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Original Article

Evaluation of COPD patients with combined detection of serum PA, SAA and PCT levels

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Abstract: Objective: To investigate the clinical significance of combined detection of serum prealbumin (PA), serum amyloid A (SAA), and procalcitonin (PCT) levels in the evaluation of patients with chronic obstructive pulmonary disease (COPD). Methods: From April 2017 to February 2019, 73 patients with exacerbations of COPD were enrolled as the study group, and 71 patients with COPD in the remission stage were enrolled as the control group. Serum PA, SAA and PCT levels were tested and compared. The diagnostic efficacies of single and combined detection of these indicators for exacerbation were explored. The correlation between each indicator and the severity of COPD was analyzed using Spearman's correlation. Results: The study group exhibited lower serum PA and higher serum SAA and PCT levels than the control group ($P < 0.05$). The sensitivity and accuracy of combined detection of serum PA, SAA, PCT levels in diagnosis of exacerbations were 98.63% (72/73) and 93.06% (134/144), higher than those of single detection ($P < 0.05$). PA level: critical group < severe group < moderate group < mild group, serum SAA and PCT levels: critical group > severe group > moderate group > mild group ($P < 0.05$). Spearman rank correlation analysis found that serum PA level was negatively correlated with the severity of exacerbations ($r < 0$, $P < 0.05$). Serum SAA and PCT levels were positively correlated with the severity of COPD exacerbations ($r > 0$, $P < 0.05$). Conclusion: Serum PA, SAA, and PCT levels were closely related to the severity of COPD exacerbations. Patients showed low expression of serum PA levels and high expression of serum SAA and PCT levels. Combined detection of serum PA, SAA, and PCT levels can significantly increase diagnostic efficacy in COPD exacerbations and can be used in clinical evaluation of the severity of COPD.

Keywords: Chronic obstructive pulmonary disease, prealbumin, amyloid, procalcitonin

Introduction

Chronic obstructive pulmonary disease (COPD) is manifested by irreversible airflow obstruction, especially in patients with COPD exacerbations [1]. The respiratory symptoms are further aggravated, which seriously threatens the physical and mental health and life safety of the patients [2, 3]. Therefore, prevention of COPD exacerbations has become a hot topic in health communities [4, 5]. Inflammatory markers are associated with the occurrence and progression of COPD. Prealbumin (PA), also called transthyretin, is one of the major proteins in the blood and one of "negative" acute-phase proteins [6]. The serum PA level decreased rapidly in response to acute infection. Serum amyloid A (SAA), a member of the apolipoprotein family, mediates the activation and chemotaxis of many inflammatory cells such as neutrophils, and thus participates in the occurrence and development of inflammatory reactions, which is indicative of the risk of respiratory failure [6]. Serum procalcitonin (PCT) levels are not only closely related to the severity of bacterial infections, but also play a vital role in the occurrence and progression of diseases. Increased PCT levels suggested the occurrence of bacterial infections in the lower respiratory tract, and can be used to assess the severity of disease and determine the type of pathogens. Therefore, it is often used as an indicator for monitoring severe systemic infections. In recent years, many studies at home and abroad have found that serum PA, SAA, and PCT levels are closely related to the occurrence, development, and severity of COPD, but there are few clinical studies on the efficacy of combined diagnosis of the three indicators [7]. In this study, 73 patients with COPD exacerba-

Table 1. Baseline data (mean ± SD)/[n (%)]

Group	Age (year)	Course of disease (years)	Gender	
			Female	Male
Study group (n = 73)	61.87±4.94	5.07±1.94	34 (46.58)	39 (53.42)
Control group (n = 71)	62.09±5.13	4.91±2.03	33 (46.48)	38 (53.52)
t/χ^2	0.262	0.483	0.000	
P	0.793	0.629	0.991	

tions were selected to explore the application value of combined detection of serum PA, SAA, and PCT levels in the evaluation of COPD patients.

