Lung function in patients with acute exacerbation and stable COPD and its correlation with serum proinflammatory cytokines and chemokines
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1. Introduction

Acute infections in patients with chronic obstructive pulmonary disease (COPD) can cause airway function deterioration and sudden pulmonary function decline, and severe cases may lead to respiratory failure[1,2]. There is irreversible airflow limitation in patients with COPD, and after local infection, the further decreased bronchial diameter and the effect of local secretion lead to severe ventilation dysfunction in patients. Studies have shown that in addition to the anatomic anomaly of small airway, massively secreted proinflammatory cytokines and chemokines are also directly involved in the deterioration of COPD, but few clinical study is about the correlation between lung function and the content of proinflammatory cytokines and chemokines in patients with COPD at present and cannot confirm that the deterioration of lung function is directly caused by inflammatory cytokines and chemokines[3-5]. In the study, patients with acute exacerbation and stable COPD were selected as the research subjects, and the differences in lung function, proinflammatory factors and chemokines were compared between the two groups of patients to clarify the internal relations among the three.

2. Materials and methods

2.1. General information

A total of 87 patients with COPD treated in our hospital between January 2013 and January 2016 were divided into observation group (n=32) at acute exacerbation phase and control group (n=55) at stable phase according to the illness. Observation group included
20 male cases and 12 female cases, they were 54-72 years old and (62.84±7.12) years old in average, and the course of COPD was 5-19 years and (11.28±7.05) years in average; control group included 34 male cases and 21 female cases, they were 52-71 years old and (61.79±7.05) years old in average, and the course of COPD was 5-18 years and (11.54±7.21) years in average. The two groups of patients showed no statistically significant difference in the distribution of gender, age and course of disease (P>0.05) and could be subsequently compared.

2.2. Lung function parameters

Spirometer (Italy, model QUAP.PFT3) was used to test the lung function of two groups of patients, and the specific indicators included forced expiratory volume in one second (FEV1), forced vital capacity (FVC), FEV1/FVC, forced expiratory flow at 75% of forced vital capacity (FEF75), peak expiratory flow (PEF) and inspiratory capacity (IC). The parameters were measured for 3 times, and the best value was selected.

2.3. Serum indexes

A total of 3 mL of fasting cubital venous blood was extracted from two groups of patients, let stand at room temperature and centrifuged under 4 °C to get supernatant and cryopreserve it in -80 °C refrigerator for test, and the specific detected indexes were as follows: (1) proinflammatory cytokines: enzyme-linked immunosorbent assay (ELISA) was used to determine interleukin-1 β (IL-1 β), interleukin-4 (IL-4), interleukin-18 (IL-18), interleukin-23 (IL-23), tumor necrosis factor α (TNF- α) and interferon γ (IFN- γ) content. (2) Chemokines: ELISA kits were used to determine Eotaxin, macrophage-derived chemokine (MDC), fractalkine (FKN), monocyte chemotactant protein 1 (MCP-1), pulmonary activation regulated chemokine (CCL18) and regulated upon activation normal T cell expressed and secreted factor (RANTES) content.

2.4. Statistical methods

Data in the study was input in software SPSS23.0, measurement data was by t test, correlation analysis was by Pearson test and P<0.05 indicated statistical significant differences.

3. Results

3.1. Lung function parameters

FEV1, FVC, FEV1/FVC, FEF75, PEF and IC levels of observation group were significantly lower than those of control group (P<0.05), shown in Table 1.

3.2. Proinflammatory cytokine content

Serum IL-1 β, IL-4, IL-18, IL-23, TNF- α and IFN- γ content of observation group were significantly higher than those of control group (P<0.05), shown in Table 2.

3.3. Serum chemokine content

Serum Eotaxin, MDC, FKN, MCP-1, CCL18 and RANTES content of observation group were significantly higher than those of control group (P<0.05), shown in Table 3.

