Effects of low molecular weight heparin on the function of blood coagulation and serum levels of TNF-\(\alpha\), CK-MB, CRP of patients with acute exacerbations of chronic obstructive pulmonary diseases and respiratory failure

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**ABSTRACT**

**Objective:** To study the effects of low molecular weight heparin on the function of blood coagulation and serum levels of tumor necrosis factor-\(\alpha\) (TNF-\(\alpha\)), creatine kinase isoenzyme (CK-MB), C-reactive protein (CRP) of patients with acute exacerbations of chronic obstructive pulmonary diseases and respiratory failure. **Methods:** A total of 80 patients with acute exacerbations of chronic obstructive pulmonary diseases and respiratory failure in our hospital from June 2014 to October 2016 were enrolled in this study. The subjects were divided into the control group (\(n=40\)) and the treatment group (\(n=40\)) randomly. The control group were treated with conventional treatment, the treatment group were treated with the conventional treatment combined with low molecular weight heparin. The two groups were treated for 7 d. The D-dimer (D-D), fibrinogen (FBG), pro thrombin time (PT), thrombin time (TT), TNF-\(\alpha\), CK-MB and CRP of the two groups before and after treatment were compared. **Results:** There were no significantly differences of the blood levels of D-D, FBG, PT and TT of the two groups before treatment. After treatment, the blood levels of D-D and FBG of the two groups were significantly lower than before treatment, and that of the treatment group were significantly lower than the control group, the PT and TT of the two groups were significantly higher than before treatment, and that of the treatment group were significantly higher than the control group. There were no significantly differences of the serum levels of the TNF-\(\alpha\), CK-MB and CRP of the two groups before treatment. After treatment, the serum levels of the TNF-\(\alpha\), CK-MB and CRP of the two groups were significantly lower than before treatment, and that of the treatment group were significantly lower than the control group. **Conclusion:** Low molecular weight heparin can significantly reduce the inflammatory factors of the patients with acute exacerbations of chronic obstructive pulmonary diseases and respiratory failure, can alleviate the patients conditions and reduce the myocardial damage.

1. Introduction

Chronic obstructive pulmonary disease (COPD) is a common clinical diseases, it is one kind of lung inflammation and chronic airway disease whose main characteristic is the persistent airflow limitation, and its clinical features are wheezing, chronic cough.

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The purpose of thorough treatment of respiratory failure, as the condition can quickly alleviate the state, but it can not achieve the purpose of thorough treatment. Low molecular weight heparin is a kind of anticoagulant drugs with stronger anti thrombosis effect than heparin, which has the function of improving the patient’s anticoagulation status and high coagulation state. This study was to investigate the effect of low molecular weight heparin on coagulation function and serum levels of CRP, CK-MB and TNF-α in patients with AECOPD complicated with respiratory failure. The results were as follows.

2. Informations and Methods

2.1. General information

The object of this study was to select 80 patients with AECOPD complicated with respiratory failure in our hospital from June 2013 to October 2016.

Inclusion criteria: (1) In accordance with "chronic obstructive pulmonary disease diagnosis and treatment guidelines (2013 Revised Edition)" in the diagnostic standard of AECOPD; (2) Accord with the diagnosis standards of respiratory failure, in particular: arterial blood gas analysis of PaO2<60 mmHg, or with PaCO2>50 mmHg;

Exclusion criteria: (1) Associated with arrhythmia, heart failure and other cardiovascular disease patients; (2) The patients with interstitial pneumonia, pulmonary embolism, pulmonary tuberculosis, bronchial asthma and other respiratory diseases; (3) It is associated with malignant tumor patients; (4) Patients with heart, brain, liver, kidney and other diseases; (5) Patients with psychiatric disorders; (6) Patients that do not cooperate with the test program.