Materials and methods

Baseline data

From April 2017 to February 2019, 73 patients with COPD exacerbations in our hospital were enrolled as the study group, and 71 patients with COPD in the remission stage were included as the control group. Inclusion criteria: Patients who met the Guidelines for the Diagnosis and Treatment of Chronic Obstructive Pulmonary Disease (2013 revised edition) [8]; those with normal coagulation function; and those who did not receive anticoagulant treatment and glucocorticoid treatment 1 month before enrollment. All study participants provided written informed consent prior to participating in the study. This study has been approved by the Ethics Committee of Shengzhou People's Hospital (The First Affiliated Hospital of Zhejiang University Shengzhou Branch). Exclusion criteria: Patients complicated with dysfunction of other important organs such as liver and kidney; those with myocardial infarction and pulmonary infarction; those with malignant tumor disease; and those with pulmonary interstitial fibrosis, typical pulmonary hypertension, bronchial asthma, connective tissue disease, pneumothorax and other lung diseases.

Methods

4 ml of fasting venous blood samples were collected in the morning and on the 2nd day after admission, placed in a reagent tube without anticoagulant, and centrifuged at 3000 r/min for 15 min. The supernatant was stored at -20°C. The levels of serum PA, SAA, and PCT were measured using the enzyme-linked immunosorbent assay kit (Shanghai Yifeng Biotechnology Co., Ltd.), and the operations were strictly performed in accordance with the kit instructions. Reference: PA: 280-350 mg/L, SAA < 3 mg/L, PCT < 0.5 μg/L.

Observation indicators

(1) Clinical data; (2) Serum PA, SAA, and PCT levels; (3) Positive cases of single detection and combined detection; (4) Using clinically confirmed results as the "gold standard", the performance of single detection and combined detection were compared. The combined detection of three indicators is considered as positive with any one positive result. (5) The serum PA, SAA, and PCT levels in the study group were evaluated by COPD Assessment Test (CAT) covering a total of 8 questions on a 5-point scale, with a total score of 40 points. Critical > 30 points, severe 20-30 points, moderate 10-19 points, and mild < 10 points. (6) Spearman's Rank correlation coefficient was used to analyze the correlation between serum PA, SAA, PCT levels and the severity of COPD.

Statistical analysis

SPSS 23.0 was used for statistical analysis. Measurement data (serum PA, SAA, PCT levels) (mean ± SD) were compared using *t* test. Comparison between multiple groups was performed using single factor analysis of variance. Count data (specificity, sensitivity, accuracy) were represented by n (%) and examined by chi-square test. The relationship between serum PA, SAA, PCT levels and the severity of COPD exacerbations was analyzed by Spearman rank correlation analysis. $P < 0.05$ indicated that the difference was statistically significant.

Results

Comparison of the baseline data

There was no significant difference in terms of age, course of disease, and gender between the two groups ($P > 0.05$, **Table 1**).

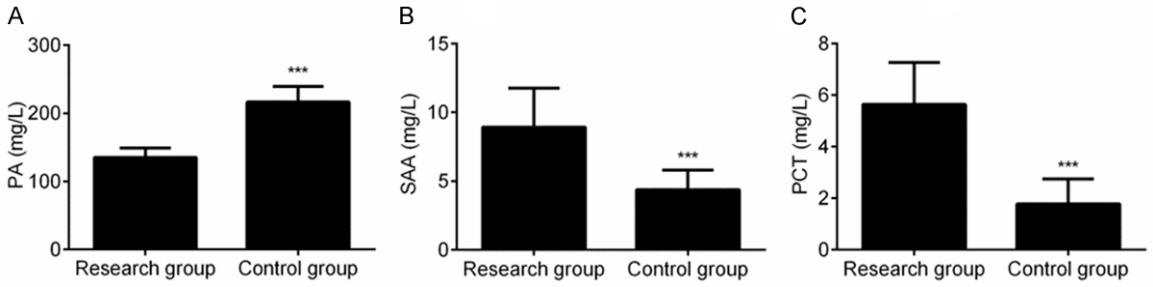

Figure 1. Comparison of serum PA, SAA and PCT levels between the two groups. The study group exhibited lower serum PA levels and higher serum SAA and PCT levels than those in the control group. Note: Compared with the control group, $^{***}P < 0.005$. A. PA; B. SAA; C. PCT.

