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Research on the diagnostic effect of PCT level in serum on patients with sepsis due to different pathogenic causes

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Abstract. – OBJECTIVE: To investigate the diagnostic effect of procalcitonin level in serum for patients with sepsis due to different pathogenic causes.

PATIENTS AND METHODS: The clinical data of 132 sepsis patients were analyzed. Those patients were admitted to the Affiliated Hospital of Medical School of Ningbo University from January 2014 to January 2017. According to the blood culture results before antimicrobial therapy, patients were divided into two groups: Gram-negative bacteria group (G- group) and Gram-positive bacteria group (G+ group). The indexes, such as SOFA score, APACHE II score, length of stay in hospital and mortality rate, were used to evaluate disease severity of the two groups. The procalcitonin, WBC, hs-CRP and NEU% were detected and compared between the two groups of patients.

RESULTS: A total of 132 pathogenic bacteria were detected in 132 patients, of which 44 patients were infected with G^- bacteria and 88 patients were infected with G^+ bacteria. Patients in G^- group were mainly infected with *Escherichia coli, Acinetobacter baumannii,* and *Klebsiella pneumoniae*, while patients in G^+ group were mainly infected with *Staphylococcus epidermidis* and *Staphylococcus aureus*. The SOFA score, APACHE II score and mortality rate in G- group were higher than those in G^+ group. The PCT levels in G^- group and G^+ group were (54.89±21.64) ng/mL and (21.13±1.30) ng/mL, respectively. The PCT level in G^- group was higher than that in G^+ group, and the difference was statistically significant between them ($p<0.05$). There was no statistically significant difference in length of stay in hospital between the two groups ($p>0.05$). There were no statistically significant differences in WBC, hs-CRP and NEU% between the two groups ($p>0.05$).

CONCLUSIONS: The procalcitonin level in serum of sepsis patients at early stage of bloodstream infection is significantly elevated and has diagnostic value for different pathogenic bacteria groups. It can also reflect the disease severity and predict the prognosis of sepsis patients.

Key Words
Sepsis, PCT, Gram-negative bacteria, Gram-positive bacteria, Diagnosis.

Introduction

Sepsis is a systematic inflammatory response syndrome caused by infection; its mortality rate ranges from 21% to 48%. The most influential factor in the prognosis of patients is bloodstream infection, so rapid early diagnosis of bloodstream infection is critical for proper treatment[1]. In clinical work, patients can be diagnosed early by identifying pathogenic bacteria, detecting auxiliary inflammatory cytokines and observing clinical symptoms. Common laboratory examinations include blood routine, procalcitonin (PCT), white blood cell count (WBC), high-sensitivity C-reactive protein (hs-CRP) and neutrophil percentage (NEU%)[2]. PCT is a kind of protein mainly produced by thyroid C-cells, which stays at a low level under normal body conditions. However, when multiple organ failure or severe fungal, bacterial and parasite infection occurs in human body, the PCT level in serum is significantly increased[3]. The focus of this study was to investigate the diagnostic effect of PCT in serum of sepsis patients caused by bloodstream infection of Gram-negative cocci and Gram-positive bacteria.

Patients and Methods

Patients

The clinical data of 132 sepsis patients admitted in the Affiliated Hospital of Medical School of Ningbo University from January 2014 to January 2017 were retrospectively analyzed. In 44 patients of G- group, 25 patients were male and

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19 patients were female, aged 18-87 years with an average of (61.23±7.22) years. In 88 patients of G+ group, 53 patients were male and 35 patients were female, aged 20-86 years with an average age of (59.86±8.04) years. There were no significant differences between the two groups in sex and age, and they were comparable.

Included criteria

1) Patients diagnosed with bloodstream infection-induced sepsis via blood culture; 2) patients aged ≥ 18 years; 3) patients with completed clinical data and follow-up data.

Excluded criteria

1) Patients with sepsis caused by burning; 2) patients who took drugs that stimulating inflammatory cytokines' release; 3) patients with thyroid cancer or small cell lung cancer; 4) patients with organ perfusion for less than 72h.

Methods

1) Before antibiotic treatment, 5 mL blood was extracted from the elbow vein of all patients, and placed in biochemical tubes. The blood was centrifuged at 3000 r/min with centrifugal radius of 10 cm for 5 m to take the upper-layer serum to be detected. The hs-CRP and PCT levels were detected by enzyme-linked immunosorbent assay. NEU% and WBC were counted by flow cytometry. 2) The Sequential Organ Failure Assessment (SOFA score) and Acute Physiology and Chronic Health Evaluation System II score (APACHE II score) were calculated according to the worst data in the first 24 h, after patients were admitted into the ICU; 3) The length of stay in hospital and mortality rate were calculated based on the 28-d outcome.

