Effect of NIPPV combined with respiratory stimulant therapy on serum markers in COPD patients with mild pulmonary encephalopathy

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ABSTRACT

Objective: To analyze the effect of NIPPV combined with respiratory stimulant therapy on serum markers in COPD patients with mild pulmonary encephalopathy. Methods: A total of 102 cases of COPD patients with mild pulmonary encephalopathy who were hospitalized in our hospital from November 2012 to February 2015 were selected as research subjects and divided into observation group 51 cases and control group 51 cases according to the different clinical treatment they received. Control group received respiratory stimulant therapy alone, observation group received NIPPV combined with respiratory stimulant therapy, and then differences in arterial blood gas, serum Ang II, CPK, LDH, IL-6, IL-8 and IL-10 levels, S-100 β, NSE, MBP, T-SOD and MDA levels as well as T3, T4 and TSH levels were compared between two groups. Results: PH value and PaO2 value of observation group after treatment were higher than those of control group, and PaCO2 level was lower than that of control group; serum Ang II, CPK, LDH, IL-6, IL-8 and IL-10 levels of observation group after treatment were lower than those of control group; serum S-100 β, NSE, MBP and MDA levels of observation group after treatment were lower than those of control group, and T-SOD level was higher than that of control group; serum T3, T4 and TSH levels of observation group after treatment were higher than those of control group. Conclusion: NIPPV combined with respiratory stimulant therapy for COPD patients with mild pulmonary encephalopathy can effectively optimize respiratory function and equilibrate body fluid environment, and it has active clinical significance.

1. Introduction

Chronic obstructive pulmonary disease (COPD) is quite common in clinical practice, pulmonary encephalopathy may occur in severe cases, and positive interventions must be taken. There is paralysis of respiratory centre in COPD patients with mild pulmonary encephalopathy, appropriate application of respiratory stimulant is quite common, but recent study has shown that long-term large-dose respiratory stimulant can lead to respiratory center failure and poor long-term prognosis[1]. In order to increase patients’ effective ventilation and decrease the work of breathing, some scholars have proposed adjuvant mechanical ventilation on the basis of respiratory stimulant therapy. Noninvasive positive pressure ventilation (NIPPV) can provide patients with certain breathing support without intubation, which is without the pain and dependence brought to patients by airway mechanical ventilation, and can both improve patients’ ventilation and improve their quality of life[2]. In the research, the effect of NIPPV combined with respiratory stimulant therapy on serum markers in COPD patients with mild pulmonary encephalopathy was mainly analyzed, hereby reported as follows.

2. Information and methods

2.1. General information

A total of 102 cases of COPD patients with mild pulmonary encephalopathy who were hospitalized in our hospital from November 2012 to February 2015 were selected as research subjects, and all of them were in line with the diagnosis for chronic
obstructive pulmonary disease of Breathing Branch of Chinese Medical Association, and were admitted to hospital because of cough of phlegm and asthma exacerbation. According to the different clinical treatment they received, all enrolled patients were divided into observation group 51 cases and control group 51 cases. Control group included 27 male cases and 24 female cases, they were 57-74 years old and the average was (65.82±5.03) years, the course of disease was 7-20 years and the average was (12.09±3.47) years; observation group included 26 male cases and 25 female cases, they were 54-76 years old and the average was (66.57±5.29) years, the course of disease was 8-23 years and the average was (12.34±3.67) years. Differences in baseline information between two groups were without statistical significance, \(P>0.05\) and they were comparable.

### 2.2. Treatment methods

Both groups received conventional treatment including anti-infection, resolving spasm and relieving asthma, dispensing phlegm, bronchiectasis and nutritional support and so on. Control group received respiratory stimulant on the basis of conventional treatment, which was as follows: nikethamide 0.375 gcx5 dissolved in 50 mL normal saline, intravenous injection over 24 h. Observation group received noninvasive positive pressure ventilation (NIPPV) combined with respiratory stimulant therapy, which was as follows: Philips multifunctional noninvasive ventilator, setting ventilation mode to S/T, respiratory frequency 16-18 times/min, intake pressure starting from 8 cmH\(_2\)O and reaching 14-16 cmH\(_2\)O within 1 h; setting inspiratory expiratory ratio to 1:2, end-expiratory pressure 5 cmH\(_2\)O and concentration of oxygen uptake about 40%, adjusting according to specific conditions in patients and maintaining blood oxygen saturation above 90%. After patients’ ventilation state was improved, discontinuous ventilation was carried out, and nasal catheter was used for low-flow continuous oxygen uptake.

