Effect of azithromycin combined with licorzinc therapy on inflammatory response and immune response in children with mycoplasma pneumonia

Qiao-Li Chai
Pediatrics Department, The Third Hospital of Yulin City, Yulin 719000, China

Objective: To study the effect of azithromycin combined with licorzinc therapy on inflammatory response and immune response in children with mycoplasma pneumonia.

Methods: A total of 150 children with mycoplasma pneumonia who were treated in our hospital between January 2014 and January 2017 were collected and divided into control group and observation group according to the random number table, with 75 cases in each group. Control group received azithromycin therapy, while observation group received azithromycin combined with licorzinc therapy. The therapies were given for the patients in both groups lasted for 14 d. The differences in serum levels of inflammatory factors, Th17/Treg cytokines and immunoglobulin were compared between the two groups before and after treatment.

Results: Before treatment, differences in serum levels of inflammatory factors, Th17/Treg cytokines and immunoglobulin were not statistically significant between two groups of patients. After treatment, serum inflammatory factors IL-6, IL-12, IL-13 and MCP-4 levels of observation group were significantly lower than those of control group; serum Th17/Treg cytokines IL-17 and IL-25 levels were significantly lower than those of control group while IL-10 and IL-35 levels were significantly higher than those of control group; serum immunoglobulin IgA, IgG and IgM levels were significantly higher than those of control group.

Conclusions: Azithromycin combined with licorzinc therapy can effectively reduce the systemic inflammatory response and optimize the immune function in children with mycoplasma pneumonia.

1. Introduction

Mycoplasma pneumonia taking on interstitial pneumonia and capillary bronchitis-like change is the most common pediatric pulmonary infectious disease. It is mainly clinically characterized by intractable cough, and it will lead to complications of cardiovascular system, nervous system, digestive system and other important viscera if not treated in time[1,2]. Azithromycin is the preferred antibiotics for treatment of mycoplasma pneumonia and belongs to the second generation of macrolides medicine. Many experiments have confirmed that it helps to control the illness in children with mycoplasma pneumonia, but the disease is still in progress in some patients, which may be associated with the deficiency of trace elements such as zinc[3,4]. Licorzinc can promote mucus secretion and epithelial cell renewal, and it has been successfully applied in the treatment of ulcers and traumatic diseases[5]. Therefore, some scholars recommend Licorzinc for the adjuvant treatment of children with mycoplasma pneumonia, but few related research is done at present. In this study, azithromycin combined with licorzinc was used in the treatment of children with mycoplasma pneumonia, and its function was discussed in terms of systemic inflammatory response, immune function and other aspects.

2. Materials and methods

2.1. Case information

A total of 150 children with mycoplasma pneumonia who were treated in our hospital between January 2014 and January 2017 were selected as the study subjects, and the families of the children
have signed the informed consent. The subjects were divided into control group and observation group based on random number table, with 75 cases in each group. Control group included 40 male cases and 35 female cases that were 1-7 years old; while observation group included 38 male cases and 37 female cases that were 1-9 years old. There was no significant difference in gender and age distribution between the two groups \((P>0.05)\), and the study was approved by the hospital ethics committee.

### 2.2. Inclusion and exclusion criteria

Inclusion criteria: (1) diagnosed with mycoplasma pneumoniae based on clinical manifestation, laboratory examination results and imaging results; (2) without history of pneumonia within 6 months prior to admission; (3) completing the whole treatment and related inspection. Exclusion criteria: (1) combined with severe congenital disorders; (2) with autonomous application of antibiotics or other treatments before admission; (3) allergic to azithromycin and licorzinc.

### 2.3. Therapy

Control group accepted routine azithromycin treatment, specifically as follows: Azithromycin Lactobionate Injection (produced by Zhejiang Zhenyuan Pharmaceutical Co., Ltd., approval No. H20020257) 10 mg/(kg·d), treatment for consecutive 3-5 d, then stopping it for 4 d, resuming treatment for 3 d, for continuous treatment of 14 d. While observation group received azithromycin combined with licorzinc therapy, specifically as follows: licorzinc granules (produced by Shandong DYNE Marine Biopharmaceutical Co., Ltd., approval No. H19993277) 1 mg/(kg·d), taken orally in twice, maximum single dose 20 mg, for continuous treatment of 14 d. The usage and dosage of azithromycin were the same as those of control group.

### 2.4. Observation indexes

Before treatment and 14 d after treatment, 3-5 mL of peripheral venous blood was extracted from two groups of children, anticoagulated, let stand at room temperature for stratification, and centrifuged at 3 500 r/min, and then the upper serum was taken cryopreserved in -70 ℃ refrigerator for test. Enzyme-linked immunosorbent assay was used to determine serum levels of inflammatory factors IL-6, IL-12, IL-13, interleukin-17 (IL-17), interleukin-25 (IL-25) as well as Treg cytokines interleukin-10 (IL-10) and interleukin-35 (IL-35). Immunoglobulin A (IgG), immunoglobulin G (IgG) and immunoglobulin M (IgM) levels in serum were detected by radioimmunoassay.

