

Low incidence of spontaneous bacterial peritonitis in asymptomatic cirrhotic outpatients

Jean-François Cadranel, Jean-Baptiste Nousbaum, Christophe Bessaguet, Pierre Nahon, Eric Nguyen-Khac, Richard Moreau, Thierry Thévenot, Christine Silvain, Christophe Bureau, Olivier Nouel, Christophe Pilette, Thierry Paupard, Arnaud Pauwels, Thierry Sapey, Jean-Didier Grangé, Albert Tran

Jean-François Cadranel, Liver, Gastroenterology and Nutrition Department, Centre Hospitalier Laennec, 60100 Creil, France

Jean-Baptiste Nousbaum, Department of Hepato-Gastroenterology, University Hospital La Cavale Blanche, 29609 Brest, France

Christophe Bessaguet, Department d'Information Médicale, Centre Hospitalier, 29000 Quimper, France

Pierre Nahon, Department of Hepato-Gastroenterology, Hôpital Jean Verdier, 93140 Bondy, France

Eric Nguyen Khac, Department of Hepato-Gastroenterology, Amiens University Hospital, 80054 Amiens, France

Richard Moreau, Department of Hepatology, Hôpital Beaujon, 92100 Clichy, France

Thierry Thévenot, Department of Hepatology, University Hospital Jean Minjoz, 25030 Besançon, France

Christine Silvain, Department of Hepato-Gastroenterology, Poitiers University Hospital, 86000 Poitiers, France

Christophe Bureau, Department of Hepato-Gastroenterology, Purpan Hospital, 31059 Toulouse, France

Olivier Nouel, Department of Hepato-Gastroenterology, Centre Hospitalier de Saint Brieuc, 22027 Saint Brieuc, France

Christophe Pilette, Department of Hepato-Gastroenterology, Centre Hospitalier, 72037 Le Mans, France

Thierry Paupard, Department of Hepato-Gastroenterology, Centre Hospitalier de Dunkerque, 59240 Dunkerque, France

Arnaud Pauwels, Department of Hepato-Gastroenterology, Centre Hospitalier de Gonesse, 95503 Gonesse, France

Thierry Sapey, Department of Hepato-Gastroenterology, Centre Hospitalier de Chateauroux, 36000 Chateauroux, France

Jean-Didier Grangé, Department of Hepatology, Hôpital Tenon, 75020 Paris, France

Albert Tran, Digestive Center, University Hospital of Nice, 06202 Nice, France

Club Francophone pour l'Etude de l'Hypertension Portale; Association Nationale des Hépatogastroentérologues des Hôpitaux Généraux de France

Author contributions: Cadranel JF and Nousbaum JB equally contributed to this work; Cadranel JF, Nousbaum JB, Silvain C, Pauwels A and Tran A designed the study; Bessaguet C analyzed the data; Cadranel JF and Nousbaum JB wrote the paper; Cadranel JF, Nousbaum JB, Nahon P, Nguyen-Khac E, Moreau

R, Thévenot T, Silvain C, Bureau C, Nouel O, Pilette C, Paupard T, Pauwels A, Sapey T, Grangé JD and Tran A collected the data and approved final version of the manuscript.

Correspondence to: Jean-François Cadranel, MD, Professor CMH, Liver, Gastroenterology and Nutrition Department, Centre Hospitalier Laennec, BP 72, 60100 Creil, France. jfrancois.cadranel@ch-creil.fr

Telephone: +33-3-44616443 Fax: +33-3-44616440

Received: July 4, 2012 Revised: September 24, 2012

Accepted: November 14, 2012

Published online: March 27, 2013

Abstract

AIM: To compare the incidence of spontaneous bacterial peritonitis in cirrhotic outpatients and inpatients undergoing therapeutic paracentesis

METHODS: From January 1 to May 31, 2004, 1041 patients from 70 different hospitals underwent 2123 therapeutic abdominal paracentesis (AP) performed as an outpatient procedure in 355 and as inpatient procedure in 686 cases respectively. The following parameters were compared prospectively between outpatients and inpatients: spontaneous bacterial peritonitis (SBP) prevalence, age, gender, cause of cirrhosis, symptoms, score and grade according to Child-Pugh classification, cirrhosis complications, antibiotics treatment, serum creatinine, platelet count and ascitic protein concentration.

