Effect of Methylprednisolone combined doxofylline on levels of serum adiponectin, MMP-9, IL-17, IL-10 and TNF-α in patients with COPD

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ABSTRACT

Objective: To exploring the effect of Methylprednisolone combined doxofylline on levels of serum adiponectin, MMP-9, IL-17, IL-10 and TNF-α in patients with COPD. Methods: A total of 84 patients were selected with COPD in our hospital for the treatment from June 2013 to June 2015, we randomly divided them into the experiment group and the control group (42 cases for each group). The experiment group was given the treatment of methylprednisolone combined doxofylline, and the control group was given the treatment of methylprednisolone combined aminophylline. After the treatment, we use ELISA method to record and detect the levels of all patients’ serum adiponectin (APN), matrix metalloproteinases9 (MMP-9), interleukin17 (IL-17), interleukin10 (IL-10) and tumor necrosis factor-α (TNF-α), and keep on related analysis according to the group work. Results: Comparing with two groups of patients before treatment, the levels of serum APN, MMP-9, IL-17, IL-10 and TNF-α had no significant difference; After treatment, the levels of serum MMP-9, TNF-α and IL-17 were significantly lower than that before treatment, and the levels of serum APN and IL-10 were significantly higher than that before treatment. The differences had statistical significance; After treatment, compared the experiment group with the control group, the levels of serum MMP-9, TNF-α and IL-17 were significantly reduced, and the levels of serum APN and IL-10 were significantly increased. The differences have statistical significance. Conclusion: It has great clinical curative effect that Methylprednisolone combined doxofylline treat patients with COPD, it can effectively improve the clinical symptoms and inflammation, safe and reliable, and it is worthy of application.

1. Introduction

Chronic obstructive pulmonary disease (COPD) is a kind of chronic obstructive airways disease with the main characteristics of a limited airflow and having irreversibility[1]. In addition to part of the genetic factors, most of the disease was due to abnormal inflammatory of lungs caused by smoking, air pollution and so on. The disease is progressively intensified and has irreversible damage in lung function. The clinical common pathological changes are chronic bronchitis and emphysema. It may be further developed into cor pulmonale and respiratory failure. Chronic obstructive pulmonary disease has high morbidity and mortality. Referring to the data of WTO, the mortality of COPD was fourth in all diseases of the world[2]. Due to the long course of disease and be relatively difficult to heal, it not only brings a lot of trouble to patients’ life, but also seriously threats to the life safety of patients. At present, the main clinical treatment methods were drug therapy such as bronchodilator and respiratory stimulants, oxygen therapy or to give up smoking. We adopted methylprednisolone combined doxofylline to treat chronic obstructive pulmonary disease and the clinical curative effect is good. Please look at the following details.
2. Informations and Methods

2.1. General information

A total of 84 patients were selected with COPD in our hospital for the treatment from June 2013 to June 2015, we randomly divided them into the experiment group and the control group. The experiment group had 42 patients, with 28 male patients, 14 female patients, ages were from 45 to 86 years old, the average (64.2±22.7) years old; The control group had 42 patients, with 27 male patients, 15 female patients, ages were from 46 to 88 years old, the average (65.6±23.1) years old. All patients met the diagnostic standards of COPD from The guideline for diagnosis and management of chronic obstructive pulmonary disease[3] made by the respilology society of Chinese medical association in 2007; All patients were in chronic bronchitis episodes, and other lung diseases were ruled out; All patients didn’t use theophylline drugs within nearly one week[4]; All patients’ brain, heart, liver and renal function had normal operation; All patients were given informed consent, and signed informed consent. Comparing and analysing the basic informations of two groups’ patients, there is no significant difference on the arterial blood gas index, age, gender, course of disease and smoking, having no statistical significance (P>0.05).