### 2.5. Statistical processing

Statistical data were recorded and calculated by the professionals, and statistical software was SPSS 20.0. Inflammatory factors, Th17/Treg cytokines, immunoglobulin and other measurement data were in terms of mean ± standard deviation, and the comparison was by \(t\) test. Statistics \(P<0.05\) was the standard of statistical significance in differences.

### 3. Results

#### 3.1. Inflammatory factors

Before treatment and 14 d after treatment, comparison of serum inflammatory factors IL-6, IL-12, IL-13 and MCP-4 levels between two groups of children was as follows: serum IL-6, IL-12, IL-13 and MCP-4 levels were not significantly different between two groups of patients before treatment \((P>0.05)\); serum IL-6, IL-12, IL-13 and MCP-4 levels of both groups after treatment were significantly lower than those before treatment, serum IL-6, IL-12, IL-13 and MCP-4 levels of observation group after treatment were lower than those of control group, and the differences were statistically significant \((P<0.05)\), shown in Table 1.

#### 3.2. Th17/Treg cytokines

Before treatment and 14 d after treatment, comparison of serum Th17/Treg cytokines IL-17, IL-25, IL-10 and IL-35 levels between two groups of children was as follows: serum IL-17, IL-25, IL-10 and IL-35 levels were not significantly different between two groups of patients before treatment \((P>0.05)\); serum IL-17 and IL-25 levels of both groups after treatment were significantly lower than those before treatment while IL-10 and IL-35 levels of both groups after treatment were significantly lower than those before treatment while IL-10 and IL-35 levels were significantly higher than those before treatment, serum IL-17 and IL-25 levels of

### Table 1

<table>
<thead>
<tr>
<th>Groups</th>
<th>Time</th>
<th>IL-6</th>
<th>IL-12</th>
<th>IL-13</th>
<th>MCP-4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>75</td>
<td>Before treatment</td>
<td>84.29±9.17</td>
<td>73.17±8.94</td>
<td>27.38±4.11</td>
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<tr>
<td></td>
<td>14 d after treatment</td>
<td>52.76±6.34</td>
<td>40.85±5.12</td>
<td>15.19±2.32</td>
<td>43.28±5.62</td>
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<tr>
<td>Observation group</td>
<td>75</td>
<td>Before treatment</td>
<td>83.76±9.42</td>
<td>72.53±8.61</td>
<td>27.19±4.07</td>
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<td>14 d after treatment</td>
<td>29.51±4.38</td>
<td>23.64±4.28</td>
<td>6.38±0.79</td>
<td>17.28±2.17</td>
</tr>
</tbody>
</table>

Note: compared with the same group before treatment, \(^*P<0.05\); compared with control group 14 d after treatment, \(^{*#}P<0.05\).
Comparison of serum immunoglobulin levels between two groups of children before and after treatment (g/L).

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>IL-17</th>
<th>IL-25</th>
<th>IL-10</th>
<th>IL-35</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>75</td>
<td>Before treatment</td>
<td>62.18±7.95</td>
<td>46.74±5.09</td>
<td>17.29±2.71</td>
<td>11.27±1.83</td>
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<td></td>
<td></td>
<td>14 d after treatment</td>
<td>40.26±5.34</td>
<td>29.65±3.41</td>
<td>24.18±3.25</td>
<td>17.64±2.97</td>
</tr>
<tr>
<td>Observation group</td>
<td>75</td>
<td>Before treatment</td>
<td>62.62±7.89</td>
<td>45.62±5.16</td>
<td>17.34±2.61</td>
<td>11.31±1.95</td>
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<td></td>
<td></td>
<td>14 d after treatment</td>
<td>23.18±4.56</td>
<td>17.34±2.19</td>
<td>35.67±4.59</td>
<td>31.55±4.68</td>
</tr>
</tbody>
</table>

Note: compared with the same group before treatment, *P<0.05; compared with control group 14 d after treatment, **P<0.05.

Table 3.
Comparison of serum immunoglobulin levels between two groups of children before and after treatment (g/L).

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>IgA</th>
<th>IgG</th>
<th>IgM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>75</td>
<td>Before treatment</td>
<td>1.42±0.17</td>
<td>13.28±1.79</td>
<td>1.41±0.17</td>
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<td></td>
<td>14 d after treatment</td>
<td>1.89±0.25</td>
<td>19.76±2.48</td>
<td>1.65±0.21</td>
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<tr>
<td>Observation group</td>
<td>75</td>
<td>Before treatment</td>
<td>1.43±0.18</td>
<td>13.31±1.85</td>
<td>1.42±0.16</td>
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<tr>
<td></td>
<td>14 d after treatment</td>
<td>2.27±0.34</td>
<td>24.15±3.07</td>
<td>2.27±0.28</td>
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</tr>
</tbody>
</table>

Note: compared with the same group before treatment, *P<0.05; compared with control group 14 d after treatment, **P<0.05.

observation group after treatment were lower than those of control group while IL-10 and IL-35 levels were higher than those of control group, and differences were statistically significant (P<0.05), shown in Table 2.

