Effect of azithromycin combined with terbutaline on the infection and systemic conditions in children with mycoplasma pneumonia

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Objective: To study the effect of azithromycin combined with terbutaline on the infection and systemic conditions in children with mycoplasma pneumonia. Methods: A total of 80 children with pneumonia who were treated in the hospital between August 2014 and February 2017 were collected and divided into control group and observation group according to the random number table method, 40 cases in each group. The control group received azithromycin therapy, the observation group received azithromycin combined with terbutaline therapy, and both therapies lasted for 6 d. The differences in systemic inflammatory response, myocardial enzyme spectrum, and liver function and so on were compared between the two groups before and after treatment. Results: Before treatment, differences in serum levels of inflammatory factors, myocardial enzyme spectrum indexes and liver function indexes were not statistically significant between the two groups. After 6 d of treatment, serum IL-2, IL-4, IL-8, IL-13, PCT, CK-MB, LDH, HBDH, ALT, AST and ALP levels of both groups of patients were significantly lower than those before treatment, and serum IL-2, IL-4, IL-8, IL-13, PCT, CK-MB, LDH, HBDH, ALT, AST and ALP levels of observation group were significantly lower than those of control group. Conclusion: Azithromycin combined with terbutaline therapy can effectively control the systemic inflammatory response and protect the heart and liver function in patients with mycoplasma pneumonia.

1. Introduction

Mycoplasma pneumonia is the pulmonary inflammatory disease easily occurs in young children, the main performance is intractable severe cough, severe cases can complicated by pleural effusion, pulmonary atelectasis, etc., and a few children had quickly progressed illness and even die(1,2). Early positively controlling systemic inflammatory response and protecting important viscera function is the principle of clinical treatment of mycoplasma pneumonia, and azithromycin, as the second generation of macrolides medicine, is mainly used for the treatment of respiratory and reproductive tract infections, and has become the main antibiotic for treatment of children with mycoplasma pneumonia(3,4). According to the latest research, azithromycin therapy alone can effectively inhibit the pathogenic bacteria, but some children still have complications of important viscera, so many scholars recommend other drugs in combination therapy. As a kind of antiasthmatic, terbutaline can excite β2 receptors and dilate bronchus, and helps to alleviate the clinical symptoms of mycoplasma pneumonia and shorten the course of disease(5,6). In this study, azithromycin and terbutaline were used together in the clinical treatment of children with mycoplasma pneumonia, and the roles were discussed from systemic infection, myocardial enzyme spectrum, liver function and other aspects.

2. Information and methods

2.1 Case information

A total of 80 children with pneumonia who were treated in the hospital between August 2014 and February 2017 were selected,
and the families of the children signed informed consent. Inclusion criteria: (1) laboratory examination results and pulmonary X-ray findings were all consistent with the diagnosis of mycoplasma pneumonia; (2) without history of pulmonary inflammation within 6 months prior to admission; (3) completing all treatment and inspection. Exclusion criteria: (1) combined with congenital heart, liver and kidney diseases; (2) combined with azithromycin and terbutaline allergy; (3) combined with serious autoimmune disease. According to the random number table method, the enrolled children were divided into control group and observation group, 40 cases in each group. Control group included 22 male cases and 18 female cases that were 1-6 years old; observation group included 21 male cases and 19 female cases that were 1-7 years old. The differences in gender and age distribution were not significant between the two groups \( (P>0.05) \), and the study was approved by the hospital ethics committee.

2.2 Therapy

Control group received azithromycin therapy, specifically as follows: azithromycin for injection (Guangdong Xinghao Pharmaceutical Co., Ltd., approved by H20066441) 8 mg/kg in normal saline 50 mL, by intravenous drip, 1 time/d, for continuous 3 d, and then switching to oral azithromycin tablets (Hainan Tianhuang Pharmacy Co., Ltd., approved by H20065786), 10 mg/kg, 1 time/d, for 3 d in a row.

