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Jahangir Khan a; Pekka Pikkarainen a; Anna-Liisa Karvonen a; Tuula Mäkelä a; Markku Peräaho a; Eeva Pehkonen a; Pekka Collin a

a Department of Gastroenterology and Alimentary Tract Surgery, Tampere University Hospital and Medical School, University of Tampere, Tampere, Finland

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Ascites: Aetiology, mortality and the prevalence of spontaneous bacterial peritonitis

JAHANGIR KHAN, PEKKA PIKKARAINEN, ANNA-LIISA KARVONEN, TUULA MÄKELÄ, MARKKU PERÄHAHO, EEVA PEHKONEN & PEKKA COLLIN

Department of Gastroenterology and Alimentary Tract Surgery, Tampere University Hospital and Medical School, University of Tampere, Tampere, Finland

Abstract

Objective. To assess the aetiology, prognosis and prevalence of spontaneous bacterial peritonitis (SBP) in patients hospitalized for ascites. The validity of an elevated (≥11 g/l) serum-ascites albumin gradient (SAAG) in the diagnostic work-up was evaluated. Mortality trends were observed over two periods of time. Material and methods. A total of 231 consecutive patients who underwent diagnostic paracentesis between February 1994 and December 1998 and January 2005 and March 2007 were included in the study. The definition of SBP comprised polymorphonuclear cell count ≥250/mm³ without evidence of other intra-abdominal source of infection. SAAG was obtained and the Child-Pugh classification applied. Survival rates were obtained from medical records. Results. The most common causes of ascites were alcohol liver cirrhosis (n=143; 62%), malignancy (n=30; 13%), non-alcoholic cirrhosis (n=11; 5%) and malignancy with cirrhosis (n=11; 5%). The prevalence of SBP in cirrhosis was 6.7% (95% CI 2.8-10.5%). Overall mortality rates at 1 month, 6 months and 1 year were 22%, 40% and 48%, respectively, and remained unchanged between the intervals. Patients with grade C liver disease had higher 1-month (26% versus 6%), and 6-month (44% versus 27%) mortality rates than grade B patients, but commensurate 1-year mortality (49% versus 47%). SAAG was ≥11 g/l in 85% of patients with obvious portal hypertension and in 30% with malignancy, ascites albumin level ≤9 g/l in 69% and 20%, respectively. Conclusions. Mortality in patients with ascites was high. The occurrence of SBP was relatively low in our series, with a high proportion of alcoholic cirrhosis. SAAG was inaccurate in differentiating ascites caused by portal hypertension or malignancy.

Key Words: Alcohol-induced disorders, ascites, liver cirrhosis, peritonitis, portal hypertension

Introduction

The prevalence of and mortality caused by liver cirrhosis is increasing in Finland concomitant with increasing alcohol consumption [1–5], the overall age-adjusted mortality being 17.2 per 100,000 per year, 26.1 for males and 8.6 for females [6]. These frequencies are similar to those reported in Southern and Western Europe, lower than those in Eastern Europe, but much higher than in the rest of Scandinavia [1,2]. Viral hepatitis is a relatively uncommon cause of liver cirrhosis in Finland.

Besides cirrhosis, portal venous hypertension caused by portal vein thrombosis, malignancy, tuberculosis peritonitis or pancreatitis can cause ascites formation [7–13]. The serum-ascites albumin gradient (SAAG) is widely applied in considering the aetiology of ascites: when SAAG is equal to or more than 11 g/l, portal hypertension is thought to be needed for ascites formation [14–19], whereas a gradient of less than 11 g/l indicates other causes.

Spontaneous bacterial peritonitis (SBP) comprises bacterial infection of the ascitic fluid when there is no evidence of an intra-abdominal source of the infection; that is, perforation or abscess. The pathogenic mechanisms of SBP are thought to be bacterial overgrowth and translocation from the intestine to the ascitic fluid via the general and lymphatic circulation [20–22]. However, bacterial culture is unreliable, and a polymorphonuclear cell (PNC) count of 250/mm³ or more in the ascitic fluid is
considered diagnostic for SBP, regardless of the result of bacterial culture [23,24].

