EXPRESSION AND CLINICAL DIAGNOSTIC VALUE OF SERUM SUPAR, NF-KB AND AQP1/5 IN PATIENTS WITH SEVERE PNEUMONIA

Wendan Wang[1,*], Qiong Wu[2], Yufeng Zeng[3]
[1]Department of Internal Medicine, The Hospital of Zhejiang University, Hangzhou 310000, Zhejiang Province, China - [2]Department of Pediatrics, Zhoushan Women and Children's Hospital, Zhoushan 316000, Zhejiang Province, China - [3]Department of Respiratory Medicine, Wenzhou Hospital of Integrated Chinese and Western Medicine, Wenzhou 325000, Zhejiang Province, China

ABSTRACT

Objective: *To investigate the expression and clinical diagnostic value of serum soluble urokinase-type plasminogen activator receptor (suPAR), nuclear factor kappa B (NF-κB) and aquaporin 1/5 (AQP1/5) in patients with severe pneumonia.*

Methods: *A total of 51 cases of severe pneumonia and 51 cases of common pneumonia, treated in our hospital from July 2018 to May 2020, were randomly selected. A total of 51 healthy subjects who simultaneously underwent a physical examination at our hospital were selected as the control group. The clinical data, serum suPAR, NF-κB and AQP1/5 levels were compared among the three groups. Pearson's correlation test was used to analyze the relationship between the serum suPAR, NF-κB, AQP1/5 levels and the intensity of severe pneumonia. Logistic regression analysis was used to examine the risk factors of severe pneumonia. A receiver operating characteristic (ROC) curve was established to analyze the clinical diagnostic value of the serum suPAR, NF-κB and AQP1/5 levels in severe pneumonia.*

Results: *In comparison with the control group, the levels of white blood cells (WBC) and neutrophil (Neu) in the severe pneumonia and common pneumonia groups were significantly increased (P < 0.05). In comparison with the common pneumonia group, the pneumonia severity index (PSI) score of the severe pneumonia group was significantly higher (P<0.05). In comparison with the control group, the serum levels of the suPAR, NF-κB and AQP1/5 in the common pneumonia group were significantly increased (P < 0.05), and in comparison with the common pneumonia group, the serum levels of the suPAR, NF-κB and AQP1/5 in the severe pneumonia group were significantly increased (P<0.05). Pearson's correlation test showed that the serum suPAR, NF-κB and AQP1/5 levels were positively correlated with the PSI score (P<0.05). An ROC curve was established. The results showed that the area under the curve of the serum suPAR, NF-κB and AQP1/5 were 0.780, 0.791, 0.775 and 0.946, respectively. The area under the curve of the combined detection was significantly higher than that of the single detection, and the specificity and sensitivity of the combined detection were significantly higher than that of the single detection. Logistic regression analysis showed that the suPAR, NF-κB and AQP1/5 were independent risk factors for the development of severe pneumonia.*

Conclusion: *The levels of serum suPAR, NF-κB and AQP1/5 in patients with severe pneumonia were significantly higher than those in patients with severe pneumonia. The levels of these indicators were of great significance for the diagnosis of severe pneumonia, and they were independent risk factors of the disease.*

Keywords: *AQP1/5, clinical diagnostic value, NF-Kb, severe pneumonia, suPAR.*

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Introduction

The lungs constitute one of the largest organs of the human body and are the only organs in which gas exchange occurs. Pneumonia is a type of inflammatory reaction involving the airway, alveoli and pulmonary interstitium. It mainly manifests as high fever, cough and expectoration, accompanied by chest pain or dyspnea. With the abuse of antibiotics, especially the increase of organ transplant patients, a large number of immunosuppressive drugs are frequently used, which makes the clinical face a variety of pathogenic bacteria and multidrug resistance and other problems. Improper treatment will result in severe pneumonia[(1)]. If the pathogenic factors cannot be removed in time, the patient's condition is often aggravated further, and multiple organ failure and other serious complications can occur that seriously

affect the quality of life and health of patients[2]. Research conducted by Wang et al.[3] confirmed that if effective treatment can be conducted in the early stages of the disease, most patients can block the progression of the disease, thus, avoiding mechanical ventilation and admission to the intensive care unit. Therefore, early diagnosis, early detection, early treatment, an improved understanding of the pathogenesis of severe pneumonia, and an improved prognosis of the patients have become the focus of clinical attention. However, at present, there is a lack of clinical indicators for the effective evaluation of severe pneumonia.

