Clinical significance of inflammatory cytokines detection in the diagnosis of chronic obstructive pulmonary disease

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ABSTRACT

Objective: To explore the changes of inflammatory cytokine levels in patients with acute exacerbations of chronic obstructive pulmonary disease (COPD) and their correlations with pulmonary function. Methods: ELISA was used to detect serum IL-8, IL-6, and TNF-α levels in COPD patients at acute exacerbation stage and stable stage. MIR Spirolab was used to detect FEV1%. IL-8, IL-6, and TNF-α levels at acute exacerbation stage and stable stage, the difference and correlations of the pulmonary function test results were observed and compared. Results: IL-8, IL-6, and TNF-α levels were increased with the increasement of the pulmonary function grade \((P<0.05)\). IL-8, IL-6, and TNF-α levels at acute exacerbation stage were significantly higher than those at stable stage \((P<0.05)\), while FEV1% was significantly lower than that at stable stage \((P<0.05)\). IL-8, IL-6, and TNF-α levels at acute exacerbation stage and stable stage were negatively correlated with FEV1%. Conclusions: IL-8, IL-6, and TNF-α, as important cytokines, are involved in the pathogenesis of COPD, and in accelerating the occurrence and development of airway inflammation, so that the airway remodeling and airflow are obstructed; therefore, the changes of their levels are of great significance in estimating COPD progression, therapeutic effect, and prognosis.

1. Introduction

Chronic obstructive pulmonary disease (COPD) is a kind of disease which can be prevented and treated, and is characterized by the incomplete reversible airflow limitation and progressively decreased lung function in the clinic with a progressive developing trend. Its morbidity and condition deferment are closely associated with the chronic non-specific airway inflammation. Pulmonary hypertension (PH) can be induced usually due to anoxia and decreased pulmonary vascular beds, which can severely affect the patients’ cardio-pulmonary function[1]. Its pathogenesis is correlated with the non-specificity of the airway and the chronic inflammatory reaction caused by the inflammatory mediators and cytokines[2]. The study is aimed to analyze the levels of IL-8, IL-6, and TNF-α and explore the correlation of cytokine levels in an acute exacerbation stage and remission stage with FEV1%.

2. Materials and methods

2.1. Clinical materials

A total of 50 patients with COPD in an acute exacerbation stage who were admitted in our hospital from February, 2013 to April, 2015 were included in the study, among which 34 were male, and 16 were female, aged from 55 to 82 years old with an average of \((67.3±11.5)\) years old; 11 cases merged with respiratory failure, and 9 merged with chronic pulmonary heart disease. All the enrolled patients had a history of chronic cough and expectoration in a different degree, were in accordance with the diagnostic criteria of “Guideline of the Diagnosis and Treatment of Chronic Obstructive Pulmonary Disease”[3], and had a definite diagnosis by the lung function and image examinations. The estimation criteria of COPD at an acute exacerbation stage: The patients’ symptoms of cough, expectoration, and dyspnea were aggravated, accompanied by respiratory failure and disorder of consciousness. Those who had acute pulmonary embolism, acute cardiovascular and cerebrovascular diseases, or were merged with pulmonary tuberculosis, malignant tumors, and severe liver and kidney failure were excluded from the study.
2.2. Methods

The morning fasting peripheral venous blood was extracted on admission before treatment and 2 weeks after routine treatments, such as anti-infection, phlegm dispersing, and dilating the bronchi, respectively. The specimens were centrifuged at 4,500 r/min for 5 min. ELISA was used to detect the serum IL-8, IL-6, and TNF-α levels. The kits were purchased from Andje Bio-technology Co. Ltd. The operation procedures were performed in strict accordance with the instructions. Master Screen Spirometer (Jaeger, German) was used to detect FEV1%.

2.3. Comprehensive assessment grading[4]

Grade A: acute aggregation times in each year less than twice, CAT<10 scores, mMRC≤1; grade B: acute aggregation times in each year less than twice, CAT>10 scores, mMRC>2; grade C: acute aggregation times in each year ≥2, CAT<10 scores, mMRC≤1; grade D: acute aggregation times in each year ≥2, CAT>10 scores, mMRC>2.

2.4. Observation indicators

The levels of IL-8, IL-6, and TNF-α with different grades were detected. The difference and correlation of IL-8, IL-6, and TNF-α levels and FEV1% at an acute exacerbation stage and stable stage were analyzed.

2.5. Statistical analysis

SPSS 18.0 software was used for statistical analysis. The measurement data were expressed as mean±SD, and t test was used. Pearson correlation analysis was performed. P<0.05 was regarded as statistically significant.

3. Results

3.1. Comparison of the IL-8, IL-6, and TNF-α levels in patients with different comprehensive assessment grades

IL-8, IL-6, and TNF-α levels were increased with the increasement of the pulmonary function grade (P<0.05) (Table 1).

