Effect of azithromycin, montelukast combined with pulmicort respulas therapy on the degree of inflammation and lung function in children with mycoplasma pneumonia

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Abstract

Objective: To analyze the effect of azithromycin, montelukast combined with pulmicort respulas therapy on the degree of inflammation and lung function in children with mycoplasma pneumonia. Methods: A total of 318 cases of children with mycoplasma pneumonia treated in our hospital from February 2013 to February 2016 were randomly divided into observation group and control group (n=159). Control group received azithromycin and montelukast therapy, observation group received azithromycin, montelukast combined with pulmicort respulas therapy, and then the degree of inmmunation, lung function, etc were compared between two groups. Results: V-T, t-PTEF/t-E, TEF25/PTEF, FEV1, FVC, FEV1/FVC and MVV values of observation group after treatment were higher than those of control group and differences in MTIF/MTEF values were not statistically significant between groups; serum CCSP value was higher than that of control group, and IL-17, MCP-4, MDC and CysLTs values were lower than those of control group. Conclusion: Azithromycin, montelukast combined with pulmicort respulas therapy can reduce the systemic inflammatory state and optimize lung function in children with mycoplasma pneumonia, and it has positive clinical significance.

1. Introduction

Mycoplasma pneumonia is the most common clinical lower respiratory disease in children, and it occurs frequently in summer and fall. Azithromycin is a more common antibiotic for mycoplasma pneumonia in children at present, it is made on the modification of the chemical structure of erythromycin, and it can obtain positive curative effect[1]. Montelukast, as selective leukotriene receptor antagonist, can strongly inhibit cysteinyl leukotriene receptor and be used in the acute phase of inflammatory diseases[2]. Pulmicort respulas also has strong local anti-inflammatory effect, is the only glucocorticoid that can be used for aerosol inhalation, and has multiple effects such as promoting the reconstruction of airway smooth muscle β2 receptor function and strengthening airway sensitivity to β2 receptor[3]. At present, many scholars recommend the joint application of above three drugs with different mechanism of action to increase the curative effect of mycoplasma pneumonia and reduce the probability of disease progression to asthma. In the study, children with mycoplasma pneumonia treated in our hospital from February 2013 to February 2016 were selected as research subjects, and the effect of azithromycin, montelukast combined with pulmicort respulas therapy on the degree of inflammation and lung function was mainly analyzed.

2. Information and methods

2.1. General information

A total of 318 cases of children with mycoplasma pneumonia
were divided into observation group and control group (n=159) according to random number table. Control group included 82 male cases and 77 female cases, they were 1-7 years old, the average age was (3.28±0.45) years, the course of disease was 3-8 d and the average course was (5.28±0.76) d; observation group included 80 male cases and 79 female cases, they were 1-8 years old, the average age was (3.46±0.49) years, the course of disease was 3-9 d and the average course was (5.31±0.74) d. the study got informed consent from children’s families and was approved by the hospital ethics committee, children were not statistically different in gender, age, course of disease and other information (P>0.05), and they could be compared subsequently.

2.2. Treatment methods

Control group received azithromycin and montelukast therapy, specifically as follows: intravenous drip of azithromycin 10 mg/(kg·d), 1 time/d, for consecutive 3-5 d; oral administration of 10 mg/(kg·d) after symptoms were controlled, 1 time/d, for consecutive 3 d; montelukast 4 mg/d for those 2-5 years old, 5 mg/d for those 6-12 years old, 1 time every night, 3 weeks as a course of treatment. Observation group received azithromycin, montelukast combined with pulmicort respulas therapy, specifically as follows: pulmicort respulas 250-500 μg/d, 1 time/d, for consecutive 7 d. The usage and dosage of azithromycin and montelukast were the same as those of control group.

2.3. Observation indexes

2.3.1. Lung function determination

Children's pulmonary function monitor was used to detect patients’ lung function parameters, and before treatment as well as three weeks after treatment, children’s tidal volume (V-T), tidal expiratory flow at 25% remaining tidal volume/peak tidal expiratory flow (TEF25/PTEF%), ratio of time to peak (t-PTEF/t-E%), mid tidal inspiratory flow/mid tidal expiratory flow (MTIF/MTEF) were determined in a quiet condition.

2.3.2. Airway sensitivity and responsiveness

At the same time point of the lung function measurements, the airway sensitivity and responsiveness were tested, and the specific indicators included forced expiratory volume in 1 second (FEV1), forced vital capacity (FVC), FEV1/FVC and maximal voluntary ventilation (MVV).

2.3.3. Serum inflammatory factors

Fasting peripheral venous blood was extracted from patients in the morning, and enzyme-linked immunosorbent assay (ELISA) was used to determine the levels of Clara cell secretory protein (CCSP), interleukin-17 (IL-17), monocyte chemotactractant protein-4 (MCP-4), macrophage-derived chemokine (MDC), cysteinyl leukotrienes (CysLTs) and other inflammatory factors.

