BACTERIAL INFECTIONS IN PATIENTS WITH LIVER CIRRHOSIS

Bakterijske infekcije kod bolesnika sa cirozom jetre

Tomislav PREVEDEN

Summary

Introduction. Liver cirrhosis is characterized by a reduced defensive reaction to bacterial infections and patients with cirrhosis are at increased risk of developing infections, sepsis and death. The most common bacterial infections in these patients are spontaneous bacterial peritonitis, urinary tract infection, pneumonia, skin and soft tissue infection and bacteremia. The most common causes are Gram negative bacteria. The aim of this study was to determine the prevalence, localization and etiology of bacterial infections in hospitalized patients with liver cirrhosis. Material and Methods. This retrospective study included 401 patients with liver cirrhosis hospitalized at the Department of Infectious Diseases, Clinical Center of Vojvodina Novi Sad in the period from 2006 to 2010. Bacterial infection was diagnosed according to clinical examination, laboratory findings, radiological examination and bacterial positive culture. Results. The prevalence of bacterial infection was 38.15% (153/401). The most common infections were pneumonia (21.56%), urinary tract infection (20.91%), and spontaneous bacterial peritonitis (18.95%). Localization of infection remained undetermined in as many as 37 patients (24.18%). Bacterial cultures were positive in 32 patients (20.91%), Gram negative bacteria were commonly isolated, mostly Escherichia coli (71.87%). The mortality rate among patients with bacterial infections was 31.37% (48/153). Conclusion. Bacterial infections are often found in patients with liver cirrhosis, the most frequent being pneumonia, urinary tract infection and spontaneous bacterial peritonitis. Gram negative bacteria, especially Escherichia coli were predominant in the etiology. The extent to which bacterial infections are taken into consideration in cases with liver cirrhosis is rather high; however, they are not proved etiologically to the satisfactory level. Key words: Liver Cirrhosis; Bacterial Infections; Risk Factors; Peritonitis; Urinary Tract Infections; Pneumonia; Escherichia coli

Sažetak

Uvod. Cirozu jetre karakteriše smanjena odbrambena reakcija organizma prema infekcijama, te pacijenti sa cirozom jetre imaju povećan rizik od bakterijskih infekcija koje mogu napredovati do sepsis i završiti smrtnim ishodom. Bakterijske infekcije se kod ovih bolesnika najčešće manifestuju kao spontani bakterijski peritonitis, infekcije urinarnog i respiratornog sistema, infekcije kože i mekih tkiva, bakteremije, a najčešći uzročnici su Gram-negativne bakterije. Cilja rada bio je da se utvrdi prevalencija, lokalizacija i etiologija bakterijskih infekcija kod hospitalizovanih bolesnika sa cirozom jetre. Materijal i metode. Retrospektivnom studijom je obuhvaćen 401 bolesnik sa cirozom jetre, hospitalizovan na Klinici za infektivne bolesti u Novom Sadu u periodu 2006–2010. godine. Dijagnoza bakterijske infekcije je postavljena na osnovu: kliničkog pregleda, laboratorijskih analiza, radioloških metoda dijagnostike i bakterioloških kultura krvi, urina, ascitesa i briseva kože. Rezultati. Prisustvo bakterijske infekcije utvrđeno je kod 153 bolesnika sa cirozom jetre (38,15%). Najčešće su bili pneumonija (21,56%), infekcija urinar-nog trakta (20,91%) i spontani bakterijski peritonitis (18,95%). Kod 37 pacijenata sa bakterijskom infekcijom (24,18%), ishodište infekcije nije utvrđeno. Bakterijske kulture su bile pozitivne kod 32 bolesnika (20,91%) i najčešće su izolovane Gram-negativne bakterije, kod 25 bolesnika (78,12%) i to Escherichia coli kod 23 bolesnika (71,87%). Smrtni ishod bakterijskih infekcija je zabeležen kod 48 bolesnika (31,37%). Zaključak. Bakterijske infekcije su često prisутne kod bolesnika sa cirozom jetre i najčešće su lokalizovane na plućima, urinarnom traktu i u abdomenu kao spontani bakterijski peritonitis. U etiologiji dominiraju Gram-negativne bakterije, pre svega Escherichia coli. Kod bolesnika sa cirozom jetre na bakterijske infekcije dovoljno mašimo, ali ih nedovoljno etiološki dokazuju.

