Influence of pidotimod combined with conventional drug therapy on the infection status and immune function of children with recurrent respiratory tract infection

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Objective: To study the influence of pidotimod combined with conventional drug therapy on the infection status and immune function of children with recurrent respiratory tract infection.

Methods: A total of 118 children with recurrent respiratory tract infection who were treated in the hospital between January 2015 and January 2017 were collected and divided into control group and observation group by random number table method, 59 cases in each group. Control group received conventional therapy, and observation group received pidotimod combined with conventional therapy. The differences in serum levels of inflammatory mediators, acute phase proteins and Th1/Th2 cytokines were compared between the two groups before and after treatment.

Results: Before treatment, the differences in serum levels of inflammatory mediators, acute phase proteins and Th1/Th2 cytokines were not statistically significant between the two groups. After 1 week of treatment, serum TNF-α, PCT, CRP, PAB, TRF and IL-4 contents of both groups of children were lower than those before treatment while IFN-γ contents as well as IFN-γ / IL-4 levels were higher than those before treatment, and serum TNF-α, PCT, CRP, PAB, TRF and IL-4 contents of observation group were lower than those of control group while IFN-γ content as well as IFN-γ / IL-4 level was higher than those of control group.

Conclusion: Pidotimod combined with conventional drug therapy can effectively inhibit the infection status and optimize the Th1/Th2 cellular immune function of children with recurrent respiratory tract infection.

1. Introduction

Children are prone to recurrent respiratory tract infection, it is related to congenital factors, immunocompromise and improper feeding, and inappropriate treatment can lead to asthma, myocardial injury and so on, seriously influence children’s quality of life and even inhibit their normal growth and development[1,2]. Anti-infection, anti-febrile and antitussive are all routine therapies for recurrent respiratory tract infections in children, but the illness still progresses in some cases, so many scholars recommend joining drugs with other mechanisms of action to enlarge the curative effect and maximize the children’s clinical benefit. Pidotimod is an immunomodulator that can enhance the phagocytic activity of macrophages and neutrophils, and help strengthen the non-specific immune response and the specific immune response[3−5]. Given that immunocompromise plays an important role in recurrent respiratory tract infections in children, pidotimod was used as adjuvant drug and added in the overall treatment of such children in this study, and the effect of combination therapy on infection status, immune function and others was discussed, now reported as follows.

2. Information and methods

2.1 Case information

A total of 118 children with recurrent respiratory tract infection who were treated in the hospital between January 2015 and January 2017 were selected as the study subjects, and the families of the children signed the informed consent. Random number table was
used to divide the children into control group and observation group, with 59 cases in each group. Control group included 31 male cases and 28 female cases that were 3-13 years old; observation group included 29 male cases and 29 female cases that were 2-14 years old. The differences in the gender and age distribution were not significant between the two groups (P>0.05), and the research was approved by the hospital ethics committee.

2.2 Inclusion criteria

(1) Clearly diagnosed with respiratory tract infection; (2) with 3 times of respiratory tract infection attack in the past 1 year; (3) cooperating with and finishing the whole treatment and related laboratory tests, and with complete clinical data collection.

2.3 Exclusion criteria

(1) Combined with severe pneumonia; (2) combined with infectious diseases of other tissue organs; (3) receiving independent drug treatment outside the hospital; (4) combined with serious congenital diseases; (5) combined with serious autoimmune diseases.

2.4 Therapy

Control group received routine therapy for children with repeated respiratory tract infection, including anti-infection, anti-febrile, antitussive, etc. Observation group, based on conventional treatment, received pidotimod combination therapy, specifically as follows: pidotimod oral liquid (Suzhou Pharmaceutical Factory, Jiangsu Wuzhong Pharmaceutical Group Corporation, approved by H20030463), 400 mg/times for acute phase, 2 times/d; 400 mg/time for non-acute phase, 1 time/d, for continuous 1 week. Routine treatment was the same as that of control group.

2.5 Observation indexes

Before treatment and after 1 week of treatment, 3.0 mL of fasting peripheral venous blood was collected from two groups of children, anti-coagulated and centrifuged at 4 ℃ (3 500 r/min, 10 min) to get the upper serum. The enzyme linked immunosorbent assay (ELISA) was used to detect the serum levels of inflammatory mediators tumor necrosis factor α (TNF-α) and procalcitonin (PCT); the serum contents of acute phase proteins C-reactive protein (CRP), prealbumin (PAB) and transferrin (TRF), and the ratio of the two was calculated.