### 2.3. Observation indicators

Before treatment, 4 h after treatment and 24 h after treatment, arterial blood was drawn from patients, and levels of blood gas such as \(pH\) value, arterial partial pressure of oxygen and arterial partial pressure of carbon dioxide (PaCO\(_2\)) were detected.

Radioimmunoassay was used to detect angiotensin II (Ang II) level; automatic biochemical analyzer was used to detect creatine phosphate kinase (CPK) and lactate dehydrogenase (LDH) levels; enzyme-linked immunosorbent assay (ELISA) was used to detect S-100 and myelin basic protein (MBP) levels as well as inflammatory factors interleukin-6 (IL-6), interleukin-8 (IL-8) and interleukin-10 (IL-10) levels; electrochemiluminescence was used to detect neuron specific enolase (NSE) level. Radioimmunoassay was used to detect serum thyroid hormone-related levels, including T\(_3\), T\(_4\) and thyroid-stimulating hormone (TSH). Xanthine oxidase was used to detect serum total superoxide dismutase (T-SOD) activity and thiobarbituric acid was used to detect malondialdehyde (MDA) level.

### 2.4. Statistical methods

SPSS 23.0 software was used to statistically analyze the data above, measurement data (Mean ± SD) was by \(t\) test, count data was by chi-square test and obtained results were determined to be statistically significant at a level of \(P<0.05\).

### 3. Results

#### 3.1. Blood gas indicators

Arterial blood was drawn from patients before and after treatment, related indicators were analyzed by blood gas analyzer, and results were as follows: differences in serum \(pH\) value, PaO\(_2\) and PaCO\(_2\) levels between two groups were without statistical significance before treatment \((P>0.05)\), \(pH\) value and PaO\(_2\) value of both groups after treatment were higher than those before treatment, PaCO\(_2\) level was lower than that before treatment \((P>0.05)\), \(pH\) value and PaO\(_2\) value of observation group after treatment were higher than those of control group, and PaCO\(_2\) level was lower than that of control group \((P<0.05)\), shown in Table 1.

#### 3.2. Serum Ang II, CPK, LDH, IL-6, IL-8 and IL-10 levels

COPD patients with mild pulmonary encephalopathy may be accompanied with abnormal levels of a series of serum indicators, peripheral venous blood was drawn, serum Ang II, CPK, LDH, IL-6, IL-8 and IL-10 levels were detected so as to judge the changes of disease in patients, and specific results were as follows: serum Ang II, CPK, LDH, IL-6, IL-8 and IL-10 levels of observation group after treatment were lower than those of control group \((P<0.05)\), shown in Table 2.

#### 3.3. Serum S-100, NSE, MBP, T-SOD and MDA levels

After patients received treatment, levels of brain injury-related indicators and oxidative stress-related indicators were detected, and detection results were as follows: serum S-100, NSE, MBP and MDA levels of observation group after treatment were lower than those of control group, and T-SOD level was higher than that of control group \((P<0.05)\), shown in Table 3.

#### 3.4. Serum T3, T4 and TSH levels

Peripheral blood was drawn from patients before and after treatment to detect levels of thyroxine-related indicators, and results were as follows: differences in serum T\(_3\), T\(_4\) and TSH levels between two groups were without statistical significance before treatment \((P>0.05)\), serum T\(_3\), T\(_4\) and TSH levels of both groups after treatment were higher than those before treatment \((P<0.05)\), and serum T\(_3\), T\(_4\) and TSH levels of observation group after treatment were higher than those of control group \((P<0.05)\), shown in Table 4.
4. Discussion

