CHANGES AND CORRELATIONS OF CRP, COAGULATION INDEXES AND BLOOD GLUCOSE LEVELS IN PATIENTS WITH SEVERE PNEUMONIA COMPLICATED BY SEPSIS

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ABSTRACT

Objective*: Recent studies show that the number of excised lymph nodes is an independent prognostic factor for colorectal cancer. Based on this Objective: To investigate the changes in C-reactive protein (CRP), coagulation parameters and blood glucose as well as their correlation in severe pneumonia patients with sepsis.*

Methods*: A total of 78 severe pneumonia patients with sepsis admitted to our hospital from January 2016 to November 2017 were enrolled in the study. The patients were assigned to an extremely serious group (n= 24), a serious group (n= 32), and a nonserious group (n= 22) according to their course of disease. The levels of serum inflammatory cytokines, such as interleukin-6 (IL-6), interleukin-10 (IL-10) and CRP; coagulation parameters, such as P-selectin and D-dimer; and blood glucose and lactate were determined in the three groups to analyze the correlation between their changes and the critical illness score in severe pneumonia patients with sepsis.*

Results*: The levels of serum IL-6, CRP, P-selectin, D-dimer, blood glucose and blood lactate were much higher in the extremely serious group than those in the serious group and the nonserious group, with a significant difference (P<0.05). The levels of serum IL-6, CRP, P-selectin, D-dimer, blood glucose and lactate were much higher in the serious group than those in the nonserious group, and the difference was statistically significant (P<0.05). The level of IL-10 was much lower in the extremely serious group than that in the other two groups, with a statistically significant difference (P<0.05), and it was much lower in the serious group than that in the nonserious group (P<0.05).*

Conclusions*: With the worsening of severe pneumonia with sepsis, the levels of IL-6, CRP, P-selectin, D-dimer, blood glucose, and blood lactate increase, whereas the level of IL-10 decreases. In addition, IL-6, CRP, P-selectin, D-dimer, blood glucose and lactate are positively related to the critical illness score, IL-10 is negatively associated with the score, and CRP is not correlated with the score.*

Keywords*: CRP, Coagulation index, Blood glucose, Level change, Correlation.*

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Introduction

Pneumonia is an inflammation of the alveoli, terminal airway and pulmonary interstitial space resulting from various pathogens or other factors, and the mortality ranks at the top among infectious diseases[1-2]. In the early stage, pneumonia is usually accompanied by tachypnea, consciousness disorders, and sleepiness. Pneumonia then turns into severe pneumonia (SP), which is related to breathing failure or significant involvement of other systems. SP usually has several complications, with sepsis being the most common in the clinical setting.

Sepsis is a systemic inflammatory response syndrome (SIRS) induced by infection with a high mortality, and it becomes life-threatening without timely treatment[3-4]. Cai J Q, et al[5] claims that coagulation parameters, inflammatory cytokines, and blood glucose play certain roles in assessing the prognoses of sepsis. However, few studies focus on the changes in these indexes in severe pneumonia patients with sepsis. Severe pneumonia patients with sepsis admitted in our hospital were involved in this study; we measured their coagulation parameters, inflammatory cytokines and blood glucose and analyzed their correlation with a critical illness score.

We then explored these values in terms of evaluating the condition of severe pneumonia patients with sepsis, and the details are presented.

Materials and methods

General materials and grouping

With the approval of a local medical ethnic committee, a total of 78 severe pneumonia patients with sepsis, who were admitted to our hospital from January 2016 to November 2017, were recruited in this study. The patients were assigned to the extremely serious group (n= 24), the serious group (n= 32) and the nonserious group (n= 22) based on their course of disease. Inclusion criteria: 0,1patients with confirmed severe pneumonia with sepsis according to the diagnostic criteria; 0,2 patients with a normal electrocardiogram; 0,3 patients without severe mental disorders; 0,4 patients with normal liver function; 0,5 patients who or whose families signed an informed consent; and 0,6 patients without severe infection. Exclusion criteria: 0,1patients with cardio-cerebrovascular diseases; 0,2 patients who received mechanical ventilation before this treatment; 0,3 patients with tracheotomy at admission; 0,4 patients without complete hospitalization materials; 0,5 patients with a trachea cannula at admission; and 0,6 patients with severe arrhythmia. There was no significant difference in age and gender among the three groups (P>0.05), as shown in table 1.

