Effects of naloxone hydrochloride on pulmonary function, blood gas changes and inflammatory factors in patients with COPD combined with respiratory failure

Juan Wu, Jun Wang, Yi Zhang

Department of Critical Care Medicine, Deyang Second People's Hospital, Deyang, Sichuan, 618000, China

ARTICLE INFO

Article history:
Received 28 Nov 2017
Received in revised form 2 Dec 2017
Accepted 7 Dec 2017
Available online 14 Dec 2017

Keywords:
Naloxone hydrochloride
COPD combined with respiratory failure
Pulmonary function
Blood gas changes
Inflammatory factors

ABSTRACT

Objective: To investigate the effects of naloxone hydrochloride on pulmonary function, blood gas changes and inflammatory factors in patients with COPD combined with respiratory failure. Methods: According to random data table method, 80 cases of COPD combined with respiratory failure were randomly divided into the control group (n=40) and observation group (n=40), patients in the control group were treated with noninvasive positive pressure ventilation on the basis of routine symptomatic treatment, on the basis of the treatment of the control group, the observation group received naloxone hydrochloride therapy. The levels of pulmonary function, blood gas changes and inflammatory factors were compared in two groups before and after treatment. Results: The levels of serum FEV1, FVC, PEF, PaCO2, PaO2, PaO2/FiO2, TNF-α and PCT in the two groups before treatment were not statistically significant. After treatment, the levels of FEV1, FVC, PEF in the control group and observation group were (70.01±0.36)%, (2.16±0.41) L, (2.98±0.45) L/s and (81.71±0.53)%, (3.65±0.55) L, (4.36±0.43) L/s, which were significantly higher than those in the same group before treatment, and the levels in observation group were significantly higher than those in the control group; the levels of PaCO2, PaO2, PaO2/FiO2 in the two groups were (59.62±6.47) mmHg, (65.53±7.36) mmHg, (323.89±10.47) mmHg and (46.59±8.26) mmHg, (73.65±8.26) mmHg, (398.64±14.06), compared with the same group before treatment, PaCO2 levels were significantly lower in both groups, and the observation group was significantly lower than the control group, PaO2, PaO2/FiO2 levels were significantly increased in both groups, and the observation group was significantly higher than the control group; the levels of TNF-α, PCT in the two groups were (23.28±4.53) pg/mL, (5.22±2.13) ng/mL and (16.61±4.12) pg/mL, (2.07±1.21) ng/mL, which were significantly lower than those in the same group before treatment, moreover, the observation group levels were significantly lower than those in the control group. Conclusion: Treatment of COPD with respiratory failure by naloxone hydrochloride can effectively reduce the level of inflammatory factors, and improved lung function and blood gas levels, which has important clinical value.

1. Introduction

COPD is a common disease characterized by airflow obstruction, accompanied by asthma, chest tightness and other symptoms, if patients do not receive timely treatment, can worsen to pulmonary heart disease and respiratory failure and other serious diseases, a serious threat to patient's life and health[1,2], so the treatment of this disease should be adhering to the principle of early detection and early treatment. The exact cause of the COPD is unclear currently, generally believed that the factors causes chronic bronchitis and obstructive pulmonary emphysema may be involved in the pathogenesis of COPD[3-6]. Naloxone hydrochloride is an opioid receptor antagonist with good clinical efficacy in the treatment of COPD disease[7,8]. This study investigated the effects of naloxone hydrochloride on the inflammatory factors, lung function and blood gas in patients with COPD combined with respiratory failure.
2. Research objects and methods

2.1 Research object

From March 2016 to August 2017, 80 patients with chronic obstructive pulmonary disease (COPD) accompanied with respiratory failure treated in our department of respiratory critical care medicine were selected as the study subjects. Inclusion criteria: (1) All patients were in line with the guidelines for the diagnosis and treatment of chronic obstructive pulmonary diseases and the diagnostic criteria for type II respiratory failure[9] developed by the respiratory diseases branch of the Chinese medical association in 2013; (2) Patients with accelerated heartbeat and dyspnea; (3) Heart rate were stable and with normal hemodynamics; (4) no other pulmonary disease; (5) patients with a clear sense can actively cooperate with the treatment. Exclusion criteria: (1) patients with severe heart, liver and kidney dysfunction; (2) autoimmune diseases; (3) suffering from cardiovascular disease; (4) failed to follow the doctor's advice to complete the treatment, half-way off. All patients were randomly divided into control group and observation group, 40 cases in each group, in the control group including 22 males and 18 females, aged 51-76 years old, with heart rate was 95-121 times/min and respiratory frequency was 25-37 times/min, disease course was 3-15 years; in the observation group, 22 males and 18 females, aged 50-75 years old, heart rate was 93-122 times/min, respiratory rate 25-38 times/min, disease course was 5-14 years. The differences in the general data of both groups was not significant (P>0.05), it was comparable. All subjects and their families were informed, signed informed consent and voluntarily joined the treatment.

