Spontaneous bacterial peritonitis: Analysis of treatment and outcome

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GH VICTOR, SM OPAL. Spontaneous bacterial peritonitis: Analysis of treatment and outcome. Can J Infect Dis 1991;2(4):147-154. Spontaneous bacterial peritonitis occurred on 44 separate occasions in 43 patients during a five year period, including 27 culture positive and 17 probable cases of spontaneous bacterial peritonitis. Alcoholic liver disease was the underlying cause of 72% of cases. Of the 27 culture positive cases, *Escherichia coli* was the most common isolate (14 cases), followed by *Klebsiella pneumoniae* (three cases), group G streptococci (three cases), group B streptococci (two cases) and one case each of five other organisms. Bacteremia occurred in 50% of cases and was the same as the peritoneal isolate 88% of the time. The overall mortality rate was 65% (66% culture positive and 60% probable spontaneous bacterial peritonitis). The mean interval between onset of symptoms and death was 10.2±8.6 days in fatal cases. Spontaneous bacterial peritonitis was felt to be a contributing cause of mortality in 70% of fatal cases. Survivors were younger (44±20 years versus 59±13, $P<0.05$) and less likely to develop renal insufficiency than nonsurvivors (38% versus 73%, $P<0.05$). Patients who were treated with an aminoglycoside were more likely to develop renal failure compared to those treated with nonaminoglycoside regimens ($P<0.05$). There was no difference in mortality rate between culture positive and culture negative spontaneous bacterial peritonitis, total peritoneal leukocyte counts, Gram-positive versus Gram-negative organisms, presence of bacteremia, or serum albumin or bilirubin levels. The mortality rate for this disease remains unacceptably high, indicating a need for the development of new strategies in the prevention, diagnosis and management of this disease.

Key Words: *Spontaneous bacterial peritonitis*

Péritonite bactérienne spontanée: Analyse du traitement et résultat

RESUME: Une péritonite bactérienne spontanée est survenue à 44 reprises distinctes chez 43 patients sur une période de cinq années – 27 cultures positives et 17 cas probables de péritonite bactérienne spontanée. Une affection hépatique éthylique était la cause sous-jacente dans 72 % des cas. Parmi les 27 cas de cultures positives, *Escherichia coli* était le germe le plus souvent isolé (14 cas), suivi de *Klebsiella pneumoniae* (trois cas), de streptocoques de groupe G (trois cas), de streptocoques de groupe B (deux cas) et d'un cas chacun de cinq autres organismes. Une bactériémie est survenue dans 50 % des cas et était identique à l'isolat péritonéal dans 88 % des cas. Le taux de mortalité global atteignait 65 % (cultures positives 66 % et péritonite bactérienne probable 60 %). L'intervalle moyen entre le début des symptômes et le décès était de 10,2±8,6 jours dans les cas fatals. On attribue la mortalité à la péritonite bactérienne

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spontanée dans 70 % des cas. Les survivants étaient plus jeunes (44±20 ans comparés à 59±13 ans, P<0,05) et moins susceptibles de développer une insuffisance rénale que les non-survivants (38 % comparés à 73 %, P<0,05). Les patients sous aminosides étaient plus sujets à une insuffisance rénale que ceux qui étaient traités par non-aminosides (P<0,05). On n'a relevé aucune différence dans le taux de mortalité des cas de péritonite bactérienne spontanée avec cultures positives et négatives, ou selon la numération leucocytaire péritonéale totale, les germes Gram positifs par rapport aux germes Gram négatifs, la présence d'une bactériémie ou les taux d'albumine sérique ou de bilirubine. Le taux de mortalité demeure inacceptablement élevé, indiquant la nécessité d'instituer de nouvelles stratégies dans la prévention, le diagnostic et le traitement de cette affection.

SPONTANEOUS BACTERIAL PERITONITIS IS A WELL described nosologic entity (1-7); nonetheless, this disease most likely represents the final endpoint in the wide clinical spectrum of ascitic fluid infection (1-5,7-11). There have been conflicting reports regarding the in-hospital mortality associated with this disease (ranging from 57 to 95%), as well as which factors portend a poor prognosis (2,3,5).

