Selected summaries

Risk of a first community-acquired spontaneous bacterial peritonitis in cirrhotics with low ascitic fluid protein levels

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The aim of the study by Guarner et al. was to determine a subgroup of cirrhotic patients with ascites and low ascitic fluid protein levels (<1gr/μL) who are at higher risk of developing a first episode of community-acquired spontaneous bacterial peritonitis (SBP) and, therefore, could benefit from long-term prophylactic antibiotic treatment.

One hundred and nine consecutive cirrhotic patients were followed-up prospectively. They were seen after discharge from the hospital, on an out-patient basis, at 2-3 months intervals. The mean follow-up period was 45 weeks. No patient had previous episodes of SBP. Exclusion criteria were ultrasonographic or cytological evidence of hepatocellular carcinoma, severe renal or hepatic dysfunction. Patients with tense ascites or refractory ascites were readmitted to the hospital and treated with paracentesis and albumin infusion. No patient received antibiotic prophylaxis during follow-up. Patients readmitted to the hospital for gastrointestinal bleeding were prophylactically treated with norfloxacin for 7 days.

Diagnosis of ascitic fluid infection was considered according to the following criteria: (1) ascitic fluid neutrophil count>250/μL with or without positive culture (SBP or neutrocytic ascites, respectively) and (2) absence of findings suggesting secondary bacterial peritonitis. A community-acquired SBP was considered in any case diagnosed during the first 72 hours of hospitalization and hospital-acquired SBP when the diagnosis of SBP was established after this period.Patients with normal ascitic fluid neutrophil count at admission, in whom SBP developed during hospitalization, were considered to have hospital-acquired SBP.

RESULTS

28 patients developed SBP during follow-up. Nine infections were acquired during hospitalization. E. coli was the most frequent organism isolated. The 1-year cumulative probability of developing SBP was 35,3%.

Of 20 variables obtained at first admission as possible predictors of SBP, 2 parameters - high bilirubin level (>3,2mg/dL) and low platelet count (<98000cells/μL) were independently associated with the higher risk of developing SBP. The investigators used the Relative Risk (RR) coefficient formula, obtained at multivariate analysis, to divide the patients into two groups: high- and low -risk groups. Half of the patients belonged to each group. In the high-risk group, the one-year propability of developing a first episode of SBP was 55%, compared to 23,5% in the low-risk group, as a consequence of a higher probability of a first community-acquired episode (47,6% vs.13.7%). The probability of developing a first nosocomial-acquired SBP was similar in both groups (13,4% vs. 11.5%).

Forty-five patients died during the follow-up period, with mortality being higher in those who developed SBP. The 1-year probability of survival was significantly higher in the low-risk group.

According to these results the authors concluded that among cirrhotic patients with low ascitic fluid protein, those with high bilirubin levels and/or low platelet count are at higher risk of developing a first episode of community-acquired SBP. Thus, they may represent a subpopulation of patients who could benefit from long-term antibiotic prophylactic treatment with selective intestinal decontamination.

COMMENT

SBP is a severe complication in cirrhotic patients with ascites. Early diagnosis and treatment are critical for improving prognosis. Diagnosis is based on the increased neutrophil count in ascitic fluid (i.e, >250 cells/mm3)

with positive ascitic fluid culture without an evident intra-abdominal surgically treatable source of infection (Tito L, Sleisinger & Fordtran's: Gastrointestinal and Liver Disease, 6th Edition). Even with early diagnosis and treatment the mortality rate is as high as 20%-40%. Because most episodes of SBP are caused by gram-negative bacteria present in the normal flora of the gut, antibiotic treatment should aim at selective decontamination of the gastrointestinal tract.

Not all patients with cirrhosis are equally susceptible to the development of SBP. Patients with the greatest risk are those who have recovered from a previous episode of SBP. The probability of developing a second episode is approximately 70% over the next year (Rimola A et al, Hepatology 1988; 8:27-31.) Another subset of cirrhotic patients at high risk for SBP are those with gastrointestinal bleeding. In these patients, the incidence of bacterial infection is 20%-40%. If only patients with ascites and GI bleeding are considered the incidence is higher (35%-60%) In these subgroups, antibiotic prophylaxis with non-absorbable selective antibiotics (such as norfloxacin) proved to be effective for the prevention of SBP. In the study by Gines et al (Gines P et al, Hepatology 1990; 12:716-724.) long term norfloxacin administration in patients with previous episode of SBP was extremely effective in the prevention of SBP recurrence. The effect of treatment on survival could not be assessed, but treatment with norfloxacin has been found to be a cost-saving measure (Younossi ZM et al, J. Hepatol 1997; 27:295-298). The efficacy of antibiotic prophylaxis in the prevention of SBP and other bacterial infections in cirrhotic patients with GI bleeding has been investigated in five randomized control trials (Rimola A et al, Hepatology 1985; 5:463-467, Soriano G et al, Gastroenterology 1992; 103:1267-1272, Blaise M et al, Hepatology 1994; 20:34-38, Pauwels A et al, Hepatology 1996; 24:802-806, Hsieh WJ et al, Am. J of Gastroenterol 1998; 93:962-966).

