EFFECT OF COMBINATION OF METHYLPREDNISOLONE AND AZITHROMYCIN ON PEDIATRIC MYCOPLASMA PNEUMONIA AND ITS EFFECTS ON PROCALCITONIN, HS-CRP, CARDIAC TRO-PONIN AND IL-2

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ABSTRACT

Objectives: To investigate the curative effect of treatment with combination of methylprednisolone and azithromycin on pediatric mycoplasmal pneumonia and its effect on procalcitonin (PCT), high sensitivity C-reactive protein (hs-CRP), cardiac troponin and IL-2.

Methods: A total of 100 cases of children diagnosed with mycoplasma pneumonia and treated in our hospital from March 2014 to March 2017 were randomly divided into control group and observation group (50 cases in each group). The control group was treated with azithromycin, while the observation group was treated with methylprednisolone combined with azithromycin. Hospital stays, treatment time, clinical symptoms, symptom disappearance time, incidence of adverse reactions, and effect of clinical treatment in the two groups were analyzed statistically. At the same time, the concentrations of PCT, hs-CRP, cardiac troponin and IL-2 in serum of the two groups were determined and analyzed before and after treatment, using magnetic particle chemiluminescence (quantitative).

Results: The total treatment effectiveness in the observation group was 96%, which was significantly higher than 84% in the control group (p < 0.05). Fever cessation time, disappearance time of cough and hales, hospital stays and healing time in the observation group were all significantly shorter than those in the control group (p < 0.05). The incidence of nausea, vomiting, abdominal pain, diarrhea, rash, injection site pain and liver function impairment in the observation group were lower than those in the control group (p < 0.05). The levels of PCT, hs-CRP, cardiac troponin in both groups decreased after treatment, while the IL-2 increased. There was a significant difference between values before and after treatment (p < 0.05). The degrees of changes in PCT, hs-CRP, cardiac troponin and IL-2 in the observation group before and after treatment were significantly higher than those in the control group. After treatment, the concentrations of PCT, hs-CRP and cardiac troponin in the observation group were lower than those in the control group, and the concentration of IL-2 in the observation group was higher than that in the control group (p < 0.05).

Conclusion: Compared with azithromycin, combination of methylprednisolone and azithromycin in the treatment of children with mycoplasma pneumoniae has better clinical efficiency and safety, lower inflammation and better immune balance.

Keywords: Pediatric mycoplasma pneumonia, Methylprednisolone, Azithromycin.

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Introduction

Mycoplasma pneumonia is a common childhood respiratory disease caused by Mycoplasma pneumoniae. The disease lasts for a long time and is associated with complicated clinical symptoms which easily lead to multiple organ damage. Therefore, the diagnosis and treatment of pediatric mycoplasma pneumonia is particularly important. At present, the commonly used therapeutic drug in clinics is azithromycin, but the clinical efficiency of this drug is low, the treatment progress is slow, and it triggers on many adverse reactions. Therefore, there is need to search for better and alternative remedies or therapies. During the treatment of mycoplasma pneumonia, the inflammation status of patients also needs to be controlled, so as to achieve effective and rapid treatment outcomes.
This study was focused on the efficiency of methylprednisolone combined azithromycin on pediatric mycoplasma pneumonia and its effect on PCT, hsCRP, cardiac troponin and inflammatory cytokine IL-2, with a view to exploring and analyzing its clinical application value.