Table 2. Results of single detection and the combined detection (n = 144)

Clinically proven	Serum PA		Serum SAA		Serum PCT		Combined detection		Total
	+	-	+	-	+	-	+	-	
+	52	21	51	22	53	20	72	1	73
-	8	63	9	62	8	63	9	62	71
Total	60	84	60	84	61	83	81	63	144

Table 3. Performance of the single detection and the combination detection [n (%), n = 144]

Detection method	Specificity	Sensitivity	Accuracy
Serum PA	88.73 (63/71)	71.23 (52/73)	79.86 (115/144)
Serum SAA	87.32 (62/71)	69.86 (51/73)	78.47 (113/144)
Serum PCT	88.73 (63/71)	72.60 (53/73)	80.56 (116/144)
Combined detection	87.32 (62/71)	98.63 (72/73)	93.06 (134/144)
χ^2	0.134	24.173	14.017
P	0.987	0.000	0.003

Comparison of serum PA, SAA, and PCT levels between the two groups

The study group exhibited lower serum PA levels and higher serum SAA and PCT levels than those in the control group ($P < 0.05$, **Figure 1**).

The performance of single and combined detection of COPD exacerbations

Clinical results confirmed that there were 73 patients with COPD exacerbations and 71 COPD patients in remission stage. Combination detection confirmed 72 patients with COPD exacerbations and 62 patients in remission stage (**Table 2**).

Single detection and combined detection of COPD exacerbation

No significant difference was found in specificity between single detection and combination detection ($P > 0.05$). In terms of sensitivity and accuracy, combination detection was higher than single detection ($P < 0.05$, **Table 3**).

Serum PA, SAA, and PCT levels in patients with COPD exacerbations

Serum PA levels were as follows: critical group < severe group < moderate group < mild group; serum SAA, PCT levels were as follows: critical group > severe group > moderate group > mild group ($P < 0.05$, **Figure 2**).

Correlation between serum PA, SAA, PCT levels and the severity of COPD exacerbations

Spearman rank correlation analysis found that serum PA levels were negatively correlated with the severity of COPD exacerbations ($r < 0$, $P < 0.05$); serum SAA and PCT levels were positively correlated with the severity of COPD exacerbations ($r > 0$, $P < 0.05$, **Table 4**).

Discussion

In recent years, the incidence of COPD has been on the rise. Data show that the incidence of COPD in people over 40 years of age is about 9%, and the incidence is proportional to the age, leading to an extremely severe prevention

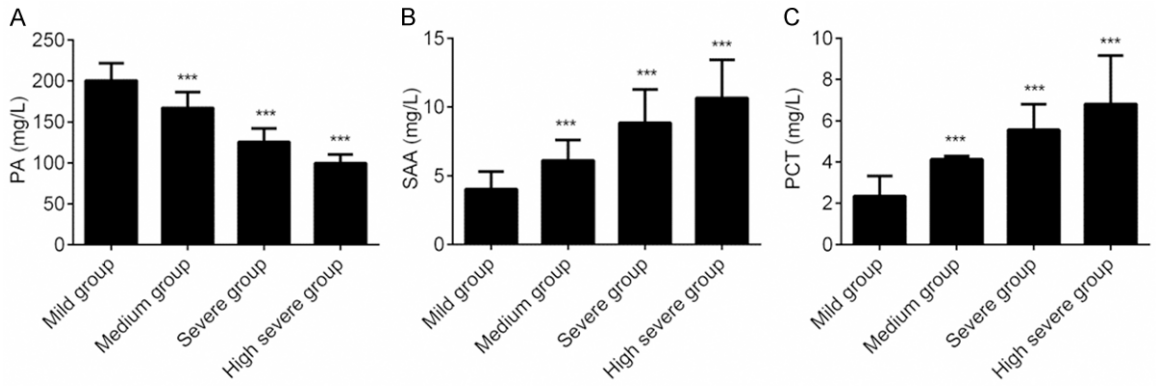

Figure 2. Comparison of serum PA, SAA and PCT levels in COPD patients with different degrees of exacerbation. Serum PA levels were as follows: critical group < severe group < moderate group < mild group; serum SAA and PCT levels were as follows: critical group > severe group > moderate group > mild group. Note: Compared with the control group, $^{***}P < 0.005$. A. PA; B. SAA; C. PCT.

