SIGNIFICANCE OF CHANGES IN SERUM SICAM-1 AND TBIL IN PATIENTS WITH ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE COMBINED WITH TYPE 2 DIABETES

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ABSTRACT

Introduction: *To explore the significance of changes in serum soluble intercellular adhesion molecule-1 (sICAM-1) and total bilirubin (TBIL) in patients with acute exacerbation of COPD combined with type 2 diabetes.*

Materials and method: *Ninety-one patients with acute exacerbation of COPD combined with type 2 diabetes were included in the case group. Ninety-one patients with acute exacerbation of COPD alone were selected as a control group. Serum sICAM-1, TBIL, and malondialdehyde (MDA) and superoxide dismutase (SOD) were compared. Receiver operating characteristic (ROC) curve was used to analyze the predictive value of serum sICAM-1 and TBIL for the development of type 2 diabetes in patients with acute exacerbations of COPD.*

Results: *Serum sICAM-1 and MDA in case group were higher than those in control group (both p<0.001); but serum TBIL and SOD in case group were the opposite (both p<0.001). In case group, serum sICAM-1 level was positively correlated with serum MDA and negatively correlated with serum SOD; and serum TBIL level was negatively correlated with serum MDA and positively correlated with serum SOD. ROC curve analysis showed that the area under ROC curve for serum sICAM-1 and TBIL level to predict acute exacerbation of COPD combined with type 2 diabetes was 0.783 (95%CI: 0.718-0.849) and 0.600 (95%CI: 0.515-0.685), respectively, the area under ROC curve of the former was larger than that of the latter.*

Conclusions: *Serum sICAM-1 and MDA levels increase and serum TBIL and SOD levels decrease in patients with acute exacerbation of COPD combined with type 2 diabetes, and the increased serum sICAM-1 and decreased TBIL levels may be related to oxidative stress in these patients. Both serum sICAM-1 and TBIL are useful for the diagnosis of COPD combined with type 2 diabetes, but the former has higher diagnostic efficacy than the latter.*

Keywords: *Chronic obstructive pulmonary disease (COPD), type 2 diabetes, soluble intercellular adhesion molecule-1 (sICAM-1), total bilirubin (TBIL), malondialdehyde (MDA), superoxide dismutase (SOD).*

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Introduction

Chronic obstructive pulmonary disease (COPD) is characterized by persistent airflow limitation that progresses in an incomplete and reversible manner. Type 2 diabetes is one of the common comorbidities of COPD[(1)]. In recent years, the number of patients with COPD combined with type 2 diabetes has been increasing. Oxidative stress directly damages airway and lung tissue, diminishes the ability of epithelial cells to participate in post-injury repair, and affects the reconstruction of the extracellular matrix[(2)]. Oxidative stress is closely associated with inflammatory lung injury and airway obstruction in COPD patients[(3)]. Oxidative stress is also strongly associated with the development of type 2 diabetes[(4)]. It has been shown that oxidative stress can cause insulin resistance and islet cell damage in COPD patients through the NF-ϰB pathway, thus participating in the development of type 2 diabetes[(5,6)]. Malondialdehyde (MDA) and superoxide dismutase (SOD) are important indicators of oxidative stress.

MDA is one of the end products of free radical lipid peroxidation reactions, and it can mediate oxidative damage and inflammatory responses in the body[7]. SOD is a metalloenzyme that catalyzes the formation of hydrogen peroxide from superoxide anions to scavenge free radicals and reduce tissue damage[8]. The levels of serum MDA and SOD can reflect the level of oxidative stress in the body.

Soluble intercellular adhesion molecule-1 (sICAM-1) is a cell adhesion molecule expressed on the alveolar epithelium and vascular endothelium and is thought to play a key role in neutrophil recruitment and transport to the lung. The increase in serum sICAM-1 level reflects the increased inflammatory response of COPD patients and can be used to assess the severity of COPD[9, 10]. Bilirubin is a potent antioxidant in the body, and it can regulate the oxidative/antioxidative processes of the body and has a protective effect on the smooth muscle of many organs[11]. It is an endogenous antioxidant that responds to antioxidant stress. Previous studies have shown that changes in serum sICAM-1 and total bilirubin (TBIL) levels are closely related to the development of both COPD and type 2 diabetes[12, 13].