The most appropriate antimicrobial regimen in the treatment of spontaneous bacterial peritonitis has yet to be defined. Aminoglycosides are frequently used in the management of this disease. These drugs may be more nephrotoxic in ascitic patients and may contribute to the metabolic complications seen in patients with severe hepatic dysfunction (12). With the advent of second and third generation cephalosporins as well as other antimicrobial agents, alternative regimens in the treatment of spontaneous bacterial peritonitis have become available to the clinician. In this report, the authors analyze their experience in the treatment of spontaneous bacterial peritonitis, comparing the results obtained with newer antimicrobial agents with those of a traditional aminoglycoside-containing regimen. The prognostic value of various clinical and laboratory parameters in determining the outcome of spontaneous bacterial peritonitis is also reviewed.

PATIENTS AND METHODS

Patient selection: A retrospective chart review was conducted at each of the five Brown University-affiliated hospitals: Rhode Island Hospital, Roger Williams General Hospital, Miriam Hospital, Veteran's Administration Hospital, and Memorial Hospital of Rhode Island. Rhode Island Hospital is a tertiary referral hospital, while the other institutions are community hospitals. The chart of any patient with a diagnosis of peritonitis over the five year study period (1981-86) was obtained and reviewed.

Criteria for inclusion as culture positive spontaneous bacterial peritonitis included: a positive peritoneal fluid culture; clinical features of ascites; and absence of a secondary cause of infection (including perforated intra-abdominal abscess determined by clinical criteria or radiographic or surgical findings, or evidenced by autopsy).

Probable spontaneous bacterial peritonitis was defined by the same criteria as culture positive spontaneous bacterial peritonitis, except that patients did not have positive peritoneal cultures. An absolute neutrophil count greater than 500×10^9/L in peritoneal fluid was required for inclusion as probable spontaneous bacterial peritonitis in the absence of other known causes of peritoneal inflammation (abscess, neoplasm, etc). Patients undergoing peritoneal dialysis were excluded from analysis.

The data collected included the following clinical features: fever, abdominal pain, hypotension, tachypnea, encephalopathy, diarrhea, nausea, vomiting, jaundice, rebound tenderness and oliguria; and the following laboratory studies: white blood cell count, bilirubin, albumin, prothrombin time, glucose, creatinine, peritoneal fluid analysis, bacteriology and method of peritoneal culture collection. It is standard practice in all of the clinical laboratories to centrifuge the ascitic fluid prior to preparation of the Gram stain. This was performed when sufficient quantities of fluid were available. The development of renal insufficiency was defined as a greater than twofold increase in baseline serum creatinine obtained 48 h or more after the initial diagnosis of spontaneous bacterial peritonitis.

Statistical analysis: The data were compiled using an IBM PC computer and analyzed using a χ^2 analysis of contingency table or an unpaired Student's t test where appropriate. Results are expressed as the mean ± standard deviation. Differences were considered statistically significant at the P<0.05 level.

RESULTS

Patient characteristics: There were 44 episodes of spontaneous bacterial peritonitis, 27 with positive peritoneal cultures and 17 with probable spontaneous bacterial peritonitis with negative peritoneal cultures. The mean patient age was

TABLE 1
Laboratory parameters in patients with spontaneous bacterial peritonitis

	Survivors (n=16)			Nonsurvivors (n=28)		
	Number	Mean	SD	Number	Mean	SD
Serum albumin (g/L)	12	24.1	8.07	24	24.6	2.17
Serum bilirubin (μmol/L)	11	117.4	48.2	25	150.5	28.8
Creatinine (μmol/L)*	13	72.1	11.4	24	176.8	58.3
Glucose (mmol/L)	11	6.69	1.8	27	8.55	5.6
Prothrombin time (s)	13	13.6	2.5	27	17.06	6.97
Serum sodium (mmol/L)	16	134	6.13	27	132	8.26
Leukocyte count (x10^9/L)	12	13,439.16	3501.7	23	14,685.6	6146.9
Characteristics of ascitic fluid						
Leukocyte count (x10^9/L) (% polymorphonuclear leukocytes)	16	15.44 (81.6)	17.62	28	17.11 (78.4)	25.22
Total protein (g/L)	16	8.6	6.1	25	12.5	8.4
Lactate dehydrogenase (U/L)	9	266.4	253.4	13	428.5	617.5
Glucose (mmol/L)	16	5.1	3.0	26	7.3	7.0
Amylase (U/L)	6	41.7	21.2	7	27.8	17.4