Materials and methods

Study object

A total of 100 patients with pediatric mycoplasma pneumonia diagnosed and treated in our hospital from March 2014 to March 2017 were randomly divided into control group and observation group, with 50 cases in each group. All patients had fever, cough, pulmonary rales and other symptoms. In the control group of 23 males and 27 females, aged from 2.3 to 12.1 years (mean = 6.8 ± 1.1 years), the total duration of illness was 2.3 - 5.6 days (mean time = 3.7 ± 0.6 days), and body temperature ranged from 38.3 to 40.2 °C (mean = 39.1 ± 0.7 °C). There were 11 mild cases, 23 moderate cases and 16 severe cases. The patients in this group were treated with azithromycin. The observation group consisted of 23 males and 27 females, aged from 2.2 to 12.3 years, with mean age of 6.6 ± 0.9 years, total duration of illness of 2.2-5.7 days (mean = 3.5 ± 0.5 days), and body temperature ranging from 38.1 to 40.3 °C (mean = 38.9 ± 0.8 °C). There were 13 mild cases, 22 moderate cases and 15 severe cases. The patients in this group were treated with combination of methylprednisolone and azithromycin. There were no significant differences between the two groups with respect to gender, age, total illness duration, body temperature and disease severity (p > 0.05).

The inclusion criteria were: positive serum mycoplasma antigen, positive cold agglutination detection, and clinical symptoms and chest X-ray consistent with the clinical diagnosis of children with pediatric mycoplasma pneumonia(5, 6). All patients were informed and agreed to participate in the study.

The exclusion criteria were: immunodeficiency; allergy to methylprednisolone or azithromycin; presence of organ disease (heart, lung, liver, kidney or any other vital organs), and mental disorders.

Therapeutic method

All patients were treated with conventional therapy including antipyretic, anti-asthma, and expectorant(6). In the control group, azithromycin (5% GS) was intravenously given through drip at a dose of 10 mg / kg daily. When the body temperature normalized, each patient was given oral azithromycin (10 mg / kg daily). On the basis of the treatment of the control group, the observation group was given methylprednisolone (prepared with 5% GS) intravenously at a dose of 1 mg / kg daily. When their body temperature normalized, they were given oral methylprednisolone at a dose of 1 mg / kg orally daily. The two groups of patients were treated for 4 days, then stopped 3d, this is a course of treatment, a total of 3 courses of treatment were conducted. Two groups of patients in the treatment of a course were evaluated for clinical treatment.

Evaluation of therapeutic effect

The observation indices were hospitalization stay, cure time, time of disappearance of clinical symptoms and signs, incidence of adverse reactions, and clinical efficiency. These were recorded in the two groups.

The evaluation criteria were cure:
• patient recovered, clinical symptoms and signs of mycoplasma pneumonia disappeared completely, absence of shadow in chest X-ray examination of the lungs;
• significantly effective: clinical symptoms and signs of children with mycoplasma pneumonia were significantly improved, shadow in chest X-ray examination of the lung almost disappeared;
• effective: clinical symptoms and signs of pediatric mycoplasma pneumonia were improved to some extent, shadow in chest X-ray examination of lungs partly disappeared;
• invalid: no improvement in clinical symptoms and signs of pediatric mycoplasma pneumonia, or symptoms even got worse; shadow in chest X-ray examination of lungs was unchanged or even expanded(7, 8).

Total effectiveness =((cured cases + significantly effective cases + effective cases) / total cases) × 100%.

Other detection index

Serum levels of PCT, hs-CRP, cardiac troponin and IL-2 were assayed before treatment, and 10 days after treatment, using magnetic particle chemiluminescence (quantitative)

Statistics analysis

Data were analyzed using SPSS18.0. Measurement data are expressed as mean ± standard deviation, and analyzed using Student’s t-test. Enumeration data was expressed as percentage and
analyzed using Chi square (χ²) test. Values of p < 0.05 were taken as indicative of statistically significant differences.

Results

Comparison of clinical efficacy between the two groups

The total effectiveness of observation group was 96%, while that of control group was 84%. The total effectiveness of the observation group was higher than that of control group (p < 0.05) (Table 1).