All the selected patients were randomly divided into the control group and the experimental group according to the random number table. In the control group, there were 22 male cases and 18 female cases; aged 51-80 years old; weight 42-71 kg, average weight (57±12) kg; have a course of 8-15 years; In the experimental group, there were 21 male cases and 19 female cases; aged 51-80 years old; weight 41-72 kg, average weight (56±14) kg; have a course of 8-15 years; In the control group, there were 22 male cases and 18 female cases; aged 52-79 years old; weight 42-71 kg, average weight (57±12) kg; have a course of 8-16 years. There was no significant difference in gender, age, weight, duration of disease between the two groups (P>0.05). All patients were informed of the study before the trial, and voluntarily signed informed consent to join this study, and this study was approved by the medical ethics committee of the hospital.

2.2 Treatment methods

After entering the group, all the patients in the control group were treated with anti-inflammatory, anti infection, correction of electrolyte imbalance, cough and phlegm, relieving asthma and a series of conventional treatment measures, especially gave invasive or non-invasive assisted breathing for patients with severe respiratory failure. The experimental group were treated with low molecular heparin calcium injection based on the treatment of control group (Purchased from Hefei branch Pharmaceutical Co., Ltd., specifications 5 000 IU/mL, the national drug standards H10980166), with 6 000 IU/time, 2 times/d for subcutaneous injection. All patients received the above appropriate treatment measures, and got a continuous treatment of 7 d.

2.3 Detection index

Check and compare the blood coagulation function indexes between the two groups before and after treatment, which include the level of D-D (D-dimer), FBG (fibrinogen), PT (prothrombin time) and TT (thrombin time).

5mL venous blood in the fasting state of the two groups before and after the treatment were exacted, and then obtained serum by centrifugal separation. The serum levels of TNF-α (tumor necrosis factor- α ), CK-MB (creatine kinase isoenzyme), CRP (C-reactive protein) in two groups before and after treatment were detected and compared. The levels of serum TNF-α and CRP were detected by enzyme linked immunosorbent assay (ELISA), and the kit was purchased from Shanghai LAN to send biological science and Technology Co., Ltd., according to the kit attached to the experimental operation. Detection of serum CK-MB levels used the immune suppression method by the application of Hitachi 7600-020 automatic biochemical analyzer.

2.4 Statistical method

We Used SPSS 19.0 software package to process the test result data, Count data used rate (%) representation and the method of χ². Mean ± SD represents measurement data, the use of t test was to compare the difference between groups, with P<0.05 as a statistically significant.

3. Results

3.1 comparison of coagulation function before and after treatment in two groups

Before treatment, plasma levels of D-D, FBG, PT and TT in the control group were (2.74±0.65) mg/L, (4.68±0.43) g/L, (8.96±2.01) s and (12.24±1.10) s, the levels in experimental group were (2.74±0.65) mg/L, (4.68±0.43) g/L, (8.96±2.01) s and (12.24±1.10) s, there was no significant difference between the two groups (P>0.05); After treatment, the levels of D-D, FBG, PT and TT in the control group were (2.12±0.53) mg/L, (3.89±0.38) g/L, (12.36±1.75) s and (13.67±1.25) s, the levels in experimental group were (1.56±0.42) mg/L, (2.14±0.21) g/L, (14.28±1.63) s and (16.32±1.32) s, Plasma D-D levels and FBG levels in the two groups were significantly lower than before treatment, and the plasma levels of D-D and FBG in the experimental group were significantly lower than those in the control group, The levels of PT and TT in the two
groups were significantly higher than before treatment, and the experimental group patients were significantly higher than those in the control group compared with the control group, the difference was significant ($p<0.05$). Please look at the table 1.

### 3.2 Comparison of serum levels of TNF-$\alpha$, CK-MB and CRP between the two groups before and after treatment

Before treatment, serum levels of TNF-$\alpha$, CK-MB and CRP in the control group were (58.34±8.26) pg/L, (30.15±4.73) U/L and (81.40±12.26) mg/L, the levels in experimental group were (59.01±8.57) pg/L, (29.86±4.32) U/L and (80.97±11.64) mg/L, there was no significant difference between the two groups ($p>0.05$); After treatment, the levels of TNF-$\alpha$, CK-MB and CRP in the control group were (30.93±4.38) pg/L, (14.38±1.84) U/L and (58.37±9.12) mg/L, the levels in experimental group were (12.74±2.14) pg/L, (5.04±0.89) U/L and (24.62±5.35) mg/L. The serum levels of TNF-$\alpha$, CK-MB and CRP in the experimental group were significantly lower than before treatment, and the serum indexes of the patients in the experimental group were significantly lower than those in the control group, all of which had significant difference ($p<0.05$). Please look at the table 2.

