Effect of pulmonary surfactant combined with mucosolvan on immune function, liver and kidney function in neonatal respiratory distress syndrome

Juan Ma, Xiao-Lei Wang, Zheng-Ying Li, Tao-Ying Chen

Department of Neonates, Wuxi People’s Hospital Affiliated to Nanjing Medical University, Jiangsu, Nanjing 214000, China

ARTICLE INFO

Objective: To explore the pulmonary surfactant combined with mucosolvan on immune function, liver and kidney function in neonatal respiratory distress syndrome, provide help for the treatment. Methods: A total of 160 cases of neonatal respiratory distress syndrome in our hospital were selected and randomly divided into observation group and control group according to the random number table method, 80 cases in each group, the control group was given conventional therapy, the observation group was given pulmonary surfactant combined with mucosolvan treatment on the basis of conventional therapy, before treatment and 3 days after treatment, the arterial blood gas correlation indexes, respiratory distress syndrome related factors, immune related factors, liver and kidney function indexes were detected in the 2 groups. Results: Compared with before treatment, in the observation group and the control group after treatment, arterial blood gas indexes PaO2, TCO2, SaO2 significantly increased, while PaCO2 significantly decreased, related cytokines KL-6, MIF-1 and HMGB-1 significantly decreased, immunologic factors IFN-γ and IL-4 significantly increased, while IL-10 and TNF-α significantly decreased, liver function indexes AST, ALT and renal function indexes BUN, CRE decreased significantly, the differences had statistically significant; compared with the control group after treatment, in the observation group after combined treatment, arterial blood gas indexes PaO2, TCO2, SaO2 significantly increased, PaCO2 significantly decreased, related cytokines KL-6, MIF-1 and HMGB-1 significantly decreased, immunologic factors IL-10 and IL-4 significantly increased, IFN-γ and TNF-α significantly decreased, liver function indexes AST, ALT and renal function indexes BUN, CRE decreased significantly; the differences had statistically significant. Conclusion: Pulmonary surfactant combined with mucosolvan can improve the respiratory distress syndrome related factors, immune function, liver and kidney function of neonates with respiratory distress syndrome, and provide important clinical help for the treatment of neonatal respiratory distress syndrome.

1. Introduction

Neonatal alveolar development is not complete, leading to pulmonary surfactant is in short supply, cause of neonatal respiratory distress syndrome, which results in neonatal shortness of breath, dyspnea and inadequate oxygen supply[1], seriously endanger the growth and health of neonates[2]. Supplement of pulmonary surfactant and promote neonatal alveolar development are the key to the treatment of neonatal respiratory distress syndrome[3], but the medicine has strong side effect, can affect the development of neonates and the function of each organ[4]. This study was to explore the effect of pulmonary surfactant combined with mucosolvan on arterial blood gas correlation indexes, respiratory distress syndrome related indicators, immune function, liver and kidney function in neonatal respiratory distress syndrome, to provide help for the treatment of neonatal respiratory distress syndrome.
2. Data and methods

2.1. General data

This study was permitted by Ethics Committee of our hospital, and implemented with informed consents from all families of neonates. 160 cases of neonatal respiratory distress syndrome in our hospital from January 2012 to January 2016 were collected, all neonates were in accordance with diagnosis standard of the fourth edition of "Practice of neonatology". According to the random number table method, 160 cases were divided into two groups, in the observation group (80 cases), there were 42 males and 38 females, 23 cases of pneumonia, 17 cases of meconium aspiration syndrome, 28 cases of asphyxia and 12 cases of septicemia, the onset time was 4-46 hours and the average was (27.7±5.8) h, aged 30-39 weeks and the average was (35.3±3.5) weeks; in the control group (80 cases), there were 41 males and 39 females, 25 cases of pneumonia, 16 cases of meconium aspiration syndrome, 26 cases of asphyxia and 13 cases of septicemia, the onset time was 5-46 h and the average was (28.4±5.6) h, aged 30-39 weeks and the average was (34.9±3.6) weeks. There were no differences in the severity of respiratory distress and weight in the two groups, with no statistical significance (P>0.05). Each neonate had no other lung disease, kidney disease, liver disease, endocrine disease and other diseases, had not received prior treatment and had detailed information before treatment.