Relevant studies have shown that soluble urokinase-type plasminogen activator receptor (suPAR), nuclear transcription factor κB (NF-κB) and aquaporin (AQP) play an important role in the early judgment of infection in the body and the prognosis of patients[4]. Therefore, the present study aimed to explore the expression and clinical diagnostic value of serum suPAR, NF-κB and AQP1/5 in the serum of patients with severe pneumonia to provide a reference for the clinical treatment of patients.

Materials and methods

General information

All patients were included in accordance with the approval of the medical ethics committee of our hospital. A total of 51 cases of severe pneumonia and 51 cases of common pneumonia, treated in our hospital from July 2018 to May 2020, were randomly selected.

Inclusion criteria:

• All patients met the diagnosis and treatment criteria for severe pneumonia[5] and common pneumonia[6];

• Patients with complete medical records could participate in the study to the end;

• Patients could cooperate with the treatment;

• All patients and their families had informed consent and signed an informed consent form.

Exclusion criteria:

• Patients with severe liver, kidney or heart dysfunction;

• Pulmonary diseases and infections caused by active pulmonary tuberculosis, pulmonary infarction or autoimmune diseases;

• Abnormal coagulation function;

• Pregnant or lactating patients.

A total of 51 healthy subjects were selected as the control group.

Observation indexes

After the participants fasted for 10 hours, 4 ml of fasting median cubital venous blood was collected the following morning. The serum and blood cells were separated by a low-temperature high-speed centrifuge at a speed of 3000 R/min. The supernatant was cryopreserved in an ultra-low temperature refrigerator at -80 °C for follow-up study.

The clinical data of the three groups were compared and included age, gender, course of disease, body mass index (BMI), smoking history, white blood cells (WBC), neutrophil (Neu) and pneumonia severity index (PSI). The serum suPAR, NF-κB and AQP1/5 levels were detected: an enzyme-linked immunosorbent assay was used to determine the suPAR and AQP1/5 levels and flow cytometry was used to determine the changes in the NF-κB levels.

Pearson's correlation test was used to analyze the relationship between the serum suPAR, NF-κB and AQP1/5 levels and the severity of the disease in patients with severe pneumonia. An ROC curve was established and the clinical diagnostic value of the serum suPAR, NF-κB and AQP1/5 levels for severe pneumonia were analyzed.

Logistic multivariate regression analysis was used to examine the risk factors affecting the development of severe pneumonia.

Statistical methods

The χ^2 test was used to analyze sex, smoking history and other count data. The measurement data such as age and serum suPAR, NF-κB and AQP1/5 levels were compared using the independent sample t-test. A comparison before and after treatment was performed using the paired sample t-test.

A comparison of the same index at various time points was performed using the repeated measures analysis of variance. The difference between the groups was compared using the independent sample t-test, and the time difference between each group was compared using the LSD-t test. The data comparison result $P<0.05$ indicated that the difference was statistically significant. The SPSS 24.0 software package was used for statistical data analysis.

Results

Comparison of the general data of each group

No significant differences were observed regarding age, gender, BMI or smoking history among the three groups ($P>0.05$). In comparison with the control group, the levels of WBC and Neu in the

severe pneumonia and common pneumonia groups were significantly higher (P<0.05). In comparison with the common pneumonia group, the PSI score of the severe pneumonia group was significantly higher (P<0.05) (Table 1).