Observation group received azithromycin combined with terbutaline, specifically as follows: Terbutaline Sulfate for Injection (Beijing Sihuan Kebao Pharmaceutical Co., Ltd., approved by H20031123) 2.5 mg was dissolved in saline 5 mL and then placed in atomizer, a single time lasted for 15-20 min, 2 times/d, for 6 d in a row. The usage and dosage of azithromycin were the same as those of control group.

2.3 Observation indexes

Before treatment and after 6 d of treatment, 2-3 mL fasting cubital venous blood was extracted from two groups of children, anticoagulated and then centrifuged at low speed to get upper serum, which was stored in deep hypothermia environment. Enzyme-linked immunosorbent assay (ELISA) was used to determine serum levels of inflammatory cytokines interleukin-2 (IL-2), interleukin-4 (IL-4), interleukin-8 (IL-8), interleukin-13 (IL-13) and procalcitonin (PCT). Automatic blood biochemical analyzer was used to determine the contents of myocardial enzyme spectrum and liver function indexes, myocardial enzyme spectrum included creatine kinase isoenzyme (CK-MB), lactate dehydrogenase (LDH) and hydroxybutyrate dehydrogenase (HBDH), and liver function indicators included alanine aminotransferase (ALT), aspartate transaminase (AST) and alkaline phosphatase (ALP).

2.4 Statistical processing

Statistical software SPSS 24.0. Inflammatory cytokines, myocardial enzyme spectrum, liver function indexes and other measurement data were in terms of mean ± standard deviation, and comparison was by t test. \( P<0.05 \) indicated statistical significance in differences.

3. Results

3.1 Inflammatory factors

Before treatment and after 6 d of treatment, comparison of serum inflammatory factors IL-2 (pg/mL), IL-4 (pg/mL), IL-8 (pg/mL), IL-13 (pg/mL) and PCT (ng/mL) levels between two groups of children was as follows: serum IL-2, IL-4, IL-8, IL-13 and PCT levels were not statistically different between the two groups before treatment \( (P>0.05) \). Compared with those before treatment, serum IL-2, IL-4, IL-8, IL-13 and PCT levels of both groups of children significantly decreased after 6d of treatment \( (P<0.05) \); compared with those of control group, serum IL-2, IL-4, IL-8, IL-13 and PCT levels of observation group significantly decreased after 6d of treatment \( (P<0.05) \), shown in Table 1.

3.2 Myocardial enzyme spectrum

Before treatment and after 6 d of treatment, comparison of serum myocardial enzyme spectrum CK-MB, LDH and HBDH levels between two groups of children was as follows: serum CK-MB, LDH and HBDH levels were not statistically different between the two groups before treatment \( (P>0.05) \). Compared with those before treatment, serum CK-MB, LDH and HBDH levels of both groups of children significantly decreased after 6d of treatment \( (P<0.05) \); compared with those of control group, serum CK-MB, LDH and HBDH levels of observation group significantly decreased after 6d of treatment \( (P<0.05) \), shown in Table 1.

<p>| Table 1. Changes in serum IL-2, IL-4, IL-8, IL-13 and PCT levels before and after treatment. |</p>
<table>
<thead>
<tr>
<th>Groups</th>
<th>( n )</th>
<th>Time</th>
<th>IL-2</th>
<th>IL-4</th>
<th>IL-8</th>
<th>IL-13</th>
<th>PCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>40</td>
<td>Before treatment</td>
<td>10.92±1.87</td>
<td>2.36±0.35</td>
<td>17.29±2.18</td>
<td>25.48±3.17</td>
<td>8.26±0.91</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6 d after treatment</td>
<td>7.53±0.84*</td>
<td>1.25±0.17*</td>
<td>11.15±1.76*</td>
<td>14.26±1.71*</td>
<td>5.12±0.64*</td>
</tr>
<tr>
<td>Observation group</td>
<td>40</td>
<td>Before treatment</td>
<td>10.84±1.79</td>
<td>2.41±0.36</td>
<td>17.42±2.06</td>
<td>25.19±3.42</td>
<td>8.31±0.95</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6 d after treatment</td>
<td>4.11±0.47*</td>
<td>0.61±0.08*</td>
<td>4.53±0.62*</td>
<td>6.88±0.75*</td>
<td>2.09±0.32*</td>
</tr>
</tbody>
</table>