2.4. Statistical methods

All data was input in statistical software SPSS 23.0, measurement data comparison between two groups was by t test, and P<0.05 was the standard of statistical significance in differences.

3. Results

3.1. Lung function determination

Differences in lung function of two groups were not statistically significant before treatment (P>0.05), V-T, t-PTEF/t-E and TEF25/PTEF% values of both groups after treatment were higher than those before treatment (P<0.05) while MTIF/MTEF values were without obvious change (P>0.05), V-T, t-PTEF/t-E and TEF25/PTEF% values of observation group were higher than those of control group.

Table 1.
Comparison of lung function index values before and after treatment (n=159).

<table>
<thead>
<tr>
<th>Groups</th>
<th>V-T (mL/kg)</th>
<th>t-PTEF/t-E</th>
<th>TEF25/PTEF</th>
<th>MTIF/MTEF</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before treatment</td>
<td>After treatment</td>
<td>Before treatment</td>
<td>After treatment</td>
</tr>
<tr>
<td>Observation</td>
<td>8.63±0.92</td>
<td>12.47±1.76</td>
<td>37.19±4.58</td>
<td>45.73±5.77</td>
</tr>
<tr>
<td>Control</td>
<td>8.71±0.95</td>
<td>10.32±1.51</td>
<td>37.87±4.09</td>
<td>40.19±4.71</td>
</tr>
<tr>
<td>t</td>
<td>0.162</td>
<td>6.214</td>
<td>0.153</td>
<td>7.394</td>
</tr>
<tr>
<td>P</td>
<td>&gt;0.05</td>
<td>&lt;0.05</td>
<td>&gt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Table 2.
Differences in airway sensitivity and responsiveness index values before and after treatment (n=159).

<table>
<thead>
<tr>
<th>Groups</th>
<th>FEV1 (L)</th>
<th>FVC (L)</th>
<th>FEV1/FVC</th>
<th>MVV (L/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before treatment</td>
<td>After treatment</td>
<td>Before treatment</td>
<td>After treatment</td>
</tr>
<tr>
<td>Observation</td>
<td>1.46±0.23</td>
<td>1.82±0.23</td>
<td>2.43±0.31</td>
<td>2.98±0.38</td>
</tr>
<tr>
<td>Control</td>
<td>1.48±0.25</td>
<td>1.59±0.18</td>
<td>2.41±0.33</td>
<td>2.56±0.35</td>
</tr>
<tr>
<td>t</td>
<td>0.162</td>
<td>5.839</td>
<td>0.114</td>
<td>5.362</td>
</tr>
<tr>
<td>P</td>
<td>&gt;0.05</td>
<td>&lt;0.05</td>
<td>&gt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>
group ($P<0.05$) while differences in MTIF/MTEF values were not statistically significant between groups ($P>0.05$), shown in Table 1.

3.2. Airway sensitivity and responsiveness

There are high airway sensitivity and responsiveness in children with mycoplasma pneumonia, the values of related indexes were determined before and after treatment, and the comparison showed that differences in FEV1, FVC, FEV1/FVC and MVV values of two groups were not statistically significant before treatment ($P>0.05$), FEV1, FVC, FEV1/FVC and MVV values of both groups after the treatment were higher than those before treatment and the increasing tendency of observation group was larger ($P<0.05$), and FEV1, FVC, FEV1/FVC and MVV values of observation group after treatment were higher than those of control group, shown in Table 2.

3.3. Serum levels of inflammatory factors

There is local airway and systemic inflammatory state in children with mycoplasma pneumonia, the balance between pro-inflammatory factor and anti-inflammatory factor will directly decide the tendency and prognosis of disease, enzyme-linked immunosorbent assay (ELISA) was used to determine inflammatory factor levels of two groups after treatment, and the results were as follows: serum CCSP level of observation group after treatment was higher than that of control group, and IL-17, MCP-4, MDC and CysLTs levels were lower than those of control group ($P<0.05$), shown in Table 3.

4. Discussion

Mycoplasma pneumonia, also called primary atypical pneumonia, is caused by mycoplasma infection, patients mainly show interstitial pneumonia and capillary bronchitis-like change, and the main clinical performance is intractable cough and lung inflammation. Mycoplasma infection is one of the main infections in children, the signs vary with the age, older children are mostly short of chest signs, infants may have the signs of obstructive emphysema, and those with severe symptoms can even show dyspnea and pleural effusion[4]. Children with mycoplasma pneumonia need active treatment to avoid complications of inflammation, and both azithromycin and montelukast are the most commonly used drugs. Azithromycin is macrolide antibiotics-sensitive, and mycoplasma pneumoniae is quite sensitive to it; montelukast is the most powerful leukotriene receptor antagonist discovered at present, and it can improve patients’ lung function[5]. In order to further improve the illness in children with mycoplasma pneumonia, some scholars recommend triple therapy to consolidate curative effect.

