HIGH LEVELS OF CRP, PCT AND HBP ARE COLLRELATED WITH PNEUMONIA SECONDARY SEPSIS

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ABSTRACT

Objective: *To investigate the value of procalcitonin (PCT), high-sensitivity C-reactive protein (hsCRP) and heparin-binding protein (HBP) in predicting sepsis secondary to pneumonia.*

Methods: *In total, 49 pneumonia patients treated in our hospital between April 2018 and March 2019 were randomly selected as the pneumonia group, and 35 patients with sepsis secondary to pneumonia were selected as the secondary sepsis group. At the same time, 45 healthy subjects who came to hospital for examination were selected as the normal group. The levels of blood lipids (serum total cholesterol (TC), triglycerides (TG), high-density lipoprotein (HDL), low-density lipoprotein (LDL)) were measured by an automatic biochemical analyser. The acute physiological and chronic health status scores (APACHE II) were compared. PCT levels were measured by fluorescence immunoquantitative analysis, hsCRP levels were measured by immunoturbidimetry, and HBP levels were measured by enzyme-linked immunosorbent assay (ELISA). A Cox regression curve model was established to analyse the independent risk factors of sepsis secondary to pneumonia. ROC curves were used to assess the value of the combined detection of CRP, PCT and HBP or single factor detection in predicting sepsis secondary to pneumonia.*

Results: *There was no significant difference in the basic data and blood lipid indexes among the three groups. The APACHE II scores in the pneumonia group and secondary sepsis group were significantly higher than those in the normal group (P<0.05). Compared with the normal group, the levels of serum PCT, hsCRP and HBP in the pneumonia group and secondary sepsis group were significantly higher (P<0.05), and the levels of PCT, hsCRP and HBP in the secondary sepsis group were significantly higher than those in the pneumonia group (P<0.05). The levels of serum PCT, hsCRP and HBP were independent risk factors for sepsis secondary to pneumonia. The ROC curve model showed that the areas under the curve of PCT, hsCRP, HBP and PCT + hsCRP + HBP were 0.876, 0.765, 0.921 and 0.969, respectively. The above indexes were beneficial in predicting sepsis secondary to pneumonia, and the predictive value of the three indexes in predicting secondary sepsis was significantly higher than that of single-factor detection.*

Conclusion: *The levels of CRP, PCT and HBP in patients with sepsis secondary to pneumonia are significantly higher than those in healthy subjects. The above indexes can be used in the diagnosis of sepsis secondary to pneumonia, and the combined prediction value of these three indexes is higher.*

Keywords: *Sepsis secondary to pneumonia, PCT, hsCRP, HBP, pneumonia, predictive value.*

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Introduction

Sepsis is a life-threatening organ dysfunction caused by the host's reaction to infection and is an important cause of death in critically ill patients. Sepsis and multifunctional disorder syndrome are outstanding problems faced by modern medicine because of their rapid progress and poor prognosis(1). Therefore, it is of great significance to find early diagnostic markers to diagnose and treat sepsis in a timely manner to delay the progress of sepsis and to reduce mortality. Procalcitonin (PCT) is a protein secreted by many different types of cells when stimulated by particular inflammatory factors, especially during bacterial infection. When the body is subjected to severe bacterial or fungal infection, sepsis or multiple organ failure, the level of PCT is significantly increased(2).

High-sensitivity C-reactive protein (hsCRP) is a nonspecific marker of acute systemic inflammation and is synthesized by the liver[3]. When the body experiences acute inflammation, trauma or infarction, the level of hsCRP is significantly increased. When the body is infected with bacteria, the level of serum hsCRP is significantly increased, and its level is positively correlated with the degree of bacterial infection[4]. Heparin-binding protein (HBP) is a multifunctional protein that has a bactericidal function and chemotactic ability to activate monocytes/macrophages and enhances the inflammatory response[5]. Some studies have found that plasma HBP concentrations have an important relationship with the severity of the condition. Through monitoring the HBP level, we can predict the shock that will occur in patients with severe infection so as to implement early intervention[6]. The value of using PCT, hsCRP and HBP to predict sepsis secondary to pneumonia was evaluated in this study.

Materials and methods

Basic information

A total of 49 patients with pneumonia treated in our hospital between April 2018 and March 2019 were randomly selected as the pneumonia group, and 35 patients with sepsis secondary to pneumonia were selected as the secondary sepsis group.

Inclusion criteria:

• Diagnostic criteria for pneumonia: according to the guidelines for the diagnosis and treatment of pneumonia formulated by the Infectious Diseases Group of the Chinese Society of Respiratory Medicine[7]. Diagnostic criteria for sepsis secondary to pneumonia: Patients met the criteria of "sepsis = infection + SOFA score ≥2"[8].