2.2 Treatment method

Experiment group used the 300 mg doxofylline injection (Rui Yang pharmaceutical co., LTD., approved by H20052239) mixing 5% glucose injection and then going on 100 mL intravenous drip. Medicine frequency: 2 times per day. The 40 mg methylprednisolone (Pfizer Manufacturing Belgium NV, approved by H20080285) mixing 100 mL 0.9% saline water was also used. Control group used 125 mg aminophylline (Tianjin Jin Yao pharmaceutical co., LTD., approved by H12020884) mixing 5% glucose injection and then going on 100 mL intravenous drip. Medicine frequency: 2 times per day. The 40 mg methylprednisolone (Pfizer Manufacturing Belgium NV, approved by H20080285) mixing 100 mL 0.9% saline water was also used. All patients’ treatment lasts a week, actively getting ready to prevent infection and prohibiting to use any drugs effecting the absorption, metabolism and excretion of theophylline during the treatment.

2.3. Therapeutic effect evaluation and detection index

Detection index included before treatment and after a week’s treatment: We collected 10ml venous blood of all fasting patients in the morning, after injecting into anticoagulant tube put them into centrifuge of 3 000 r/min for 15 min, then separated the upper layer of the serum and placed them into -70 °C stored under test. Enzyme-linked immunosorbent assay (ELISA) was used, respectively testing serum APN, MMP-9, IL-17, IL-10 and TNF-α levels of each group’s patients. We chose human ELISA kit produced by Linco co., LTD., the specific process operation in accordance with the manual instructions.

2.4 Statistical method

We carry on data statistics and analysis using SPSS 19.0 statistical software, mean ± standard deviation representing measurement data. using t test and χ² test to compare between groups of measurement data and count data. Their differences were statistically significant (P<0.05).

3. Results

3.1 Comparison of changes on serum adiponectin, MMP-9 and TNF-α levels before and after treatment for both groups’ patients

Serum adiponectin, MMP-9 and TNF-α levels in both groups’ patients had no significant difference compared with those before treatment (P>0.05); Serum MMP-9 and TNF-α levels after treatment were significantly lower than those before treatment, the difference was statistically significant (P<0.05). But serum adiponectin level was significantly higher than that before treatment. After comparison with the control group after treatment, serum MMP-9 and TNF-α levels of experiment group significantly reduced, serum adiponectin level was significantly increased, the difference was statistically significant (P<0.05) (Table 1).

3.2 Comparison of serum IL-17 and IL-10 levels before and after treatment for both groups’ patients

Serum IL-17 and IL-10 levels of two groups’ patients showed

<table>
<thead>
<tr>
<th>Index</th>
<th>Experiment group (n=42)</th>
<th>Control group (n=42)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before treatment</td>
<td>After treatment</td>
</tr>
<tr>
<td>APN (mg/L)</td>
<td>7.63±1.58</td>
<td>16.58±5.06 *</td>
</tr>
<tr>
<td>MMP-9 (ng/mL)</td>
<td>0.61±0.24</td>
<td>0.36±0.15 *</td>
</tr>
<tr>
<td>TNF-α (ng/mL)</td>
<td>34.61±8.51</td>
<td>17.36±7.95 *</td>
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</table>

Ps: Compared with the same group before treatment, *P<0.05; Compared with the control group after treatment, †P<0.05.
no significant difference before treatment (P>0.05); Serum IL-17 after treatment were significantly lower than that before treatment, the difference was statistically significant (P<0.05). But serum IL-10 level was significantly higher than that before treatment. After compared with the control group after treatment, serum IL-17 of experiment group after treatment were significantly decreased and serum IL-10 level was significantly increased. The difference was statistically significant (P<0.05)(Table 2).

4. Discussion

The reason of onset and progression for chronic obstructive pulmonary disease is complex. Its pathogenesis is not fully explained. But it is generally believed that the root cause of its onset and development lies in the chronic inflammatory response of whole body or local part[5-8]. Chronic inflammation is caused by persistent inflammatory factors of damaging tissue. Its main features are inflammatory cells aggregation and various elevated serum inflammatory markers such as TNF-α. This paper mainly discussed that the role of serum adiponectin, MMP-9, IL-17, IL-10 and TNF-α in the COPD pathogenesis.