2.2 Treatment methods

Both groups received routine treatment, including bronchial dilation, enhanced sputum drainage, controlled pulmonary infection, enhanced nutritional support, and correction of water and electrolyte balance in patients. The patients in both groups were treated with VPAP II series multi-function bi-level ventilator from Reesee Australia for noninvasive positive pressure ventilation. Machine parameters were set as: suction pressure was 6-8 cmH2O, expiratory pressure was 2-3 cmH2O (1 cmH2O = 0.098 kPa), according to the patient condition during the ventilation process gradually increased the above parameters, maximum suction pressure increased to 15-20 cmH2O, maximum expiratory pressure increased to 5-6 cmH2O, respiratory frequency was 12-20 times/min, down-regulated the above parameters until the patient's condition improved. Inhaled oxygen levels were set as 40% during treatment and oxygen flow was set as 4-6 L/min. Each ventilation for 4-6 h, 3 times a day. The changes of respiratory rate, heart rate, pH, PaCO2 and PaO2 value were observed and recorded at any time. Based on the above treatment, the observation group was given intravenous infusion of naloxone hydrochloride (the manufacturer was Chongqing Yaoyou Pharmaceutical Co., Ltd., approval number (H20060062), 5 µ g/kg (naloxone dissolved in 50 mL of sodium chloride solution), 1 time a day, continuous intravenous infusion for 5 d.

2.3 Indexes detection

(1) Pulmonary function detection: Before and after treatment, percentage of the forced expiratory volume at the first second occupied the predicted value (FEV1%), forced vital capacity (FVC) and maximum expiratory flow (PEF) were detected by HI-801type pulmonary function detection instrument. Blood gas parameters detection: 5 mL of radial artery blood was extracted from the two groups before and after treatment, partial pressure of carbon dioxide (PaCO2), arterial partial pressure of oxygen (PaO2), oxygenation index (PaO2/FiO2) were measured by ABL80 blood gas analyzer (Denmark). (3) Serum inflammatory factors detection: Before and after treatment, patients were extracted 10 mL of venous blood, put into ordinary tube for a few minutes, then 3 000 r/min, centrifuged for 10 min, the supernatant collected in the EP tube, placed in -20 °C refrigerator for detection. TNF-α (tumor necrosis factor-α) was detected by radioimmunoassay, the kit was purchased from Shanghai Hengyuan Biological Company; PCT (procalcitonin) detection by enzyme-linked immunosorbent assay, kit was purchased from Shanghai Yanhao Biological Technology Co., Ltd.

2.4 Statistical analysis

All the data in the study were analyzed by SPSS 22.0 software. The measurement data were analyzed by t-test and mean value plus or minus standard deviation (Mean± SD). P<0.05 was considered as significant difference.

3. Results

3.1 Comparison of pulmonary function of both group before and after treatment

Before and after treatment, comparison of pulmonary function in two groups as shown in Table 1. Before treatment, there was no significant difference in FEV1, FVC and PEF between the two groups (P>0.05). The levels of FEV1, FVC and PEF in the control group and the observation group were (70.01 ± 0.36)% , (2.98 ± 0.45) L/s and (81.71 ± 0.53)% , (3.65 ± 0.55) L and (4.36 ± 0.43) L/s, respectively. Compared with the same group before treatment, the levels of FEV1, FVC and PEF in both groups were significantly increased (P<0.05), and the observation group was significantly higher than the control group (all P<0.05).

<table>
<thead>
<tr>
<th>Table 1. Comparison of lung function of both group before and after treatment.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group</strong></td>
</tr>
<tr>
<td>Control group</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Observation group</td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>

Note: Compared with before treatment intergroup, *P<0.05; compared with in the control group after treatment " † P<0.05.