$P<0.05$; no other parameter showed statistical significance

58.3 years (range three to 91). The mean age of survivors (44±20 years) was less than that of nonsurvivors (59±13 years) ($P<0.05$). Three patients were younger than 14 years old. One patient (age four years) had two separate episodes of peritonitis with two different organisms. The study population consisted of 41 Whites, one Black, and two Hispanics; the male/female ratio was 3.4/1. Alcoholic liver disease was the most common cause of ascites, accounting for 72% (32 of 44) of all patients studied. Other forms of liver disease included chronic active hepatitis (three patients); neoplastic liver disease (three patients); Wilson's disease (one patient); and cryptogenic cirrhosis (four patients). One patient had nephrotic syndrome as the cause of ascites.

Clinical features: The major clinical features observed included abdominal pain, fever, hypotension and jaundice. The most common presenting symptom was abdominal pain, which was noted in 28 of 44 cases (63%). Fever defined by an oral temperature of 38°C or greater at the time of diagnosis was found in only 18 cases (40%). Hypotension defined as systolic blood pressure less than 100 mmHg was found in 18 cases (46%). Nausea and vomiting were noted in 18 cases (40%). Jaundice and tachypnea (greater than 20/min) were reported in 17 cases (38%). Encephalopathy was noted in 13 cases (29%); rebound tenderness in 12 (27%); diarrhea in seven (15%); and oliguria in two (4). The diagnosis of spontaneous bacterial peritonitis was made in four asymptomatic patients with progressive ascites.

Laboratory studies: Laboratory data disclosed myriad abnormalities primarily attributable to severe liver dysfunction. The only parameter of any apparent prognostic significance was the serum creatinine at diagnosis, which was significantly higher in nonsurvivors (176.8±58.3 μmol/L) compared to survivors of spontaneous bacterial peritonitis (72.1±11.4 μmol/L; $P<0.05$). The pertinent laboratory findings are summarized in Table 1.

Peritoneal fluid findings: The ascitic fluid was noted to be cloudy in 24 of 28 specimens examined. The mean leukocyte count in culture positive spontaneous bacterial peritonitis was 14,135x10^9/L (range 770 to 63,700); the mean leukocyte count in probable spontaneous bacterial peritonitis was 8359x10^9/L (range 1100 to 28,350) (not significant). Each patient had greater than 500x10^9/L neutrophils in the ascitic fluid, except one patient with culture positive spontaneous bacterial peritonitis. This patient had *Clostridium tertium* cultured from the blood and peritoneal fluid, and died seven days from the onset of spontaneous bacterial peritonitis from disseminated intravascular coagulation and refractory hypotension. This patient's initial peritoneal tap had 710x10^9/L total white blood cells with 433x10^9/L neutrophils. The mean leukocyte count was found to be greater than 10,000x10^9/L in both survivors and nonsurvivors. A polymorphonuclear leukocyte predominance was found in all patients, with a mean of 78.3% of total leukocytes in the peritoneal fluid.

Gram stain of the ascitic fluid was positive in only four of 37 episodes (11%); the organisms visualized were morphologically similar to those ultimately cultured. The results of peritoneal fluid analysis are shown in Table 1. The peritoneal fluid findings did not differ significantly between culture positive and probable spontaneous bacterial peritonitis patients, nor between patients who

TABLE 2
Bacteriology of spontaneous bacterial peritonitis and blood isolates

Organism	Ascitic fluid	Blood
Escherichia coli	14	5
Klebsiella pneumoniae	3	1
Klebsiella oxytoca	1	1
Group G streptococci	3	2
Group B streptococci	2	2
Aeromonas hydrophila	1	1
Enterococcus faecalis	1	1
Clostridium tertium	1	1
Listeria monocytogenes	1	—
Bacteroides fragilis	1	—