The frequency of SBP is reported to range from 8% to 35% in patients with ascites requiring hospitalization [25-30]. The most common pathogens are Gram-negative bacilli, particularly Escherichia coli, or Gram-positive cocci such as Streptococcus pneumoniae [31,32]. Life expectancy is short, in-hospital mortality is 17–43% [33-36], and only 31–78% survived one year after the onset of SBP [37-39]. Of the patients surviving their first SBP, 33–69% developed a new episode within one year [37,38]. The prognosis is strongly influenced by the Child-Pugh classification: SBP patients with grade C liver disease have higher mortality rates than those with grade B during the first year, 74% and 20%, respectively [40].

The aim of the present study was to assess the aetiology and prognosis of ascites and the occurrence of SBP in patients with ascites. The validity of SAAG in the diagnostic work-up was evaluated. Since alcohol consumption and mortality caused by cirrhosis have increased considerably in Finland, we decided to observe the trends within two periods of time.

Material and methods

The study population comprised consecutive patients who had undergone diagnostic paracentesis for ascites in Tampere University Hospital, with a catchment area of 400,000 inhabitants. Group I was collected between February 1994 and December 1998 and comprised 94 patients. Group II was collected from January 2005 to March 2007 and comprised 137 patients. None of the patients received antibiotic treatment or prophylaxis prior to the investigation. When more than one paracentesis test was performed during the same hospital visit, only the first was included in the analysis. The PNC count, albumin level and bacterial culture were analysed in ascites fluid samples. Serum albumin was measured simultaneously to obtain SAAG. The Child-Pugh classification was applied. The cause of ascites was ascertained on the basis of all available data: disease history, clinical findings and subsequent follow-up. Patients were diagnosed with SBP when the PNC count in ascitic fluid was 250/mm³ or more regardless of the culture results, and when there was no evidence of other intra-abdominal source of infection. Ascites was considered malignant when confirmed clinically, or by cytology or histology. In some cases the aetiology turned out to be multifactorial; for instance, liver cirrhosis and malignant ascites.

Statistical analysis

Statistical testing was done with the SPSS statistical software using the Mann-Whitney U-test, the χ² test, the Kruskal-Wallis H-test and the Fisher exact test, and by calculating the 95% confidence intervals (CIs), when applicable; p-values ≤0.05 were considered statistically significant. Survival rates were measured by obtaining the date of death from the medical records (Statistics, Finland), and depicted by Kaplan-Meier curves. This study was carried out according to the Helsinki Declaration and was approved by the Ethics Committee of Tampere University Hospital.

Results

The demographic data are presented in Table I. The most common aetiology for ascites was alcohol liver cirrhosis, occurring in 62%. There was no difference in the distribution of aetiologies between the study periods. Only five (2.2%) patients had viral hepatitis as the cause of cirrhosis; these cases occurred in the later period and all had hepatitis C. Eleven patients had malignancy with cirrhosis: 1 metastasized pancreatic carcinoma and 10 hepatocellular cancers. In patients with multifactorial aetiologies, 1 had pancreatitis and portal vein thrombosis, 2 had pancreatitis and cirrhosis and 1 patient had portal vein

<table>
<thead>
<tr>
<th>Aetiology</th>
<th>n (male)</th>
<th>Mean age (range)</th>
<th>Child A/B/C</th>
<th>SBP n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>231 (72%)</td>
<td>57 (30-94)</td>
<td>1/49/177 (4)*</td>
<td>12 (5.2%)</td>
</tr>
<tr>
<td>All patients with cirrhosis</td>
<td>165 (74%)</td>
<td>55 (30-82)</td>
<td>0/23/141 (1)</td>
<td>11 (6.7%)</td>
</tr>
<tr>
<td>Alcohol liver cirrhosis</td>
<td>143 (75%)</td>
<td>54 (30-73)</td>
<td>0/19/123 (1)</td>
<td>11 (7.7%)</td>
</tr>
<tr>
<td>Malignancy</td>
<td>30 (63%)</td>
<td>62 (40-94)</td>
<td>0/18/11 (1)</td>
<td>0</td>
</tr>
<tr>
<td>Non-alcoholic cirrhosis</td>
<td>11 (55%)</td>
<td>60 (43-78)</td>
<td>0/3/8</td>
<td>0</td>
</tr>
<tr>
<td>Others**</td>
<td>8 (100%)</td>
<td>64 (45-81)</td>
<td>0/2/6</td>
<td>0</td>
</tr>
<tr>
<td>Unclear</td>
<td>28 (64%)</td>
<td>58 (42-81)</td>
<td>1/6/19 (2)</td>
<td>1 (3.6%)</td>
</tr>
</tbody>
</table>

*No data available; **comprising cardiac (3), veno-occlusive (1) and multifactorial aetiologies (4).
thrombosis and cirrhosis. All patients were followed-up for a minimum of 12 months.

