonitis caused by gram-negative organisms.

Risk factors	Survivors (n = 96)	Nonsurvivors (n = 76)	Unadjusted HR (95% CI)	P	Model 1		Model 2	
					Adjusted HR (95% CI)	P	Adjusted HR (95% CI)	P
Age, mean years ± SD	54.5 ± 11.4	57.4 ± 9.84	1.02 (1.00–1.04)	.086	…		…	
Sex			1.46 (0.84–2.54)	.182	…		…	
Male	64	59	…		…		…	
Female	32	17	…		…		…	
Child-Pugh classification								
Class B	23 (24.0)	8 (10.5)	1		…		…	
Class C	73 (76.0)	68 (89.5)	2.50 (1.14–5.44)	.021	2.48 (1.13–5.44)	.024	2.45 (1.12–5.38)	.025
Concomitant hepatocellular carcinoma	31 (32.3)	36 (47.4)	1.62 (1.02–2.55)	.040	1.70 (1.07–2.69)	.025	1.75 (1.10–2.77)	.017
Previous antibiotics use within 90 days	36 (37.5)	35 (46.1)	1.24 (0.79–1.96)	.357	…		…	
Nosocomial infection	38 (39.6)	44 (57.9)	1.81 (1.14–2.88)	.012	…		…	
Gastrointestinal bleeding ⩽7 days after illness onset	15 (15.6)	17 (22.4)	1.40 (0.81–2.40)	.228	…		…	
Presentation with acute renal failure	22 (22.9)	47 (61.8)	3.49 (2.17–5.62)	<.001	3.35 (2.03–5.50)	<.001	3.35 (2.03–5.50)	<.001
Presentation with septic shock	12 (12.5)	27 (35.5)	2.65 (1.65–4.27)	<.001	2.38 (1.46–3.87)	<.001	2.35 (1.44–3.83)	.001
Antimicrobial resistance								
Third-generation cephalosporins	7 (7.3)	18 (23.7)	2.29 (1.34–3.90)	.002	Not applicable		1.89 (1.09–3.27)	.023
Quinolones	16 (16.7)	20 (26.3)	1.38 (0.83–2.31)	.217	…		…	
ESBLs	3 (3.1)	8 (10.5)	1.79 (0.86–3.74)	.119	…		…	
Receipt of inappropriate antibiotics	6 (6.3)	17 (22.4)	2.35 (1.36–4.05)	.002	1.95 (1.11–3.41)	.020	Not applicable	

NOTE. Data are no. (%) of patients, unless otherwise indicated. In model 1, antimicrobial resistance (third-generation cephalosporins) was excluded for analysis. In model 2, initial inappropriate antibiotics therapy was excluded for analysis. ESBLs, extended-spectrum β-lactamases.

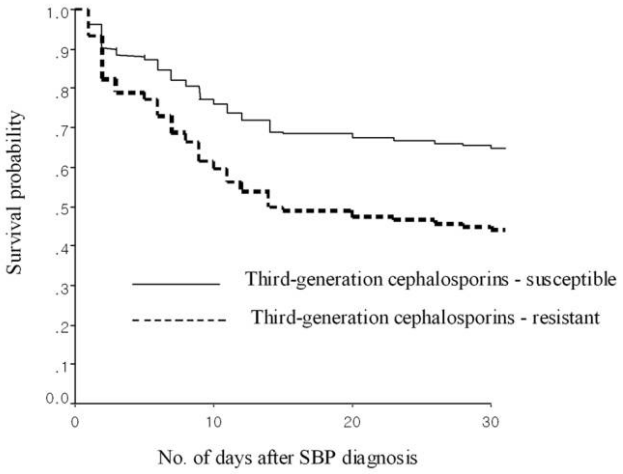

Figure 1. Survival curve for patients with spontaneous bacterial peritonitis (SBP), by gram-negative organism, according to third-generation cephalosporin resistance ($P = .023$).

tional hazards Cox regression models, third-generation cephalosporin resistance was found to be an independent factor associated with 30-day mortality ($P < .05$) (model 2 in table 4). The survival curve also shows that patients with third-generation cephalosporin–resistant SBP had a significantly lower probability of survival than did patients with third-generation cephalosporin–susceptible SBP ($P = .023$) (figure 1).

Prior use of antibiotics, nosocomial acquisition of pathogens, and presentation with acute renal failure or septic shock occurred more frequently among patients with third-generation cephalosporin–resistant SBP than among patients with third-generation cephalosporin–susceptible SBP (table 5). Multivariate analysis showed that previous use of third-generation cephalosporins, nosocomial acquisition of pathogens, and presentation with acute renal failure were independent factors associated with third-generation cephalosporin resistance (table 5).