• The study was approved by the ethics committee of the hospital;

• Informed consent signed by the patient and his or her family;

• The patient medical record data is complete and the patient can cooperate with treatment.

Exclusion criteria:

• Lactation or pregnancy;

• The death of patients or the patient no longer wanted to participate in the study;

• Concurrent infectious diseases such as hepatitis b. There were 29 males and 20 females in the pneumonia group, aged 35~74 years old, with an average age of 53.27±3.73 years. There were 22 males and 13 females in the secondary sepsis group, aged 37~72 years old, with an average age of 54.11±4.53 years. At the same time, 45 healthy subjects were selected as the normal group, including 26 males and 19 females, aged 37~73 years old, with an average age of 55.13±6.48 years.

Observation indexes

The age and other basic information of the patients were collected. The levels of total cholesterol (TC), triglycerides (TG), high-density lipoprotein (HDL) and low-density lipoprotein (LDL) in the three groups were measured by an automatic biochemical analyser. Comparisons of the Acute Physiology and Chronic Health Evaluation II (APACHE II) scores were made between groups, along with the PCT, hsCRP and HBP levels. PCT was determined by fluorescence immunoquantitative analysis, the hsCRP level was determined using immunoturbidimetry, and the HBP level was determined by ELISA.

A Cox regression model was established to analyse the independent risk factors of sepsis secondary to pneumonia. ROC curve was used to analyse the value of CRP, PCT and HBP combined detection or independent detection in the early prediction of sepsis secondary to pneumonia.

Statistical methods

The SPSS 20.0 software package was used for statistical data analysis. Univariate analysis of variance and the least significant difference (LSD) t-test were used for comparing the measurement data. Statistical data were compared by the chi squared test. The ridit test was used to compare the grade data. A Cox regression model was established to analyse the independent risk factors of sepsis secondary to pneumonia. A ROC curve was used to analyse the value of CRP, PCT and HBP combined detection or independent detection in the early prediction of sepsis secondary to pneumonia. A value of $P<0.05$ was considered to be statistically significant.

Results

Comparison of clinical data in each group

There was no significant difference in age, gender or other basic data between the pneumonia group, the secondary sepsis group and the normal group ($P>0.05$). There was no significant difference in TG, TC, LDL or HDL among the three groups ($P>0.05$). Compared with the pneumonia group, the secondary sepsis group APACHE II scores were significantly increased ($P<0.05$) (Table 1).

Index	Pneumonia group (n=49)	Secondary sepsis group (n=35)	Normal group (n=45)
Gender (man/woman)	29/20	22/13	26/19
Age (years)	53.27±3.73	54.11±4.53	55.13±6.48
TC (mmol/L)	4.27±0.85	4.16±1.04	4.08±0.84
TG (mmol/L)	1.51±0.39	1.48±0.42	1.47±0.51
LDL (mmol/L)	3.23±0.51	3.18±0.52	3.13±0.46
HDL (mmol/L)	1.62±0.43	1.52±0.68	1.47±0.57
APACHE II (score)	2.52±1.69	11.37±4.68[a]	-

Table 1: Comparison of clinical data.
Note: a indicates P<0.05 compared with the pneumonia group.

Comparison of PCT, hsCRP and HBP levels

Compared with the normal group, the PCT, hsCRP and HBP levels in the pneumonia group and the secondary sepsis group were significantly increased (P<0.05), and the PCT, hsCRP and HBP levels in the secondary sepsis group were significantly higher than those in the pneumonia group (P<0.05) (Table 2).

Group	n	PCT (μg/L)	hsCRP (mg/L)	HBP (ng/mL)
Normal group	45	0.33±0.25	1.32±1.28	10.24±2.13
Pneumonia group	49	1.27±0.72	40.86±24.55	14.43±2.08
Secondary sepsis group	35	4.59±0.44	97.81±38.16	27.47±3.14
F		986.852	163.391	582.444
P		<0.001	<0.001	<0.001

Table 2: Comparison of PCT, hsCRP and HBP levels (x±s).
Note: a indicates P<0.05 compared with the normal group, b indicates P<0.05 compared with the pneumonia group.

Analysis of independent risk factors affecting sepsis secondary to pneumonia

A Cox regression curve model was analysed. The results showed that the serum PCT, hsCRP and HBP levels and the APACHE II scores are independent risk factors for sepsis secondary to pneumonia (Table 3).