Currently there are few reports concerning the correlation between serum sICAM-1, TBIL and oxidative stress in patients with COPD combined with type 2 diabetes. In addition, there are also few reports on using serum sICAM-1 and TBIL to diagnose COPD combined with type 2 diabetes. The objective of this study was to explore the content changes in serum sICAM-1 and TBIL and oxidative stress indicators MDA and SOD in patients with acute exacerbation of COPD combined with type 2 diabetes, analyze the correlation between serum sICAM-1 and MDA levels and serum TBIL and SOD, and study the application value of serum sICAM-1 and TBIL in the diagnosis of acute exacerbation of COPD combined with type 2 diabetes.

Materials and methods

Clinical materials

This study was approved by the Medical Ethics Committee of our hospital. All patients signed an informed consent form.

A total of 91 patients with acute exacerbation of COPD combined with type 2 diabetes admitted to our hospital from April 2019 to February 2022 were included in the case group.

The inclusion criteria were as follows:

• Met the diagnostic criteria of COPD, with clinical manifestation of grade II (moderate) acute exacerbation;

• With diabetic symptoms such as polyuria, polydipsia, and unexplained body mass reduction, plasma glucose ≥7.0 mmol/L on 3 consecutive days, and confirmed with type 2 diabetes;

• And no other pulmonary diseases shown on chest X-ray.

The exclusion criteria were as follows:

• Patients who had taken glycemic control, anti-infective and other related drugs before inclusion in the study;

• With acute and chronic complications of diabetes;

• With concomitant diseases such as gout, hypertension, acute and chronic nephritis, thyroid disease and malignancy;

• Women during pregnancy and lactation;

• Patients with COPD combined with type 2 diabetes who were not in acute exacerbation period.

A total of 91 patients admitted to our hospital during the same period with acute exacerbation of COPD alone were selected as the control group.

Methods

Venous blood specimens of patients in the two groups were collected before admission to the hospital. The level of sICAM-1 in serum specimens was measured by ELISA. Serum TBIL levels were measured using a fully automated biochemical analyzer. A thiobarbituric acid colorimetric assay was used to measure MDA content. SOD content was measured by xanthine oxidase method.

The correlation between serum sICAM-1, TBIL and oxidative stress indicators (MDA and SOD) in patients with acute exacerbation of COPD combined with type 2 diabetes in the case group was analyzed. Receiver operating characteristic (ROC) curve was used to analyze the predictive value of serum sICAM-1 and TBIL for the development of type 2 diabetes in patients with acute exacerbations of COPD.

Statistical analysis

SPSS 25 0 was used for data analysis. Measurement data were expressed by mean ± standard deviation, and independent sample t-test was used. Counting data were expressed by n (%) and chi-square test was used. Correlation between serum sICAM-1, TBIL and oxidative stress indexes (MDA, SOD) was analyzed by Pearson correlation. Predictive value of serum sICAM-1 and TBIL in the

development of type 2 diabetes in patients with acute exacerbation of COPD was evaluated by ROC curve. The difference was statistically significant at $p<0.05$.

Results

Among the 91 patients in the case group, 50 (54.95%) were male and 41 (45.05%) were female, aged 65.57±4.68 years old. Among the 91 patients in the control group, 48 (52.75%) were male and 43 (47.25%) were female, aged 64.40±4.95 years old.

Serum sICAM-1 and MDA in the case group were higher than those in the control group (both $p<0.001$); and serum TBIL and SOD in the case group were lower than those in the control group (both $p<0.001$), as shown in Table 1.

Index	Case group (n=91)	Control group (n=91)	P- value
Serum sICAM-1 (μg/L)	160.08±15.21	142.05±10.92	<0.001
Serum TBIL (μmol/L)	9.49±0.98	12.24±1.03	<0.001
Serum MDA (nmol/mL)	8.91±0.67	8.00±0.64	<0.001
Serum SOD (NU/ mL)	60.12±4.53	75.40±5.80	<0.001

Table 1: Comparison of serum sICAM-1, TBIL levels and oxidative stress indicators.