Ključne reči: Ciroza jetre; Bakterijske infekcije; Faktori rizika; Peritonitis; Infekcije urinar-nog trakta; Pneumonija; Escherichia coli

Introduction

Bacterial infections are often present in patients with liver cirrhosis, often leading to the progression of liver failure, occurrence of complications such as gastrointestinal bleeding, hepatic encephalopathy, hepatorenal syndrome and acute exacerbation of chronic liver failure. They are present on admission or develop during hospitalization in 30–40% of patients with liver cirrhosis and are responsible for fatal outcome in 30–50% of patients [1-3]. They result from immune dysfunction incurred during cirrhosis and the patients with cirrhosis are at increased risk of acquiring bacterial infection, deve-
Preveden T. Bacterial infections in patients with liver cirrhosis

Bacterial infections of disease. Clinical examination and determination of the acute phase inflammatory markers, such as C-reactive protein (CRP) and procalcitonin (PCT), may raise suspicion of the presence of a bacterial infection, which can be proved by taking bacterial cultures. Exacerbation of the disease and adverse outcome can be prevented by introducing adequate antibiotics as soon as possible [14]. In patients with liver cirrhosis who have had previous bleeding from esophageal varices, spontaneous bacterial peritonitis presence, or some other bacterial infection, it is recommended to apply prophylactic oral antibiotic treatment for seven days per month for the purpose of selective intestinal decontamination [15, 16].

The aim of this study was to determine the prevalence, localization and etiology of bacterial infections in hospitalized patients with liver cirrhosis.

**Material and Methods**

This retrospective study included 401 patients with liver cirrhosis hospitalized at the Department of Infectious Diseases, Clinical Center of Vojvodina Novi Sad during the period from 2006 to 2010. Diagnosis of bacterial infection was based on clinical examination (fever, visible infections of skin and soft tissue), laboratory findings such as elevated markers of acute phase inflammatory markers (CRP, PCT), bacterial positive culture of urine, blood, ascites and skin swabs. Diagnosis of SBP was based on diagnostic paracentesis and finding the absolute number of polymorphonuclears in ascitic liquid ≥250/mm³. Diagnosis of pneumonia was based on chest X-ray which verified the changes in the lung parenchyma corresponding to an inflammatory process. The data were analyzed by statistical package SPSS version 13.0, and the results are shown in graphs and tables created in Microsoft Office Excel 2007.

**Results**

Of 401 patients included in the study, 153 were found to have bacterial infection (38.15%). The most common infections were urinary tract infections, pneumonia and SBP, which were proved in 33/153 (21.56%), 32/153 (20.91%) and 29/153 patients (18.94%), respectively. Infections of skin and soft tissue were found in 13/153 patients (8.49%), while bacteremia was present in 9/153 patients (5.88%).

**Table 1.** Type of bacterial isolates taken for bacteriological cultures (N=32)

<table>
<thead>
<tr>
<th></th>
<th>Escherichia coli</th>
<th>Staphylococcus species</th>
<th>Pseudomonas aeruginosasa</th>
<th>Enterococcus fecalis</th>
<th>Total Ukupno</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine culture/Urinokultura</td>
<td>19</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>21</td>
</tr>
<tr>
<td>Hemoculture/Hemokultura</td>
<td>4</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>9</td>
</tr>
<tr>
<td>Skin swab/Bris kože</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Total/Ukupno</td>
<td>23</td>
<td>7</td>
<td>1</td>
<td>1</td>
<td>32</td>
</tr>
</tbody>
</table>
The test performed failed to determine the localization of bacterial infections in 37/153 patients (24.18%).

Localization of bacterial infection in our patients is shown in Graph 1.

Positive bacterial culture confirmed the etiological diagnosis of bacterial infection in 32/153 patients (20.91%). These 32 positive bacterial cultures were as follows: 21 positive urine culture, 9 positive hemocultures and two positive swab cultures of skin taken from the site of infection. Of 33 patients with signs of bacterial infection of the urinary tract, positive urine culture was obtained in 32/33 (96.97%), all 9 patients with bacteremia had positive bacterial hemocultures (100%). Positive bacteriological culture swab provided bacteriological confirmation only in 2/13 (6.25%) patients with infection of skin and soft tissue. The diagnosis of SBP was based on the increased number of polymorphonuclear leukocytes in ascitic fluid (≥250 /mm³), while the bacterial culture sampled from the ascitic fluid remained sterile. Thirty two patients were diagnosed with pneumonia on the basis of changes in chest X-ray and elevated parameters of acute inflammation phase (CRP, PCT), which proved to be normalized after treatment with antibiotics on the check-up.

Of 32 patients, Gram-negative bacteria were isolated in 25 (78.12%), whereas Gram-positive bacteria were isolated in 7 patients (21.83%). Escherichia coli and Staphylococcus species were isolated in 23 (71.87%) and 7 patients (21.87%), respectively. One patient was found to have Pseudomonas aeruginosa (3.13%) and Enterococcus fecalis was also found in one patient (3.13%). Types of bacterial isolates in patients with liver cirrhosis and bacterial infection are shown in Graph 2.