Group	Severe pneumonia group	Common pneumonia group	Control group	χ^2/t	*P*
Age (years)	53.86±10.85	54.20±10.76	52.81±12.59	0.20	0.823
Gender					
Female	32(62.75)	30(58.82)	33(64.71)	0.165	0.685
Male	19(37.25)	21(41.18)	18(35.29)		
Course of the disease (days)	8.15±1.10	8.33±1.13	-	0.815	0.417
BMI (kg/m^2)	24.09±1.96	23.34±2.04	24.20±1.96	2.83	0.062
Smoking history	36(70.59)	33(64.71)	31(60.78)	1.097	0.578
WBC (×10^9/L)	19.23±3.46	12.04±2.99	5.98±1.49	291.01	<0.001
Neu (%)	85.48±5.37	72.34±8.79	52.25±7.65	260.31	<0.001
PSI score (points)	99.57±25.98	72.24±20.85	-	5.859	<0.001

Table 1: Comparison of the general data of each group.

Comparison of the serum levels of suPAR, NF-κB and AQP1/5 in each group

In comparison with the control group, the serum levels of the suPAR, NF-κB and AQP1/5 in the patients with common pneumonia were significantly increased (P<0.05). In comparison with the normal pneumonia group, the levels of the serum suPAR, NF-κB and AQP1/5 in the severe pneumonia group were significantly increased (P<0.05) (Table 2).

Group	Cases	suPAR (ng/mL)	NF-κB	AQP1/5 (μg/L)
Control group	51	4.68±1.58	0.36±0.04	0.45±0.09
Common pneumonia group	51	7.48±2.11	0.74±0.10	0.53±0.05
Severe pneumonia group	51	10.86±2.71	1.06±0.14	0.66±0.14
F		102.51	602.19	56.91
P		<0.001	<0.001	<0.001

Table 2: Comparison of the serum levels of the suPAR, NF-κB and AQP1/5 in each group ($\bar{x}\pm s$).

The correlation between the serum suPAR, NF-κB and AQP1/5 levels and the illness severity in patients with severe pneumonia

Pearson's correlation test showed that the serum suPAR, NF-κB and AQP1/5 levels in patients with severe pneumonia were significantly positively correlated with the PSI scores (P<0.05) (Table 3).

Indexes	PSI score	
	r	*P*
suPAR	0.405	<0.05
NF-κB	0.101	<0.05
AQP1/5	0.167	<0.05

Table 3: The correlation between the serum suPAR, NF-κB and AQP1/5 levels and the illness severity in patients with severe pneumonia.

The clinical diagnostic value of the serum suPAR, NF-κB and AQP1/5 levels for severe pneumonia

An ROC curve was established, and the results showed that the area under the curve of the serum suPAR, NF-κB and AQP1/5 was 0.780, 0.791, 0.775, 0.946, respectively.

The combined area under the curve of the three elements was significantly higher than that of a single test, and the specificity and sensitivity of the combined detection of the three elements were significantly higher than that of the single detection (Table 4).

Indexes	Area under the curve	Sensitivity (%)	Specificity (%)	*P*	95%CI	
					max	min
suPAR	0.780	81.94	74.13	<0.001	0.888	0.682
NF-κB	0.791	80.21	73.68	<0.001	0.901	0.681
AQP1/5	0.775	79.35	75.88	<0.001	0.883	0.658
suPAR + NF-κB +AQP1/5	0.946	90.13	92.83	<0.001	0.991	0.882

Table 4: The clinical diagnostic value of the serum suPAR, NF-κB and AQP1/5 levels for severe pneumonia.

Risk factors affecting the development of severe pneumonia

Logistic multivariate regression analysis showed that the suPAR, NF-κB and AQP1/5 are independent risk factors that affect the development of severe pneumonia (Table 5).

Indexes	Wald value	Standard deviation	B	P value	0.888
suPAR	14.268	0.033	-0.111	<0.001	0.901
NF-κB	13.415	0.020	-0.084	<0.001	0.883
AQP1/5	11.283	0.023	-0.069	<0.001	0.991

Table 5: Risk factors affecting the development of severe pneumonia.