Table 1:
Comparison of lung function parameters between two groups.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Case No.</th>
<th>FEV1 (L)</th>
<th>FVC (L)</th>
<th>FEV1/FVC</th>
<th>FEF75 (L/s)</th>
<th>PEF (L/s)</th>
<th>IC (L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation group</td>
<td>32</td>
<td>1.18±0.19</td>
<td>2.16±0.28</td>
<td>49.37±5.12</td>
<td>0.34±0.04</td>
<td>4.37±0.51</td>
<td>1.42±0.18</td>
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<tr>
<td>Control group</td>
<td>55</td>
<td>1.67±0.21</td>
<td>2.83±0.31</td>
<td>58.62±6.45</td>
<td>0.52±0.06</td>
<td>5.37±0.69</td>
<td>1.86±0.21</td>
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<tr>
<td>t</td>
<td></td>
<td>5.285</td>
<td>5.893</td>
<td>8.293</td>
<td>5.834</td>
<td>6.293</td>
<td>5.372</td>
</tr>
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<td>P</td>
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<td>&lt;0.05</td>
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</tr>
</tbody>
</table>

Table 2
Comparison of serum proinflammatory cytokine levels between two groups (ng/L).

<table>
<thead>
<tr>
<th>Groups</th>
<th>Case No.</th>
<th>IL-1 β (pg/L)</th>
<th>IL-4 (pg/L)</th>
<th>IL-18 (pg/L)</th>
<th>IL-23 (pg/L)</th>
<th>TNF- α (pg/L)</th>
<th>IFN- γ (pg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation group</td>
<td>32</td>
<td>4.83±0.51</td>
<td>88.63±9.12</td>
<td>89.36±9.43</td>
<td>52.47±5.88</td>
<td>3.92±0.41</td>
<td>8.93±0.91</td>
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<tr>
<td>Control group</td>
<td>55</td>
<td>2.04±0.23</td>
<td>50.27±5.89</td>
<td>35.47±4.12</td>
<td>27.69±3.42</td>
<td>0.92±0.09</td>
<td>2.16±0.33</td>
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<tr>
<td>t</td>
<td></td>
<td>5.384</td>
<td>9.384</td>
<td>8.732</td>
<td>6.393</td>
<td>5.395</td>
<td>7.293</td>
</tr>
<tr>
<td>P</td>
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Table 3
Comparison of serum chemokine content between two groups.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Case No.</th>
<th>Eotaxin (μg/L)</th>
<th>MDC (ng/L)</th>
<th>FKN (ng/L)</th>
<th>MCP-1 (μg/L)</th>
<th>CCL18 (μg/L)</th>
<th>RANTES (μg/L)</th>
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</thead>
<tbody>
<tr>
<td>Observation group</td>
<td>32</td>
<td>154.82±20.43</td>
<td>643.28±79.34</td>
<td>382.64±40.12</td>
<td>4.02±0.51</td>
<td>2.48±0.31</td>
<td>30.27±3.69</td>
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<td>Control group</td>
<td>55</td>
<td>60.32±7.19</td>
<td>192.47±25.12</td>
<td>170.53±19.27</td>
<td>2.18±0.27</td>
<td>0.92±0.11</td>
<td>8.54±0.91</td>
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<td>11.293</td>
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<td>10.284</td>
<td>5.384</td>
<td>5.728</td>
<td>7.923</td>
</tr>
<tr>
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<td>&lt;0.05</td>
<td>&lt;0.05</td>
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</table>
control group ($P<0.05$), shown in Table 3.

3.4. Correlation between lung function parameters and the content of proinflammatory cytokines and chemokines

Pearson test showed that lung function parameters FEV1, FVC, FEV1/FVC, FEF75, PEF and IC levels in patients with COPD were negatively correlated with the content of proinflammatory cytokines IL-1 $\beta$, IL-4, IL-18, IL-23, TNF-$\alpha$ and IFN-$\gamma$ as well as chemokines Eotaxin, MDC, FKN, MCP-1, CCL18 and RANTES ($P<0.05$).

4. Discussion

COPD is mainly characterized by irreversible airway function change, lung function at stable phase is in good condition and patients are without significant discomfort, and when acute infections occur, COPD progresses rapidly and is generally characterized by the deterioration of lung function. After acute infection, airway spasm and massively produced inflammatory airway secretions in patients with COPD further weaken patients’ pulmonary ventilation and gas exchange function, and severe cases may induce type II respiratory failure[6]. FEV1, FVC, FEV1/FVC, FEF75, PEF, IC and other lung function indexes in patients with acute exacerbation COPD and stable COPD were detected in the study in order to clarify the lung function changes in different phases of COPD[7-9]. The results showed that FEV1, FVC and FEV1/FVC levels of observation group with acute exacerbation COPD were lower. FEV1, FVC and FEV1/FVC have been the commonly recognized clinical lung function indexes, their levels reduce with the deterioration of lung function, the above results indicate that patients with acute exacerbation COPD are accompanied by significant lung function decline, and this is the inevitable result after the pathological change of airway and lung tissue in patients with COPD after acute infection. What factors are specifically involved in the deterioration of lung function in patients with COPD? Opinions vary at present, but the inflammatory factor theory and chemokine theory have received more recognition, and the role of inflammatory cytokines and chemokines in COPD progression will be further analyzed in the study.