Written consents were obtained from all subjects. This study was approved by the Ethics Committee of the Affiliated Hospital of Medical College of Ningbo University.

Statistical Analysis

Statistical Product and Service Solutions (SPSS) 19.0 software (IBM Corp. IBM SPSS Statistics for Windows, Armonk, NY, USA) was used for statistical comparison. The measurement data were presented as mean ± standard, and *t*-test was used for intergroup comparisons. Enumeration data were presented as [n (%)], and chi-square test was used for intergroup comparisons. $p<0.05$ suggested that the difference was statistically significant.

Results

Distribution of Pathogenic Bacteria

A total of 132 pathogenic bacteria were detected in 132 patients, of which 44 patients were infected with G- bacteria and 88 patients were infected with G+ bacteria. Patients in G- group were mainly infected with *Escherichia coli, Acinetobacter baumannii* and *Klebsiella pneumoniae*, while patients in G+ group were mainly infected with *Staphylococcus epidermidis, Staphylococcus aureus* and *Staphylococcus aureus* (Table I).

Comparison of Disease Degree

The SOFA score, APACHE II score and mortality rate in G- group were higher than those in G+ group, and the differences were statistically significant ($p<0.05$). There was no statistically significant difference in length of stay in hospital between the two groups ($p>0.05$) (Table II).

Table I. Distribution of pathogenic bacteria.

G^- group	Strain number (n, %)	G^+ group	Strain number (n, %)
Escherichia coli	20 (45.45)	Staphylococcus epidermidis	25 (28.47)
Acinetobacter baumannii	9 (20.45)	Staphylococcus human	20 (22.72)
Klebsiella pneumoniae	6 (13.63)	Staphylococcus aureus	14 (15.90)
Pseudomonas aeruginosa	4 (9.09)	Enterococcus faecium	9 (10.22)
Enterobacter cloacae	2 (4.57)	Staphylococcus haemolyticus	8 (9.09)
Proteus mirabilis	1 (2.27)	Staphylococcus xylose	2 (2.27)
Bacterioides	1 (2.27)	Staphylococcus Kirschner	2 (2.27)
Rhizobium radiobacter	1 (2.27)	Staphylococcus saprophyticus	2 (2.27)
		Enterococcus faecalis	2 (2.27)
		Staphylococcus aureus	1 (1.13)
		Streptococcus oralis	1 (1.13)
		Staphylococcus lentus	1 (1.13)
		Green Staphylococcus	1 (1.13)

Table II. Comparison of disease degree.

Group	Cases (n)	Sofa score (score)	Apache II score (score)	Length of stay (d)	Mortality (n, %)
G^- group	44	7.51±1.61	25.54±9.13	19.68±9.04	6 (13.63)
G^+ group	88	6.79±1.52	21.89±7.56	17.14±10.26	5 (5.68)
χ^2/t		2.549	2.377	1.652	7.158
p		0.016	0.033	0.098	0.019

Comparisons of PCT, WBC, hs-CRP and NEU%

The PCT levels in G- group and G+ group were (54.89±21.64) ng/mL and (21.13±1.30) ng/mL, respectively. The PCT level in G- group was higher than that in G+ group, and the difference was statistically significant ($p<0.05$). There were no statistically significant differences in WBC, hs-CRP and NEU% between the two groups ($p>0.05$) (Table III).

Discussion

Sepsis caused by bloodstream infection is a serious infectious disease, and early diagnosis and appropriate clinical treatment are important means to reduce the mortality rate of patients[4]. The early clinical manifestation of bloodstream infection is fever. Clinically blood culture is regarded as the golden standard for bloodstream infection. However, because the test needs to take a long time, and the positive rate of results is low, the collection of specimens easily leads to normal skin flora contaminated. Thus, its application is limited in the diagnosis of bloodstream infection[5,6]. PCT is originally extracted from cell culture fluid of thyroid tumor, a peptide hormone, in recent years, which has been widely used in the early diagnosis of bacterial infection as a marker[7]. And in serum, PCT level has lower degradation rate and better stability[8] than other inflammatory indicators. Therefore, this study explored the diagnostic effect of PCT level in serum on sepsis patients caused by different pathogens, in order to provide a reference for the later clinical treatment.