<table>
<thead>
<tr>
<th>Groups</th>
<th>N</th>
<th>Cure</th>
<th>Significantly effective</th>
<th>Effective</th>
<th>Invalid</th>
<th>Total effectiveness (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>50</td>
<td>21 (42%)</td>
<td>18 (36%)</td>
<td>9 (18%)</td>
<td>2 (4%)</td>
<td>96%*</td>
</tr>
<tr>
<td>Control</td>
<td>50</td>
<td>17 (34%)</td>
<td>13 (26%)</td>
<td>12 (24%)</td>
<td>8 (16%)</td>
<td>84%</td>
</tr>
</tbody>
</table>

Table 1: Comparison of the clinical efficacy between the two groups [n (%)]. * p < 0.05, compared with the control group

Comparison of improvement in clinical symptoms and signs, hospitalization stays and cure time between the two groups

Fever clearance time, cough clearance time, rales clearance time, hospital stay and the cure time in the observation group were shorter than those in the control group (p < 0.05) (Table 2).

<table>
<thead>
<tr>
<th>Groups</th>
<th>N</th>
<th>Fever clearance time</th>
<th>Cough clearance time</th>
<th>Rales clearance time</th>
<th>Hospital stay</th>
<th>Cure time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>50</td>
<td>3.39±0.98</td>
<td>8.42±1.58</td>
<td>4.08±0.87</td>
<td>6.23±1.28</td>
<td>11.23±3.29</td>
</tr>
<tr>
<td>Control</td>
<td>50</td>
<td>4.67±1.04</td>
<td>12.58±2.49</td>
<td>6.41±1.38</td>
<td>10.16±2.09</td>
<td>15.27±4.58</td>
</tr>
<tr>
<td>p</td>
<td></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 2: Comparison of improvement in clinical symptoms and signs, hospitalization stays and cure time between the two groups (d).

Comparison of adverse reactions between the two groups

In the observation group, the incidence of nausea and vomiting, abdominal pain, diarrhea, skin rash, injection site pain and hepatic dysfunction were all lower than those in the control group (p < 0.05) (Table 3).

<table>
<thead>
<tr>
<th>Groups</th>
<th>N</th>
<th>Nausea and vomiting</th>
<th>Abdominal pain and diarrhea</th>
<th>Skin rash</th>
<th>Injection site pain</th>
<th>Hepatic dysfunction</th>
<th>Total number of adverse reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>50</td>
<td>3 (6%)</td>
<td>2 (4%)</td>
<td>2 (4%)</td>
<td>3 (6%)</td>
<td>2 (4%)</td>
<td>12 (24%)</td>
</tr>
<tr>
<td>Control</td>
<td>50</td>
<td>8 (16%)</td>
<td>7 (14%)</td>
<td>5 (10%)</td>
<td>9 (18%)</td>
<td>4 (8%)</td>
<td>33 (66%)</td>
</tr>
<tr>
<td>p</td>
<td></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 adverse reactions between the two groups [n (%)].

Comparison of changes in PCT, hs-CRP, cardiac troponin and IL-2 before and after treatment between the two groups

The levels of PCT, hs-CRP, cardiac troponin and IL-2 in both groups decreased after treatment, and there were significant differences between pre- and post-treatment values (p < 0.05). The changes in PCT, hs-CRP, cardiac troponin and IL-2 before and after treatment in the observation group were significantly higher than those in the control group. After treatment, the levels of PCT, hs-CRP and cardiac troponin in the observation group were lower than those in the control group, and the IL-2 in the observation group was higher than that in the control group (p < 0.05) (Table 4).

<table>
<thead>
<tr>
<th>Groups</th>
<th>N</th>
<th>IL-2 (µg/ml) Before treatment</th>
<th>IL-2 (µg/ml) After treatment</th>
<th>hs-CRP (mg/L) Before treatment</th>
<th>hs-CRP (mg/L) After treatment</th>
<th>PCT (µg/L) Before treatment</th>
<th>PCT (µg/L) After treatment</th>
<th>Cardiac troponin (ng/ml) Before treatment</th>
<th>Cardiac troponin (ng/ml) After treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>50</td>
<td>3.21±0.46</td>
<td>1.23±0.21*</td>
<td>4.98±0.12*</td>
<td>0.21±0.08*</td>
<td>25.53±1.05</td>
<td>2.18±1.11</td>
<td>11.80±1.25</td>
<td>0.83±0.19*</td>
</tr>
<tr>
<td>Control</td>
<td>50</td>
<td>3.23±0.53</td>
<td>3.09±0.68*</td>
<td>24.98±2.98</td>
<td>4.23±0.82*</td>
<td>10.18±4.26</td>
<td>2.17±1.05</td>
<td>10.09±4.66</td>
<td>0.83±0.19*</td>
</tr>
</tbody>
</table>

