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Diagnostic value of serum procalcitonin level in the diagnosis of the spontaneous bacterial peritonitis

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Abstract

Introduction: Spontaneous bacterial peritonitis (SBP) is an infectious ascitic fluid with an unknown intra-abdominal source. Rapid diagnosis of infection can improve prognosis in cirrhotic patients.
Objectives: We aim to determine the diagnostic value of serum procalcitonin (PCT) and C-reactive protein (CRP) in SBP.
Patients and Methods: In this cross-sectional study, we included 120 cirrhotic patients with possible diagnosis of SBP asities. Serum and ascitic fluid samples were taken from the patient before initiating antibiotics. The ascitic fluid parameters, serum levels of CRP, PCT and white blood cells were measured and the diagnostic value of the CRP and PCT were evaluated.
Results: Of 120 patients, 59.16% had confirmed SBP. PCT with a cutoff of 0.8 ng/mL and CRP with cutoff of 10.5 mg/L had a sensitivity of 90.91% and 86.11% and specificity of 91.5% and 81.25% respectively in diagnosing of SBP. Considering PCT above 0.8 ng/mL and CRP above 10.5 mg/L both, they had the sensitivity and specificity of 96.87% and 83.92% in detecting SBP in cirrhotic patients.
Conclusion: Serum PCT and CRP levels could predict SBP in cirrhotic patients while PCT had the most sensitivity and specificity. Considering both parameters, the sensitivity will increase, but the specificity is decreasing. Both PCT and CRP levels could be used as a less invasive method compared to ascites fluid analysis in diagnosing SBP.

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Introduction

Spontaneous bacterial peritonitis (SBP) is a serious complication in cirrhotic patients (1,2) with a prevalence rate of 10%-30% (3). Mortality rate has been increased by four times in these patients with bacterial infection (4). SBP is associated with poor prognosis and high hospitalization time (5-8).

Early diagnosis of SBP can improve the prognosis (6) since it is difficult to treat in decompensated cirrhotic patients due to mismatch clinical symptoms and biochemical parameters of ascites (9).

According to the guidelines, the gold standard method for SBP diagnosis is ascites culture positivity for bacterial pathogen and polymorphonuclear cells (PMN) count >250 cells/μL. However, SBP is not confirmed in 60% of patients with SBP symptoms and high PMN count in ascites (2,10). Hypersplenism (11) or hepatic encephalopathy (12) cause leukocytosis, which can mask the symptoms and is the certain specific problem in diagnosis of SBP. Paracentesis will not be necessary if the serum biological marker is found to detect SBP (10).

Key point

In a cross-sectional study on 120 cirrhotic patients with primary diagnosis of spontaneous bacterial peritonitis (SBP), we found serum procalcitonin and C-reactive protein levels could predict SBP.

Procalcitonin (PCT) is a precursor of calcitonin that secreted from thyroidal and extra-thyroidal tissues and is a new and suitable marker to diagnose bacterial infection. Bacterial infection induces PCT gene expression then PCT secretes in various tissues (13). Several studies were performed on the accuracy of PCT to diagnose SBP.

Objectives

In this study we aimed to evaluate the value of serum PCT detection in the diagnosis of SBP in cirrhotic patients.

Patients and Methods

Participants and procedure

In this cross-sectional study, 120 cirrhotic patients with the primary diagnosis of SBP who were admitted in Imam Reza and Sina hospitals, Tabriz, Iran (March 2015 to March 2016), were included. Inclusion criteria included SBP since patients with hypertension, heart failure, diabetes, autoimmune disease, receiving prophylactic antibiotics, receiving immunosuppressant drugs and sepsis due to other bacterial infections were excluded.

Diagnostic paracentesis of ascitic fluid was performed and sent for analysis. According to the results, patients were divided into two groups of confirmed SBP and non-SBP. Patients were considered as: (1) SBP if ascitic analysis showed PMN ≥250 cells/μL, positive culture or both, (2) non-SBP if none of these criteria was documented.

Sampling was performed before antibiotic administration. Samples of ascitic fluid were taken under complete aseptic conditions and were sent for leukocyte count, biochemical analysis (glucose, protein and LDH) and ascites fluid culture. At the same time, serum samples were taken for measurement of leukocyte count, glucose, CRP and PCT. PCT were measured by enzyme-linked immunosorbent assay (ELISA) technique using human PCT ELISA kit (Rosh Inc., USA) and Cobas E 411 analyzer. Laboratory tests were compared between the two groups.