General materials	Sum	Extremely serious group	Serious group	Nonserious group	F/χ^2	*p*
n	78	24(30.77%)	32(41.03%)	22(28.21%)		
Mean age (years)	39±14	41±13	39±13	38±15	0.296	0.745
Gender					1.544	0.462
Male	43(55.13)	11(25.58)	20(46.51)	12(27.91)		
Female	35(44.87)	13(37.14)	12(34.29)	10(28.57)		

Table 1: Comparison of the general materials of the three groups [n (%)].

Determination standards

The maximum difference between the physiological parameters and the laboratory results of the patient was conducted using a critical illness score within 24 hours of admission. Extremely serious group: scores <70; serious group: 70 < scores <80; and nonserious group: scores>80

Determination methods

A total of 3 ml of peripheral venous blood under fasting and within 24 hours of admission was drawn from all patients, and the blood samples were centrifuged at 3500 r/min for 5 min and then stored at -80 °C after the serum was separated. The levels of serum IL-6, IL-10, CRP, P-selectin, and D-dimer were detected with an immunochemistry analyzer, blood glucose with the enzymic method, and blood lactate by colorimetry.

Observation parameters

The changes in serum IL-6, IL-10, CRP, and P-selectin and D-dimer, blood glucose, and blood lactate in severe pneumonia patients with sepsis were observed, and the correlation between these parameters and the critical illness score of these patients was analyzed.

Statistical analysis

All data were analyzed by SPSS22.0 software. The measurement data are expressed as the mean±SD, and the t-test was used for the comparison between groups, whereas one-way ANOVA or the Kruskal-Wallis rank-sum test was used for multigroup comparisons. The enumeration data were analyzed using a Chi-square test, and correlations were analyzed using Pearson correlation analysis. The differences were considered statistically significant when p<0.05.

Results

Comparison of the levels of IL-6, IL-10 and CRP among the three groups

The levels of IL-6 and CRP were much higher in the extremely serious group than those in the serious group and nonserious group, and the difference was statistically significant (P<0.05); these levels were also much higher in the serious group than those in the nonserious group, with a statistically significant difference (P<0.05). However, the level of IL-10 was much lower in the extremely serious group than that in the other two groups, and the difference was statistically significant (P<0.05); additionally, the level was much lower in the serious group than that in the nonserious group, with a statistically significant difference (P<0.05), as shown in table 2.

Group	IL-6 (pg/ml)	IL-10 (ng/l)	CRP (mg/l)
Extremely serious group (n=24)	236.03±120.11	14.62±12.02	51.23±24.52
Serious group (n=32)	120.96±75.02	20.13±9.63	37.62±12.03
Nonserious group (n=22)	33.42±18.78	33.02±20.68	14.65±6.98
H	63.411	9.643	11.374
P	<0.001	0.008	0.003

Table 2: Comparison of the levels of IL-6, IL-10 and CRP among the three groups ($\bar{x}\pm s$).

Comparison of the levels of P-selectin and D-dimer among the three groups

The levels of P-selectin and D-Dimer were much higher in the extremely serious group than those in the serious group and nonserious group, and the difference was statistically significant (P<0.05); the levels were also much higher in the serious group than those in the nonserious group, with a statistically significant difference (P<0.05), as shown in table 3.

Group	P-selectin (ng/ml)	D-dimer (ug/ml)
Extremely serious group (n= 24)	251.96±101.56	7.59±5.78
Serious group (n= 32)	171.85±75.23	2.51±1.29
Nonserious group (n= 22)	63.25±40.69	0.69±0.40
F	74.807	38.746
P	<0.001	<0.001

Table 3: Comparison of the levels of P-selectin and D-dimer among the three groups ($\bar{x}\pm s$).