RESULTS: SBP was observed in 91 patients. In the whole population the SBP prevalence was 8.7% (95%CI: 7.2-10.6) it was 11.7% (95%CI: 9.5-14.3) in inpatients and 3.1% (95%CI: 1.7-5.5) in outpatients ($P < 0.00001$). SBP prevalence was 8.3% (95%CI: 4.3-15.6) in symptomatic outpatients vs 1.2% (95%CI: 0.4-3.4) in asymptomatic outpatients ($P < 0.002$). Patients undergoing outpatient AP were significantly different from

those undergoing inpatient AP; they were older (61.1 ± 11.1 years *vs* 59.4 ± 11.7 years; $P = 0.028$), cause of cirrhosis was less often alcohol (83.7 *vs* 88.2% ; $P < 0.001$), Child-Pugh score was lower (8.9 *vs* 10.1 ; $P < 0.001$) and more often B than C (63.7% *vs* 38% ; $P < 0.001$). In addition, in outpatients the platelet count was higher (161 ± 93 Giga/L *vs* 143 ± 89 Giga/L; $P = 0.003$), serum total bilirubin concentration was lower (38.2 ± 60.7 $\mu\text{mol/L}$ *vs* 96.3 ± 143.3 $\mu\text{mol/L}$; $P < 0.0001$), and ascitic protein concentration higher (17.9 ± 10.7 g/L *vs* 14.5 ± 10.9 g/L; $P < 0.001$) than in inpatients.

CONCLUSION: In asymptomatic cirrhotic outpatients, the incidence of spontaneous bacterial peritonitis is low thus exploratory paracentesis could be avoided in these patients without significant risk.

© 2013 Baishideng. All rights reserved.

Key words: Liver cirrhosis; Ascites; Ascitic fluid; Bacterial infections; Paracentesis; Peritonitis

Cadranel JF, Nousbaum JB, Bessagnet C, Nahon P, Nguyen-Khac E, Moreau R, Thévenot T, Silvain C, Bureau C, Nouel O, Pilette C, Paupard T, Pauwels A, Sapey T, Grangé JD, Tran A. Low incidence of spontaneous bacterial peritonitis in asymptomatic cirrhotic outpatients. *World J Hepatol* 2013; 5(3): 104-108 Available from: URL: <http://www.wjgnet.com/1948-5182/full/v5/i3/104.htm> DOI: <http://dx.doi.org/10.4254/wjh.v5.i3.104>

INTRODUCTION

Therapeutic abdominal paracentesis (AP) is the recommended treatment for patients with ascites resistant or refractory to medical treatment^[1]. Many cirrhotic patients with ascites are regularly hospitalized for AP. Good clinical practice guidelines of the American Association for the Study of Liver Diseases^[2] recommend performing ascitic fluid analysis in association with AP in order to search for two serious complications: bacterial peritonitis and neutrocytic ascites^[3,4]. However, except in cases where infection is suspected, the usefulness of this approach is not clearly established in outpatients. Indeed several retrospective and prospective studies have shown that spontaneous bacterial peritonitis (SBP) is very rare or even absent in outpatients^[5-10]. These data are probably related to differences in demographic data and liver diseases severity and/or characteristics of ascitic fluid between inpatients and outpatients. However such probable differences have not been properly studied. The present study is ancillary to the prospective multicenter study of the usefulness of Multistix[®] strip for the detection of SBP already published^[11]. The aims were to compare the incidence of SBP in outpatients and inpatients undergoing AP and to look for factors associated with low SBP prevalence in outpatients (if these data were confirmed).

MATERIALS AND METHODS

Patients

The present study is a retrospective analysis of data from a prospective study involving all consecutive cirrhotic patients with ascites, undergoing therapeutic abdominal paracentesis (AP) followed from January 1 to May 31, 2004 in 70 French participating centers under the authority of the "Club Francophone pour l'Etude de l'Hypertension Portale" (CFHTP) and the "Association Nationale des Hépatogastroentérologues des Hôpitaux Généraux de France" (ANGH). Centers affiliated with the CFHTP were academic hospitals and centers affiliated with the ANGH were primary referral hospitals.

