Effect of adjuvant tiotropium bromide therapy on the oxygenation function and inflammatory response in patients with COPD and type II respiratory failure

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ARTICLE INFO

Article history:
Received 7 Jul 2016
Received in revised form 17 Jul 2016
Accepted 12 Jul 2016
Available online 24 Jul 2016

Keywords:
COPD
Type II respiratory failure
Tiotropium bromide
Oxygenation function
Inflammatory response

ABSTRACT

Objective: To explore the effect of adjuvant tiotropium bromide therapy on the oxygenation function and inflammatory response in patients with COPD and type II respiratory failure. Methods: a total of 58 patients with COPD and type II respiratory failure treated in our hospital between August 2012 and January 2016 were collected and divided into observation group (n=29) and control group (n=29) according to the single blind randomized control method. Control group of patients received clinical routine treatment, and observation group of patients received adjuvant tiotropium bromide therapy on the basis of routine treatment. Before treatment and 30d after treatment, spirometer was used to determine pulmonary ventilation function; blood gas analyzer was used to test oxygenation function indexes; enzyme-linked immunosorbent assay (ELISA) was used to detect serum inflammatory factor levels. Results: Before treatment, differences in pulmonary ventilation function, oxygenation function and serum inflammatory factor levels were not statistically significant between two groups of patients. 30d after treatment, FEV1, FEF75%, PEF, PaO2/FiO2, DO2 and O2ER levels of observation group were significantly higher than those of control group while VO2 level was significantly lower than that of control group; serum IL-1β, IL-18, IL-27 and CRP levels were significantly lower than those of control group. Conclusion: Adjuvant tiotropium bromide treatment can optimize the pulmonary ventilation and oxygenation function and reduce systemic inflammatory response in patients with COPD and type II respiratory failure.

1. Introduction

Chronic obstructive pulmonary disease (COPD) is the airway function injury disease caused by recurrent chronic bronchitis, acute COPD onset can be complicated with respiratory failure, and type II respiratory failure is the most common[1,2]. The treatment of COPD combined with type II respiratory failure is trickier than that of COPD alone, the effect of increasing oxygen supply, eliminating phlegm, resisting pathogen and other conventional treatments is limited for such patients, and other drugs are required for adjuvant therapy[3]. Tiotropium bromide is the selective anticholinergic agent that inhibits the smooth muscle M3 receptor to generate bronchiectasis effect, its curative effect on optimizing the conditions of patients with COPD has been reported by many researches, but its effect on the specific pulmonary ventilation/gas exchange function and serum inflammation-related parameters is less covered[4-5]. In the following study, the effect of adjuvant tiotropium bromide therapy on the oxygenation function and inflammatory response in patients with COPD and type II respiratory failure was analyzed.

2. Information and methods

2.1 General information

A total of 58 patients with COPD and type II respiratory failure treated in our hospital between August 2012 and January 2016 were included, the patients themselves learned about the research process
and signed the informed consent, and the research was approved by the hospital ethics committee. Inclusion criteria: (1) conforming to the diagnostic criteria for COPD established by world health organization; (2) the oxygen partial pressure (PaO<sub>2</sub>) < 60 mmHg and CO<sub>2</sub> partial pressure (PaCO<sub>2</sub>) > 50 mmHg; (3) not treated with antibiotics, etc before admission; (4) without pulmonary tumor diseases. Exclusion criteria: (1) with basic severe heart, liver and kidney dysfunction; (2) associated with systemic infectious disease caused by other reasons; (3) with long-term use of corticosteroids; (4) the patients or families voluntarily gave up treatment. According to single blind randomized control method, 58 patients were divided into observation group (n=29) and control group (n=29). Observation group included 15 male cases and 14 female cases, they were 45-78 years old, and the course of COPD was 6-25 years and (14.28±2.76) years in average; control group included 16 male cases and 13 female cases, they were 43-79 years old, and the course of COPD was 7-26 years and (13.76±2.88) years in average. The two groups of patients were not statistically different in the distribution of gender, age and course of COPD (P>0.05).

2.2 Treatment methods

Control group of patients received clinical routine therapy for patients with COPD and type II respiratory failure, which was as follows: oxygen uptake, eliminating phlegm by ambroxol (TIPR Pharmaceutical Co., LTD., approved by H20123026) and anti-infection by piperacillin (Reyoung Pharmaceutical Co., LTD, approved by H20110134). Based on above treatment, observation group of patients received tiotropium bromide treatment, which was as follows: inhalation of 20 μg of tiotropium bromide dry powder (Chiatai Tianqing Pharmaceutical Group Co., LTD., approved by H20060454) every morning, 1 time/d for continuous 30 d of treatment.