Occurrence of spontaneous bacterial peritonitis

Twelve patients (5.2%) had SBP, and each of them grade C liver disease. Eleven of the 12 had alcohol liver cirrhosis and in 1 patient the cause of ascites remained unknown. None of the SBP patients had active gastrointestinal (GI) bleeding during hospitalization. The prevalence of SBP in patients with cirrhosis was 6.7% (95% CI 2.8–10.5%). The frequency of SBP in patients with cirrhosis was 4.7% in group I (earlier series) and 7.9% in group II (later series), p = 0.532. Only four (33%) SBP patients yielded a positive ascitic fluid bacterial culture.

Mortality

The overall and subgroup mortalities are summarized in Table II. Figure 1 shows the survival curves for different aetiologies of ascites. There were no differences in the mortality figures between group I and group II. Patients with Child-Pugh grade C liver disease had increased early mortality when compared with those with grade B disease, but the percentages were commensurate after one year of follow-up (49% and 47%, respectively). The mortality rate for SBP patients was not increased statistically significantly (p = 0.360).

Serum-ascites albumin gradient

The serum and ascites albumin concentrations and SAAG in all patients and the most typical patient subgroups are summarized in Table III. Patients with malignancy as the cause of ascites were found to have higher serum and ascites albumin levels and lower SAAGs than other patients (p < 0.0001). There was, however, a considerable overlap. The sensitivity and specificity (patients with missing data were omitted) for detecting malignancies using SAAG <11 g/l were 66.7% (18/27) and 91.5% (140/153), respectively. A high ascites albumin level was a more sensitive indicator of malignancy, with 77.8% (21/27) sensitivity and 74.5% (114/153) specificity using a cut-off value of 9 g/l. Nine (75%) out of 12 SBP cases had ≥11 g/l SAAG, 2 cases (17%) had <11 g/l; data were missing in one case (8%). Low serum and ascites albumin levels and elevated SAAG were associated with increased 1-month (p = 0.006, p = 0.008 and p = 0.028, respectively) and 6-month (p = 0.022, p = 0.006 and p = 0.054, respectively), but not 1-year (p = 0.164, p = 0.3 and p = 0.895, respectively) mortality.

Discussion

Alcoholic liver cirrhosis was the most common reason for ascites in our series. There were no significant changes in the distribution of aetiologies for different aetiologies of ascites. There were no

Table II. Overall and subgroup (group I = earlier, group II = later series) mortality among ascites patients.

<table>
<thead>
<tr>
<th>Aetiology</th>
<th>One-month mortality</th>
<th>Six-month mortality</th>
<th>One-year mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% (95% CI)</td>
<td>% (95% CI)</td>
<td>% (95% CI)</td>
</tr>
<tr>
<td>Overall</td>
<td>22 (16–27)</td>
<td>40 (33–46)</td>
<td>48 (41–55)</td>
</tr>
<tr>
<td>Group I</td>
<td>20 (12–28)</td>
<td>38 (28–48)</td>
<td>42 (32–53)</td>
</tr>
<tr>
<td>Group II</td>
<td>23 (15–30)</td>
<td>41 (33–50)</td>
<td>51 (43–60)</td>
</tr>
<tr>
<td>Child-Pugh classification</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>6 (0–13)</td>
<td>27 (14–40)</td>
<td>47 (32–61)</td>
</tr>
<tr>
<td>C</td>
<td>26 (19–32)</td>
<td>44 (36–51)</td>
<td>49 (41–56)</td>
</tr>
<tr>
<td>Aetiology</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol liver cirrhosis</td>
<td>21 (14–28)</td>
<td>36 (28–44)</td>
<td>41 (32–49)</td>
</tr>
<tr>
<td>Malignancy</td>
<td>17 (3–31)</td>
<td>53 (34–72)</td>
<td>77 (61–93)</td>
</tr>
<tr>
<td>Non-alcoholic cirrhosis</td>
<td>18 (0–45)</td>
<td>18 (0–45)</td>
<td>36 (2–70)</td>
</tr>
<tr>
<td>Malignancy with cirrhosis</td>
<td>64 (30–98)</td>
<td>91 (71–100)</td>
<td>100%</td>
</tr>
<tr>
<td>Spontaneous bacterial peritonitis</td>
<td>33 (2–65)</td>
<td>50 (17–83)</td>
<td>58 (26–91)</td>
</tr>
</tbody>
</table>