2.2. Treatment methods

The control group was given conventional treatment, mainly included mechanical ventilation, improvement of pulmonary microcirculation, prevention of related complications, protection of liver and kidney function of neonates and related basic nursing and other conventional medical services related to neonatal respiratory distress syndrome. The observation group was given pulmonary surfactant (source: Beijing Shuang He modern medical technology Co., Ltd, the dosage was 70 mg /kg) combined with mucosolvan (J20031314, Shanghai boehringer ingelheim pharmaceutical Co., Ltd, the dosage was 2 times per day, 2.5 mL/once) treatment between the two groups before treatment and had detailed information before treatment. Before treatment and 3 d after treatment, 1ml of peripheral blood was collected from neonates, the supernatant was collected after centrifugation and stored at -80 °C for subsequent detection. The levels of related indexes about alveolar cell surface antigen (KL-6), alveolar cell surface antigen (MIF-1), high mobility group protein 1 (HMGB-1), interferon-γ (IFN-γ), interleukin-4 (IL-4), interleukin-10 (IL-10), tumor necrosis factor-α (TNF-α) were detected by enzyme linked immunoassay kit (Shanghai meilian biological technology Co., Ltd, Shanghai senxiong biotech industrial Co., Ltd, Shanghai Jingkang biological engineering Co., Ltd). Wuhan Huamei biological engineering Co., Ltd, Jiangsu Jingmei biotechnology Co., Ltd), related operations were carried out strictly according to the kit instructions.

2.3. Liver and kidney function detection

The indexes of liver and kidney function about alanine aminotransferase (ALT), aspartate aminotransferase (AST), blood urea nitrogen (BUN), creatinine (CRE) were detected by Hitachi automatic biochemical analyzer (Model: 7180, Japan).

2.4 Statistical method

The related indexes of neonates with respiratory distress syndrome were statistically analyzed by SPSS 17.0 statistical software, measurement data were described as mean ± standard deviation, comparison between the observation group and the control group by t test; values of P<0.05 were considered to be statistically significant.

3. Results

3.1. Comparison of arterial blood gas before and after treatment between the two groups

Analysis of arterial blood gas in neonates with respiratory distress syndrome by hematology analyzer found that there was no significant difference in the comparison of blood gas indexes between the two groups before treatment (P>0.05); compared with before treatment, in the observation group after pulmonary surfactant combined with mucosolvan treatment, the arterial blood gas indexes of PaO2, TCO2, SaO2 significantly increased and PaCO2 significantly decreased, respectively, the levels of which were (93.26±7.25) mmHg, (31.34±1.96) mmol/L, (98.93±7.78)%,(35.53±6.22) mmHg, difference existence statistics significance (P<0.05); in the control group after conventional treatment, the levels of PaO2, TCO2, SaO2 significantly increased and PaCO2 significantly decreased, the difference was statistically significant (P<0.05); compared with the control group after treatment, the arterial blood gas indexes of PaO2, TCO2, SaO2 significantly increased and PaCO2 significantly decreased in the observation group after combined treatment, there
were statistically significant differences between the two groups \((P<0.05)\). See table 1.