2.3 Observation indexes

2.3.1 Pulmonary ventilation function

Immediately after admission and 30 d after treatment, the spirometer (Shanghai Jumu Medical Equipment Co., LTD., model AS-507) was used to determine the ventilation function of two groups of patients, including forced expiratory volume in one second (FEV1), maximal expiratory flow in 75% vital capacity (FEF75%) and peak expiratory flow (PEF).

2.3.2 Pulmonary oxygenation function

Immediately after admission and 30 d after treatment, 1 mL of radial artery blood was extracted from two groups of patients at the same point in time, the blood gas analyzer (Nanjing Liaicheng Trade Co., LTD., model AC2013467) was used to detect oxygenation indexes, including oxygenation index (PaO<sub>2</sub>/FiO<sub>2</sub>), oxygen consumption (VO<sub>2</sub>), oxygen delivery (DO<sub>2</sub>) and oxygen uptake rate (O<sub>2</sub>ER).

2.3.3 Inflammatory response

Immediately after admission and 30 d after treatment, 2 mL of cubital venous blood was extracted from two groups of patients at the same point in time and then centrifuged to get supernatant and cryopreserve it in -80 °C refrigerator (Beijing Aochuangxingye Technology Development Co., LTD., model DW-86L388A) for test, and ELISA was used to determine serum inflammatory factors interleukin-1 β (IL-1 β), interleukin-18 (IL-18), interleukin-27 (IL-27) and C-reactive protein (CRP) levels.

2.4 Statistical methods

SPSS 15.0 software was used for statistical processing, measurement data was in terms of Mean ± SD, measurement data comparison before and after treatment was by paired t test, measurement data comparison between groups was by routine t test and P<0.05 indicated statistical significance in differences.

3. Results

3.1 Pulmonary ventilation function

Before and after treatment, comparison of pulmonary ventilation function indexes FEV1(L), FEF75%(L/s) and PEF(L/s) between two groups of patients was as follows: before treatment, differences in FEV1, FEF75% and PEF levels were not statistically significant between two groups of patients (P>0.05). 30 d after treatment, FEV1, FEF75% and PEF levels of both groups were significantly higher than those before treatment, and differences were statistically significant (P<0.05). 30 d after treatment, FEV1, FEF75% and PEF levels of observation group were significantly higher than those of control group, and differences were statistically significant (P<0.05), shown in Table 1.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>FEV1 Before treatment</th>
<th>FEV1 After treatment</th>
<th>FEF75% Before treatment</th>
<th>FEF75% After treatment</th>
<th>PEF Before treatment</th>
<th>PEF After treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>29</td>
<td>1.68±0.21</td>
<td>2.97±0.36</td>
<td>2.09±0.24</td>
<td>2.56±0.07</td>
<td>3.76±0.39</td>
<td>5.63±0.67</td>
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<tr>
<td>Control</td>
<td>29</td>
<td>1.71±0.28</td>
<td>2.17±0.18</td>
<td>2.08±0.23</td>
<td>2.33±0.05</td>
<td>3.68±0.41</td>
<td>4.21±0.53</td>
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<tr>
<td>t value</td>
<td></td>
<td>0.283</td>
<td>6.832</td>
<td>0.116</td>
<td>5.371</td>
<td>0.271</td>
<td>7.192</td>
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<tr>
<td>P value</td>
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<td>&lt;0.05</td>
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</tbody>
</table>

Table 1. Comparison of pulmonary ventilation function index levels before and after treatment.
Comparison of serum inflammatory factor levels before and after treatment.

Table 3.

Comparison of serum inflammatory factor levels before and after treatment.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
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<th>After treatment</th>
<th>Before treatment</th>
<th>After treatment</th>
<th>Before treatment</th>
<th>After treatment</th>
<th>Before treatment</th>
<th>After treatment</th>
<th>Before treatment</th>
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<tr>
<td>Observation</td>
<td>29</td>
<td>84.25±9.11</td>
<td>112.17±15.09</td>
<td>312.46±15.38</td>
<td>309.72±32.64</td>
<td>764.23±85.18</td>
<td>831.52±98.67</td>
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<td>0.29±0.03</td>
<td>0.18±0.02</td>
<td>0.21±0.02</td>
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<tr>
<td>Control</td>
<td>29</td>
<td>83.09±9.43</td>
<td>92.74±9.64</td>
<td>306.48±13.28</td>
<td>276.83±30.18</td>
<td>764.23±85.18</td>
<td>831.52±98.67</td>
<td>0.14±0.05</td>
<td>0.28±0.05</td>
<td>0.14±0.05</td>
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</tr>
<tr>
<td>P value</td>
<td></td>
<td>&gt;0.05</td>
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</table>