Comparison of the levels of blood glucose and lactate among the three groups

Group	Blood glucose (mmol/L)	Blood lactate (mmol/L)
Extremely serious group (n= 24)	14.56±2.98	2.88±0.39
Serious group (n= 32)	10.21±2.86	1.93±0.35
Nonserious group (n= 22)	7.83±2.63	0.78±0.29
F	33.829	209.703
P	<0.001	<0.001

Table 4: Comparison of the levels of blood glucose and lactate among the three groups ($\bar{x}\pm s$).

The levels of blood glucose and lactate were much higher in the extremely serious group than those in the serious and nonserious group, with a statistically significant difference (P<0.05); the levels were also much higher in the serious group than those in the nonserious group, and the difference was statistically significant (P<0.05), as shown in table 4.

Correlation between the levels of the coagulation parameters, inflammatory cytokines, blood glucose and blood lactate and the critical illness score

IL-6, P-selectin, D-dimer, blood glucose and blood lactate levels were positively correlated with the critical illness score, IL-10 was negatively related to the score, and CPR had no correlation with the score, as shown in table 5.

	IL-6	P-selectin	D-dimer	Blood glucose	Blood actate	IL-10	CRP
r	0.643	0.307	0.709	0.364	0.568	-0.401	0.204
P	<0.001	0.006	<0.001	0.001	<0.001	<0.001	0.073

Table 5: Correlation between the levels of the coagulation parameters, inflammatory cytokines, blood glucose and blood lactate and the critical illness score.

Discussions

Severe pneumonia is characterized by substantial pulmonary inflammation resulting from various pathogens, including pneumococcal, staphylococcus aureus, and anaerobic bacteria, and it is easily complicated by severe sepsis. This results in dehydration, coma, shock, and hypotension. With a fast onset, sepsis is serious, it progresses rapidly, and it is susceptible to a missed diagnosis, which leads to high mortality[6-8]. Epidemiological surveys suggest that the mortality of sepsis has exceeded that of myocardial infarction and is only inferior to that of heart disease[9].

In recent years, organ function support technologies and anti-infection therapies have shown some curative effect on treating severe pneumonia with sepsis, but it easily gives rise to iatrogenic diseases due to many therapeutic paradoxes that exacerbate the disease. Consequently, its mortality is still 30%~70% and negatively influences a human being's health and quality of life. Some articles[10-11] claim that P-selectin, IL-18 and blood glucose can be considered clinical parameters, assessing the severity and progress of severe pneumonia patients with sepsis. Therefore, researching the changes in CRP, coagulation parameters and blood glucose in severe pneumonia patients with sepsis may be of significance in evaluating and treating these kinds of patients.

Cytokines are a group of polypeptide-like regulatory substances with high biological activity that include cell stimulating factors, interleukins, tumor necrosis factors, and interferon. It is reported[12] that the levels of IL-6, IL-10 and CRP have corresponding changes in the blood when inflammation occurs. As a stimulating agent of inflammatory response, IL-6 can induce the proliferation and differentiation of T cells to participant in the immune response of the body. In addition, IL-6 can also induce B cell differentiation and antibody production, and it plays a major role in regulating hematopoiesis and nerve cell regeneration. IL-10 is a multifunctional negative regulation factor that is secreted by activated B cells, Th2 cells and monocytes with domination of immunological suppression. Furthermore, it can resist inflammatory mediators, and it plays an important role in cellular biological regulation, severe infectious diseases, tumor growth, transplant immunity, and autoimmune diseases.