3.2. Comparison of serum cytokines before and after treatment between the two groups

Analysis of serum related cytokines in neonates with respiratory distress syndrome by enzyme linked immunosorbent assay found that there was no significant difference in the comparison of serum related cytokines between the two groups before treatment \((P>0.05)\); compared with before treatment, the related cytokines KL-6, MIF-1, HMGB-1 significantly decreased in the observation group after combined treatment, respectively, the levels of which were \((18.37±29.16)\) U/L, \((147.39±25.43)\) \(\mu\)g/L, \((7.52±1.92)\) \(\mu\)g/L, difference existence statistics significance \((P<0.05)\); in the control group after conventional treatment, the related cytokines KL-6, MIF-1 significantly increased and IL-10, TNF-\(\alpha\) significantly decreased, difference existence statistics significance \((P<0.05)\); compared with the control group after treatment, the related immune factors IFN-\(\gamma\), IL-4 significantly increased and IL-10, TNF-\(\alpha\) significantly decreased, difference existence statistics significance \((P<0.05)\); compared with before treatment, the related immune factors IL-10, IL-4 significantly increased and IFN-\(\gamma\), TNF-\(\alpha\) significantly decreased in the observation group after combined treatment, there were statistically significant differences between the two groups \((P<0.05)\). See table 2.

3.3. Comparison of serum immune factor before and after treatment between the two groups

Analysis of serum related immune factors in neonates with respiratory distress syndrome by enzyme linked immunosorbent assay found that there was no significant difference in the comparison of serum related immune factors between the two groups before treatment \((P>0.05)\); compared with before treatment, respectively, the levels of which were \((24.23±8.12)\) \(\text{ng/L}\), \((417.19±14.95)\) \(\text{pg/mL}\), \((13.72±3.51)\) \(\text{ng} / \text{L}\), \((24.23±8.12)\) \(\text{ng} / \text{L}\), difference existence statistics significance \((P<0.05)\); in the control group after conventional treatment, the related immune factors IFN-\(\gamma\), IL-4 significantly increased and IL-10, TNF-\(\alpha\) significantly decreased, difference existence statistics significance \((P<0.05)\); compared with the control group after treatment, the related immune factors IL-10, IL-4 significantly increased and IFN-\(\gamma\), TNF-\(\alpha\) significantly decreased in the observation group after combined treatment, there were statistically significant differences between the two groups \((P<0.05)\). See table 3.

3.4. Comparison of liver and kidney function before and after treatment between the two groups

Analysis of liver and kidney function in neonates with respiratory distress syndrome by enzyme linked immunosorbent assay found that there was no significant difference in the comparison of indexes of liver and kidney function between the two groups before treatment \((P>0.05)\); compared with before treatment, hepatic function indexes AST, ALT and renal function indexes BUN, CRE significantly decreased in the observation group after combined treatment, respectively, the levels of which were \((32.88±1.09)\) U/L.

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

<table>
<thead>
<tr>
<th>Group</th>
<th>Time</th>
<th>PaO(_2) (mmHg)</th>
<th>PaCO(_2) (mmHg)</th>
<th>TCO(_2) (mmol/L)</th>
<th>SaO(_2) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>After treatment</td>
<td>62.19±7.49</td>
<td>48.24±5.32</td>
<td>25.42±1.69</td>
<td>87.25±8.02*</td>
</tr>
<tr>
<td>Observation</td>
<td>Before treatment</td>
<td>41.28±6.91</td>
<td>63.13±5.84</td>
<td>21.23±1.42</td>
<td>81.42±7.64</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>93.26±7.25*</td>
<td>35.53±6.22*</td>
<td>31.34±1.96*</td>
<td>98.93±7.78*</td>
</tr>
</tbody>
</table>

Note: compared with intra-group before treatment, \(P<0.05\); compared with the control group after treatment \(P<0.05\).

### Table 2.
Comparison of serum cytokines before and after treatment between the two groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>Time</th>
<th>KL-6 (U/L)</th>
<th>MIF-1 ((\mu)g/L)</th>
<th>HMGB-1 ((\mu)g/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>Before treatment</td>
<td>485.62±53.13</td>
<td>678.48±91.38</td>
<td>325.73±24.31*</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>258.28±35.91</td>
<td>325.73±24.31*</td>
<td>13.65±1.78*</td>
</tr>
<tr>
<td>Observation</td>
<td>Before treatment</td>
<td>481.28±59.52</td>
<td>683.23±89.62</td>
<td>25.22±3.92*</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>118.37±29.16*</td>
<td>147.39±25.43*</td>
<td>7.52±1.92*</td>
</tr>
</tbody>
</table>

Note: compared with intra-group before treatment, \(P<0.05\); compared with the control group after treatment \(P<0.05\).