3.2 Pulmonary oxygenation function indexes

Before and after treatment, comparison of pulmonary oxygenation function indexes PaO2/FiO2, VO2(mL/min), DO2(mL/min) and O2ER between two groups of patients was as follows: before treatment, differences in PaO2/FiO2, VO2, DO2 and O2ER levels were not statistically significant between two groups of patients (P>0.05). 30d after treatment, PaO2/FiO2, DO2 and O2ER levels of both groups were significantly higher than those before treatment while VO2 levels were significantly lower than those before treatment, and differences were statistically significant (P<0.05). 30d after treatment, PaO2/FiO2, DO2 and O2ER levels of both groups were significantly higher than those before treatment while VO2 levels were significantly lower than those before treatment, and differences were statistically significant (P<0.05). 30d after treatment, PaO2/FiO2, DO2 and O2ER levels of both groups were significantly higher than those before treatment while VO2 levels were significantly lower than those before treatment, and differences were statistically significant (P<0.05), shown in Table 2.

3.3 Inflammatory response

Before and after treatment, comparison of serum inflammatory factors IL-1β (pg/mL), IL-18 (pg/mL), IL-27 (ng/L) and CRP (mg/L) between two groups of patients was as follows: before treatment, differences in serum IL-1β, IL-18, IL-27 and CRP levels were not statistically significant between two groups of patients (P>0.05). 30d after treatment, serum IL-1β, IL-18, IL-27 and CRP levels of both groups were significantly lower than those before treatment, and differences were statistically significant (P<0.05). 30d after treatment, serum IL-1β, IL-18, IL-27 and CRP levels of both groups were significantly lower than those before treatment, and differences were statistically significant (P<0.05). 30d after treatment, serum IL-1β, IL-18, IL-27 and CRP levels of both groups were significantly lower than those before treatment, and differences were statistically significant (P<0.05), shown in Table 3.

4. Discussion

Pulmonary ventilation/gas exchange dysfunction is the pathological basis of patients with COPD, and when acute inflammation occurs, pulmonary dysfunction is further aggravated until respiratory failure occurs. Tiotropium bromide belongs to long-acting anticholinergic agent, dilates airway smooth muscle while expands the cross-sectional area of airway, directly reduces the pulmonary ventilation resistance and realizes the optimization of pulmonary ventilation function[6,7]. FEV1, FEF75% and PEF are the most common clinical pulmonary oxygenation indexes, there are declined FEV1, FEF75% and PEF levels in most patients with COPD, and the decline extent is consistent with the illness of COPD[8]. It was found in the study that compared with control group, observation group were with higher FEV1, FEF75% and PEF levels 30d after treatment, confirming the role of tiotropium bromide in optimizing patients’ ventilation function.

Type II respiratory failure refers to the oxygen partial pressure decrease (<60 mmHg) and the carbon dioxide partial pressure increase (>50 mmHg), and in addition to increased ventilation resistance and ventilation dysfunction in patients with COPD, pulmonary oxygenation dysfunction is the core mechanism of its occurrence[9,10]. Patients with COPD and type II respiratory failure have severe local and systemic inflammatory response, the secretions accumulate within local lung lesions, and local atelectasis may even appear[11]. There is ventilation/blood flow imbalance in lung tissue with poor ventilation or atelectasis, the inhaled oxygen cannot be effectively displaced into the blood circulation, and the CO2 produced during circulation cannot diffuse into the alveoli in time, leading to oxygenation dysfunction. PaO2/FiO2 is the most intuitive index to reflect pulmonary oxygenation function, and constant PaO2/FiO2 declining indicates the ventilation dysfunction within the lungs. VO2, DO2 and O2ER represent pulmonary oxygen supply and oxygen consumption balance state, and if the oxygen consumption is continuously greater than the oxygen supply, stubborn hypoxemia and oxygenation disorder will appear in the body[12]. It was found in the study that compared with control group, observation group were with higher PaO2/FiO2, DO2 and O2ER levels and lower VO2 level, indicating that the adjuvant tiotropium bromide treatment can
optimize the pulmonary oxygenation state, and this is mainly directly related to its role in relieving airway smooth muscle dysfunction, reducing bronchospasm, remitting airway hyperresponsiveness, and so on.

There is local airway inflammation in patients with COPD. COPD is aggravated in the case of acute onset of inflammation and triggers type II respiratory failure, so the systemic inflammatory state is the core mechanism leading to disease progression and continuously aggravated inflammatory response is also the factor expression changes after tiotropium bromide inhalation treatment of patients with COPD. \cite{4,5}.

To sum up, it is concluded as follows: adjuvant tiotropium bromide treatment can optimize the pulmonary ventilation and oxygenation function and reduce systemic inflammatory response in patients with COPD and type II respiratory failure, and it’s worth popularization and application in clinical practice in the future.

References


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