Units are number of isolates

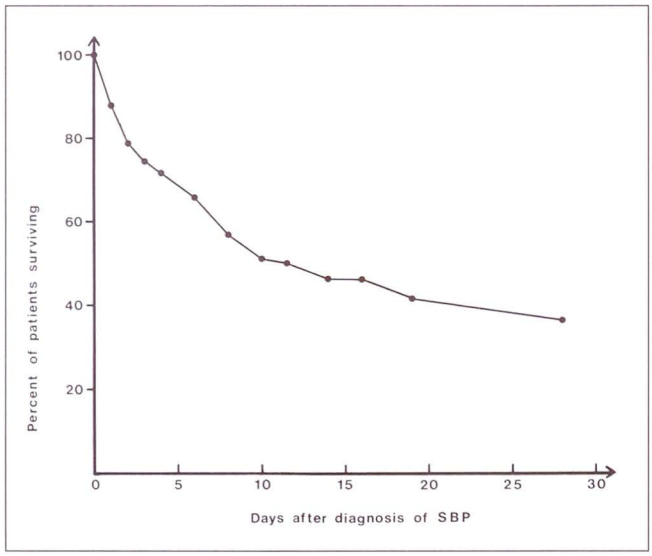

Figure 1) *Survival curve following the onset of spontaneous bacterial peritonitis*

ultimately survived and those who died from spontaneous bacterial peritonitis.

Bacteriology: Peritoneal fluid microbial isolates and blood isolates are shown in Table 2. The most common isolate was *Escherichia coli*, accounting for 50% of culture positive cases, followed by *Klebsiella pneumoniae* (11%) and group G streptococci (11%). Enterobacteriaceae accounted for 66% of the peritoneal isolates found in this study.

Treatment and outcome: All patients received antibiotic therapy within 12 to 24 h of paracentesis. Sixteen patients survived the illness, and 27 did not (65% mortality). In patients who died, the mean interval between the onset of symptoms and death was 10.2±12.6 days (Figure 1).

In the survivors, seven patients were treated with a combination of a beta-lactam antibiotic and an aminoglycoside; four were treated with a beta-lactam alone; and five were started on a combination of a beta-lactam and an aminoglycoside, the latter being stopped within 72 h because of susceptibility of the identified organism. Of interest is that aminoglycoside levels were therapeutic in eight patients, subtherapeutic in one, and not done for unknown reasons in four. If the aminoglycoside was stopped prior to the patient receiving three doses, a level was not felt to be indicated and therefore was not taken into account.

In the nonsurvivors, 22 patients were treated with a combination of a beta-lactam antibiotic and an aminoglycoside; five were treated with a beta-lactam alone. Aminoglycoside levels were therapeutic in three patients, toxic in five, subtherapeutic in one, and not done in nine. Within the limits of a retrospective study, the dosing of the beta-lactams appeared quite adequate in all but two regimens, in which suboptimal doses were used (one survivor and one nonsurvivor). There were no significant differences in the antimicrobial regimens employed in survivors compared to the treatment regimens given to nonsurvivors.

The causes of death included disseminated intravascular coagulation (19%), pneumonia (19%), cardiac failure (19%), hepatic insufficiency (15%), hepatorenal syndrome (11%) and gastrointestinal hemorrhage (7%). Approximately 73% of nonsurvivors developed evidence of renal failure during their hospital course.

In the survivors, the mean duration of therapy was 10.6±8.8 days. Only two survivors had evidence of persistent renal insufficiency during their hospital course. Survivors were younger (44±20 years versus 59±13; $P<0.05$) and less likely to develop renal insufficiency than nonsurvivors (38% versus 73%; $P<0.04$). Aminoglycoside-containing regimens led to an increased risk of nephrotoxicity compared to nonaminoglycoside-containing regimens (10 of 20 versus one of 13; $P<0.05$).

DISCUSSION

Spontaneous bacterial peritonitis is part of a continuum of ascitic fluid infections which have remarkably different clinical presentations and implications. 'Bacterascites' exists when there are less than 250×10^9/L polymorphonuclear cells and ascitic fluid culture is positive. The significance of this entity is not known. It has been hypothesized that organisms in the ascitic fluid can be cleared by host defence mechanisms – including opsonization and macrophages – without an influx of neutrophils. It is known that some patients with positive cultures have cleared these organisms spontaneously without antimicrobial therapy (8,13).