Note: comparison within group before and after treatment, \( * P<0.05 \); compared with control group after 6d of treatment, \( ^P<0.05 \).
of children significantly decreased after 6 d of treatment ($P<0.05$); compared with those of control group, serum CK-MB, LDH and HBDH levels of observation group significantly decreased after 6 d of treatment ($P<0.05$), shown in Table 2.

### Table 2.
Changes in serum CK-MB, LDH and HBDH levels before and after treatment.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>CK-MB</th>
<th>LDH</th>
<th>HBDH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>40</td>
<td>Before treatment</td>
<td>18.36±2.11</td>
<td>205.48±2.71</td>
<td>217.62±25.85</td>
</tr>
<tr>
<td>Observation</td>
<td>40</td>
<td>Before treatment</td>
<td>11.64±1.85</td>
<td>151.32±18.54</td>
<td>160.82±18.74</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6 d after treatment</td>
<td>18.29±2.32</td>
<td>204.59±23.65</td>
<td>216.59±24.71</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6 d after treatment</td>
<td>7.03±0.86</td>
<td>113.18±13.69</td>
<td>125.47±15.83</td>
</tr>
</tbody>
</table>

Note: comparison within group before and after treatment, $P<0.05$; compared with control group after 6 d of treatment, $P<0.05$.

### 3.3 Liver function indexes

Before treatment and after 6 d of treatment, comparison of serum liver function indexes ALT, AST and ALP levels between two groups of children was as follows: serum ALT, AST and ALP levels were not statistically different between the two groups before treatment ($P>0.05$). Compared with those before treatment, serum ALT, AST and ALP levels of both groups of children significantly decreased after 6 d of treatment ($P<0.05$); compared with those of control group, serum ALT, AST and ALP levels of observation group significantly decreased after 6 d of treatment ($P<0.05$), shown in Table 3.

### Table 3.
Changes in serum ALT, AST and ALP levels before and after treatment.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>ALT</th>
<th>AST</th>
<th>ALP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>40</td>
<td>Before treatment</td>
<td>48.22±5.61</td>
<td>42.67±5.19</td>
<td>164.38±20.29</td>
</tr>
<tr>
<td>Observation</td>
<td>40</td>
<td>Before treatment</td>
<td>39.61±4.52</td>
<td>33.82±3.76</td>
<td>104.72±15.88</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6 d after treatment</td>
<td>48.63±5.72</td>
<td>43.51±5.47</td>
<td>163.75±21.52</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6 d after treatment</td>
<td>27.85±4.17</td>
<td>25.19±2.84</td>
<td>81.63±9.27</td>
</tr>
</tbody>
</table>

Note: comparison within group before and after treatment, $P<0.05$; compared with control group after 6 d of treatment, $P<0.05$.

### 4. Discussion

Mycoplasma pneumonia is caused by mycoplasma infection, shows the changes of interstitial pneumonia/capillary bronchitis, and is the most important type of pneumonia in children. The disease severity varies in children with mycoplasma pneumonia, mild cases are only manifested as persistent cough and low-grade fever, and severe cases can be combined with pulmonary atelectasis, necrotizing pneumonia and even death[7,8]. Choosing the reasonable treatment is the most reliable way to control systemic inflammation in early stage and optimize the outcome, azithromycin has been successfully applied in the treatment of the disease, and it is with wide antibacterial spectrum, can quickly reach the infected area, and has good tissue permeability[9,10]. However, some cases show that there is still have obvious cough or wheezing in children after active anti-inflammatory treatment, which not only prolongs the course of disease, but may also cause other complications. Terbutaline has high selectivity to airway β 2 receptors, which can dilates the bronchus after application, and help relieve the coughing or wheezing. Terbutaline was added on the basis of azithromycin therapy in this study, and the effects on systemic inflammation and other tissue organs in children with bronchial pneumonia were explored.