Index	Wald	*P*	95% CI	
			Upper Limit	Lower Limit
Gender	0.177	0.647	1.322	0.715
Age	1.141	0.258	1.177	0.927
TC	3.242	0.072	0.925	0.653
TG	6.625	0.054	1.337	1.319
LDL	2.467	0.086	1.316	0.775
HDL	2.727	0.063	1.151	0.826
APACHE II	3.708	<0.001	0.934	0.832
PCT	9.147	<0.001	0.865	0.672
hsCRP	7.758	<0.001	0.924	0.825
HBP	8.416	<0.001	0.849	0.671

Table 3: Analysis of independent risk factors of sepsis secondary to pneumonia.

The value of PCT, hsCRP and HBP in predicting sepsis secondary to pneumonia, either independently or jointly

A ROC curve model was established, and the results showed that the areas under the curve for PCT, hsCRP, HBP and PCT + hsCRP + HBP were 0.876, 0.765, 0.921 and 0.969, respectively. The above indexes were beneficial in predicting sepsis secondary to pneumonia, and the combined value of the three indexes was significantly higher than that of a single index (Table 4).

Index	Specificity (%)	Sensitivity (%)	Area Under Curve	Negative Predictive Value	Positive Predictive Value	Accuracy
PCT	82.69	64.25	0.876	71.36	87.17	74.15
hsCRP	69.11	75.74	0.765	69.88	73.15	82.18
HBP	91.08	67.73	0.921	73.53	88.17	76.04
PCT+ hsCRP+ HBP	94.36	87.26	0.969	78.53	94.74	89.12

Table 4: Value of PCT, hsCRP and HBP in predicting sepsis secondary to pneumonia alone or in combination.

Discussion

Sepsis is a systemic inflammatory response syndrome caused by an infection or a high degree of disease. Pathogens that cause sepsis mainly include bacteria, fungi and viruses. In the absence of timely treatment, sepsis may develop into septic shock and even multiple organ failure, threatening the life and health of the patient, leading to a significant increase in patient mortality. Pneumonia is the most common cause of sepsis[9]. The early prediction of sepsis secondary to pneumonia is of great significance for early sepsis treatment and to improve patient prognosis.

PCT is one of the precursors of calcitonin and is part of the CAPA protein family. PCT levels are normally very low; however, when the body is infected, PCT is released into the blood, and its serum level is significantly increased[10].

PCT levels can reflect the activity of the systemic inflammatory reaction and also have great significance for the early diagnosis of infectious diseases and for the guidance of antibiotic treatment. As disease develops, the PCT level is correlated with the degree of infection or disease[11]. In this study, the PCT levels in patients with pneumonia and sepsis secondary to pneumonia were significantly higher than those in the normal group (P<0.05). The levels of PCT in the secondary sepsis group were significantly higher than those in the pneumonia group (P <0.05). The results of this study are similar to the findings of Troia et al.[12].

HsCRP is an acute phase protein that is synthesized by the liver cells. It enhances the phagocytic function of leucocytes and combines with platelet activating factor to promote the synthesis of macrophage tissue factor; it also regulates the functions of lymphocytes and mononuclear/ macrophages[13]. HsCRP can reflect the degree of inflammation and the degree of injury, and it is highly sensitivity. When the body experiences viral infections, cardiovascular system diseases and surgery, the level of hsCRP is significantly increased; however, hsCRP has some limitations regarding the specificity of disease diagnosis[14]. The hsCRP levels in the patients with pneumonia and sepsis secondary to pneumonia were higher than those in the normal group ($P<0.05$).

The levels of hsCRP in the secondary sepsis group were significantly higher than those of the pneumonia group ($P<0.05$). The HBP protein was isolated from neutrophils for the first time by Shafer et al. and has sterilization and chemotaxis abilities[15]. HBP is mainly stored in the polynucleoblasts and secretory granules, and it is the only granular protein that can be released into the extracellular environment by the secretion of polymorphonuclear cells. HBP levels are low in the normal physiological state. When the body becomes infected, polymorphonuclear cells are stimulated and they release HBP, substantially increasing the HBP levels[16].

It has been reported that the serum HBP level is closely related to the state of microcirculation and to the degree of inflammation in the body[17]. In the current study, the level of HBP in the secondary sepsis group was significantly higher than that of the pneumonia group and the normal group ($P <0.05$).

The area under the ROC curve was used to compare and evaluate secondary sepsis using PCT, hsCRP, HBP and PCT + hsCRP + HBP. Values closer to 1 when the area under the ROC curve is greater than 5 indicate a better diagnostic effect[18].

The results showed that the areas of PCT, hsCRP, HBP and PCT + hsCRP + HBP were 0.876, 0.765, 0.921 and 0.969, respectively, and the sensitivity and specificity of the diagnoses were 64.25%, 82.69%, 75.74%, 69.11%, 67.73%, 91.08%, 87.26% and 94.08%, respectively.

In conclusion, the levels of CRP, PCT and HBP in patients with sepsis secondary to pneumonia were significantly higher than those of healthy subjects.

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