Failure of these mechanisms to clear the infection may result in a polymorphonuclear neutrophil response and onset of the clinical syndrome of spontaneous bacterial peritonitis.

Culture negative neutrocytic peritonitis has been described by Runyon and Hoefs (9). Although this entity has been reported to be caused by other underlying diseases (14-16), it is believed that it represents a variant of spontaneous bacterial peritonitis, and that insensitive culture techniques may account for at least some cases of peritoneal fluid infections with negative culture results (9,17).

Secondary bacterial peritonitis occurs as a result of leakage of organisms into the ascitic fluid via a perforated viscus or a contiguous focus of infection such as an intra-abdominal abscess. Clinical symptoms and signs are very similar to those of spontaneous bacterial peritonitis, and it may prove difficult to distinguish some cases of secondary bacterial peritonitis from spontaneous bacterial peritonitis on clinical grounds alone. Ascitic fluid analysis may help in the differentiation of these two entities by monitoring the protein content, microbiology and response of the ascitic neutrophil count to antimicrobial therapy (10,11).

Pathogenesis: The pathogenesis of spontaneous bacterial peritonitis is not entirely understood. A number of possible routes of infection have been proposed. A primary bacteremia with subsequent infection of the ascitic fluid may occur in some patients, as positive blood cultures have been found in more than one-half of patients with spontaneous bacterial peritonitis (8,18). Similarly, some patients with spontaneous bacterial peritonitis also have evidence of other sources of infection, including the urinary tract and pneumonia, and it is plausible that hematogenous seeding can lead to ascitic fluid infection.

It has been noted that patients with cirrhosis have defects in their reticuloendothelial systems, resulting in delayed clearance of bacteremia. Rimola et al (19) have shown that patients with depressed phagocytic activity are more likely to develop sustained bacteremia. Intrahepatic shunting has been described by Hoefs et al (20); this may well be another important factor disrupting the clearance of microorganisms by the liver. Other defects that have been described in cirrhotic patients include impaired neutrophil function, deficient ascitic fluid complement activity, poor opsonic activity and low immunoglobulin levels (21). These defects in host defences may further contribute to the propensity of ascitic fluid to become infected in decompensated liver disease.

Transmural migration of bacteria across the bowel wall (22) and ascending infection from the female genital tract (23) have also been mentioned as possible precipitating events leading to spontaneous bacterial peritonitis.

Invasive procedures may predispose to peritonitis by generating bacteremia or by transferring organisms directly to the ascitic fluid. Endoscopy, bladder catheterization and paracentesis itself often accompany hospital admissions for hepatic decompensation, and have been speculated to be potential risk factors for spontaneous bacterial peritonitis. Transient bacteremia following endoscopy has been documented, but it is unclear if this procedure itself causes spontaneous bacterial peritonitis (24). Only four patients had paracentesis prior to diagnosis of spontaneous bacterial peritonitis, with an interval between paracentesis and onset of symptoms of three to 14 days. Three patients underwent lower endoscopic procedures prior to the onset of symptoms, and two of these individuals subsequently developed enteric Gram-negative bacilli in their peritoneal fluid. None of these patients received antibiotic prophylaxis prior to these procedures. As suggested by Rimland and Hand (13), studies addressing the use of prophylactic antibiotics prior to invasive procedures in ascitic patients should be considered.

Diagnosis: Spontaneous bacterial peritonitis has become a well recognized disorder and is being diagnosed with increasing frequency. The exact prevalence of this disease is not known but has been estimated to be as high as 27% in non-alcoholic cirrhotic patients (1).