DISCUSSION

In the present study, we described the clinical and microbiological characteristics of nosocomial versus community-acquired SBP. To our knowledge, this is the largest study to have compared the clinical characteristics and outcomes of patients with nosocomial SBP with those of patients with community-acquired SBP.

Nosocomial infections are associated with the emergence of drug-resistant bacteria in a broad spectrum of pathological conditions; however, little is known about nosocomial SBP in cirrhotic patients [11]. In a previous study, Bert et al. [13] observed that nosocomial SBP isolates were significantly more resistant to antibiotics than community-acquired isolates. However, the treatment outcome of nosocomial SBP (10-day mortality rate) was not significantly different from community-acquired SBP. In contrast, our results showed that nosocomial acquisition affected adversely the outcome of SBP. Nosocomial infection was strongly associated with mortality in our multivariate analysis, even after adjustments were made for underlying illness and other confounding variables. Our data suggest

Table 5. Risk factors associated with resistance to third-generation cephalosporins in patients with spontaneous bacterial peritonitis, by gram-negative organism.

	Resistance status to third-generation cephalosporins			Multivariate analysis	
Risk factor	Resistant ($n = 28$)	Susceptible ($n = 144$)	Univariate P	OR (95% CI)	P
Age, mean years ± SD	56.3 ± 9.6	55.7 ± 11.1	.875	…	
Sex			.404		
Male	22	102		…	
Female	6	42		…	
Child-Pugh classification					
Class B	5 (17.9)	24 (16.7)		…	
Class C	23 (82.1)	119 (82.6)	>.99	…	
Concomitant hepatocellular carcinoma	13 (46.4)	56 (38.9)	.456	…	
Previous antibiotics use within 90 days					
All	20 (71.4)	54 (37.5)	.001	…	
Third-generation cephalosporins	15 (53.6)	36 (25.0)	.002	2.76 (1.05–7.25)	.040
Quinolones	12 (42.9)	24 (16.7)	.002	…	
Nosocomial infection	23 (82.1)	63 (43.8)	<.001	7.02 (2.30–21.47)	.001
Gastrointestinal bleeding ⩽7 days after illness onset	7 (25.0)	26 (18.1)	.342	…	
Presentation with acute renal failure	21 (75.0)	50 (34.7)	<.001	8.29 (3.00–22.92)	<.001
Presentation with septic shock	11 (39.3)	29 (20.1)	.028	…	

NOTE. Data are no. (%) of patients, unless otherwise indicated.

that the acquisition site of infection (i.e., nosocomial infection) may influence the outcome of patients with SBP and that a new therapeutic strategy is needed for the management of nosocomial SBP.

Because the underlying illnesses in nosocomial SBP were more severe (as determined by Child-Pugh score) than in community-acquired SBP, it may be presumed that nosocomial SBP may have a worse prognosis because of the greater severity of underlying illness. However, after adjusting for other prognostic factors associated with mortality, nosocomial SBP was still identified as an independent risk factor for mortality in this study. Not surprisingly, the severity of underlying illness and initial inappropriate antibiotic therapy were also prognostic factors of mortality.

Third-generation cephalosporins, such as cefotaxime, were the most frequently prescribed antibiotics for empirical therapy, regardless of the source of infection acquisition in our study. Consequently, 40.5% of patients with nosocomial SBP received inappropriate initial antimicrobial therapy, and most of them had SBP caused by antimicrobial-resistant gram-negative bacilli. Third-generation cephalosporin resistance was associated with previous use of antibiotics within 90 days and nosocomial infection. Our results suggest that third-generation cephalosporins may not be the optimal choice for the first-line treatment of nosocomial SBP, especially in populations with a high prevalence of gram-negative bacilli with resistance to third-generation cephalosporins. These results correspond with the results of a recent study, which reported that initial treatment with cefotaxime failed more frequently than expected, and an increase in health care–related infections with antibiotic-resistant pathogens may explain this finding [16].

Our study has some limitations. First, it was observational, and thus unknown risk factors for mortality might have been unequally distributed between the 2 groups. Second, patients with bacteria ascites (defined by a positive ascitic fluid culture result without an increased polymorphonuclear leukocyte count) or culture-negative neutrocytic ascites (defined by an ascitic fluid polymorphonuclear leukocyte count $\geqslant$250 cells/mm^3 and a negative culture result) were not included in this study. Patients with these conditions are sometimes treated with antibiotics in clinical practice; thus, selection bias may have occurred, because we only included patients with culture-proven SBP in this study. For example, our study showed that fever was more common in patients with nosocomial SBP and abdominal pain was more common in patients with community-acquired SBP. It is unlikely that the initial presenting symptoms of patients with nosocomial SBP were different from those of patients with community-acquired SBP. Thus, those findings could be explained in part by selection bias. Finally, our study was performed at a single, large institution, and the results may or may not be applicable to other hospitals.