Ethical issues

The ethics committee of Tabriz University of Medical Sciences approved the study protocol (IR.TBZMED.REC.1395.548). The study was conducted according to the 1964 Helsinki Declaration and its later amendments. All participants gave written informed consent. This paper is the result of pathology residency thesis of Lachin Brtari at this university.

Statistical analysis

All data were analyzed using SPSS software (version 23; SPSS Inc., Chicago, IL). The results are expressed as Mean ± standard deviation or percentage. Kolmogorov-Smirnov test was used to assess normal distribution of data. Chi-square test, Fischer's exact test, independent *t* test or Mann-Whitney U test were used to compare data between groups. Receiver operating characteristic (ROC) analysis was used to compute the sensitivity, specificity, positive predictive value and negative predictive value. Accordingly, $P < 0.05$ was considered significant.

Results

Of 120 patients, 61 (50.8%) patients were female with mean age of 56.43 ± 16.28 years. SBP was found in 71 patients (59.16%). Ascites fluid culture was positive in 33 cases (27.5%) with *E. coli* as the most common pathogen (33.3%). There was no difference between patients with and without SBP regarding age and gender (Table 1). SBP patients had significantly higher ascitic protein, PMN and LDH and lower ascitic glucose levels. The PCT and CRP levels were also significantly higher in SBP patients (Table 1).

Accordingly, the receiver operating characteristic (ROC) curve analysis showed that the ascites PMN (AUC: 0.840, $P = 0.001$), PMN percentages [AUC (area under the curve); 0.955, P: 0.001)], serum PCT (AUC: 0.972, $P = 0.001$), and CRP (AUC: 0.898, $P = 0.001$) were all able to predict SBP (Figures 1 and 2).

Table 2 demonstrates the diagnostic values of PMN, PMN percentages, serum PCT and CRP in predicting SBP. Ascitic PMN and serum PCT had the highest sensitivity, while only the specificity for PCT was higher. CRP alone had lower sensitivity and specificity compared to other parameters.

Considering PCT above 0.8 ng/mL and CRP above 10.5 mg/L together, they could detect SBP with sensitivity and specificity of 96.87% and 83.92%, respectively.

Discussion

SBP, a severe complication in cirrhotic patients, is usually considered as ascites fluid infection without other contagious sources (11,14). Since the 1970s, when SBP was described for the first time, its mortality rate declined from 80% to 30% due to early diagnosis and appropriate antibiotic treatment (15,16). An acceptable method for SBP diagnosis is ascitic fluid paracentesis and PMN measurement or culture. PMN counts ≥ 250/μL in ascites has been adopted as a diagnostic criterion of SBP, even if the culture is negative for bacteria (7,17,18).

Several markers have been investigated for ascitic fluid infection such as CRP, PCT and PMN (19,20). According to studies, various reports have been published about the

Table 1. Demographic data and laboratory findings in patients

Variable	SBP	Without SBP	*P* value
Age	55.54±17.44	57.86±14.5	0.48
Gender			0.13
Male	36 (54.5%)	23 (42.6%)	
Female	30 (45.5%)	31 (57.4%)	
Ascites analysis			
Glucose (mg/dL)	110.69±31.14	136.31±42.91	0.001*
Protein (g/dL)	2.21±1.12	1.72±1.12	0.02*
PMN (cells/μL)	515.19±505.83	173.04±30.81	0.001*
PMN (percentage)	78.37±12.21	39.29±19.76	0.001*
LDH	400.32±54.3	242.94±53.94	0.04*
Serum analysis			
WBC (cells/mL)	11771.21±7156.65	9846.30±6157.76	0.12
Glucose (mg/dL)	134.54±76.76	139.27±62.93	0.72
Procalcitonin (ng/mL)	6.98±5.39	0.53±0.09	0.001*
CRP (mg/L)	22.63±12.21	8.63±4.24	0.001*

SBP, Spontaneous bacterial peritonitis; PMN, polymorphonuclear; LDH, Lactate dehydrogenase.

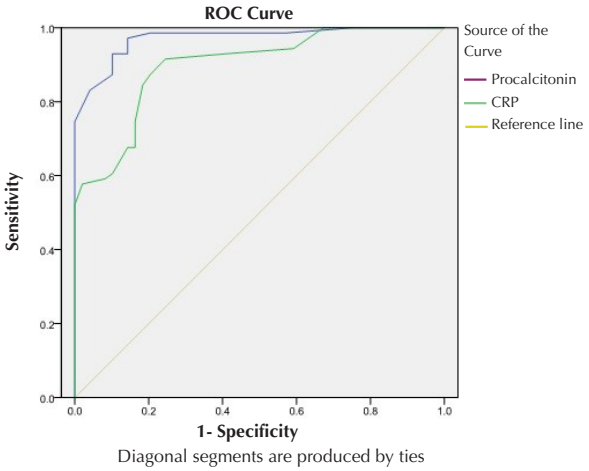

Figure 1. Receiver operating characteristic curves of serum procalcitonin, CRP in detecting SBP.