Pulmicort respulas belongs to inhaled corticosteroid, and it can act on the airway to exert potent anti-inflammatory effect while promote the reconstruction of airway smooth muscle 2 receptor function and enhance the airway sensitivity to 2 agonist. In the study, pulmicort respulas was added in the treatment of children with mycoplasma pneumonia, and then the changes of treatment effect were observed. Pulmonary function test is of important significance in the diagnosis of respiratory diseases, especially the respiratory disease in children, and it can assess the disease severity and drug treatment effect[6,7]. TBFV loop has gradually replaced maximum expiratory flow-volume curve (MEFV) in infant lung function test, the changes of lung function index values during treatment were detected at first in the study, and the results showed that the lung function of both groups was optimized after treatment, V-T, t-PTEF/t-E and TEF25/ PTEF values of observation group were higher while MTIF/MTEF value was without obvious change. The above results suggest that mycoplasma pneumonia mainly involves the small airway and causes smaller damage to the large airway, and also indicate that azithromycin, montelukast combined with pulmicort respulas therapy is more effective in optimizing pulmonary function, which is consistent with the results of related literature reports.

Mycoplasma infection can induce airway injury and increase airway responsiveness, it was mainly because that it causes the production of inflammatory factors such as lymphocytes and macrophages, and persistent infection stimulation can eventually cause chronic airway inflammation and airway stenosis[8,9]. Ventilation and air exchange dysfunction caused by airway hyperresponsiveness of mycoplasma pneumonia can cause type respiratory failure (hypoxemia and hypercapnia) in children, which increases the compensatory respiratory frequency and further aggravates the ventilation and air exchange dysfunction. Reducing airway hyperresponsiveness is the key step in the treatment of mycoplasma pneumonia, and also an important link judging the validity of treatment[10]. In the study, FEV1, FVC, FEV1/FVC and MVV values of observation group were higher than those of control group, indicating that the airway hyperresponsiveness was under control after systemic treatment. Relevant studies have shown that the airway hyperresponsiveness in children with mycoplasma pneumonia is persistent and can last until 3 months after treatment, and so for such patients, continuous airway response monitoring should be strengthened after treatment so as to avoid disease progression to asthma[11,12].

Mycoplasma pneumoniae, as a specific antigen, can also induce

| Table 3.  |
| Comparison of serum levels of inflammatory factors after treatment ($n=159$), |
| Groups | CCSP (μg/L) | IL-17 (ng/L) | MCP-4 (pg/mL) | MDC (pg/mL) | CysLTs (pg/mL) |
| Observation | $11.64±1.93$ | $9.63±1.12$ | $45.37±5.11$ | $573.28±78.11$ | $831.26±95.73$ |
| Control | $8.73±0.95$ | $12.78±1.65$ | $76.19±8.53$ | $856.63±94.31$ | $1254.77±134.27$ |
| t | $7.282$ | $8.192$ | $8.974$ | $12.843$ | $15.482$ |
| P | $<0.05$ | $<0.05$ | $<0.05$ | $<0.05$ | $<0.05$ |
the body to produce corresponding antibody and cytokines through allergic reaction, and directly participate in the chronic airway inflammation. There are a large number of inflammatory cytokines in the airway and circulation of children with mycoplasma pneumoniae, and persistent high state of inflammatory factors is also the main cause of protracted course of disease[13]. In the study, serum levels of inflammatory factors were further monitored after treatment in order to make clear the exact curative effect of triple therapy. Clara cell secretory protein (CCSP) is the main secretory protein of Clara cells, is an important endogenous anti-inflammatory factor, and participates in airway repair and anti-inflammatory immune. Interleukin-17 (IL-17) is secreted by the helper T cell 17 (Th17), is a kind of proinflammatory factor, and is directly involved in the mediation of inflammatory response. Monocyte chemoattractant protein-4 (MCP-4) mainly comes from the mononuclear epithelial cells, and may selectively recruit Th2 cells to inflammatory sites and trigger the immune inflammatory injury[14]. Macrophage-derived chemokine (MDC) is a potent chemotactic agent that can recruit eosinophils to the airway and prompte them to release a variety of toxic proteins, causing bronchial mucosal epithelial damage and inflammatory cell infiltration[15]. Cysteinyl leukotrienes (CysLTs) is the general designation of leukotriene C4, D4 and E4, is the most powerful bronchoconstrictor and also mucus hypersecretion inducer, and can increase microvascular permeability, block cilia movement and cause the occurrence of wheeze and cough[16]. The study results showed that serum CCSP value of observation group was higher after treatment, and IL-17, MCP-4, MDC and CysLTs values were lower, indicating that azithromycin, montelukast combined with pulmicort respulas therapy effectively inhibited the generation of pro-inflammatory factors, increased the secretion of anti-inflammatory factors, and eventually optimized the conditions in children with mycoplasma pneumonia.

To sum up, it is concluded as follows: azithromycin, montelukast combined with pulmicort respulas therapy can optimize the lung function and improve the systemic inflammatory state in children with mycoplasma pneumoniae pneumonia and its significance. J Clin Pediatr 2014; 32(10): 948-950.

References