### 4. Discussion

COPD is a global medical disease, which is the world’s fourth leading cause of death, and it has become a serious public health problem[13]. The incidence of COPD in our country is 8.2%, the incidence of the disease in the world is as high as 10%, and in recent years its incidence rate increases year by year[14,15]. Most COPD patients with respiratory failure are often associated with respiratory failure for longer duration, and got recurrent episodes of acute attack, thus seriously affecting the health of the patient[16]. AECOPD patients with respiratory failure due to chronic hypoxia in the state, the cause of secondary polycythemia, platelet aggregation, plasma fibrinogen levels rise higher thrombosis caused by the state, resulting in high blood viscosity[17]. Therefore, it is of great clinical significance to choose the treatment measures for the treatment of AECOPD patients with respiratory failure. Low molecular weight heparin is degraded by heparin, because it has a stronger anti clotting factor Xa activity, and therefore has a stronger anti thrombosis effect than heparin. Low molecular weight heparin by heparin degradation, because of its stronger anti coagulation factor Xa activity, so it has stronger antithrombotic effect than heparin at the same time, the incidence of bleeding is low, reduces spontaneous bleeding, thrombocytopenia heparin and other adverse reactions, are widely used clinically. At the same time, the incidence of bleeding is low, which reduces the incidence of spontaneous bleeding, thrombocytopenia and other adverse reactions, so it has been widely used in clinical practice[18,19]. This study was to investigate the effect of low molecular weight heparin on the function of blood coagulation and serum levels of TNF-$\alpha$, CK-MB, CRP of AECOPD patients with respiratory failure, so as to provide a clinical basis for the treatment of AECOPD patients with respiratory failure for clinical rational use of effective treatment measures.

The results of this study show that: Before treatment, there was no significant difference in the plasma levels of D-D, FBG, PT and TT between the two groups, and ($p>0.05$); After treatment, Plasma D-D levels and FBG levels in the two groups were significantly lower than before treatment, and the plasma levels of D-D and FBG in the experimental group were significantly lower than those in the control group, The levels of PT and TT in the two groups were significantly higher than before treatment, and the experimental group patients were significantly higher than those in the control group, the difference was significant ($p<0.05$). It suggested that low molecular weight heparin could significantly improve the coagulation function of patients with AECOPD complicated with respiratory failure. This may be due to low molecular weight heparin can activate fibrinolytic system, thereby preventing platelet aggregation, prevent the formation of permanent platelet clots, in addition, it can improve the function of blood coagulation and prevent thrombosis by changing the blood flow dynamics[20]. The results of this study also show that, before treatment, there was no significant difference
in serum levels of CRP, CK-MB and TNF-α (P>0.05); After treatment, the serum levels of the TNF-α, CK-MB and CRP of the two groups were significantly lower than before treatment, and that of the treatment group were significantly lower than the control group (P<0.05). It suggested that low molecular weight heparin could significantly decrease the serum inflammatory factors in patients with AECOPD complicated with respiratory failure, and reduce the myocardial damage. TNF-α and CRP are two important inflammatory factors, which can be used in the evaluation of drug therapy. CK-MB is a kind of myocardial enzyme, which can be used to evaluate the degree of myocardial injury[21]. It is reported in the literature that the inflammatory response is the main pathological basis of AECOPD, and it is an important factor to cause disease progression[22]. Low molecular weight heparin can effectively relieve the patient's condition by improving the coagulation function, which is conducive to the elimination of inflammatory reaction and reduce the myocardial injury[23].

To sum up, low molecular weight heparin can significantly reduce the level of serum inflammatory factors in patients with AECOPD and respiratory failure, an alleviats the patients' conditions and reduce the myocardial damage, so it is worth to be popularized in clinical application.

Reference