Mycoplasma infection activates mononuclear macrophages and prompts them to secrete a large number of inflammatory mediators, which cause local and systemic inflammatory response in lung, and further form tissue damage and a variety of clinical manifestations[11,12]. IL-2 and IL-8 are the most typical pro-inflammatory factors, which can induce neutrophils to aggregate and further release other inflammatory factors to form inflammatory amplification. IL-4 and IL-13 are anti-inflammatory factors that are reactively released after the occurrence of inflammatory reaction, and can neutralize the effect of some pro-inflammatory factors and inhibit the expansion of inflammatory response[13]. PCT is a new type of late inflammatory marker, its content does not change obviously in patients with mild infection, and the content increases significantly in patients with moderate and severe acute infection[14]. In this study, differences in serum levels of inflammatory cytokines were compared between the two groups before and after treatment, and it was found that compared with those before treatment, serum IL-2, IL-4, IL-8, IL-13 and PCT levels of both groups of children decreased after 6d of treatment; further compared with those of control group, serum IL-2, IL-4, IL-8, IL-13 and PCT levels of observation group were lower after 6d of treatment, confirming that the azithromycin combined with terbutaline therapy can more effectively inhibit the systemic inflammatory response in children with mycoplasma pneumonia.

Around 25% of children with mycoplasma pneumonia can be complicated by complications of heart, liver, kidney and other important tissue organs, and cardiac dysfunction is mostly caused by direct mycoplasma or indirect inflammatory factor injury to myocardial cells. After myocardial injury, myocardial enzyme spectrum indexes in cells can be released to the outside of cells, they further penetrate into the blood circulation, so abnormally highly expressed myocardial enzyme spectrum in serum mostly indicates that children with mycoplasma pneumonia are complicated by myocardial injury[15,16]. In the study, differences in serum levels of myocardial enzyme spectrum indexes were compared between...
the two groups before and after treatment, and it was found that compared with those before treatment, serum CK-MB, LDH and HBDH levels of both groups of children decreased after treatment; further compared with those of control group, serum CK-MB, LDH and HBDH levels of observation group were lower after 6d of treatment, confirming that azithromycin combined with terbutaline therapy can more effectively protect the cardiac function and reduce the myocardial injury caused by the pathogen itself or inflammation in children with mycoplasma pneumonia.

The liver is one of the most vulnerable organs in children with mycoplasma pneumonia, which is characterized by the high expression of various liver-specific enzymes in serum[17]. ALT and AST are the most common indicators of liver function, and their levels can significantly increase when liver function injuries exceed the compensatory range, which can be used to determine the severity of liver injury[18]. ALP is an enzyme that is widely distributed in the human body and discharged out of the gallbladder from the liver, and its serum levels can pathologically rise in the case of liver dysfunction, which can be used to help determine liver function injury. In the study, differences in serum levels of these liver function indexes were compared between the two groups before and after treatment, and it was found that compared with those before treatment, serum ALT, AST and ALP levels of both groups of children decreased after treatment; further compared with those of control group, serum ALT, AST and ALP levels of observation group were lower after treatment, confirming that azithromycin combined with terbutaline therapy can more effectively reduce liver damage and protecting liver function.

To sum up, it is concluded that azithromycin combined with terbutaline therapy for children with mycoplasma pneumonia can effectively reduce the level of systemic inflammation and relieve the heart and liver damage, it is more efficient and reasonable than azithromycin therapy alone, and it is worthy of popularization and application in clinical practice in the future.

References