Acute exacerbation COPD is mainly caused by acute airway infection, bacteria or virus prompts mononuclear macrophages to secrete massive proinflammatory factors, and massive accumulation of proinflammatory factors within the local airway can further contain patients’ anti-inflammatory ability and immune function until systemic inflammatory cascade occurs. Research has shown that serum levels of IL-6, IL-8 and other proinflammatory factors in patients with active COPD are significantly higher than those in patients with stable COPD, and it is speculated that they are directly involved in COPD progression[10]. IL-1 $\beta$, IL-4, IL-18, IL-23, TNF-$\alpha$ and IFN-$\gamma$ are the clinically confirmed proinflammatory factors and play an important role in a variety of pneumonia or infectious diseases, serum levels of the above proinflammatory factors of two groups of patients with COPD were determined in the study, and it was found that serum IL-1 $\beta$, IL-4, IL-18, IL-23, TNF-$\alpha$ and IFN-$\gamma$ content of patients with acute exacerbation COPD were significantly higher than those of patients with stable COPD. After COPD patients are infected by bacteria or viruses, proinflammatory factors can accelerate neutrophil activation and make it produce "respiratory burst", which stimulates the migration of neutrophils to airway endothelial cells and pulmonary epithelial cells[11,12]. At the same time, studies have found that proinflammatory factors can activate a variety of signaling pathways, and their levels are directly correlated with the severity of pulmonary infectious diseases. The above results indicate that proinflammatory factors are involved in the COPD transformation from stable phase to acute exacerbation phase, and are one of the important media of COPD progression.

Chemokines can recruit inflammatory factors, neutrophils, eosinophils and other pathogenic cells in local lesions, causing the accumulation of inflammatory mediators and continuous enlargement of inflammatory response in local lesions. Chemokines can further expand the role of proinflammatory factors and play an important role in the process of the inflammatory cascade[13,14]. Eotaxin can cause local infiltration of eosinophils; MDC and MCP-1 can induce local infiltration of mononuclear macrophages; FKN is a new type of chemokine that is considered to play a key role in the process of T lymphocyte and monocyte recruitment and adhesion to blood vessel walls[15,16]. Foreign studies have found that pulmonary activation regulated CCL18 expression level in patients with COPD is higher than that in healthy people, and it is further secreted in acute exacerbation COPD and can be a reliable indicator for disease prognosis[17,18]. RANTES can regulate T cell activation and secretion. It was found in the study that serum levels of above chemokines in patients with acute exacerbation COPD were higher than those in patients with stable COPD, indicating that massive secretion and aggregation of chemokines is one of the important factors that cause COPD progression.

The above research has made it clear that lung function deteriorates and serum levels of proinflammatory factors and chemokines increase in patients with acute exacerbation COPD, and at present, there is still no clear literature that reports the correlation between lung function change and the levels of proinflammatory factors and chemokines. In the study, Pearson test was used to analyze the correlation between lung function change and serum levels of proinflammatory factors and chemokines in patients with COPD, and it was found that the lung function in patients with COPD were negatively correlated with proinflammatory factors IL-1 $\beta$, IL-4, IL-18, IL-23, TNF-$\alpha$ and IFN-$\gamma$ as well as chemokines Eotaxin, MDC, FKN, MCP-1, CCL18 and RANTES content. It indicates that massively secreted proinflammatory factors and chemokines directly lead to disease progression and lung function deterioration in patients with COPD, and they are the core factors causing the acute
exacerbation of COPD.

To sum up, it is concluded as follows: lung function declines in acute exacerbation COPD, the changes in levels of both proinflammatory cytokines and chemokines are involved in it, and they can be the new approach for the intervention in COPD.

References