Chen Y[13], et al found that patients infected with the flu have greatly decreased levels of IL-10. CRP, which is an acute phase protein secreted by the liver, is low in health human serum but may largely increase in patients with acute infections or tissue injury such as trauma, bacterial infections, burns, and regional ischemia. Previous studies have proven that CPR is a major marker reflecting the severity of inflammation. Dang R and his fellow colleagues revealed that the level of CRP increases with the worsening of severe pneumonia, and the higher the CRP is, the worse the prognoses. The findings of this study suggest that the levels of IL-6 and CRP are much higher in the extremely serious group than those in the serious group and nonserious group, while the level of IL-10 largely declines with the worsening of severe pneumonia and sepsis, which is consistent with the results of previous studies[12-14]. This finding further demonstrates that IL-6, IL-10 and CRP can reflect the inflammatory severity of the body. The analysis of the correlation between inflammatory cytokines and the critical illness score suggests that IL-6 is positively related to the critical illness score, while IL-10 is negatively related to the score, which indicates that inflammatory cytokines are significant in assessing the progress of severe pneumonia with sepsis.

P-selectin, a member of the adhesion molecule selectin family, is rapidly fused to the plasma membrane and expressed on its surface with the stimulation of histamine, complement, thrombin and reactive oxygen, and the remainder is released into the blood to become a soluble P-selectin. Kim K J, et al[15] reported that the increase in soluble P-selectin suggests the activation of platelets. Normal blood circulation relies on the dynamic equilibrium between plasmin and inhibitory enzymes. This equilibrium is broken when coagulation occurs, and fibrins are degraded into pieces with the action of thrombin; then, r-chain connects these pieces into a D-dimer. A previous study suggested that as a molecular marker reflecting fibrinolytic function, D-dimer is of significance in diagnosing pulmonary embolism (PE), deep venous thrombosis (DVT), and venous thromboembolism (VTE).

Tang G, et al[16] discovered that the increase in D-dimer suggests thrombosis. At the same time, Zhou H T, et al[17] found that D-dimer is an independent marker for assessing the prognoses of sepsis. The findings of this study reveal that the levels of P-selectin and D-dimer are much higher in the extremely serious group than those in the serious group and nonserious group, which coincides with the report of Han Y[18]. A possible reason is that sepsis gives rise to a massive release of cytokines and inflammatory mediators such as interleukin, tumor necrosis factor and endothelin, which thereby causes an imbalance of the coagulation and anti-coagulation system. The findings of this study also suggest that the levels of P-selectin and D-dimer are positively associated with the critical illness score, which indicates that severe pneumonia patients with sepsis have activated platelets that can induce the synthesis of inflammatory cytokines and participate in the process of the inflammatory response and thrombosis. Glucose, which is an important component of the human body, can provide power for the normal operation of various organs and tissues, and glucose in the blood is blood sugar. Blood glucose is maintained at a relatively stable level in normal conditions but increases when the body is in a pathological state such as intracranial hemorrhage, diabetes and myocardial infarction.

Sachwani G R, et al[19] claimed that the level of blood glucose can predict the severity of organ injury in sepsis patients, and the mortality of these patients increases with the elevation of blood glucose concentration. Lactate is a middle product of in vivo glucose metabolism, and it increases when anoxia occurs. Therefore, glucose metabolism processes such as strenuous exercise, glycolysis, and

dehydration can also increase lactate. Joynt G M, et al[20] indicated that the level of blood lactate can indicate the severity of potential disease. The outcomes of this study suggest that the levels of blood glucose and blood lactate increase with the worsening of the disease, which is consistent with the results previous studies[19,20]. This indicates that the levels of blood glucose and blood lactate can temper the severity of severe pneumonia with sepsis to some extent. Further analysis on the correlation between blood glucose and blood lactate and the critical illness score suggests that blood glucose and blood lactate are positively related to the severity of sepsis and indicates that the combined detection of blood glucose and blood lactate can assist in the early diagnosis and assessment of severity.

In summary, IL-6, CRP, P-selectin, D-dimer, blood glucose and blood lactate increase, but IL-10 decreases with the worsening of severe pneumonia with sepsis. Furthermore, IL-6, P-selectin, D-dimer, blood glucose and blood lactate are positively related to the critical illness score, IL-10 is negatively associated with the score, and CRP has no correlation with the score.

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