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>IL-8</th>
<th>IL-6</th>
<th>TNF-α</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>19</td>
<td>64.89±14.32</td>
<td>62.35±11.25</td>
<td>17.12±4.55</td>
</tr>
<tr>
<td>B</td>
<td>16</td>
<td>77.65±12.43</td>
<td>74.25±10.41</td>
<td>20.11±3.76</td>
</tr>
<tr>
<td>C</td>
<td>8</td>
<td>93.71±18.31</td>
<td>90.22±18.07</td>
<td>28.51±4.68</td>
</tr>
<tr>
<td>D</td>
<td>7</td>
<td>115.85±22.15</td>
<td>107.23±17.17</td>
<td>34.11±6.74</td>
</tr>
<tr>
<td>F</td>
<td></td>
<td>22.351</td>
<td>23.702</td>
<td>26.422</td>
</tr>
<tr>
<td>P</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td></td>
</tr>
</tbody>
</table>

3.2. Comparison of IL-8, IL-6, and TNF-α levels and FEV1% at an acute exacerbation stage and stable stage

IL-8, IL-6, and TNF-α levels at acute exacerbation stage were significantly higher than those at stable stage (P<0.05), while FEV1% was significantly lower than that at stable stage (P<0.05) (Table 2).

3.3. Correlation analysis

IL-8, IL-6, and TNF-α levels at acute exacerbation stage and stable stage were negatively correlated with FEV1% (r = -0.598, -0.625, -0.498, r = -0.511, -0.745, -0.549) (P<0.05) (Table 3).

4. Discussion

COPD is the most common chronic disease in the respiratory system with a high morbidity, disability rate, and fatality rate, and an increasing morbidity trend, and is characterized by incomplete reversible airflow limitation and progressively decreased lung function, in which PH is a common complication usually due to anoxia and decreased pulmonary vascular beds[5]. COPD mainly occurs in the aged population. With the gradual aggravated condition, the pulmonary heart disease, respiratory failure, and other severe complications will occur, which can affect the patients’ living qualities. The main pathological basis of COPD is the chronic non-specific inflammation of the airway. The airway inflammation is mainly infiltrated by the lymphocytes, neutrophils, and alveolar macrophages. The activated inflammatory cells can release many inflammatory mediators and cytokines which are involved in the development of inflammation, while IL-8 and IL-6 are the important cytokines for developing airway inflammation in COPD patients[6]. TNF-α is secreted and produced by the mononuclear-macrophages, and is involved in the adhesion and infiltration of monocytes and...
lymphocytes during the inflammation process, thus leading to airway and lung injuries and inducing the production of cytokines\[7,8\].

IL-8 is synthetized and secreted by Th1 cells with main functions of chemotaxis and activating the neutrophils and T lymphocytes to promote the aggregation in the tracheal epithelium, and can suppress the apoptosis of neutrophils, thus leading to the alveolar epithelium and pulmonary vascular wall and aggravating the inflammatory reaction. IL-8, coexisted with IL-3, can also promote the synthesis of eosinophils and basophils and mastocytes to release the histamine, thus causing the bronchospasm and airway obstruction, and is involved in the occurrence and development of COPD\[9,10\]. IL-6 is secreted by the lymphocytes and is a cytokine produced by the reaction of various cells, such as T cells, monocytes, and vascular endothelial cells, can activate and promote the neutrophils to aggregate in the inflammation site, delay the cell apoptosis, release the elastin and ROS, leading to an increased capillary permeability and pulmonary interstitial edema, aggravating the inflammatory reaction, and inducing the synthesis of hepatocytes in an acute phase and the release of C-reactive protein to play a defense role, and is also involved in the airway remodeling of COPD\[10-12\]. IL-8, IL-6, and TNF-\(\alpha\) levels in COPD patients are higher than those in the normal individuals, moreover, those levels at the acute exacerbation stage are higher than those at the stable stage; accordingly, detection of IL-8, IL-6, and TNF-\(\alpha\) levels is of certain significance in estimating the condition and prognosis. Therefore, IL-8, IL-6, and TNF-\(\alpha\) in the pathogenesis of COPD are closely associated with the inflammation, and can reflect the infection degree of airway and systemic inflammation to a certain extent. It is reported that IL-8, IL-6, and TNF-\(\alpha\) at the acute exacerbation stage are significantly higher than those at the stable stage\[12\], which is in accordance with the results in the study, showing that the above cytokine levels are positively correlated with COPD, and monitoring of the change of the levels can accurately reflect the patients’ conditions.

The results in the study showed that IL-8, IL-6, and TNF-\(\alpha\) levels were increased with the increase of the pulmonary function grade \((P<0.05)\); IL-8, IL-6, and TNF-\(\alpha\) levels at acute exacerbation stage were significantly higher than those at stable stage \((P<0.05)\), while FEV1% was significantly lower than that at stable stage \((P<0.05)\), showing that IL-8, IL-6, and TNF-\(\alpha\) in COPD patients are involved in the occurrence and development of COPD together, and can trigger or aggravate the airway inflammation in order to promote the development and deferment. FEV1% predicated value is an accurate indicator to measure the lung function in patients with COPD in the clinic. The results in the study showed that IL-8, IL-6, TNF-\(\alpha\), and FEV1% in COPD patients at the acute exacerbation stage and the stable stage were negatively correlated, probably in that the high expression of cytokines can promote the excessive secretion of airway mucus to block the airway, thus leading to a reduced FEV1% predicated value.

In conclusion, IL-8, IL-6, and TNF-\(\alpha\), as important cytokines, are involved in the pathogenesis of COPD, and in accelerating the occurrence and development of airway inflammation, so that the airway remodeling and airflow are obstructed; therefore, the changes of their levels are of great significance in estimating COPD progression, therapeutic effect, and prognosis.

References

[12] Yao DZ, Xu YS, Xie YH. Correlation research on the changes of IL-8, IL-6, and TNF-\(\alpha\) levels in aged patients with COPD at the acute exacerbation stage with the pulmonary function. Modern Hosp 2014; 14(6): 17-19.