Chronic obstructive pulmonary disease (COPD) is a clinical common respiratory disease that is manifested as increased respiratory resistance and decreased alveolar effective ventilation and can significantly increase patients’ work of breathing and oxygen consumption, ultimately leading to respiratory failure. Aggravated COPD and increased CO2 retention will damage patients’ brain nerve cells, affect cortical excitability and thus generate a series of neurological symptoms, clinically called pulmonary encephalopathy[3,4]. COPD patients with mild pulmonary encephalopathy have higher mortality rate and must receive positive therapeutic interventions. For respiratory center damage in COPD patients with mild pulmonary encephalopathy, respiratory stimulant becomes conventional treatment means. Nikethamide is the typical respiratory stimulant that can stimulate respiratory center, accelerate respiratory frequency, increase alveolar ventilation and reduce respiratory oxygen consumption. But study has shown long-term use of respiratory stimulant can lead to patients’ ventilator fatigue and may cause a series of side effects in long term[5]. NIPPV means that in the case that there is no need of tracheal intubation, various techniques are used to increase the ventilation in patients with spontaneous breathing, the clinical application of NIPPV technique has been increasing in recent years, and many studies have confirmed that the technique can practically reduce patients’ tracheal intubation rate and case fatality rate. NIPPV can be used as the first-line treatment method in cases of acute respiratory failure or the preferred mechanical ventilation in cases of ineffective drug treatment. In the research, NIPPV treatment was added on the basis of respiratory stimulant application, and the performance of patients in blood gas indicators and serum indicators was mainly observed. Respiratory dysfunction and effective alveolar hypoventilation in COPD patients with pulmonary encephalopathy can directly lead to decreased arterial partial pressure of oxygen and increased partial pressure of carbon dioxide, and CO2 retention may lead to respiratory acidosis and decreased arterial pH value. Blood gas levels are essential for diagnosis of COPD, so blood gas levels are also the indicators of the main consideration in judging treatment effect of patients with COPD[6,7]. In the research, arterial PH value increased, PaO2 value was improved and PaCO2 value decreased after observation group received treatment, it indicated that effective ventilation in patients increased and CO2 retention was improved, the main reason was that that NIPPV provided the patients with

### Table 1
Comparison of arterial blood gas indicator levels between two groups before and after treatment.

<table>
<thead>
<tr>
<th>Groups</th>
<th>pH value</th>
<th>PaO2 (mmHg)</th>
<th>PaCO2 (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BT 4 h AT</td>
<td>24 h AT</td>
<td>BT 4 h AT</td>
</tr>
<tr>
<td>Observation</td>
<td>7.12±0.14</td>
<td>7.30±0.14</td>
<td>7.38±0.11</td>
</tr>
<tr>
<td>Control</td>
<td>7.13±0.15</td>
<td>7.21±0.14</td>
<td>7.29±0.12</td>
</tr>
<tr>
<td>t</td>
<td>0.143</td>
<td>5.232</td>
<td>6.923</td>
</tr>
<tr>
<td>P</td>
<td>&gt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

BT: Before treatment; AT: after treatment.

### Table 2
Comparison of serum Ang II, CPK, LDH, IL-6, IL-8 and IL-10 levels between two groups after different treatment.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Ang II (pg/mL)</th>
<th>CPK (μ/L)</th>
<th>LDH (μ/L)</th>
<th>IL-6 (pg/mL)</th>
<th>IL-8 (pg/mL)</th>
<th>IL-10 (pg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>41.82±3.54</td>
<td>89.34±3.64</td>
<td>192.37±13.23</td>
<td>21.28±1.73</td>
<td>31.04±2.83</td>
<td>24.27±2.12</td>
</tr>
<tr>
<td>Control</td>
<td>70.93±5.71</td>
<td>153.28±11.35</td>
<td>275.48±23.51</td>
<td>29.05±2.45</td>
<td>42.57±3.95</td>
<td>33.96±3.04</td>
</tr>
<tr>
<td>t</td>
<td>8.293</td>
<td>7.135</td>
<td>9.485</td>
<td>6.284</td>
<td>7.486</td>
<td>8.284</td>
</tr>
<tr>
<td>P</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

### Table 3
Comparison of serum S-100β, NSE, MBP, T-SOD and MDA levels between two groups after treatment.

<table>
<thead>
<tr>
<th>Groups</th>
<th>S-100β (ng/L)</th>
<th>NSE (μg/L)</th>
<th>MBP (ng/mL)</th>
<th>T-SOD (μ/mL)</th>
<th>MDA (nmol/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>21.83±1.52</td>
<td>15.49±1.36</td>
<td>1.92±0.14</td>
<td>88.36±7.25</td>
<td>6.13±0.57</td>
</tr>
<tr>
<td>Control</td>
<td>30.74±2.76</td>
<td>20.60±1.93</td>
<td>2.76±0.21</td>
<td>59.52±5.09</td>
<td>10.42±0.92</td>
</tr>
<tr>
<td>t</td>
<td>7.942</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>P</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

