Influence of low molecular heparin on blood coagulation function and lung function in AECOPD patients

Rui Deng *

Department of Internal Medicine, Fifth People’s Hospital of Sichuan Province, Sichuan, Chengdu 610031, China

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ABSTRACT

Objective: To explore the influence of low molecular heparin on the blood coagulation function and lung function in acute exacerbation of chronic obstructive pulmonary disease (AECOPD) patients. Methods: A total of 100 cases AECOPD patients were divided into observation group and control group according to the present order and odd number by half. They were all given AECOPD conventional symptomatic treatment, on this basis, patients in the observation group were treated with low molecular heparin, 10 d after treatment, arterial blood gas index such as oxygen partial pressure (PaO₂), oxygen saturation (SaO₂), carbon dioxide partial pressure (PaCO₂), pulmonary function index such as FEV₁ and FVC, blood coagulation function index such as fibrinogen (Fib), D-dimer (D-D), activated partial blood coagulation time (APTT) live enzymes, plasma prothrombin time (PT), thrombin time (TT) between two groups before and after treatment were compared. Results: Compared with before treatment, the levels of PaO₂, SaO₂, FEV₁ and FVC, FEV₁/FVC in control group after treatment were significantly elevated, PaCO₂, D-D were significantly reduced, the difference were statistically significant (all \( P<0.05 \)); The levels of PaO₂, SaO₂, FEV₁ and FVC, FEV₁/FVC, PT, TT and APTT in observation group after treatment were significantly increased, and were significantly higher than the control group after treatment, PaCO₂, D-D, Fib were significantly lower, and were lower than the control group after treatment, the differences were statistically significant (all \( P<0.05 \)). Conclusions: AECOPD patients treated with low molecular heparin can help to improve the arterial blood gas, lung function and blood coagulation function.

1. Introduction

Chronic obstructive pulmonary disease (COPD) is a common syndrome in respiratory department of internal medicine, it is characteristic by airflow limitation and progressive development and accompanied chronic airway inflammation[1,2]. In patients with acute exacerbation of COPD (AECOPD), due to the increased release of inflammatory mediators, it may cause carbon dioxide retention, hypoxemia, smooth muscle spasm and prethrombotic state and decreased lung function, which aggravate COPD condition[3,4]. In addition to anticoagulant, Heparin has a variety of other pharmacological effects and biological activities, including anti allergy, anti-inflammatory, reduce airway resistance and anti free radical damage[5,6]. Our study investigated the effects of low molecular heparin on the lung and blood coagulation function in the treatment of patients with AECOPD.

2. Materials and methods

2.1. General information

A total of 100 AECOPD patients who was admitted in the
Department of internal medicine, the Fifth People's Hospital of Sichuan Province from August 2013 to October 2015 were selected as the research object, who all met the following conditions: ① Meet COPD diagnostic criteria, and in acute exacerbation stage; ② Without the history of drug allergy and drug contraindications; ③ Did not receive anticoagulation therapy recently; ④ Excluded patients with coagulation dysfunction and bleeding tendency; ⑤ Excluded patients with cardiovascular and cerebrovascular diseases, liver and kidney dysfunction, diabetes and other diseases; ⑥ Excluded patients with pulmonary embolism, asthma and other lung diseases; ⑦ Excluded patients with recent trauma or malignant tumor. According to the order, the patients were divided into two groups, each 50 cases. In the observation group, male 38 cases, female 12 cases; age from 65 to 100 years old with an average (78.65±19.38) years; the course from 1 to 11 years with an average (4.31±2.20) years. In the control group, male 40 cases, female 10 cases; age from 67 to 98 years old with an average (78.08±18.87) years; the course from 1.5 to 14 years with an average (4.57±2.31) years. There were no significant differences between the two groups.

2.2. Treatment methods

After diagnosis, they were treated by AECOPD conventional basic treatment, including expectorant, antispasmodic, anti-inflammatory, anti infection and oxygen inhalation. In addition, the observation group patients were treated with low molecular heparin, abdominal subcutaneous injected 5 000 units low molecular Heparins Calcium injection, once a day, for 10 d.

2.3. Observation indexes

2.3.1. Arterial blood gas

Blood gas analyzer (GEM premier 3000 blood gas analyzer) was used to detect the Arterial blood gas indexes before and after treatment, including partial pressure of oxygen (PaO2), oxygen saturation (SaO2) and carbon dioxide partial pressure (PaCO2).