Juan Wu et al./ Journal of Hainan Medical University 2017; 23(22): 37-40
course of clinical treatment needs to overcome respiratory muscle permeability, brain stroma and brain cell edema, therefore in the treatment, endorphin, enkephalin, and dynorphin as endogenous respiratory inhibitors, are crucial role in respiratory and neurological functions. Related studies have shown that COPD patients with respiratory failure occurs, adding tissue hypoxia, resulting in β-endorphin increasing in plasma, damages the body; and β-endorphin as endogenous respiratory inhibitors, are involved in the regulation of body system functions, and when their content is increased in large quantities, it will make the brain stem nerve cell’s sensitivity to carbon dioxide reduce and their respiratory function may be inhibited[18,19]. Therefore, when COPD with respiratory failure appears, adding naloxone hydrochloride treatment based on non-invasive mechanical ventilation, use of its ability to pass through the blood-brain barrier to excite the respiratory center, to improve the symptoms of hypercapnia and hypoxia, eliminate β-endorphin effect on respiratory inhibition, thereby speeding the consciousness recovery, improving ventilation in order to reduce mortality. Also has the effect of improving brain metabolism, protecting brain cells and reducing edema in the brain region. The results of this study revealed that in terms of pulmonary function and blood gas parameters, the levels of FEV1, FVC and PEF in the control group and the observation group were significantly higher than those in the same group before treatment (P<0.05), and the observation group was significantly higher than control group (P<0.05). The PaCO2 levels of the control group and the observation group were significantly decreased than those before treatment (P<0.05), and the observation group was significantly lower than the control group after treatment (all P<0.05).

Note: Compared with before treatment intergroup, *P<0.05; compared with in the control group after treatment †P<0.05.

### 3.2 Comparison of blood gas changes of both group before and after treatment

Blood gas changes in both groups before and after treatment as shown in Table 2. Before treatment, there was no significant difference in PaCO2, PaO2 and PaO2/FiO2 between the two groups (P>0.05). The levels of PaCO2, PaO2 and PaO2/FiO2 in control group and observation group were (59.62 ± 6.47) mmHg, (65.53 ± 7.36) mmHg, (323.89 ± 10.47) and (46.59 ± 6.64) mmHg, (73.65 ± 8.26) mmHg, (398.64 ± 14.06) respectively. PaCO2 levels in both groups were significantly decreased than that in the same group before treatment (P<0.05), and the observation group was significantly lower than the control group, the PaO2 and PaO2/FiO2 levels were significantly increased (P<0.05), and the observation group was significantly higher than the control group (P<0.05).

### 3.3 Comparison of inflammatory factors of both group before and after treatment

Before and after treatment comparison of inflammatory factors in both group as shown in Table 3. Before treatment, serum TNF-α and PCT levels in both groups were similar, with no significant difference (P>0.05). After treatment, the levels of TNF-α and PCT in the control and observation groups were (23.28 ± 4.53) pg/mL, (5.22 ± 2.13) ng/mL and (16.61 ± 4.12) pg/mL and (2.07 ± 1.21) ng/mL respectively, after treatment, the levels of TNF-α and PCT in both groups were significantly decreased than those before treatment (P<0.05), and the levels in the observation group were significantly lower than those in the control group after treatment (all P<0.05).

### 4. Discussion

In recent years, as environmental pollution continues to worsen, the number of smokers continues to increase, and the incidence of chronic obstructive pulmonary disease has also increased year by year[10,11]. Studies have shown that COPD is associated with increased airway resistance leading to respiratory airflow limitation and gas exchange abnormalities, after long-term airflow limitation, respiratory muscle fatigue, easily leading to CO2 retention and hypoxia, resulting in an increase of cerebral vascular wall permeability, brain stroma and brain cell edema, therefore in the course of clinical treatment needs to overcome respiratory muscle fatigue and reduce contractility caused by increased endogenous positive end-expiratory pressure, to prevent secondary occurrence of respiratory failure[12-14]. COPD patients with type II respiratory failure mainly have the following clinical symptoms: hypoxemia, dyspnea, shortness of breath and chest tightness, hypercapnia, severe cases can cause hypoxia, leading to electrolyte imbalance in the body[15,16].