In patients with acute exacerbation of COPD combined with type 2 diabetes in the case group, serum sICAM-1 level was positively correlated with serum MDA and negatively correlated with serum SOD ($r=0.437$, $p<0.001$; $r=-0.429$, $p<0.001$); and serum TBIL level was negatively correlated with serum MDA and positively correlated with serum SOD ($r=-0.657$, $p<0.001$; $r= 0.580$, $p<0.001$), as shown in Table 2.

Index	Serum MDA		Serum SOD	
	Correlation value r	p-value	Correlation value r	p-value
Serum sICAM-1	r=0.437	p<0.001	r=-0.429	p<0.001
Serum TBIL	r=-0.657	p<0.001	r= 0.580	p<0.001

Table 2: Correlation analysis of serum markers in the case group.

ROC curve analysis showed that the area under the ROC curve for serum sICAM-1 and TBIL level to predict acute exacerbation of COPD combined with type 2 diabetes was 0.783 (95%CI: 0.718-0.849) and 0.600 (95%CI:0.515-0.685), respectively.

The area under the ROC curve of the former was larger than that of the latter, and the best cut-off value for serum sICAM-1 was 148.22 μg/L and for serum TBIL was 11.63 μmol/L, as shown in Table 3 and Figures 1 and 2.

Prediction index	Area under ROC curve	95% CI	The best cut off values	Sensitivity (%)	Specificity (%)
Serum sICAM-1	0.783	0.718--0.849	148.22 μg/L	70.8	64.5
Serum TBIL	0.600	0.515--0.685	11.63μmol/L	74.2	50.6

Table 3: Value of serum sICAM-1 and TBIL levels in predicting acute exacerbation of COPD combined with type 2 diabetes.

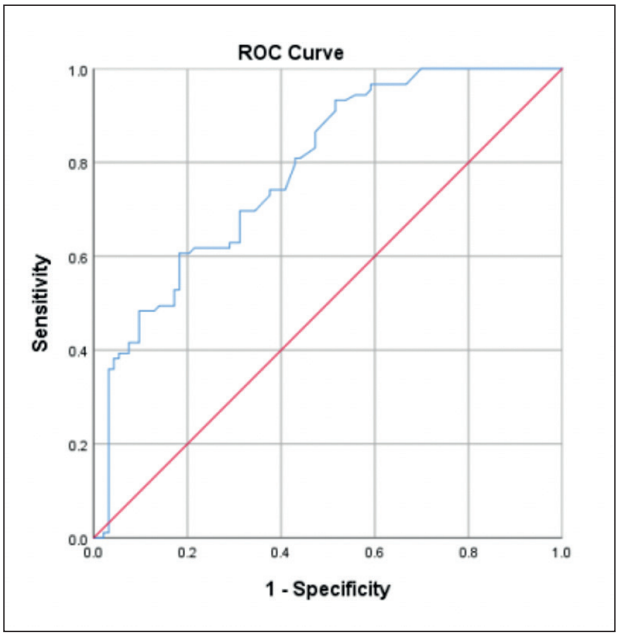

Figure 1: ROC curve of serum sICAM-1 level for evaluation of acute exacerbation of COPD combined with type 2 diabetes.

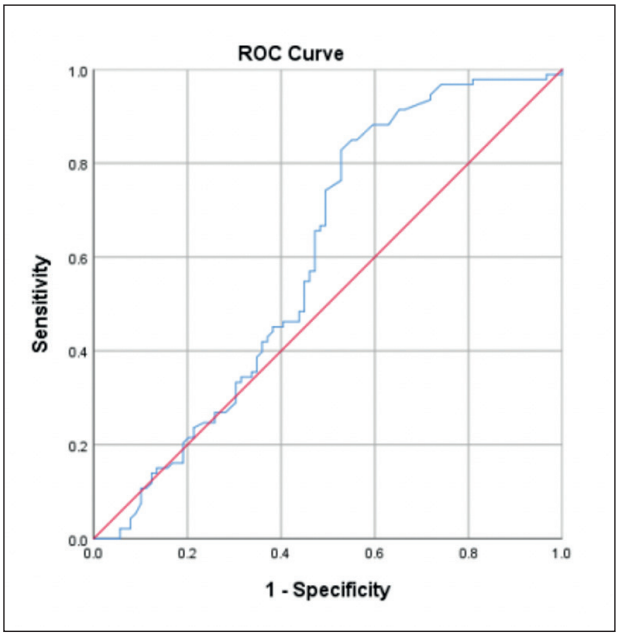

Figure 2: ROC curve of serum TBIL level for evaluation of acute exacerbation of COPD combined with type 2 diabetes.