The results of this study showed that a total of 132 pathogenic bacteria were detected in 132 patients, of which 44 patients were infected with G- bacteria and 88 patients were infected with G+ bacteria. The PCT levels in G- group and G+ group were (54.89±21.64) ng/mL and (21.13±1.30) ng/mL, respectively. The PCT level in G- group was higher than that in G+ group, and the difference was statistically significant between them ($p<0.05$). It has been pointed out that[9], G+ cocci pathogens were mainly from respiratory infection, but the G- Bacillus were mainly from digestive infection, which suggested that G+ cocci pathogens lead to the disease because of the exotoxin, whose dominant sector of exotoxin is extremely unstable protein that is vulnerable to damage. The G- Bacillus leads to disease because of endotoxin, whose main sector is lipopolysaccharide, affecting macrophages and neutrophils, and promoting the production of interleukin-1, interleukin-6, tumor necrosis factor -α and other cytokines. These cytokines induce PCT produced in neuroendocrine cells of spleen, liver, lung and kidney, leading to an increase in PCT level in patients. PCT level in serum of patients in G- group was higher than that in G+ group, which can provide the main basis for identifying the main pathogens of sepsis patients clinically, so as to select the appropriate antimicrobial drugs for treatment[10]. WBC refers to counting the number of white blood cells contained in unit volume of blood. If bleeding and infection occur, WBC level will be significantly increased[11]. Hs-CRP is a C-reactive protein in plasma, also known as high-sensitivity C-reactive protein[12]. It is a common indicator to distinguish low-level inflammatory state[13]. NEU contains ly-

Table III. Comparisons of PCT, WBC, hs-CRP and NEU%.

Group	Cases (n)	Pct (ng/ml)	Hs-crp (mg/l)	Wbc ($\times10^9$/l)	Neu%
G^- group	44	54.89±21.64	124.66±31.25	13.58±2.71	77.25±41.32
G^+ group	88	21.13±1.30	111.36±31.83	14.64±2.74	66.93±37.65
χ^2/t		2.524	1.935	1.693	1.949
p		0.018	0.060	0.087	0.055

sozyme, myeloperoxidase, alkaline phosphatase, lysozyme, acid hydrolase and other enzymes, which are relevant to cell digestion and phagocytosis. So if the body is infected, NEU% will be increased[14]. However, there were no statistically significant differences in WBC, hs-CRP, NEU% between the two groups in this study (p>0.05). This result shows that PCT is more specific and sensitive than traditional inflammatory markers, such as WBC, hs-CRP and NEU%, for the identification of bloodstream infections in sepsis patients, and the number of WBC in microbial infection is more or less. The unskilled or non-standard operation may have an impact on cell counting. The SOFA score is a quantitative assessment index that dynamically describes the organ dysfunction of sepsis patients, with simple standard, and the results are easy to be obtained with objective reliability. The hemodynamic changes of patients can better reflect the severity of sepsis in patients[15]. APACHE II score consists of three parts, age score, acute physiology score and chronic health score. The higher the score is, the more severe the patient will be. It is a common indicator evaluating the condition and prognosis of ICU patients[16]. The results of this study showed that the SOFA score, APACHE II score and mortality rate in G- group were higher than those in G+ group, and the differences were statistically significant (p<0.05). There was no statistically significant difference in length of stay in hospital between the two groups (p>0.05). This result suggests that the disease of G- bacillus patients is more serious and the prognosis is worse.

Conclusions

We observed that in the early stage of bloodstream infection in sepsis patients, PCT level in serum is elevated significantly, which has diagnostic value for different pathogenic bacteria. Also, it can reflect the severity of disease and predict the prognosis of patients.

Conflict of interest

The authors have no conflicts of interest to declare.

