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Full Length Research Paper

Emergence of gram positive bacteria as a causal agents of spontaneous bacterial peritonitis

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It has been suggested that the profile of spontaneous bacterial peritonitis has changed, and severe infections caused by resistant bacteria species have started to emerge. The aim of this work was to evaluate the recent changes in bacteria causing spontaneous bacterial peritonitis in cirrhotic patients. In this study, records of laboratory and ascitic fluid cultures data of 100 cirrhotic patients, with SBP, in the retrospective period from October 2007 to October 2008 and 120 patients with SBP in the prospective period from October 2011 to October 2012, were subjected to laboratory tests, ascitic fluid sent for bacterial culture along with routine biochemical and cytological examination were done. Results showed that the overall culture positivity rate was higher in prospective study period 39(32.5 %) versus retrospective period 35(35 %) p>0.05 and the main bacterial isolates were *E. coli* and *Klebsiellapneumoniae*. Gram positive bacteria (GPB) were isolated more frequently in the prospective than retrospective period 16 (41%) versus 10 (28.6%). Conclusion: There is an emergence of Gram positive bacteria as a causal agents of SBP.

Keywords: Spontaneous bacterial peritonitis, gram-positive bacteria and infection.

INTRODUCTION

Spontaneous bacterial peritonitis (SBP) is a frequent and serious complication that occurs in 10-30% of patients with cirrhosis and ascites. SBP is associated with high mortality rates 20-40% that were previously attributed to the severity of cirrhosis (Subhas et al., 2013). Recently several factors have been shown to contribute to the prognosis of the disease; these include associated bactera emia, hepatocellular carcinoma and the microbiological characteristics of the causative agent of the infection (Nevine et al., 2008). Over 70% of the SBP episodes were produced by Gram-negative enteric bacilli-*Escherichia coli* and *Klebsiella pneumonia*, which were the frequently isolated micro-organisms (Garcia-Tsao 2004). It has been suggested that the microbiological causes of SBP and the susceptibility of the causative organisms to antibiotics are changing. Changes in the microbial causes of SBP and bacterial antibiotic resistance patterns vary according to the location and time (Nevine et al., 2008; Jiu-Cong et al., 2010). This recent changes in its microbial etiology may have several important implications for the management and treatment of SBP and suggestions have been made for verifying the efficacy of current guidelines. Empiric

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antibiotic therapy should be initiated before the results of ascitic fluid cultures are available, which is guided by knowledge of the microbial spectrum of spontaneous bacterial peritonitis in a particular population (Amjad et al., 2011).

The aim of this study was to evaluate the possible changes of isolated bacteria in Egyptian cirrhotic patients with SBP.

PATIENTS AND METHODS

This study has been conducted at the department of internal medicine, Ain Shams University hospital Egypt after approval by the ethical committee of our institution.

Retrospective study period (October 2007 to October 2008).We retrospectively examined the medical records and the microbiology laboratory files of patients diagnosed clinically with SBP and who yielded positive results in ascitic fluid culture. The records were reviewed for the following data: age, sex, liver disease, Child–Pugh score, cause of cirrhosis, gastrointestinal bleeding, renal impairment, blood and ascitic fluid laboratory data and culture results.

Prospective study period **(**October 2011 to October 2012**):**

All patients with decompensated cirrhosis, ascites and clinical signs of SBP were enrolled in the study. The diagnosis of cirrhosis was established on the basis of clinical examination, biochemical test and instrumental examination and/or liver biopsy. The severity of the liver disease in each patient was classified at entry according to the Child-Pugh scores. The diagnosis criteria for SBP involved a combination of positive ascitic fluid culture and an ascetic poly morpho nuclear (PMN) leukocyte count of >250 cells/mm3 with no evidence of intra-abdominal source of infection. The diagnosis of culture-negative neutrocytic ascites (CNNA) was based on a negative ascitic bacterial culture, PMN count >250 cells/mm3, there was no antibiotics given within 7 days and no evident intra-abdominal source of infection or an alternative explanation for the elevated PMN count (Sheer and Runyon 2005). We excluded patients who showed a sign of free air in their abdominal X-ray and had a recent history of surgery or trauma which increased the possibility of secondary peritonitis rather than SBP.