### Table 4
Comparison of serum T3, T4 and TSH levels between two groups before and after treatment.

<table>
<thead>
<tr>
<th>Groups</th>
<th>T3 (μg/L)</th>
<th>T4 (μg/L)</th>
<th>TSH (mU/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BT 4 h AT</td>
<td>24 h AT</td>
<td>BT 4 h AT</td>
</tr>
<tr>
<td>Observation</td>
<td>1.14±0.12</td>
<td>1.32±0.12</td>
<td>1.56±0.14</td>
</tr>
<tr>
<td>Control</td>
<td>1.13±0.11</td>
<td>1.20±0.12</td>
<td>1.29±0.13</td>
</tr>
<tr>
<td>t</td>
<td>0.127</td>
<td>5.674</td>
<td>6.885</td>
</tr>
<tr>
<td>P</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>
appropriate respiratory pressure, and on the basis of respiratory stimulant, it could better trigger the occurrence of breathing and the maintenance of respiratory rhythm while decrease the work of respiratory muscle and reduce the incidence rate of respiratory muscle fatigue after excessive application of respiratory stimulant. Angiotensin II (Ang II) has strong bioactivity, which can exert potent vasoconstriction effect and participate in the formation of pulmonary arterial hypertension. Recent study has found that Ang II may be involved in the occurrence of cerebral edema and aggravate cerebral hypoxia and ischemia, and there is prevalent high Ang II level in patients with brain tissue injury[8]. Both creatine phosphate kinase (CPK) and lactate dehydrogenase(LDH) are intracellular enzymes that mainly exist in astrocytes and neurons, their contents in serum are little under physiological conditions, they can be released into bloodstream in cases of cell injury, and therefore, their levels in serum can reflect tissue injury to a certain extent. Many studies have shown that CPK and LDH contents may increase in brain tissue hypoxia condition, and meantime, due to increased brain cell membrane permeability under hypoxic condition, CPK and LDH are released into intercellular space and enter into bloodstream through damaged blood-brain barrier, which leads to significantly elevated CPK and LDH activity. COPD patients themselves are accompanied with certain degree of systemic inflammatory response, and in cases of pulmonary encephalopathy, a variety of inflammatory factors with certain degree of systemic inflammatory response, and in cases of pulmonary encephalopathy, a variety of inflammatory cascade reaction, which in turn aggravates COPD and forms a vicious circle[9,10]. IL-6, IL8 and IL-10 are all important inflammatory factors in human body, IL-6 can promote the release of IL8 and IL-10, and study has shown that for COPD patients with pulmonary encephalopathy, significantly increased serum inflammatory factor levels mostly indicate poor prognosis. In the research, values of above indicators in serum of two groups were compared after treatment, and results showed that serum Ang II, CPK, LDH, IL-6, IL-8 and IL-10 levels of observation group all decreased, indicating that after NIPPV combined with respiratory stimulant therapy could effectively reduce the degree of brain injury in COPD patients with pulmonary encephalopathy, improve body’s antioxidant capacity and help the recovery of disease.

Study has shown that patients with pulmonary encephalopathy may have low thyroid hormone syndrome, and the reduction in serum T3 and T4 level has certain correlation with prognosis. The reasons of T3, T4 and TSH levels of observation group elevated after treatment, indicating that combined therapy could optimize patients' thyroxine level and indirectly reflect the relieved brain tissue injury in patients. In cases of CORD with pulmonary encephalopathy, the body is in stress state, and increased secretion of cortisol will lead to reduced ability of T3 to convert to T4 as well as further decrease of serum T3 level. T4 mainly decreases in the liver, and liver function damage may occur in patients with pulmonary encephalopathy and lead to increased T4 level, the occurrence of negative feedback and inhibited secretion of T3 and T4. In normal cases, there is positive feedback of T3 and T4 in the body, which may lead to increased TSH level, but there are changes of brain hypoxia in patients with pulmonary encephalopathy and feedback is not functional, severe hypoxia may even cause decreased TSH level, and the decrease is positively correlated with the degree of brain injury[15]. In the research, serum T3, T4 and TSH levels of observation group elevated after treatment, indicating that combined therapy could optimize patients' thyroxine level and indirectly reflect the relieved brain tissue injury in patients. To sum up, it is concluded as follows: NIPPV combined with respiratory stimulant therapy for COPD patients with mild pulmonary encephalopathy can effectively optimize respiratory function and equilibrate body fluid environment, and it’s worth popularization in clinical practice in the future.
References