Table 4. Correlation between serum PA, SAA and PCT levels and the severity of COPD

Indicators	*r*	*P*
PA	-0.742	0.000
SAA	0.566	0.000
PCT	0.691	0.000

situation [9-11]. Periods of COPD were categorized as phases of remission and exacerbations. Among them, patients are critically ill during exacerbations. If not diagnosed and treated in a timely manner, it will lead to a high risk of death [12-14]. Therefore, it is of great significance to explore an effective method to distinguish remission from exacerbation.

This study showed that the serum PA level in the study group was lower than that in the control group, while the serum SAA and PCT levels in the study group were higher than those in the control group ($P < 0.05$). PA levels in critical group were lower than those in mild group, while serum SAA and PCT levels in critical group were higher than those in mild group. The serum PA level was negatively correlated with the severity of COPD exacerbations, and the serum SAA and PCT levels were positively correlated with the severity of COPD. Serum SAA and PCT levels are highly expressed, and detection of them is helpful to determine the severity of COPD. The serum PA level drops rapidly during acute infection and is often used clinically to evaluate and monitor the nutritional status of patients [15]. The study of Gong and other researchers [16] has found that the serum PA level of children with acute sepsis was significantly lower than that of children in recovery and healthy children. SAA participates in the development of inflammatory reactions [17]. Increased serum SAA levels are more common in respiratory diseases such as acute respiratory distress syndrome, viral infections, and COPD. The study of Yu has [18] found that the serum SAA levels of patients with cerebral infarction were significantly higher than those of healthy controls and have some connection with TOAST subtype, and it is often used as an indicator of cerebral infarction in acute stage. PCT is one of the glycoproteins with good stability, and its level is very low in healthy people [19, 20]. However, when inflammation or infection occurs, the serum PCT level will increase sharply. Therefore, it is often used to determine the degree of infection and prognosis in clinic. Studies have found that the serum PCT level is less than 0.5 μg/L. When infection occurs, large amounts of PCT could be secreted by extra-thyroid. The rise usually begins 2 to 4 hours after infection, and peaks at 16 to 32 hours. With the effective infection control, its level will gradually drop to the normal range [21]. In the study of Xu [22], serum PCT level was positively correlated with the severity of COPD patients in the exacerbation phase ($P < 0.05$), which was consistent with the results of this study. This further indicated that PCT was unusually high in COPD patients in the exacerbation phase, and it increased with the aggravation of the disease, which could be used as an indicator to evaluate the disease condition. Fan and other

researchers [23] showed that the serum PCT level of patients with acute pancreatitis was significantly higher than that of healthy people, and the serum PCT level reached a peak on the 4th day of admission. Serum PCT levels are not only closely related to the severity of bacterial infections, but are also involved in the occurrence and progression of diseases. Increased levels can predict the occurrence of bacterial infections in the lower respiratory tract. It is often used to monitor severe systemic infections [24-26]. The expression level of PCT is also correlated with the severity of COPD, which is mostly used to evaluate the treatment efficacy and prognosis of COPD exacerbations.

In this study, there was only 1 case of missed diagnosis by the combined detection, and the rate of missed diagnosis was 1.37%, indicating that the combined detection of PA, SAA and PCT levels could reduce the missed diagnosis rate in patients with exacerbation of COPD. This study showed that the combined detection of serum PA, SAA and PCT levels in the exacerbation of COPD had a sensitivity of 98.63% and an accuracy of 93.06%, higher than those of the single detection ($P < 0.05$), suggesting that combined detection can significantly improve the diagnostic sensitivity and accuracy of patients in the exacerbation period and could aid the early diagnosis. However, there are still some deficiencies in this study, such as small sample size, no healthy control group, and no correlation analysis among various indicators. Therefore, a large sample size and multi-center study is still needed in the later stage.

In summary, the levels of serum PA, SAA, and PCT are closely related to the severity of COPD exacerbations. The combined detection of serum PA, SAA, and PCT levels showed higher sensitivity and accuracy in the diagnosis of COPD patients with exacerbations and could be used in clinical evaluation of the severity of COPD.

Disclosure of conflict of interest

None.

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