### Table 3.
Comparison of serum immune factors before and after treatment between the two groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>Time</th>
<th>IFN-(\gamma) (ng/L)</th>
<th>TNF-(\alpha) (ng/L)</th>
<th>IL-4 (pg/mL)</th>
<th>IL-10 (ng/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>Before treatment</td>
<td>96.33±10.37</td>
<td>55.58±8.29</td>
<td>117.49±14.54</td>
<td>39.42±4.12</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>282.59±13.34*</td>
<td>41.01±7.88*</td>
<td>201.52±16.12*</td>
<td>13.72±3.43*</td>
</tr>
<tr>
<td>Observation</td>
<td>Before treatment</td>
<td>95.46±13.24*</td>
<td>56.15±8.33</td>
<td>119.64±13.84</td>
<td>40.23±3.15</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>141.40±12.12*</td>
<td>24.23±8.12*</td>
<td>417.19±14.95*</td>
<td>27.13±3.51*</td>
</tr>
</tbody>
</table>

Note: compared with intra-group before treatment, \(P<0.05\); compared with the control group after treatment \(P<0.05\).
significant differences between the two groups (observation group after combined treatment, there were statistically and renal function indexes BUN, CRE significantly decreased in the control group after treatment, hepatic function indexes AST, ALT and renal function indexes BUN, CRE significantly decreased, group after conventional treatment, hepatic function indexes AST, ALT and renal function indexes BUN, CRE significantly decreased in the observation group after combined treatment, there were statistically significant differences between the two groups (P<0.05). See table 4.

4. Discussion

Respiratory distress syndrome is a kind of pulmonary diffuse injury caused by various factors, which increases alveolar surface tension in patients with respiratory distress syndrome, resulting in atelectasis, reduces the gas exchange area, leading to neonatal shortness of breath, progressive dyspnea, insufficient oxygen supply, respiratory failure caused by severe inspiratory three depression sign[5]. The incidence of neonates with low birth weight, cesarean neonates, neonatal asphyxia during delivery and neonates of diabetic mothers are high. The acute symptoms of weight and acute occurrence of neonatal respiratory distress syndrome easily lead to a variety of complications[6]. Mechanical ventilation to treat neonatal respiratory distress syndrome is commonly used in clinical treatment at present, mechanical ventilation can maintain a positive pressure in respiratory cycle, increase the functional residual capacity and effectively prevent alveolar collapse, plays an important role in increasing gas exchange area, reducing energy loss, etc[7]. The study found that after mechanical ventilation treatment in the control group, the indexes were improved, and has an important role in the treatment of neonatal respiratory distress syndrome. Mainly due to mechanical ventilation therapy can repair collapsed alveoli, increase the functional residual capacity, improve the ventilation/perfusion ratio, and also improve the alveolar oxygenation function and lung compliance correspondly[8,9]. The improvement of related pulmonary function is conducive to the synthesis and secretion of pulmonary surfactant and neonatal alveolar maturation, so as to achieve the purpose of treatment of respiratory distress syndrome objective[10]. However, the treatment of neonatal respiratory distress syndrome with mechanical ventilation alone is slow, and the mechanical ventilation treatment for long term in neonates often leads to ventilator associated pneumonia and other complications.