Diagnosis of cirrhosis relied on clinical, biological and morphological criteria. Patients were admitted either for treatment of ascites or for complications of cirrhosis (*i.e.*, infection, gastrointestinal bleeding, hepatic encephalopathy, alcoholic hepatitis, acute renal failure, hepatocellular carcinoma), or were treated in an ambulatory setting (outpatients). These outpatients were eligible for inclusion whether they presented with or without signs of SBP, according to the following criteria defined by Jeffries *et al*^[5] and Castellote *et al*^[10]: temperature above 38°C or below 36.5°C , chills, abdominal tenderness suggestive of peritonitis, developing or worsening hepatic encephalopathy, gastrointestinal bleeding within the last 15 d, acute renal failure (defined by an increase in the serum creatinine level to above 133 $\mu\text{mol/L}$) and arterial hypotension (systolic arterial pressure below 80 mmHg). These signs, suggestive of infection, were carefully searched for at admission by a senior physician. Exclusion criteria were: chylous ascites and ascites not related with portal hypertension (*i.e.*, pancreatic ascites, peritoneal tuberculosis, and peritoneal carcinomatosis). Patients with hemoperitoneum complicating hepatocellular carcinoma were also excluded^[11].

Paracentesis

Ascitic fluid was examined for leukocyte counts and polymorphonuclear leukocytes counts/ μL , total protein and bacteriological status. Ascitic fluid was centrifuged at 2500 g for 10 min. A smear was stained with Giemsa. Total and differential cell counts were made with an optical microscope. Bacterial cultures were obtained by bedside inoculation of 10 mL of ascitic fluid into aerobic and anaerobic bottles (BacT/ALERT, Biomérieux, France)^[12].

Each sample of ascitic fluid was tested for urine using Multistix 8 SG[®] according to the technique described by the manufacturer. All reagent areas were immersed in ascitic fluid and the strip was removed immediately^[11].

The strips were tested independently by each investigator and by a nurse, each of whom were unaware of the results of ascitic cytological examination at the time of reading. All strips were read manually^[11]. AP was repeated during the period of the study for a maximum of 8 paracenteses for each patient. The study protocol was approved by the local ethics committee of the University Hospital of Brest, France.

Table 1 Characteristics of the 1041 patients who underwent diagnostic or therapeutic paracentesis

| Characteristics | |
|---|--------------|
| Male, <i>n</i> (%) | 748 (71.9) |
| Age (yr), mean (range) | 60 (25-93) |
| Median number of paracenteses | 2 |
| Cause of cirrhosis, <i>n</i> (%) | |
| Alcohol | 840 (80.7) |
| Alcohol + viral hepatitis (B or C) | 52 (5) |
| Viral hepatitis | 88 (8.4) |
| Hemochromatosis | 6 (0.6) |
| Others | 55 (5.3) |
| Child-Pugh score, <i>n</i> (%) | |
| A | 0 |
| B | 470 (45.2) |
| C | 571 (54.8) |
| Prothrombin time (%), median (range) | 52 (20-85) |
| Serum bilirubin (μmol/L), median (range) | 30 (10-812) |
| Albumin (g/L), median (range) | 29 (16.5-53) |
| Platelet count (10 ⁹ cells/mL), median (range) | 130 (15-684) |
| Serum creatinine (μmol/L), median (range) | 80 (22-474) |

Table 2 Comparison between outpatients and inpatients

| | Outpatients | Inpatients | <i>P</i> value |
|--------------------------------------|-------------|--------------|----------------|
| Age (yr) | 61.1 ± 11.1 | 59.4 ± 11.7 | < 0.03 |
| Alcohol (%) | 83.7 | 88.2 | < 0.001 |
| Child-Pugh score (mean) | 8.9 | 10.1 | < 0.001 |
| Child-Pugh score B vs C (%) | 63.7/36.3 | 38.0/62.0 | < 0.001 |
| Bilirubin (μmol/L) | 38.2 ± 6.7 | 96.3 ± 143.3 | < 0.0001 |
| Platelets (10 ⁹ cells/mL) | 161 ± 93 | 143 ± 89 | < 0.003 |
| Ascitic protein concentration (g/L) | 17.9 ± 10.9 | 14.5 ± 10.9 | < 0.001 |

Statistical analysis

The following parameters were compared between outpatients and inpatients: SBP prevalence, age, gender, cause of cirrhosis, symptoms, score and grade according to Child-Pugh classification, cirrhosis complications, antibiotics treatment, serum creatinine, platelet count and ascitic protein concentration.

Statistical analysis was performed using the SPSS package (SPSS Inc., Chicago, United States). Results were expressed as mean and standard deviation with range unless specified otherwise. Quantitative characteristics (age, bilirubin, platelet count, *etc.*) were compared between the two patients populations by Student's *t* test. Depending on the qualitative characteristics (cause of cirrhosis, Child-Pugh score, *etc.*) proportional differences between the two populations were studied by χ^2 test.