Initial reports suggested a male predominance of patients with spontaneous bacterial peritonitis (2,5). However, of the 18 cases in this study from non-Veteran's Administration hospitals, 10 were female. This supports the view of Rimland and Hand (13) that there may not be any sex predilection in this syndrome. The clinical features of spontaneous bacterial peritonitis in this series are generally similar to those in previously published reports (Table 3). The most common symptom was abdominal pain (63%), which is consistent with other studies (59 to 80%). Fever, vomiting and hypotension were the next most common presenting symptoms (40%). Conn and Fessel (2) found that fever was present in over 80% of patients. This finding appears to be less common in recent series (5,8,13) including the current study, in which fever was seen in only 40% of patients. Encephalopathy is being reported less frequently than in original reports (5,6,8,13), and may relate to earlier diagnosis of spontaneous bacterial peritonitis and improved management of encephalopathy. Nausea, diarrhea, hypotension and hypothermia were found infrequently in this series.

Evaluation of peritoneal fluid is essential in the

TABLE 3
Comparative analysis of previous reports of clinical signs and symptoms of spontaneous bacterial peritonitis

	Rimland and Hand (13)	Weinstein et al (5)	Hoefs et al (8)	Conn and Fessel (2)	Present study
Fever	42%	68%	54%	81%	40%
Abdominal pain	59%	79%	51%	78%	68%
Vomiting	60%	—	—	—	40%
Diarrhea	23%	—	—	—	15%
Encephalopathy	—	54%	46-51%	73%	29%
Hypotension	36%	14%	5%	69%	40%

Results are presented as percentages of patients exhibiting a given clinical factor. — Not commented upon. Numbers in parentheses are references

diagnosis of spontaneous bacterial peritonitis. Other laboratory parameters (complete blood count, chemistries, clotting studies, etc) are nonspecific and of little value in the diagnosis of spontaneous bacterial peritonitis. Controversy exists as to the usefulness of the peritoneal leukocyte count as a predictor of infection. In a recent extensive review of spontaneous bacterial peritonitis, a polymorphonuclear leukocyte count greater than 500×10^9/L was found to be the best single predictor of infected ascitic fluid with a sensitivity, specificity and diagnostic accuracy of 87, 98 and 97%, respectively (6). Gram stain of the peritoneal fluid was disappointing in the present study, with only 11% of specimens revealing positive stains. It is conceivable that Gram stains were not uniformly carried out on centrifuged specimens in this study due to insufficient quantities of peritoneal fluid. It has been previously shown that Gram stain will reveal organisms in up to 55% of cases when the ascitic fluid is centrifuged (1,2). Previously published reports have found Gram stain positivity in 22 to 75% of cases (3,5).

The ascitic protein level in patients with spontaneous bacterial peritonitis is characteristically low and may reflect poor opsonic activity, thereby potentiating the risk of ascitic fluid infection (25). This parameter is also useful in differentiating secondary peritonitis from spontaneous bacterial peritonitis (11,26).

Organisms: The predominance of aerobic Gram-negative bacilli as a cause of spontaneous bacterial peritonitis in liver disease has been well substantiated (3,5,8,13). Among the streptococcal species, *Streptococcus pneumoniae* was not isolated in the current series. This organism has been frequently associated with spontaneous bacterial peritonitis in children with nephrotic syndrome (2,27,28).

There were three cases of peritonitis due to group G streptococcus (two-thirds bacteremic). This organism is most commonly found on the skin and in the upper respiratory tract and is an unusual isolate in spontaneous bacterial peritonitis. Despite the contention that anaerobic organisms may play a significant role in spontaneous bacterial peritonitis (29), only two cases of anaerobic organisms in the ascitic fluid (*Bacteroides fragilis* and *C tertium*) were noted. Anaerobic bacteria may not proliferate in the ascitic environment for a number of reasons, including high oxygen content (30). In addition to routine cultures of peritoneal fluid, inoculation of blood culture bottles with ascitic fluid may increase the sensitivity of bacterial growth more than twofold (17). Recently, inoculation of ascitic blood in a tryptic soy broth blood culture media not only resulted in improved culture results, but also shortened time for detection of bacterial growth (31).

Prognosis: Hoefs et al (8) observed early as well as delayed mortality rates in spontaneous bacterial peritonitis. A similar pattern was found in the present study, with 48% of all deaths occurring within the first 48 h of diagnosis, followed by a gradual decline in the survivor curve over the next 14 to 21 days (Figure 1). Spontaneous bacterial peritonitis was felt to be a contributing cause of mortality in 70% of fatal cases.