In conclusion, nosocomial SBP, which is more frequently caused by antibiotic-resistant organisms, has a poorer outcome than community-acquired SBP. Nosocomial acquisition was found to be significantly associated with higher mortality rates, along with inappropriate initial antimicrobial therapy and third-generation cephalosporin resistance. Third-generation cephalosporin may not be appropriate for the empirical treatment of SBP in cirrhotic patients with an increased risk of resistant isolates, particularly in patients with nosocomial SBP.

Acknowledgments

Potential conflicts of interest. All authors: no conflicts.

References

1. Sort P, Navasa M, Arroyo V, et al. Effect of intravenous albumin on renal impairment and mortality in patients with cirrhosis and spontaneous bacterial peritonitis. N Engl J Med **1999**; 341:403–9.
2. Guarner C, Sola R, Soriano G, et al. Risk of a first community-acquired spontaneous bacterial peritonitis in cirrhotics with low ascitic fluid protein levels. Gastroenterology **1999**; 117:414–9.
3. Thuluvath PJ, Morss S, Thompson R. Spontaneous bacterial peritonitis: in-hospital mortality, predictors of survival, and health care costs from 1988 to 1998. Am J Gastroenterol **2001**; 96:1232–6.
4. Llovet JM, Moitinho E, Sala M, et al. Prevalence and prognostic value of hepatocellular carcinoma in cirrhotic patients presenting with spontaneous bacterial peritonitis. J Hepatol **2000**; 33:423–9.
5. Park YH, Lee HC, Song HG, et al. Recent increase in antibiotic-resistant microorganisms in patients with spontaneous bacterial peritonitis adversely affects the clinical outcome in Korea. J Gastroenterol Hepatol **2003**; 18: 927–33.
6. Rimola A, Garcia-Tsao G, Navasa M, et al. Diagnosis, treatment and prophylaxis of spontaneous bacterial peritonitis: a consensus document. J Hepatol **2000**; 32:142–53.
7. Bacon BR. Cirrhosis and its complications. In: Fauci AS, Braunwald E, Kasper DL, et al., eds. Harrison's principles of internal medicine. 17th ed. New York: McGraw-Hill Companies, **2008**:1971–80.
8. Caruntu FA, Benea L. Spontaneous bacterial peritonitis: pathogenesis, diagnosis, treatment. J Gastrointestin Liver Dis **2006**; 15:51–6.
9. Felisart J, Rimola A, Arroyo V, et al. Cefotaxime is more effective than is ampicillin-tobramycin in cirrhotics with severe infections. Hepatology **1985**; 5:457–62.
10. Runyon BA, McHutchison JG, Antillon MR, Akriviadis EA, Montano AA. Short-course versus long-course antibiotic treatment of spontaneous bacterial peritonitis: a randomized controlled study of 100 patients. Gastroenterology **1991**; 100:1737–42.
11. Campillo B, Richardet JP, Kheo T, Dupeyron C. Nosocomial spontaneous bacterial peritonitis and bacteremia in cirrhotic patients: impact of isolate type on prognosis and characteristics of infection. Clin Infect Dis **2002**; 35: 1–10.
12. Novella M, Sola R, Soriano G, et al. Continuous versus inpatient prophylaxis of the first episode of spontaneous bacterial peritonitis with norfloxacin. Hepatology **1997**; 25:532–6.
13. Bert F, Andreu M, Durand F, et al. Nosocomial and community-acquired spontaneous bacterial peritonitis: comparative microbiology and therapeutic implications. Eur J Clin Microbiol Infect Dis **2003**; 22:10–5.
14. Song JY, Jung SJ, Park CW, et al. Prognostic significance of infection acquisition sites in spontaneous bacterial peritonitis: nosocomial versus community acquired. J Korean Med Sci **2006**; 21:666–71.
15. Clinical and Laboratory Standards Institute (CLSI). Performance standards for antimicrobial susceptibility testing: fifteenth informational supplement M100–S16. Wayne, PA: CLSI, **2006**.
16. Angeloni S, Leboffe C, Parente A, et al. Efficacy of current guidelines for the treatment of spontaneous bacterial peritonitis in the clinical practice. World J Gastroenterol **2008**; 14:2757–62.