A recent metanalysis of these studies showed that prophylactic treatment was not only effective in reducing infection but was also associated with a reduction in short -term mortality (Bernard B et al, Hepatology 1999; 29:1655-1661).

Although antibiotic prophylaxis is currently accepted in cirrhotic patients with gastrointestinal bleeding during hospitalization and in survivors of an episode of SBP, long term primary antibiotic prophylaxis in cirrhotic patients with low ascitic fluid protein levels is controversial. Ruynon was the first to show in a prospective study that 15% of cirrhotic patients with low ascitic protein levels developed SBP during hospitalization, compared to 2% of patients with ascitic protein levels >1g/dl (Runyon BA et al, Gastroenterology 1986; 91:1343-1346). This observation was then evaluated in other prospective studies (Grange JD et al, J. Hepatol 1998; 29:430-436, Llach J et al, Hepatology 1992; 16:724-727, Andreu M et al, Gastroenterology 1993; 104:1133-1138, Novella M et al, Hepatology 1997; 25:532-536).

In these studies the 1-year probability of developing SBP in this subgroup of cirrhotic patients varied from 20%-43%. In the more recent study by Grange et al. (Grange JD et al, J. Hepatol 1998; 29:430-436), the only placebo-controlled trial published up to now, in the six-month follow-up period, the probability of severe gram-negative infection (including SBP) was approximately 11% in the non-treated group compared to 0% in the norfloxacin-treated group. On the other hand only 9% of patients in the placebo group developed SBP, indicating a very low incidence of SBP in this subset of cirrhotic patients. Neither of the studies mentioned above, showed benefit in patient survival. Thus, recommending primary prophylaxis in all these patients is not justified. Additional studies are needed to identify subpopulations of patients with low ascitic protein levels who are at higher risk for SBP.

The study by Guarner et al adds important new information regarding the risk of SBP in cirrhotics with a low ascitic fluid protein level. As described earlier, 109 consecutive patients were studied for a period of 45 weeks. 28 patients developed a first episode of SBP. The one-year cumulative probability of the infection was 35%. Previous studies by the same authors have shown similar results (Novella M et al, Hepatology 1997; 25:532-536).

Twenty variables were estimated as possible predictors of SBP and 2 of them (bilirubin>3,2g/dl and platelet count<98000/mm3) were significantly associated with a higher risk of developing SBP. The investigators used the Relative-Risk formula and divided the patients into low- and high- risk groups (RR<1,09 and RR>1.09, respectively). In the high-risk group the 1-year probability of developing SBP was 55%. This is the highest percentage reported so far. The percentage of patients with Child C cirrhosis was 58%. The RR formula is not easily applicable and perhaps an easier approach would be to use of a combination of the identified parameters at specific cut-off levels. The low platelet count could be attributed to hypersplenism and indirectly to portal hypertension [G Garcia-Tsao et al, Abstract. Hepatology 1997; 26:4 360A (927)]. Furthermore, the Child score was higher in patients who developed SBP than in those who did not.

In previous studies the highest percentages of SBP were observed when more patients with Child C cirrhosis were included. The high bilirubin level also denotes an altered liver function but it could also be attributed to worsening of portal hypertension (the predominant type of bilirubin is not specified).

The study, has succeeded in identifying a subgroup of patients with low ascitic protein levels, with no history of episode of SBP who could benefit from prophylactic antibiotic treatment. Yet, such therapy cannot be recommended until the proposed risk factors are validated in prospective placebo-controlled trials with inclusion of only high-risk patients. Apart from the prevention of infection, the effect of primary prophylaxis on survival should also be estimated. Until then, long-term antibiotic prophylaxis should only be used in cirrhotic patients hospitalized with gastrointestinal hemorrhage or in those with a previous episode of SBP. Also, prophylactic treatment is strongly recommended to prevent SBP recurrence in cirrhotics waiting for transplantation [(N Chalasani et al, Abstract. Hepatology 1997; 26:4 491A (1451)].

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