Weinstein et al (5) noted a poor outcome in patients with elevated bilirubin (greater than 8 mg/dL), low albumin (less than 2.5 g/dL), encephalopathy, or a ratio of greater than 0.85 polymorphonuclear neutrophils in blood or ascitic fluid. A better prognosis was associated with a temperature greater than 38°C. In all patients, an indicator of a poor prognosis was renal insufficiency (creatinine greater than 2.1 mg/dL) at diagnosis or within three days of admission; this was a similar finding in the present study. Cummings et al (7) have also recently reported that patients with spontaneous bacterial peritonitis and a serum creatinine greater than 185 μmol/L had a 90% mortality for hospitalization compared with a 50% mortality in patients with normal renal function.

Management: The therapeutic approach to the management of spontaneous bacterial peritonitis has undergone significant changes over the past three decades. Initially, Conn and Fessel (2) recommended cephalothin and kanamycin. Subsequently, ampicillin and gentamicin have been recommended to cover Gram-negative bacilli,

principally *E coli*, as well as the group D streptococci (5). It is now recognized that aminoglycosides increase the risk of renal dysfunction in cirrhotic patients (12,32). Routine laboratory parameters such as serum creatinine levels may not accurately reflect the glomerular filtration rate in the face of ascites (33).

New antimicrobial agents including beta-lactam drugs and 4-quinolones are potential alternatives to aminoglycosides in the treatment of ascitic patients. In a recent randomized clinical trial comparing cefotaxime with ampicillin/tobramycin, it was found that this third generation cephalosporin covered approximately 98% of the bacterial pathogens isolated and was less nephrotoxic than the aminoglycoside-containing regimen in cirrhotic patients (34). Although cephalosporins are effective against Gram-negative bacilli, one of the deficiencies of these agents is the lack of activity against enterococci. Cefoxitin has been frequently used in spontaneous bacterial peritonitis, since it provides adequate anaerobic coverage as well as aerobic Gram-negative coverage (35). It is of interest that to date no randomized controlled trial has been performed comparing ampicillin/aminoglycoside with cefoxitin in the treatment of spontaneous bacterial peritonitis syndrome.

With the development of beta-lactamase inhibitors (36), monobactams (aztreonam) (37), and imipenem-cilastatin (38), there are now additional therapeutic alternatives in spontaneous bacterial peritonitis. Experience with these agents and the 4-quinolones is limited at present (37). A recent prospective trial by Grange et al (39) demonstrated promising results with amoxicillin-clavulanic acid in the treatment of spontaneous bacterial peritonitis.

The ideal regimen for this syndrome has yet to be determined. Bacterial culture results and susceptibility data will dictate adjustments in the antibiotic regimen. While the optimal duration of antimicrobial therapy for spontaneous bacterial peritonitis is not known, Fong et al (40) have suggested that the duration of therapy be dictated by the response to treatment. Monitoring of peritoneal fluid neutrophil counts may permit termination of antimicrobials several days earlier than the 'standard' 10 to 14 day course of therapy. Repeat paracentesis is of paramount importance to determine if the leukocyte count in the ascitic fluid is diminishing. It may be useful to repeat this procedure at 48 h to ensure that antibiotic therapy is efficacious, and to rule out secondary bacterial peritonitis (10). As the mortality associated with culture negative neutrocytic ascites is significant, it is prudent to treat this entity in a fashion similar to treatment of spontaneous bacterial peritonitis (9).

Because of the mortality for spontaneous bacterial peritonitis and the high frequency of recurrence, alternative strategies for prevention and treatment must be developed. Prophylactic antibiotic therapy may be of benefit under specific circumstances. Oral nonabsorbable antibiotics have been shown to reduce the incidence of infection in cirrhosis with gastrointestinal hemorrhage (41). Similarly, transient bacteremia has been documented following endoscopic procedures, and perhaps antibiotic prophylaxis may reduce the potential for hematogenous seeding of the peritoneal fluid during invasive procedures. Antibiotic trials will be needed to determine if prophylaxis will be of any benefit. Diuretic therapy has been reported to increase the opsonic activity of ascitic fluid and may be of potential benefit in the prevention of spontaneous bacterial peritonitis (42).

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