RESULTS

One thousand and forty one cirrhotic patients with ascites, undergoing therapeutic paracentesis (AP) were studied. A total of 2123 paracenteses were performed. The procedure was performed as an outpatient procedure in 355 cases (34.1%) and in hospitalized patients (inpatients) in 686 cases (65.9%). The main characteristics of the patients are shown in Table 1; cirrhosis was related with alcohol in 80.6% of cases, to viral hepatitis in 8.5% patients

Table 3 Prevalence of spontaneous bacterial peritonitis in asymptomatic outpatients in main published series

| Ref. | No. of patients | No. of paracenteses | Prevalence of spontaneous bacterial peritonitis |
|---|-----------------|---------------------|---|
| Jeffries <i>et al</i> ^[5] | 29 | 118 | 0 (0%) |
| Evans <i>et al</i> ^[8] | 427 | 427 | 15 (3.5%) |
| Romney <i>et al</i> ^[9] | 67 | 270 | 0 (0%) |
| Castellote <i>et al</i> ^[10] | 40 | 204 | 1 (0.5%) |
| Present study | 355 | 976 | 1.2 |

and to several causes in 5% (Table 1).

Data concerning Multistix[®] performance for the SBP diagnosis have been published elsewhere and will not be described here^[11]. One hundred and seventeen SBP were observed in 91 out of 1041 patients undergoing 2123 paracenteses. Cultures were positive in 56 patients. SBP incidence was 8.7% (95%CI: 7.2-10.6) in the whole population, 11.7% (95%CI: 9.5-14.3) in inpatients and 3.1% (95%CI: 1.7-5.5) in outpatients (*P* < 0.00001). SBP incidence was 8.3% (95%CI: 4.3-15.6) in symptomatic outpatients vs 1.2% (95%CI: 0.4-3.4) in asymptomatic outpatients (*P* < 0.002).

Patients undergoing AP as an outpatient procedure differed significantly from those undergoing inpatient AP (Table 2); outpatients were older (61.1 ± 11.1 vs 59.4 ± 11.7 years, *P* = 0.028), cause of cirrhosis was less often alcohol (83.7% vs 88.2%; *P* < 0.001), Child-Pugh score was lower (mean score was 8.9 vs 10.1; *P* < 0.001) and more often B than C (63.7% vs 38%, *P* < 0.001). In addition, in outpatients the platelet count was higher [(161 ± 93) × 10⁹ cells/mL vs (143 ± 89) × 10⁹ cells/mL; *P* = 0.003], serum total bilirubin concentration was lower (38.2 ± 60.7 μmol/L vs 96.3 ± 143.3 μmol/L; *P* < 0.0001), and ascitic protein concentration was higher (17.9 ± 10.7 g/L vs 14.5 ± 10.9 g/L; *P* < 0.001) than in inpatients (Table 2).

DISCUSSION

In this study, 1041 cirrhotic patients underwent 2123 paracenteses with ascitic fluid analysis and two Multistix 8 SG strip determination^[11]. Eighty percent of the patients had alcoholic cirrhosis and 44.2% were stage C cirrhosis according to the Child-Pugh classification. The incidence of SBP in asymptomatic outpatients was 1.2%. Our study thus confirms the low incidence of SBP in outpatients considered as asymptomatic according to well-defined clinical criteria^[5,8,9]. In the two studies published in abstract form only, the incidence of SBP in outpatients was 0% in the first study (78 paracenteses performed in 26 patients)^[6] and 0% in the second (173 paracenteses study performed in 51 patients)^[7]. In the 4 studies published as peer-reviewed articles, including a paracenteses number ranging from 118 to 427, the incidence of SBP ranged from 0% to 3.5% (Table 3). In addition, Runyon^[2] recently reported a 2% incidence of SBP in a series of 400 paracenteses performed in two years in an outpatient setting. In a study performed by one of the coauthors