2.3.2. Lung function

Pulmonary function instrument (RSFJ1000, Chengdu sunrise Electrical Appliance Co. Ltd.) was used to detect the lung function indexes before and after treatment, including forced vital capacity (FVC), forced expiratory volume in one second (FEV1) and calculated FEV1/FVC.

2.3.3. Coagulation function

Coagulation analyzer (RAC-100 Automatic Coagulation Analyzer) was used to detect the coagulation function indexes before and after treatment, including fibrinogen (FIB), D-Dimer (D-D), activated partial thromboplastin time (APTT), prothrombin time (PT) and thrombin time (TT).

2.4. Statistical analysis

SPSS 18.0 software was used for statistical analysis, the measurement data were expressed as mean±SD, the data in the group and between the group was compared by t test, P<0.05 was considered as statistically significant difference.

3. Results

3.1. Changes of arterial blood gas indexes before and after treatment

There were no significant differences in PaO2, SaO2 and PaCO2 between the two groups before treatment (P>0.05); After treatment, both two groups' SaO2 and PaO2 were significantly higher, while PaCO2 was significantly lower, and the differences were significant (P<0.05), in the observation group after treatment, SaO2 and PaO2 were (80.12±10.54) mmHg and (98.62±1.08)% which were significantly higher than those in the control group after treatment, while PaCO2 was (45.65±11.43) mmHg which was significantly lower than that in the control group after treatment, the differences were statistically significant (P<0.05) (Table 1).

3.2. Changes of pulmonary function indexes before and after treatment

There were no significant differences in FEV1, FVC and FEV1/FVC between the two groups before treatment (P>0.05); After treatment, both two groups' pulmonary function indexes were significantly increased, and the differences were significant (P<0.05), in the observation group after treatment, FEV1, FVC and FEV1/FVC were (1.75±0.32) L, (2.24±0.63) L and (78.12±6.68)% which were significantly higher than those in the control group after treatment (Table 2).

3.3. Changes of coagulation function indexes before and after treatment

There were no significant differences in PT, TT, APTT, Fib and D-D between the two groups before treatment (P>0.05); In the control group after treatment, D-D was significantly reduced (P<0.05), while other indexes had no significant differences (P>0.05); In the observation group after treatment, PT, TT and APTT were (18.45±3.03) s, (14.24±3.1) s and (35.83±4.86) s, which were significantly higher than those before treatment and in the control group after treatment (Table 3).
Table 1
Changes of arterial blood gas indexes before and after treatment.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Cases</th>
<th>Time</th>
<th>PaO2 (mmHg)</th>
<th>SaO2 (%)</th>
<th>PaCO2 (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation group</td>
<td>50</td>
<td>Before treatment</td>
<td>65.59±9.91</td>
<td>88.80±9.53</td>
<td>54.49±8.22</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>80.12±10.54</td>
<td>98.62±1.08</td>
<td>45.65±11.43</td>
</tr>
<tr>
<td>Control group</td>
<td>50</td>
<td>Before treatment</td>
<td>66.08±10.32</td>
<td>87.35±10.18</td>
<td>54.02±8.18</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>73.21±11.01</td>
<td>94.42±4.36</td>
<td>50.36±10.68</td>
</tr>
</tbody>
</table>

Compared with before treatment, \( P<0.05 \); Compared with the control group after treatment, \( P<0.05 \).

Table 2
Changes of pulmonary function indexes before and after treatment.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Cases</th>
<th>Time</th>
<th>FEV1 (L)</th>
<th>FVC (L)</th>
<th>FEV1/FVC (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation group</td>
<td>50</td>
<td>Before treatment</td>
<td>1.03±0.20</td>
<td>1.69±0.45</td>
<td>60.94±5.71</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>1.75±0.32</td>
<td>2.24±0.63</td>
<td>78.12±6.68</td>
</tr>
<tr>
<td>Control group</td>
<td>50</td>
<td>Before treatment</td>
<td>1.01±0.22</td>
<td>1.65±0.39</td>
<td>61.21±4.98</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>1.35±0.30</td>
<td>1.91±0.57</td>
<td>70.68±6.39</td>
</tr>
</tbody>
</table>

Compared with before treatment, \( P<0.05 \); Compared with the control group after treatment, \( P<0.05 \).