Discussion

Severe pneumonia is a common infectious disease caused by bacteria and viruses in intensive care units. With the development of the social economy and the deterioration of the living environment, the incidence of pneumonia has increased significantly, particularly among the elderly. These individuals have low body resistance and a weakened cough reflex, and most have basic diseases. Once infection occurs, the underlying diseases are easily aggravated. These conditions can even develop into severe pneumonia and can cause death in certain cases[7]. However, due to a lack of understanding of the disease and a lack of specific detection methods, a misdiagnosis or missed diagnosis is common. Additionally, the irrational use of antibiotics and the emergence of bacterial resistance has increased the level of difficulty of clinical treatment. Therefore, an effective index for the early diagnosis of severe pneumonia is required.

As a variant of the urokinase-type plasminogen activator receptor (uPAR), suPAR is produced through the hydrolysis of the uPAR in plasmin, chymotrypsin, elastase and other proteins. It is formed by the shedding of the cell surface and exists in the cerebrospinal fluid, serum, urine, bronchoalveolar lavage fluid and other body fluids. It is involved in cell adhesion, proteolysis, immune activation, tumor cell infiltration and signal transduction, and other physiological processes[8]. Studies have found that the serum suPAR level is closely related to the activation level of the body's immune system, and its level is a direct reflection of the activation degree of the body's immune system, which is not affected by diet[9]. It has been reported that suPAR is significantly increased in infectious diseases and tumors, and its level is closely related to the pathological process and prognosis of[10]. The results of the present study showed that the level of serum suPAR was significantly higher than that of the individuals who had common pneumonia and the healthy subjects, which was significantly related to the patient's condition, and it was an important risk factor for the development of severe pneumonia.

NF-κB is a nuclear transcription factor that is necessary for the expression of inflammatory mediator genes. Haizhou et al.[11] found that when severe infection occurs, numerous activated inflammatory cells participate in the infection. Tumor necrosis factor-α (TNF-α), C-reactive protein (CRP) and other major inflammatory mediators and cytokines involved in the inflammatory response of severe pneumonia are transcripts that are regulated by NF-κB. Furthermore, NF-κB may be the key to regulating the inflammatory response of severe pneumonia. Inhibiting the activation of NF-κB in the body can significantly reduce the expression of downstream mRNA and proteins (for example, a variety of pro-inflammatory cytokines) and prevent multi-organ damage induced by lipoproteins or cytokines. The results of this study demonstrated that NF-κB was significantly increased in patients with severe pneumonia, and its levels effectively reflected the changes in a patient's condition[12]. This may be because NF-κB can regulate inflammatory mediators such as TNF-α, causing an abundance of inflammatory mediators to be released, thereby initiating and expanding the inflammatory cascade and aggravating the development of the disease[13].

AQP is a type of protein with specific permeability to water, which widely exists in many tissues and cell membranes and is extremely important for maintaining the homeostasis of the internal and external environments. Studies have confirmed that AQP expression levels of alveolar epithelial cells and capillary endothelial cells in patients with acute lung injury are significantly reduced[14]. The AQP in the lungs includes AQP1, AQP3, AQP4, AQP5, AQP8 and AQP9. It is expressed in various parts of the lungs and participates in the movement of water molecules. AQP1 and AQP5 have been the primary focus of research concerning lung inflammatory diseases. AQP1 is widely distributed in vascular endothelial cells, which can increase the water permeability of cell membranes. AQP5 is widely expressed in alveolar epithelial cells and plays an important role in removing water from the alveoli and maintaining water balance inside and outside the cells. According to reports, decreased expression of AQP5 is an important indicator of a lung injury[15]. The results of this study revealed that with the aggravation of pneumonia patients, the level of AQP1/5 increased significantly. Thus finding is of great value for the diagnosis of severe pneumonia.

In summary, the serum levels of suPAR, NF-κB and AQP1/5 in patients with severe pneumonia were significantly increased. The levels of the above-mentioned indicators are of great significance for the diagnosis of severe pneumonia, and they are independent risk factors that affect the disease.

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Corresponding Author:
Wendan Wang
Zhejiang University Zijingang Campus Hospital, No. 866 Yuhangtang Road, Xihu District, Hangzhou City, Zhejiang Province, China
Email: rv1gsg@163.com
(China)