of this study, including more than 500 paracenteses of ascitic fluid in cirrhotic ascitic patients on long-term ofloxacin treatment, the incidence of bacterial peritonitis was zero^[9]. In their retrospective study of 427 cirrhotic patients seen in a single outpatient clinic, Evans *et al*^[8] analyzed 427 exploratory paracenteses performed over a 6-year period. Their exclusion criteria were similar to those used by Jeffries *et al*^[5]; however patients receiving primary or secondary prophylaxis with norfloxacin were excluded. The incidence of SBP in the study performed by Evans *et al*^[8] was 1.4% and that of neutrocytic ascites was 2.1% (giving a combined incidence of 3.5%). In the prospective multicenter study of Romney *et al*^[9] the incidence of SBP was nil and it was 0.5% in the recent study of Castellote *et al*^[10] (Table 3). The incidence of SBP in asymptomatic outpatients found in our large prospective multicenter study was thus comparable to that of these 4 studies^[5,8-10]. Our data confirm on a large scale that asymptomatic outpatients have a very low or even null risk of SBP. Although in our study the incidence of SBP in asymptomatic outpatients was less than 1.5%, it rose to more than 8% when symptoms and signs of infection were present underlining the validity of the criteria of Jeffries *et al*^[5] and Romney *et al*^[9]. When considering the whole population of outpatients, the incidence of SBP remained however significantly lower than that of inpatients ($P < 10^{-5}$). Although the reasons for such differences in SBP incidence between inpatients and outpatients are probably related to differences in demographic data and liver diseases severity and/or characteristics of ascitic fluid between inpatients and outpatients, these data had not been studied in previously published series. In the present study, outpatients differed significantly from inpatients: cause of cirrhosis was less often alcohol, Child-Pugh score was lower and more often B than C, platelet count was higher and serum total bilirubin concentration was lower; in addition, ascitic protein concentration was higher in outpatients. Several factors associated with SBP have been reported including: variceal bleeding, liver failure, low ascitic protein concentration and past history of SBP^[13] leading to antibioprophylaxis in bleeding cirrhotic patients, in those with SBP history and/or low ascitic protein concentration^[13]. It has been suggested, then shown, that cirrhotic patients with low platelet count, high serum bilirubin level^[14], Child-Pugh C, hyponatremia or renal failure were at higher risk of SBP and that primary prophylaxis was particularly indicated in these settings^[14,15]. It is noteworthy that outpatients in the present study presented with lower Child-Pugh score, higher serum bilirubin level; lower platelet count and higher ascitic protein concentration than inpatients accounting for the lower SBP incidence observed in this group.

In conclusion, the results of our study confirm that SBP is rare in outpatients undergoing exploratory paracentesis. The reason for this rarity is the lower frequency of SBP risk factors in these patients. Exploratory paracentesis could be avoided in most of the cases. However, we need to clarify the predictive factors associated with

no risk of SBP in this setting.

ACKNOWLEDGMENTS

The authors thank LFB Laboratories for their support and Mrs. Myriam Lombard for her assistance in preparing the manuscript.

COMMENTS

Background

Therapeutic abdominal paracentesis is the recommended treatment for patients with ascites resistant or refractory to medical treatment. Good clinical practices guidelines recommend performing ascitic fluid analysis in association with abdominal paracentesis to search for bacterial peritonitis. However, except in cases where infection is suspected the usefulness of this approach is not clearly established in cirrhotic outpatients.

Innovations and breakthroughs

The results of this large scale study confirm that spontaneous bacterial peritonitis is rare in cirrhotic outpatients undergoing exploratory paracentesis. The reasons for this rarity are the lower frequency of spontaneous bacterial peritonitis risk factors in these patients. Patients undergoing abdominal paracentesis in an outpatient setting differed significantly from those undergoing inpatient abdominal paracentesis: they were significantly older, cause of cirrhosis was less often alcohol, Child-Pugh score was significantly lower and more often B than C, platelet count was higher, serum total bilirubin concentration was significantly lower and ascitic protein concentration was higher.

Applications

The study results suggest that exploratory paracentesis could be avoided in most cases of asymptomatic cirrhotic outpatients, according to well-defined clinical criteria.

Peer review

The question is not new and results were rather predictable, however few actual results were available in the literature. Statistical differences occur even in the presence of small numerical differences because of the large number of patients. Nevertheless the substantial sample is in itself a bonus and therefore findings should be accepted.