Table 4: Comparison of changes in PCT, hs-CRP, cardiac troponin and IL-2 before and after treatment between the two groups. * p < 0.05, compared with value before treatment; # p < 0.05, compared with control group

Discussion

Mycoplasma pneumonia is one of the most common forms of lower respiratory tract infection in children and is also one of community-acquired pneumonia. According to statistics, mycoplasma pneumonia accounts for 10 - 70% of community-acquired pneumonia, and the proportion is increasing\(^9, 10\). Mycoplasma pneumonia easily leads to pediatric fever, cough and other illnesses, often accompanied by extra-pulmonary complications. Due to the fact that children's tissues and organs are not yet fully developed, the serious condition causes damage to other organs. Azithromycin has a long half-life and low metabolic rate in the body, so it has a long acting time and low effect. Methylprednisolone is a mid-acting glucocorticoid that has a strong anti-infective function and can improve therapeutic efficiency by modulating inflammatory cytokines\(^11\) and reducing the inflammatory response\(^12\). At the same time, safety is particularly important during the drug
treatment of pediatric mycoplasma pneumonia. In this study, methylprednisolone combined with azithromycin treatment was significantly better than treatment with azithromycin alone, and adverse reaction was significantly reduced, which is consistent with the findings of Meyer Sauteur et al.\(^{13}\). Studies by Lee et al.\(^{14}\) also found that the clinical symptoms of refractory mycoplasma pneumonia improved with methylprednisolone.

In clinical treatment, changes in inflammatory cytokines are also a means of monitoring pediatric mycoplasma pneumonia and evaluating the therapeutic effect of drugs. In related studies on mycoplasma infection, expression of inflammatory factors such as anti-inflammatory and pro-inflammatory cytokines may occur, so it is important to monitor changes in inflammatory markers in the course of treatment\(^{15}\). Interleukin-2 (IL-2) is an anti-inflammatory factor that induces its own response to the death of T-cells and maintains the immune system. In this study, after the treatment of pediatric mycoplasma pneumonia with methylprednisolone combined with azithromycin, IL-2 improvement was significantly higher than that in azithromycin-alone treatment, and thus the patient’s infection was better controlled.

Procalcitonin (PCT) is a marker of the severity of the inflammation in the body, and its levels are high when the patient is infected, but are decreased when the inflammation disappears\(^{16}\). In cancer patients or patients with immune disease, the concentration of CRP changes very minimally\(^{17}\). High sensitivity C-reactive protein (hs-CRP) which is synthesized in the liver, is also a marker of the body’s inflammatory response. The concentration of hs-CRP in healthy humans is very low. However, when the body is infected, the concentration of hs-CRP rises sharply, and is positively correlated with the degree of infection\(^{18}\).

In this study, after treatment with methylprednisolone combined with azithromycin or azithromycin alone, the concentrations of PCT and hs-CRP were both decreased, and the combined treatment had better outcomes, indicating that methylprednisolone combined with azithromycin can achieve better anti-inflammation effect. Pediatric mycoplasma pneumonia has higher incidence of myocardial damage\(^{19}\). Cardiac troponin reflects the degree of myocardial damage in patients, the higher the concentration, the more serious the damage. In this study, the results showed that methylprednisolone combined with azithromycin treatment was better in repairing myocardial cells and effectively controlling myocardial damage.

**Conclusion**

Methylprednisolone combined with azithromycin treatment for pediatric mycoplasma pneumonia has a good effect. Compared with azithromycin, the treatment efficiency and safety was significantly improved to better control the patient’s inflammatory state and improve anti-inflammatory ability, reduce inflammation, maintain immune balance and improve heart function, with high potential for clinical application.

**References**

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