This study explored the treatment of pulmonary surfactant combined with mucosolvan in neonates with respiratory distress syndrome. Study found that neonates in the use of pulmonary surfactant and mucosolvan on the basic of mechanical ventilation therapy can significantly improve their arterial blood gas, ensure adequate oxygen supply, make up the defect of insufficient pulmonary surfactant in neonates, and conducive to the alveolar development and pulmonary surfactant further production. The study found that after combined treatment, the levels of neonatal serum cytokines KL-6, MIF-1 and HMGB-1 were significantly lower than those in control group neonates. Impaired alveolar type II epithelial cells often secrete a surface antigen KL-6, related studies showed that the KL-6 content was positively correlated with the mean pressure and peak pressure of the patient’s airway, and negatively correlated with the patient’s oxygenation index, KL-6 can be used as an indicator to judge the degree of alveolar epithelial injury[11, 12]. The main function of KL-6 is through promoting the secretion of platelet-derived growth factor and transforming growth factor-β 1 to promote lung fibroblast proliferation and induce fibrosis, at the same time, damage the alveolar oxygenation function[13], which affect the health of neonates seriously, mucosolvan can repair the damaged alveolar[14], thereby reducing the secretion of KL-6. MIF-1 is a kind of polypeptide secreted by macrophages, which can cause persistent infiltration of inflammatory cells in the alveolar and secretion of inflammatory cytokines and NO, improve the proliferation and activation of T cells, inhibit the migration of mononuclear macrophages[15,16]; HMGB1 has a cascade amplification effect on inflammation[17]. Pulmonary surfactant and mucosolvan can significantly reduce the content of KL-6, MIF-1, HMGB-1, decrease the probability of pulmonary inflammation, prevent the occurrence of complications[18]. Numerous studies show that the changes of Th1/Th2 cells play an important role in the respiratory distress syndrome[19], Th1 cells mainly secrete IFN-γ, TNF-α and other pro-inflammatory factors, have strong cytotoxic effect on inflammatory cells, and can mediate the cellular immune response[20]. Th2 cells mainly secrete IL-4, IL-10 and other related cytokines, with anti-inflammatory mediators to achieve the purpose of promoting the production of antibodies and the conductor liquid immune response[21]. The study found that compared with the control group, after application of pulmonary surfactant and mucosolvan, neonatal serum IL-10, IL-4 increased significantly and

Table 4.
Comparison of liver and kidney function before and after treatment between the two groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>Time</th>
<th>AST (U/L)</th>
<th>ALT (U/L)</th>
<th>BUN (mmol/L)</th>
<th>CRE (μmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>Before treatment</td>
<td>39.29±1.07</td>
<td>41.18±1.17</td>
<td>10.80±2.15</td>
<td>91.62±8.78</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>35.91±1.10</td>
<td>39.48±1.09</td>
<td>8.73±2.18</td>
<td>87.25±7.93</td>
</tr>
<tr>
<td>Observation</td>
<td>Before treatment</td>
<td>38.97±1.05</td>
<td>41.13±1.13</td>
<td>10.91±2.13</td>
<td>91.51±8.93</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>32.88±1.09</td>
<td>36.43±0.98</td>
<td>7.21±2.10</td>
<td>83.76±7.47</td>
</tr>
</tbody>
</table>

Note: compared with intra-group before treatment, *P<0.05; compared with the control group after treatment †P<0.05
IFN-γ, TNF-α significantly decreased. Showed that pulmonary surfactant and mucosolvan can reduce neonatal inflammatory reaction, help to maintain Th1/Th2 balance and achieve the effect of protecting the body[22]. As external drugs, mucosolvan has side effects on the body, through further detection of liver and kidney function, the author found that compared with the control group after treatment, the hepatic function indexes AST, ALT and renal function indexes CRE, BUN significantly decreased in the observation group after combined treatment, the liver and kidney function of neonates were improved after combined treatment. The reason could be after combined treatment, neonatal hepatic function improved, the less reason was more than the amount of toxin induced by drugs, thus reducing the effect on liver and kidney function[23].

In conclusion, pulmonary surfactant combined with mucosolvan can improve the arterial blood gas correlation indexes, respiratory distress syndrome related indicators, immune related factors, liver and kidney function indexes in neonatal respiratory distress syndrome, and provide important clinical help for the treatment of neonatal respiratory distress syndrome.

References