References

1) Koch FR, Wagner CL, Jenkins DD, Caplan MJ, Perkel JK, Rollins LG, Katikaneni LD, Mulvihill DM. Sex differences in cerebral blood flow following chorioamnionitis in healthy term infants. J Perinatol 2014; 34: 197-202.
2) Soares AC, Araújo RN, Carvalho-Tavares J, Gontijo Nde F, Pereira MH. Intravital microscopy and image analysis of Rhodnius prolixus (Hemiptera: Reduviidae) hematophagy: the challenge of blood intake from mouse skin. Parasitol Int 2014; 63: 229-236.
3) Kitanovski L, Jazbec J, Hojker S, Derganc M. Diagnostic accuracy of lipopolysaccharide-binding protein for predicting bacteremia/clinical sepsis in children with febrile neutropenia: comparison with interleukin-6, procalcitonin, and C-reactive protein. Support Care Cancer 2014; 22: 269-277.
4) Vanker N, Ipp H. The use of the full blood count and differential parameters to assess immune activation levels in asymptomatic, untreated HIV infection. S Afr Med J 2013; 104: 45-48.
5) Hashi S, Masuda S, Kikuchi M, Uesugi M, Yano I, Omura T, Yonezawa A, Fujimoto Y, Ogawa K,Kaido T, Uemoto S, Matsubara K. Assessment of four methodologies (microparticle enzyme immunoassay, chemiluminescent enzyme immunoassay, affinity column-mediated immunoassay, and flow injection assay-tandem mass spectrometry) for measuring tacrolimus blood concentration in Japanese liver transplant recipients. Transpl P 2014; 46: 758-760.
6) Medina F, Quintremil S, Alberti C, Barriga A, Cartier L, Puente J, Ramírez E, Ferreira A, Tanaka Y, Valenzuela MA. Tax posttranslational modifications and interaction with calreticulin in MT-2 cells and human peripheral blood mononuclear cells of human T cell lymphotropic virus type-I-associated myelopathy/tropical spastic paraparesis patients. Aids Res Hum Retrov 2014; 30: 370-379.
7) Cohn B. Can procalcitonin differentiate sepsis from systemic inflammatory response syndrome without infection? Ann Emerg Med 2014; 63: 631-632.
8) Bishop BM, Bon JJ, Trienski TL, Pasquale TR, Martin BR, File TM Jr. Effect of introducing procalcitonin on antimicrobial therapy duration in patients with sepsis and/or pneumonia in the Intensive Care Unit. Ann Pharmacother 2014; 48: 577-583.
9) Naffaa M, Makhoul BF, Tobia A, Kaplan M, Aronson D, Azzam ZS, Saliba W. Procalcitonin and interleukin 6 for predicting blood culture positivity in sepsis. Am J Emerg Med 2014; 32: 448-451.
10) Westhorpe CL, Maisa A, Spelman T, Hoy JF, Dewar EM, Karapanagiotidis S, Hearps AC, Cheng WJ, Trevillyan J, Lewin SR, Sviridov D, Elliott JH, Jaworowski A, Dart AM, Crowe SM. Associations between surface markers on blood monocytes and carotid atherosclerosis in HIV-positive individuals. Immunol Cell Biol 2014; 92: 133-138.
11) Yilmaz H, Cakmak M, Inan O, Darcin T, Akcay A. Can neutrophil-lymphocyte ratio be independent risk factor for predicting acute kidney injury in patients with severe sepsis? Renal Failure 2015; 37: 225-229.
12) Uyanik V, Tuglu C, Gorgulu Y, Kunduracilar H, Uyanik MS. Assessment of cytokine levels and hs-CRP in bipolar I disorder before and after treatment. Psychiat Res 2015; 228: 386-392.

13) Zhang XF, Zhang XQ, Wu CC, Wu HW, Wei D. Application value of procalcitonin in patients with central nervous system infection. Eur Rev Med Pharmacol Sci 2017; 21: 3944-3949.

14) Verneris MR, Arshi A, Edinger M, Kornacker M, Natkunam Y, Karimi M, Cao YA, Marina N, Contag CH, Negrin RS. Low levels of Her2/neu expressed by Ewing's family tumor cell lines can redirect cytokine-induced killer cells. Clin Cancer Res 2005; 11: 4561-4570.

15) Okazaki H, Shirakabe A, Hata N, Yamamoto M, Kobayashi N, Shinada T, Tomita K, Tsurumi M, Matsushita M, Yamamoto Y, Yokoyama S, Asai K, Shimizu W. New scoring system (APACHE-HF) for predicting adverse outcomes in patients with acute heart failure: evaluation of the APACHE II and Modified APACHE II scoring systems. J Cardiol 2014; 64: 441-449.

16) Lee M, Lee JH, Oh S, Jang Y, Lee W, Lee HJ, Yoo JJ, Choi WM, Cho YY, Cho Y, Lee DH, Lee YB, Yu SJ, Yi NJ, Lee KW, Kim YJ, Yoon JH, Suh KS, Lee HS. CLIF-SOFA scoring system accurately predicts short-term mortality in acutely decompensated patients with alcoholic cirrhosis: a retrospective analysis. Liver Int 2015