Discussion

Diabetes can be involved in the inflammatory process of COPD through cellular and humoral immune mechanisms, and it makes COPD patients more susceptible to exacerbation by factors such as infection[14]. Oxidative stress occurs when the body is exposed to various harmful stimuli, and it is the result of a persistent imbalance between free radical production and oxidative defense and can lead to tissue damage[15]. Oxidative stress has an important role in the development of diabetes and COPD. The oxidants/antioxidants are in a dynamic balance in the body under physiological conditions. During acute exacerbations of COPD, infection increases oxide production and decreases clearance ability, resulting in an imbalance in oxide/antioxidant levels[16]. The severity of free radical attack on the body's cells can be indirectly reflected by the level of MDA through the measurement of MDA, an end product of free radical metabolism[17].

SOD is a metalloenzyme that catalyzes the formation of hydrogen peroxide from superoxide anions to scavenge free radicals and reduce tissue damage, reflecting the antioxidant capacity of the body[18]. Antioxidants such as SOD can reduce the production of free radicals, directly destroy free radicals in the body, and enhance the body's antioxidant capacity to protect against oxygen radical pathological damage and lipid peroxidation pathological damage during stress[19], so it is possible to prevent the development of COPD in patients with type 2 diabetes. In this study, we found that serum MDA level in the case group was higher than that in the control group, and serum SOD in the case group was lower than that in the control group, suggesting that the degree of oxidative stress is more severe in patients with type 2 diabetes combined with acute exacerbations of COPD than in patients with acute exacerbations of COPD alone.

The abnormal expression of sICAM-1 was closely related to the degree of glycemic control[20]. Lower bilirubin levels lead to a reduction in the body's antioxidant capacity[12]. Previous studies have shown that serum bilirubin concentrations are associated with the development of COPD, diabetes and other diseases[21-22]. The results of this study showed that serum sICAM-1 in the case group was higher than that in the control group, and serum TBIL in the case group was lower than that in the control group, suggesting that the endogenous antioxidant capacity is weaker and the oxidative/antioxidative imbalance is more severe in patients with acute exacerbation of COPD combined with type 2 diabetes than in patients with acute exacerbation of COPD alone.

The further analysis showed that serum sICAM-1 level in the case group was positively correlated with serum MDA level and negatively correlated with serum SOD level; and serum TBIL level was negatively correlated with serum MDA level and positively correlated with serum SOD level, indicating that elevated serum sICAM-1 and decreased TBIL may be associated with oxidative stress in patients with acute exacerbation of COPD combined with type 2 diabetes; and changes in sICAM-1 and TBIL levels may be used as serum markers for the determination of type 2 diabetes in combination with acute exacerbation of COPD. It is worthwhile to further investigate whether downgrade serum sICAM-1 levels and upgrade TBIL levels can delay the complication of type 2 diabetes in patients with acute exacerbation of COPD. The ROC curve analysis revealed that the value of serum sICAM-1 and TBIL tests was best for the diagnosis of acute exacerbation of COPD combined with type 2 diabetes. This shows that the diagnostic efficacy of both serum sICAM-1 and TBIL is high in screening for type 2 diabetes in patients with acute exacerbation of COPD, and the former is better than the latter.

The limitation of this study was that the sample size was limited and other factors affecting serum sICAM-1 and TBIL could not be fully excluded. Although the single index test of serum sICAM-1 and TBIL has certain effect, it still has great limitations. The efficacy of the combined test of serum sICAM-1 and TBIL on the diagnosis of type 2 diabetes in patients with acute exacerbation of COPD was not studied in this paper, and further research is needed. In addition, all patients were from the same hospital, which also has limitations.

Conclusion

Serum sICAM-1 and MDA levels increase and serum TBIL and SOD levels decrease in patients with acute exacerbation of COPD combined with type 2 diabetes, and the increased serum sICAM-1 and decreased TBIL levels may be related to oxidative stress in these patients. Both serum sICAM-1 and TBIL are useful for the diagnosis of COPD combined with type 2 diabetes, but the former has higher diagnostic efficacy than the latter.

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