Detailed history , physical examination and Laboratory tests including complete blood count, prothromb in activity (PTA) and routine liver , kidney biochemistry tests blood glucose , viral hepatitis markers, abdominal ultra sonography and , diagnostic paracentesis was performed under aseptic measures with a biochemical analysis(LDH, glucose, albumin, total protein, SAAG), cytological examination and bacteriological examination including (Gram stain, Leishman stain, Ziehl Neelsen stain, total leukocytic count, differential leucocyte count, microbiological culture at admission **Bacterial culture:** Ascitic fluid was placed in blood culture bottles, incubated at 37℃ for 7 days, and examined daily for turbidity. At least 10 mL of ascitic fluid was inoculated into in (BD BACTEC) blood culture bottle. All isolated organisms in the culture were tested for antimicrobial susceptibility according to the diffusion methods. To assess the clinical outcome in those patients, the response to treatment was assessed 72h after Cefotaxime 2 gmi.v every 8 hours and mortality rate within 30 days. The initial responses included resolution of fever, leucocytosis, and PML in ascitic fluid; and failure of response consisted of absence of improvement or clinical deterioration or death of patients. Treatment failure is defined as the reduction in the PMN count of less than 25% as compared with the pre-treatment value and/or if the culture failed to change to negative culture (Tolga et al., 2010).

The collected data were coded, tabulated, and statistically analyzed using SPSS program, software version 17. Using the chi-square and the t-test The data were considered significant if p values were less than 0.05.

RESULTS

During the retrospective period100 episodes of SBP were clinically recorded in the retrospective study period and 120 cases were noted in prospective study period. The clinical characteristics of the patients showed that Hepatitis C virus followed by hepatitis B virus were the most frequent causes of liver cirrhosis, abdominal pain and fever were the most common presenting symptoms in both study periods (P > 0.05).

The clinical characteristics of both groups are shown in (table1).

Ascitic fluid culture positive rate was (39(32.5 %) in the prospective study versus (35(35 %) the retrospective study period (p>0.05), Gram-negative bacilli were the main organisms isolated during the two study periods (23 (59%) in the prospective versus 25(71.4%) in the retrospective P< 0.05) and *E. coli* was the most common species recovered from patients followed by *K. pneumoniae*. (19 (48.7%) and 4 (10.3 %) versus 20(57.1%) and 5 (14.3%); P < 0.05 in the prospective as opposed to retrospective period). Gram- positive bacteria were found more frequently in SBP patients of the prospective as opposed to retrospective period 16 (41%) episodes were caused by GPB in the prospective period and were caused by *Staphylococcus epidermidis* (8(20.5%)and *Streptococcus viridians* (8(20.5 %), while 10 (28.6%) patients 5 (14.3 %) were caused by *Staphylococcus epidermidis* and 5 (14.3 %) were caused by *Streptococcus viridans* in the retrospective period(table 2).

Assessment of clinical response 72 hours after initial antimicrobial therapy in patients of prospective study period showed that treatment failure rate was 14/120

Table 1.

	Retrospective period	Prospective period
Age	51+9	51+8
Child A/B/C	5(5%)/50(50%/45(4%)	24(20)/30(25%)/66(55%)
Ascitic PMN	406+77	621+86
A.Albumin (g/dl)	1.1+0.5	1.2+0.5
A.Glucose (mg/dl)	117+10	124+14
A.LDH (IU/L)	210+20	196+17
SAAG	1.6+0.4	1.5+0.38

Tables 2. Ascitic culture results in both study periods

Ascitic culture		**Retrospective**	**Prospective**	**P**
Negative culture		65(65%)	81(67.5%)	>.05
Positive culture		35(35%)	39(32.5%)	>.05
Gram –ve	***E-coli***	20(57.1%)	19(48.7%)	<.05
	Klebsiellapneumoniae	5(14.3%)	4(10.3%)	<.05
Gram +ve	***Staphylococcus epidermidis***	5(14.3%)	8(20.5%)	<.05
	Streptococcus pneumoniae	5(14.3%)	8(20.5%)	<.05

(11.7%) and mortality within 30 days was 18/120 patients (15%).