Table 3
Changes of coagulation function indexes before and after treatment.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Cases</th>
<th>Time</th>
<th>PT (s)</th>
<th>TT (s)</th>
<th>APTT (s)</th>
<th>Fib (g/L)</th>
<th>D-D (μg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation group</td>
<td>50</td>
<td>Before treatment</td>
<td>10.10±2.51</td>
<td>12.84±3.56</td>
<td>33.31±4.41</td>
<td>3.68±0.65</td>
<td>321.65±44.82</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>18.45±3.03</td>
<td>14.24±3.14</td>
<td>35.83±4.86</td>
<td>2.25±0.38</td>
<td>187.81±20.89</td>
</tr>
<tr>
<td>Control group</td>
<td>50</td>
<td>Before treatment</td>
<td>10.04±2.37</td>
<td>12.26±2.76</td>
<td>33.20±4.62</td>
<td>3.02±0.53</td>
<td>317.87±43.65</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>11.13±2.46</td>
<td>12.32±3.09</td>
<td>33.14±4.82</td>
<td>3.14±0.40</td>
<td>301.89±33.43</td>
</tr>
</tbody>
</table>

Compared with before treatment, \( P<0.05 \); Compared with the control group after treatment, \( P<0.05 \).

4. Discussion

The coagulation and fibrinolysis imbalance, pre thrombotic and blood coagulation state in AECOPD patients may be due to the following:

1. Hyperfibrinolysis, hypercapnia, infection and hypoxia cause vascular endothelial injury and activation of coagulation, resulting in the activation of the fibrinolytic enzyme and the increased fibrin deposition, in addition, inflammatory stimulation will consume the body coagulation factors, resulting in the fibrinolytic system and the increased blood D-D and Fib; 2. Inflammatory response, a large number of inflammatory mediators are activated and released, through the direct effect to damage lung tissue; and inflammatory mediators activates coagulation factor, initiates the extrinsic and intrinsic coagulation pathway, cause a series of coagulation reaction, and increase the release of various types of coagulant to accelerate platelet activation and coagulation. 3. Blood viscosity change, in order to adapt to long-term hypoxia environment, the body could increase the number and the ability to transport oxygen of red blood cells, if hypoxia, the energy metabolism of red blood cells will change, the adaptability and the ability of deformation decrease, the aggregation ability increase, and the red blood cell aggregation increase the blood viscosity.

Heparin is clinical commonly used physiological anticoagulant, we used low molecular heparin for AECOPD treatment and we found that only D-D was significantly lower in the conventional therapy control group, PT, TT and APTT were significantly higher in the observation group treated with low molecular heparin, and were significantly higher than those in the control group after treatment, Fib and D-D were significantly decreased, and were significantly lower than those in the control group after treatment. D-D is a soluble degradation product produced by cross linked fibrin. It is a sensitive index to reflect the body’s high coagulation state and a specific fiber soluble marker, its content is very low in normal human blood, but increased obviously when the body is in fibrinolysis activity and activated thrombosis in blood vessels[10,11]. Fib, on the one hand can be directly as a coagulation factor to participate in the coagulation reaction; On the other hand, Fib is an important transmitter of platelet aggregation, which promotes platelet aggregation and affects the viscosity of blood[12,13]. By binding with anti-thrombin, heparin can inhibit the activity of thrombin, in addition, heparin can reduce platelet aggregation, inhibit blood visible component aggregation, lower blood viscosity and high coagulation state, improve microcirculation, prevent thrombosis and play a powerful anticoagulant effect in vivo and vitro[14–16].

Due to the increased release of inflammatory mediators, AECOPD patients’ lung injury, resulting in a progressive decline in lung function[17]. Our study also found that in the observation group after treatment, PaO2, SaO2, FVC, FEV1, FEV1 / FVC were significantly increased while PaCO2 was significantly reduced compared with those in the control group after treatment, and the differences were statistically significant. The results showed that low molecular heparin helps to improve arterial blood gas and pulmonary function in AECOPD patients. The reasons may be that low molecular heparin has other pharmacological effects and biological activity. On the one hand, heparin competitive binding of P-selectin and L-selectin, modulate the inflammatory cascade, prevent leukocyte adhesion activation, play an anti-inflammatory role, reduce the release of inflammatory mediators, reduce the inflammation of lung...
tissue damage and protect the lung function[18,19]. On the other hand, heparin can increase uptake and utilization ability of oxygen in tissues, correct hypoxia, improve microcirculation, relieve microvascular constriction and bronchial spasm, reduce airway pressure, reduce pulmonary arterial hypertension, prevent the proliferation of vascular smooth muscle, improve hypoxemia and pulmonary ventilation and enhance heart and lung function[20,21].

In summary, Heparin has a variety of other pharmacological effects and biological activities in addition to anticoagulant. Clinical use of heparin for AECOPD treatment can significantly improve patients’ arterial blood gas, lung function and blood coagulation function.

References