Cardiac, veno-occlusive and multifactorial aetiologies are not depicted owing to the small number of cases.
or mortality between the observation periods. Child-Pugh C disease was associated with poor short-term outcome, yet not with decreased 1-year survival when compared to Child-Pugh B disease. This finding reflects the large proportion of carcinoma patients in the latter group. In non-malignant cirrhosis, patients with grade C disease had increased 1-year mortality when compared to grade B patients (49% versus 22%). The overall occurrence of SBP (6.7%) in cirrhosis was significantly lower in our series than typically reported (11–35%) [25–29], though Wallerstedt et al. reported a frequency of 8% in Sweden [30]. It has been suggested by Kaymakoglu et al. that the prevalence of SBP is higher in the subgroup of cirrhosis patients whose ascites is caused by viral hepatitis rather than by alcohol [41], whereas Lata et al. came to the opposite conclusion [28]. In the present study, SBP occurred in all except one case with uncertain aetiology concomitantly with alcoholic liver disease. This study confirmed previous data indicating that ascitic fluid culture has a poor sensitivity for SBP. SAAG was higher in patients with apparent portal hypertension, but the gradient did not reliably exclude malignant diseases from portal hypertension. There was significant overlapping of SAAG in different aetiologies of ascites. In fact, the ascites albumin cut-off level of 9 g/l was found to be more sensitive in indicating a possible malignant cause for the ascites.

Mortality in patients with ascites remained similar and relatively high throughout the study period. SBP occurred in only 6.7% of patients with cirrhosis in our series, with a high proportion of alcohol liver disease, and was not clearly associated with decreased survival. We conclude that SAAG was not superior to the determination of ascites albumin concentration in differentiating portal hypertension from malignancy as the cause of ascites.

Acknowledgements

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Table III. Median serum and ascites albumin levels and the serum-ascites albumin gradient (SAAG) in the most common ascites subgroups.

<table>
<thead>
<tr>
<th>Aetiology</th>
<th>S-albumin g/l (range)</th>
<th>A-albumin g/l (range)</th>
<th>A-albumin ≤9 g/l</th>
<th>SAAG g/l (range)</th>
<th>SAAG ≥11 g/l</th>
<th>Data missing n</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>24 (9–44)</td>
<td>7 (0–33)</td>
<td>139 (60%)</td>
<td>16 (0–39)</td>
<td>174 (75%)</td>
<td>19 (8%)</td>
</tr>
<tr>
<td>Apparent portal hypertension</td>
<td>24 (14–42)</td>
<td>6 (0–26)</td>
<td>114 (69%)</td>
<td>16 (7–28)</td>
<td>140 (85%)</td>
<td>12 (7%)</td>
</tr>
<tr>
<td>Alcohol liver cirrhosis</td>
<td>23 (14–39)</td>
<td>6 (0–26)</td>
<td>99 (69%)</td>
<td>16 (7–28)</td>
<td>123 (86%)</td>
<td>8 (6%)</td>
</tr>
<tr>
<td>Non-alcoholic cirrhosis</td>
<td>26 (20–42)</td>
<td>8 (3–26)</td>
<td>7 (64%)</td>
<td>20 (9–23)</td>
<td>8 (73%)</td>
<td>2 (18%)</td>
</tr>
<tr>
<td>Malignancy with cirrhosis</td>
<td>24 (20–31)</td>
<td>4 (1–12)</td>
<td>8 (73%)</td>
<td>19 (14–26)</td>
<td>9 (82%)</td>
<td>2 (18%)</td>
</tr>
<tr>
<td>Malignancy</td>
<td>29 (15–38)</td>
<td>21 (4–33)</td>
<td>6 (20%)</td>
<td>7 (0–25)</td>
<td>9 (30%)</td>
<td>3 (10%)</td>
</tr>
</tbody>
</table>

Declarations of interests: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

References