DISCUSSION

Empirical antibiotic therapy with a high activity against the most frequently seen microorganisms in SBP should be initiated before the definitive results of ascitic fluid cultures have been ascertained. The current spectrum of causative microorganisms and their antibiotic sensitivity should be redefined at regular time intervals. In our study classic spontaneous bacterial peritonitis was diagnosed in (39(32.5 %) versus (35(35 %), where as its variants, culture negative neutrocytic ascites was diagnosed in 81(67.5%) versus (65(65%) in the prospective opposed to the retrospective study period respectively. None of the patients in the study was diagnosed as bacterascites. (Iqbal et al., 2004), supports our findings as they reported classic spontaneous bacterial peritonitis in 33.3% of the cases whereas culture negative neutrocytic ascites was found in 66.7% of the cases. None of the patients in their study was diagnosed having bacterascites. (Rajput et al., 1999). found classic spontaneous bacterial peritonitis in 34.5% of their patients whereas culture negative neutrocytic ascites and bacterascites in 62.1% and 3.4% of their cases respectively. Another study by (Mohamed et al., 2010), the values are classical SBP 37.93%, CNNA 55.17% and BA 6.89%. The low proportion of positive ascitic fluid cultures is probably due to that SBP is an infection of low microbial concentration (Badawy et al., 2013). For the same reason, a therapy based on the isolation of the responsible bacteria is seldom achievable and antibiotic treatment cannot be delayed to the moment when microbiological results are available (Badawy et al., 2013).

E. coli was and still the most frequent offending organism as a cause of SBP in cirrhotic patients with ascites 19 (48.7%) versus 20(57.1%) in the prospective as opposed to retrospective period, however, there is an increasing incidence of Gram-positive bacteria in the prospective opposed to retrospective period 16(40%) versus 10(28.6%). These results are in line with the findings of other studies on microbial spectrum of spontaneous bacterial peritonitis. (Mohamed et al., 2010), reported *E. Coli* in (61.55%) and *Streptococci* in (15.38%) in their study while **Zhang** and his colleagues (Zhang et al., 2000), reported that *E. coli* was the most common species (47.8%) recovered from patients; followed by *K. pneumoniae* (28.1%). Gram- positive bacteria were found more frequently in SBP patients of the prospective as opposed to retrospective period (25% versus 13%). The increasing pattern of Gram-positive bacteria in SBP has been attributed to antibiotic therapy used as primary or

secondary prophylaxis. Norfloxacin, ciprofloxacin and ofloxacin are effective drugs for the prevention of bacterial infections in cirrhotic patients, they show a broader antimicrobial spectrum and higher systemic absorption characteristics that may be prone to the development of infections caused by gram-positive cocci more drug resistant gram-negative bacilli in long-term treatment (Wong et al., 2005).

Moreover, the increasing number of invasive procedures and hospitalizations of cirrhotic patients (which promotes the presence of these kinds of bacteria). As the bacterial translocation is the main pathogenesis in SBP, also there is a possibility for Gram-positive bacteria to reach ascitic fluid from the same source and by the same route[14,15]. All these features indicated that the microbial etiology and spectrum of SBP in cirrhosis may have changed under the circumstances.

Assessment of clinical response 72 hours after initial antimicrobial therapy in patients of prospective study period showed that treatment failure rate was 14/120 (11.7%) and mortality within 30 days was 18/120 patients (15%).

The increase in antibiotic resistant bacteria has become a real threat to the effective treatment of SBP infections in recent years (Park et al., 2003). Cephalosporins may no longer be effective in the empiric treatment of SBP cases, this may explain the high treatment failure and mortality rate in patients of this study as they were all initially treated with cephalosporins, Other factors which may be responsible include under-nourishment, poverty, and advanced liver disease. A recent study suggested that cirrhotics who were on antibiotic prophylaxis were more likely to be infected with ESBL-producing organisms, and should be started empirically on second line antibiotics such as carbapenems upon diagnosis (Garcia-Tsao 2001).

CONCLUSION

The bacterial isolates from spontaneous bacterial peritonitis in cirrhotic patients with ascites had shown an increasing incidence of SBP caused by Gram-positive bacteria. This may have some implications in their management, and should be taken into account in empirical antibiotic treatment.

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