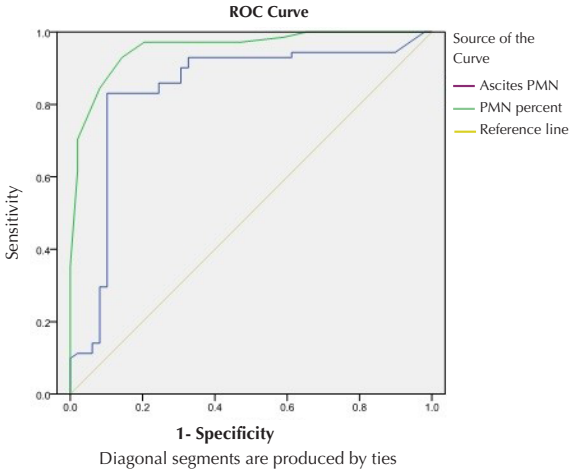

Figure 2. Receiver operating characteristic curves of ascites PMN and PMN percentage in detecting SBP.

Table 2. Diagnostic value of variables in predicting SBP

Variable	Cutoff	Sensitivity	Specificity	NPV	PPV
PMN percentage	62.5	90.54%	91.30%	85.71%	94.37%
PMN (cells/μL)	252	92.12%	78.57%	89.80%	83.1%
Procalcitonin (ng/mL)	0.8	90.91%	91.50%	84.78%	93.59%
CRP (mg/L)	10.5	86.11%	81.25%	79.59%	87.32%

NPV, negative predictive value; PPV, positive predictive value.

diagnostic value of these tests (21).

Our study demonstrated that PCT with a cutoff value of 0.8 ng/mL had a sensitivity of 90.91% and specificity of 91.50%. Abdel-Razik et al (3) reported a high sensitivity and specificity for PCT above 0.94 ng/mL in diagnosing SBP. Wu et al (22) reported low sensitivity (77.5%) and specificity (60.4%) with a similar cut-off value of PCT. While, Hamed et al (23) reported the cut-off value of serum PCT in SBP was 0.495 ng/mL with sensitivity and specificity of 90% and 92%, respectively (23).

In general, in various studies, different amounts of cutoff value of PCT 0.38 ng/mL to 0.94 ng/mL have been reported with different sensitivities and specificities, and a standard cutoff has not been reported, yet (22, 24-26).

CRP, an acute phase protein, is synthesized by the liver and secreted into the blood plasma within hours in response to the tissue damage, infection and inflammation (27,23).

According to our study, serum CRP with the cutoff value of 10.5 mg/L had the sensitivity and specificity of 86.11% and 81.25%, respectively. Different studies have demonstrated similar results (22,26). Hamed et al (23) demonstrated the same cutoff value for CRP with a higher sensitivity (91%) and specificity (97%). Additionally, Metwally et al (27) indicated a sensitivity and specificity of 86.4% and 66% for CRP >13.5 mg/L. A cut-off value of 35 mg/L was also reported by Sood and colleagues (28).

In the present study, results showed that PMN and PMN percentage with a cutoff value of 252 cells/ml and 62.5%, respectively, had a sensitivity of 92.12% and 90.54%, and the specificity of 78.57% and 91.30%, respectively. Wang et al (24) reported at a cutoff value of 75.0% in PMN percentage, the sensitivity and specificity would be 83.03% and 92.7%, respectively. According to the study by Abdel-Razik et al (3) PMN at a cut-off point 265/mm^3 could predict SBP with a sensitivity of 91% and specificity of 73.8%.

Conclusion

Serum levels of PCT and CRP could predict SBP in cirrhotic patients with PCT having the most sensitivity and specificity. Considering both parameters, the sensitivity will increase, but the specificity is decreasing. Both PCT and CRP levels could be used as a less invasive method compared to ascites fluid analysis in diagnosing SBP.

Limitations of the study

The small sample of the patients and single-center study were the limitations of the current study.

Ethical considerations

Ethical issues including plagiarism and double publication have been completely observed by the authors.

Conflicts of interest

We have no conflicts of interest.

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