### 3.3. Immunoglobulin

Before treatment and 14 d after treatment, comparison of serum immunoglobulin IgA, IgG and IgM levels between two groups of children was as follows: serum IgA, IgG and IgM levels were not significantly different between two groups of patients before treatment (P>0.05); serum IgA, IgG and IgM levels of both groups after treatment were significantly higher than those before treatment, serum IgA, IgG and IgM levels of observation group after treatment were significantly higher than those of control group, and differences were statistically significant (P<0.05), shown in Table 3.

### 4. Discussion

The incidence of mycoplasma pneumonia is extremely high in children, and azithromycin, as an antimicrobial sensitive antibiotic, has been successfully applied in treatment of mycoplasma pneumonia, but the illness in some patients has not been effectively controlled after azithromycin application alone, so many scholars recommend the combined use of other mechanisms of drugs to expand the curative effect. The latest studies have shown that the probability of deficiency of trace elements is high in children, and many scholars think it may be related to the enhancement of the child's constitution, but the specific change of the immune function is not clear. Th17 and Treg cells are the newly discovered T cell subgroups, Th17 cells can release effector cytokines IL-17 and IL-25, and promote and amplify the inflammatory response[13,14]. Treg cells have a negative immunomodulatory effect, and inhibit T lymphocyte activation and proliferation by secreting cytokines IL-10 and IL-35. There is the imbalance of Th17/Treg in children with mycoplasma pneumoniae, and the specific expression is strong Th17 cell secretion and inhibited Treg cell synthesis[15,16]. In the study, Th17/Treg cytokine contents in serum were compared between the two groups before and after treatment, and it was found that compared with those before combined with licorzinc was used in the treatment of children with mycoplasma pneumoniae, and the difference in the therapeutic effect of drug combination and azithromycin alone was discussed.

Local pulmonary and systemic inflammatory response is the main pathological change of mycoplasma pneumoniae, and the degree of inflammatory response is highly consistent with the illness severity[8,9]. IL-6, IL-12 and IL-13 are the typical pro-inflammatory factors, which can be increasingly released early after mycoplasma infection, further induce neutrophils to accumulate in the affected area, and aggravate local inflammation in the lung[10,11]. McP-4 is a pro-inflammatory factor derived from mononuclear epithelial cells, which can selectively recruit Th2 cells to inflammatory sites and trigger inflammatory injury[12]. In this study, the degrees of systemic inflammation before and after the treatment were first compared between the two groups, and the results showed that compared with those before treatment, serum IL-6, IL-12, IL-13 and MCP-4 levels of both groups were significantly lower after treatment; further compared with control group, the observation group were with lower serum IL-6, IL-12, IL-13 and MCP-4 levels after treatment, confirming that licorzinc combination therapy based on azithromycin can further reduce the systemic inflammatory response and macroscopically optimize the treatment effect.

The application of licorzinc can increase the amount of trace element zinc in the children, and many scholars think it may be related to the enhancement of the child's constitution, but the specific change of the immune function is not clear. Th17 and Treg cells are the newly discovered T cell subgroups, Th17 cells can release effector cytokines IL-17 and IL-25, and promote and amplify the inflammatory response[13,14]. Treg cells have a negative immunomodulatory effect, and inhibit T lymphocyte activation and proliferation by secreting cytokines IL-10 and IL-35. There is the imbalance of Th17/Treg in children with mycoplasma pneumoniae, and the specific expression is strong Th17 cell secretion and inhibited Treg cell synthesis[15,16]. In the study, Th17/Treg cytokine contents in serum were compared between the two groups before and after treatment, and it was found that compared with those before...
treatment, serum IL-17 and IL-25 levels of both groups were lower while IL-10 and IL-35 levels were higher after treatment; further compared with control group, the observation group were with lower serum IL-17 and IL-25 levels, and higher IL-10 and IL-35 levels after treatment, confirming that the azithromycin combined with licorzinc treatment is more effective in inhibiting Th17 cell function and increasing Treg cell synthesis.

The humoral immune dysfunction is also the important reason for the occurrence and progress of mycoplasma pneumoniae, and IgA has antibacterial antivirus effect in the immune regulation; IgM has bacteriolytic and high antigen-binding effect; IgG plays a major role in anti-infection and has immunological effects such as regulating phagocytes and neutralizing toxins[17,18]. There are different levels of decreased immunoglobulin expression in children with mycoplasma pneumoniae, and the above immunoglobulin contents are highly consistent with the disease severity. In this study, serum immunoglobulin contents were compared between the two groups of patients, and it was found that compared with those before treatment, serum IgA, IgG and IgM levels of both groups were higher after treatment; further compared with the control group, the observation group were with higher serum IgA, IgG and IgM levels after treatment, confirming that azithromycin combined with licorzinc is more effective in strengthening the humoral immunity of the children.

Azithromycin combined with licorzinc therapy can effectively decrease the systemic inflammatory response, balance Th17/Treg cell function and enhance the humoral immune function in children with mycoplasma pneumoniae, it is a reliable way for clinical treatment of children with mycoplasma pneumoniae, and it is worthy of popularization and application in clinical practice in the future.

References