The results showed that serum MMP-9, TNF-α, IL-17 levels in patients with chronic obstructive pulmonary disease before treatment were significantly reduced (P<0.05). But adiponectin and IL-10 levels were significantly increased (P<0.05). It indicated that MMP-9, TNF-α and IL-17 may participate in the airway obstruction, while adiponectin and IL-10 levels increased with the treatment’s progression, suggesting that they may play an important role in the anti-inflammatory. The related studies have shown that adiponectin plays an important role in the anti-inflammatory in the onset process of COPD, which mainly shows inhibiting the secretion of inflammatory chemokines such as IL-17, IL-8 and reducing the synthesis of macrophage TNF-α. Related research also has shown that adiponectin can combine with airway epithelial cells and adiponectin receptor 1 caused by macrophages, promoting the content of IL-8 and TNF-α, while the rise in concentration of IL-8 helps the promotion of adiponectin and adiponectin receptor 1, resulting in cascading amplification effects to play a role in anti-inflammatory[11,12]. Because adiponectin level significantly increases with the exacerbation of course, related studies also point out its pro-inflammatory role. But this study shows that adiponectin play a role in anti-inflammatory factors in the COPD course. Therefore, specific roles of adiponectin in the COPD development remains to be discussed. MMP-9 as a kind of matrix metalloproteinases, its main function is to degrade and remodel the dynamic balance of extracellular matrix[13]. Its function is to decompose the structure compound within the respiratory tract and lung, which can effectively participate in the reconstruction of the respiratory tract and lung. It also can effectively regulate the activity of other cytokines and protease, therefore elastic enzyme activity in the lung can abnormally elevate, contributing to the development of COPD. IL-17 is an early starting factor of inflammatory response induced by T cell, being able to promote the release of proinflammatory cytokines, which will increase the inflammatory response. IL-17 can promote the secretion of IL-6 and TNF-α, thus effecting the building of airway fibrous connective tissue and the hyperplasia of smooth muscle. Therefore it can be involved in the regulation of COPD airway remodeling. And IL-10, as a kind of the few inhibitory cytokines, can effectively inhibit the production of proinflammatory cytokines and activated cytokines produced by T cells, also can effectively inhibit the activities of harmful inflammatory factors such as IL-8 and TNF-α[14]. TNF-α is mainly produced by mononuclear macrophages, which can stimulate alveoli to make it fibrosis, and induce the production of IL-8[15] participating in the whole course of COPD.

Theophylline drugs for the treatment of airway disease are commonly used, which can effectively relax the bronchial smooth and alleviate the bronchospasm. Doxofylline is methyl-xanthine derivatives and a kind of bronchodilator which can directly act on bronchus. On the one hand, it can inhibit the effect of airway smooth muscle cells such as phosphodiesterase and reduce the intracellular Ca²⁺ concentration, thus relaxing the bronchial smooth muscle; On the other hand, it can inhibit the synthesis and release of airway inflammatory cytokines to protect the airway. Related research has showed that the effect of doxofylline on airway relaxation is 10-15 times of aminophylline[16-18]. Doxofylline can effectively inhibit the activity of inflammatory cells elastase, thus inhibiting its metabolic reactions and preventing the synthesis of inflammatory cells[19,20]. In this study, the effect of doxofylline group’s treatment is significantly better than that of aminophylline group. Doxofylline can effectively inhibit the TNF-α level and promote the IL-10 level.

Table 2.
Comparison of serum IL-17 and IL-10 levels before and after treatment for both groups’ patients.

<table>
<thead>
<tr>
<th>Index</th>
<th>Experiment group (n=42)</th>
<th>Control group (n=42)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before treatment</td>
<td>After treatment</td>
</tr>
<tr>
<td>IL-17 (ng/L)</td>
<td>234.61±34.51</td>
<td>127.36±13.95*</td>
</tr>
<tr>
<td>IL-10 (ng/mL)</td>
<td>10.61±2.51</td>
<td>27.36±2.95*</td>
</tr>
</tbody>
</table>

*Ps: Compared with the same group before treatment, *P<0.05; Compared with the control group after treatment, #P<0.05.
In summary, the clinical efficacy of methylprednisolone combined doxofylline on the treatment of chronic obstructive pulmonary disease is remarkable. Being able to effectively improve the clinical symptoms and inflammation, safe and reliable, it should be widely applied.

Reference