The principle of noninvasive positive pressure ventilation is to connect the ventilator with the patient through the nasal mask, positive pressure supported by the ventilator to complete the ventilation treatment. This method does not need tracheotomy or endotracheal intubation to establish the artificial airway. Therefore, This method is less damage, more conducive to patient rehabilitation, is currently common treatment for COPD disease. Naloxone hydrochloride is a synthetic endogenous opioid receptor blocker that specifically blocks endogenous opioids, such as beta-endorphin, enkephalin, and dynorphin[17]. These substances play a crucial role in respiratory and neurological functions. Related studies have shown that when COPD patients with respiratory failure occurs, the synthesis and release of β-endorphin in patients, adding tissue hypoxia, resulting in β-endorphin increasing in plasma, damages the body; and β-endorphin as endogenous respiratory inhibitors, are involved in the regulation of body system functions, and when their content is increased in large quantities, it will make the brain stem nerve cell’s sensitivity to carbon dioxide reduce and their respiratory function may be inhibited[18,19]. Therefore, when COPD with respiratory failure appears, adding naloxone hydrochloride treatment based on non-invasive mechanical ventilation, use of its ability to pass through the blood-brain barrier to excite the respiratory center, to improve the symptoms of hypercapnia and hypoxia, eliminate β-endorphin effect on respiratory inhibition, thereby speeding the consciousness recovery, improving ventilation in order to reduce mortality. Also has the effect of improving brain metabolism, protecting brain cells and reducing edema in the brain region. The results of this study revealed that in terms of pulmonary function and blood gas parameters, the levels of FEV1, FVC and PEF in the control group and the observation group were significantly higher than those in the same group before treatment (P<0.05), and the observation group was significantly higher than control group (P<0.05). The PaCO2 levels of the control group and the observation group after treatment were significantly decreased (P<0.05), and the observation group was significantly lower than the control group, the PaO2, PaO2/FiO2 levels were significantly increased (P<0.05); compared with in the control group after treatment †P<0.05.

### Table 2.

Comparison of blood gas changes of both group before and after treatment.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Treatment time</th>
<th>PaCO2 (mmHg)</th>
<th>PaO2 (mmHg)</th>
<th>PaO2/FiO2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>40</td>
<td>Before treatment</td>
<td>71.91 ± 8.03</td>
<td>52.19 ± 6.79</td>
<td>300.41 ± 12.56</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>59.62 ± 6.47</td>
<td>65.53 ± 7.36</td>
<td>323.89 ± 10.47</td>
</tr>
<tr>
<td>Observation group</td>
<td>40</td>
<td>Before treatment</td>
<td>72.12 ± 8.15</td>
<td>51.83 ± 6.68</td>
<td>299.85 ± 13.15</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>46.59 ± 6.64</td>
<td>73.65 ± 8.26</td>
<td>398.64 ± 14.06</td>
</tr>
</tbody>
</table>

Note: Compared with before treatment intergroup, *P<0.05; compared with in the control group after treatment †P<0.05.

### Table 3.

Comparison of inflammatory factors of both group before and after treatment.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Treatment time</th>
<th>TNF-α (pg/mL)</th>
<th>PCT (ng/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>control group</td>
<td>40</td>
<td>Before treatment</td>
<td>45.36 ± 8.95</td>
<td>11.03 ± 2.59</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>23.28 ± 4.53*</td>
<td>5.22 ± 2.13*</td>
</tr>
<tr>
<td>Observation group</td>
<td>40</td>
<td>Before treatment</td>
<td>46.51 ± 9.02</td>
<td>10.97 ± 2.94</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>16.61 ± 4.12**</td>
<td>2.07 ± 1.21**</td>
</tr>
</tbody>
</table>

Note: Compared with before treatment intergroup, *P<0.05; compared with in the control group after treatment †P<0.05.
<0.05), and the observation group was significantly higher than the control group, the difference was statistically significant \((P<0.05)\). The results suggested that naloxone hydrochloride can significantly improve the patient’s lung function and blood gas parameters, which may be due to naloxone hydrochloride can effectively block the increase of \(\beta\)-endorphin, improve the bronchial smooth muscle contract and thereby effectively improve pulmonary circulation.

In addition, studies have reported that COPD complicated with respiratory failure is closely related to airway inflammation, and inflammatory factors such as IL-6, IL-8 and TNF-\(\alpha\) are released massively when inflammation occurs\([20]\). TNF-\(\alpha\) is an inflammatory factor mainly secreted by monocytes-macrophages. It has a variety of immune functions and can mediate inflammatory responses, is an important substance of airway inflammation. PCT, as a glycoprotein, is almost undetectable in healthy human and its plasma levels are significantly increased when severe bacterial, fungal, parasitic infections and sepsis occur\([21]\). PCT is not only used as an acute index for differential diagnosis, but also an important parameter for monitoring inflammation in vivo. In addition, PCT can promote the increase of serum IL-6 and TNF-\(\alpha\) in vivo\([22]\). The results of this study showed that the levels of TNF-\(\alpha\) and PCT in the control group and the observation group after treatment were significantly decreased than those in the same group before treatment, and the observation group was significantly lower than the control group \((P<0.05)\). The results indicated that naloxone hydrochloride can effectively relieve the inflammatory reaction in patients and promote the rehabilitation of patients. The specific mechanism remains to be further explored.

In conclusion, The use of naloxone hydrochloride based on noninvasive positive pressure ventilation in COPD with respiratory failure can effectively relieve the level of inflammatory factors, improve pulmonary function and blood gas levels, has a very important clinical value.

**Reference**