REFERENCES

- 1 Moore KP, Wong F, Gines P, Bernardi M, Ochs A, Salerno F, Angeli P, Porayko M, Moreau R, Garcia-Tsao G, Jimenez W, Planas R, Arroyo V. The management of ascites in cirrhosis: report on the consensus conference of the International Ascites Club. *Hepatology* 2003; **38**: 258-266 [PMID: 12830009]
- 2 Runyon BA. Management of adult patients with ascites due to cirrhosis: an update. *Hepatology* 2009; **49**: 2087-2107 [PMID: 19475696]
- 3 Silvain C, Besson I, Ingrand P, Mannant PR, Fort E, Beauchant M. Prognosis and long-term recurrence of spontaneous bacterial peritonitis in cirrhosis. *J Hepatol* 1993; **19**: 188-189 [PMID: 8301039]
- 4 Jouët P, Grangé JD. Bacterial flora and cirrhosis. *Gastroenterol Clin Biol* 2003; **27**: 738-748 [PMID: 14586247]
- 5 Jeffries MA, Stern MA, Gunaratnam NT, Fontana RJ. Unsuspected infection is infrequent in asymptomatic outpatients with refractory ascites undergoing therapeutic paracentesis. *Am J Gastroenterol* 1999; **94**: 2972-2976 [PMID: 10520854]
- 6 Stern MA, Chalasani N, Strauss RM. Is it cost effective and necessary to routinely analyse ascitic fluid in an asymptomatic outpatient population of cirrhotic? (Abstract). *Hepatology* 1994; **19**: 1271A
- 7 Kolle L, Ortiz J, Ricart E, Sabaat M, Sola-Vera J, Minana J, Soriano G, Guarner C, Vilardell S. Ascitic fluid culture is not necessary in asymptomatic cirrhotic outpatients undergoing repeated therapeutic paracentesis (Abstract). *Hepatology*

- 1996; **24**: 445A
- 8 **Evans LT**, Kim WR, Poterucha JJ, Kamath PS. Spontaneous bacterial peritonitis in asymptomatic outpatients with cirrhotic ascites. *Hepatology* 2003; **37**: 897-901 [PMID: 12668984]
- 9 **Romney R**, Mathurin P, Ganne-Carrié N, Halimi C, Medini A, Lemaître P, Gruaud P, Jouannaud V, Delacour T, Boudjema H, Pauwels A, Chaput JC, Cadranel JF. Usefulness of routine analysis of ascitic fluid at the time of therapeutic paracentesis in asymptomatic outpatients. Results of a multicenter prospective study. *Gastroenterol Clin Biol* 2005; **29**: 275-279 [PMID: 15864178]
- 10 **Castellote J**, Girbau A, Maisterra S, Charhi N, Ballester R, Xiol X. Spontaneous bacterial peritonitis and bacterascites prevalence in asymptomatic cirrhotic outpatients undergoing large-volume paracentesis. *J Gastroenterol Hepatol* 2008; **23**: 256-259 [PMID: 17683477]
- 11 **Nousbaum JB**, Cadranel JF, Nahon P, Khac EN, Moreau R, Thévenot T, Silvain C, Bureau C, Nouel O, Pilette C, Paupard T, Vanbiervliet G, Oberti F, Davion T, Jouannaud V, Roche B, Bernard PH, Beaulieu S, Danne O, Thabut D, Chagneau-Derode C, de Lédinghen V, Mathurin P, Pauwels A, Bronowicki JP, Habersetzer F, Abergel A, Audigier JC, Sapey T, Grangé JD, Tran A. Diagnostic accuracy of the Multistix 8 SG reagent strip in diagnosis of spontaneous bacterial peritonitis. *Hepatology* 2007; **45**: 1275-1281 [PMID: 17464969]
- 12 **Runyon BA**. Paracentesis of ascitic fluid. A safe procedure. *Arch Intern Med* 1986; **146**: 2259-2261 [PMID: 2946271]
- 13 **Rimola A**, García-Tsao G, Navasa M, Piddock LJ, Planas R, Bernard B, Inadomi JM. Diagnosis, treatment and prophylaxis of spontaneous bacterial peritonitis: a consensus document. International Ascites Club. *J Hepatol* 2000; **32**: 142-153 [PMID: 10673079]
- 14 **Guarner C**, Solà R, Soriano G, Andreu M, Novella MT, Vila MC, Sàbat M, Coll S, Ortiz J, Gómez C, Balanzó J. Risk of a first community-acquired spontaneous bacterial peritonitis in cirrhotics with low ascitic fluid protein levels. *Gastroenterology* 1999; **117**: 414-419 [PMID: 10419924]
- 15 **Fernández J**, Navasa M, Planas R, Montoliu S, Monfort D, Soriano G, Vila C, Pardo A, Quintero E, Vargas V, Such J, Ginès P, Arroyo V. Primary prophylaxis of spontaneous bacterial peritonitis delays hepatorenal syndrome and improves survival in cirrhosis. *Gastroenterology* 2007; **133**: 818-824 [PMID: 17854593]

P- Reviewer Faintuch J **S- Editor** Zhang DN
L- Editor Hughes D **E- Editor** Li JY