Regarding the type of the material sample for bacteriological culture, Escherichia coli was isolated in 19 out of 21 bacteriologically positive urine culture, whereas Pseudomonas aeruginosa and Enterococcus fecalis was isolated in one sample, each.

Of 9 positive blood cultures, Staphylococcus spp. was isolated in 5 samples and Escherichia coli in 4 samples. Staphylococcus spp. was isolated from both positive skin swab samples. The type of bacterial isolates taken for bacteriological culture is given in Table 1.

Lethal outcome of bacterial infections in patients with liver cirrhosis was reported in 31.37% of cases (48/153), while healing was achieved in 68.63% of patients (105/153).

Discussion

The results of this study indicate that bacterial infections often occur in patients with liver cirrhosis, in 38.15% of cases, which is consistent with the earlier studies. A similar prevalence of bacterial infection in patients with cirrhosis of 37.8% was reported by M. Drang et al., a group of Romanian authors, who stressed that the infection often passed without symptoms [17]. It is believed that the patients with liver cirrhosis and gastrointestinal bleeding are particularly prone to bacterial infections, which occur in about 45% of cases [7]. Having analyzed the occurrence of sepsis in patients with cirrhosis, Arvaniti V. et al. concluded that the occurrence of sepsis and multiorgan dysfunction in patients with terminal liver cirrhosis increased mortality four times [18]. Lethal outcome in 31.37% of patients with bacterial infection and cirrhosis in our study is consistent with the literature data.

According to the literature the most common types of bacterial infections in patients with liver cirrhosis are SBP, urinary tract infections and pneumonia, followed by infections of the skin and soft tissue infections, bacteremia and other infections [8, 9]. The distribution of types of bacterial infections in our study is consistent with the literature data since it has been found that the most commonly occurring infections are urinary tract infection (21.56%), pneumonia (20.91%), and SBP (18.94%).
Similar distribution of types of bacterial infections was found by Preda CM et al., a group of Romanian authors as well as by Fernandez J et al., a group of Spanish authors [19, 20]. What is worrying is the fact that the type of infection remained undetermined in ¼ (24.18%) of the patients in our study. The available literature does not offer such information because the studies only show the distribution of type or localization of infection without specifying whether there are undetermined types of infections. The group of patients with “undetermined type of infection” consisted of patients who had prolonged fever and elevated acute phase parameters, which disappeared after antibiotic treatment. It should be emphasized that this study was retrospective and data were not recorded precisely during hospitalization, CRP and PCT were not routinely taken in all patients, the patients did not undergo a detailed examination in order to confirm the presence of infection. In other words, more attention was paid to the treatment of liver cirrhosis and its decompensation than to the type of infection. Diagnostic paracentesis was not performed routinely in patients with ascites, and since it is known that SBP often goes asymptomatic, diagnostic paracentesis should be done in case of occurrence of ascites [21, 22].

The results of bacterial cultures in our study agree with literature data which also indicate that Gram-negative bacteria, especially Escherichia coli are predominant. According to recent data, approximately 65% of bacterial infections in patients with liver cirrhosis are caused by Gram-negative bacteria, that being somewhat less than in our study where that participation was 78.12% [21]. It is important to emphasize that our study gave data on positive bacterial cultures in only 20.91% of the cases, which is not satisfactory because this percentage is much higher in the literature, ranging from 40-70% [2, 19]. This small number of positive bacterial cultures in our study is unsatisfactory, but it should be taken into consideration that this was a retrospective study of hospitalized patients, whose samples for bacterial cultures were not taken routinely or frequently enough, that there may have been some inappropriate sampling, storage and transport of samples. In addition, a considerable number of patients had been taking antibiotics before sampling for bacteriological culture and the presence of a bacterial infection in hospitalized patients was not always taken into consideration.

Conclusion

Bacterial infections often occur in patients with liver cirrhosis. Therefore, they should be taken into consideration in patients with liver cirrhosis and acute exacerbation of the disease, i.e. decompensation in order to make the early etiological diagnosis and introduce antibiotics that cover the most common Gram-negative and Gram-positive bacteria as early as possible. A great number of positive bacterial cultures must be obtained in order to enhance the favorable outcome of bacterial infections in patients with liver cirrhosis. Even before receiving the results of bacterial cultures, biomarkers of acute phase of inflammation, such as C-reactive protein and procalcitonin, must be looked for because they raise suspicion of the presence of bacterial infection. A detailed clinical examination, sampling material for bacteriological culture, and paracentesis of ascites and chest X-ray may confirm the presence of bacterial infection, and thus appropriate antibiotic therapy can be introduced on time. It most often involves the application of third generation cephalosporins or quinolones for a period of 10-14 days. Consequently, if bacterial infections in patients with liver cirrhosis are taken into consideration, their influence on mortality can be decreased, the duration of treatment can be shortened and treatment costs can be reduced.

References