<table>
<thead>
<tr>
<th></th>
<th>Groups</th>
<th>n</th>
<th>Before treatment</th>
<th>After treatment</th>
<th>Before treatment</th>
<th>After treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>59</td>
<td>20.38±2.71</td>
<td>11.61±1.85</td>
<td>263.81±30.42</td>
<td>142.36±17.82</td>
<td>5.61±0.67</td>
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<tr>
<td>Observation group</td>
<td>59</td>
<td>20.47±2.85</td>
<td>6.02±0.78</td>
<td>267.94±31.52</td>
<td>96.53±10.72</td>
<td>5.59±0.64</td>
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<tr>
<td>t</td>
<td>0.283</td>
<td>9.281</td>
<td>0.351</td>
<td>13.276</td>
<td>0.184</td>
<td>8.263</td>
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<tr>
<td>P</td>
<td>&gt;0.05</td>
<td>&lt;0.05</td>
<td>&gt;0.05</td>
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<td>&gt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Note: compared with same group before treatment, *P<0.05.

2.6 Statistical processing

Inflammatory mediators, acute phase proteins, Th1/Th2 cytokines and other measurement data were in terms of mean ± standard deviation and compared by t test. Statistical software adopted in the study was SPSS 24.0 and statistic P<0.05 indicated statistical significance in differences.

3. Results

3.1 Inflammatory mediators

Comparison of serum inflammatory mediators TNF-α (ng/mL) and PCT (µg/L) contents between two groups of children before treatment and after 1 week of treatment was as follows: before treatment, the differences in serum TNF-α and PCT contents were not significant between the two groups (P>0.05); after 1 week of treatment, serum TNF-α and PCT contents of both groups of children were lower than those before treatment (P<0.05), and serum TNF-α and PCT contents of observation group were lower than those of control group (P<0.05), shown in Table 1.

3.2 Acute phase proteins

Comparison of serum acute phase proteins CRP (mg/L), PAB (mg/L) and TRF (g/L) contents between two groups of children before treatment and after 1 week of treatment was as follows: before treatment, the differences in serum CRP, PAB and TRF contents were not significant between the two groups (P>0.05); after 1 week of treatment, serum CRP, PAB and TRF contents of both groups of children were lower than those before treatment (P<0.05), and serum CRP, PAB and TRF contents of observation group were lower than those of control group (P<0.05), shown in Table 2.
Comparison of serum Th1/Th2 cytokine contents between two groups of children before and after treatment.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Before treatment</th>
<th>After treatment</th>
<th>Before treatment</th>
<th>After treatment</th>
<th>Before treatment</th>
<th>After treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>59</td>
<td>12.8±2.14</td>
<td>22.7±2.85</td>
<td>68.7±2.31</td>
<td>51.6±2.87</td>
<td>0.21±0.03</td>
<td>0.40±0.05</td>
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<tr>
<td>Observation group</td>
<td>59</td>
<td>12.76±1.58</td>
<td>34.8±4.42</td>
<td>68.59±2.24</td>
<td>40.7±3.77</td>
<td>0.23±0.03</td>
<td>0.71±0.08</td>
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</table>

Note: compared with same group before treatment, *P*<0.05.

### 3.3 Th1/Th2 cytokines

Comparison of serum Th1/Th2 cytokines IFN-γ (ng/mL) and IL-4 (pg/mL) contents as well as their ratio IFN-γ/IL-4 levels between two groups of patients before treatment and after 1 week of treatment was as follows: before treatment, the differences in serum Th1 cytokine IFN-γ and Th2 cytokine IL-4 contents as well as their ratio IFN-γ/IL-4 levels were not significant between the two groups (*P*>0.05); after 1 week of treatment, serum IFN-γ contents as well as IFN-γ/IL-4 levels of both groups of children were higher than those before treatment while IL-4 contents were lower than those before treatment (*P*<0.05), and serum IFN-γ content as well as IFN-γ/IL-4 level of observation group was higher than those of control group while IL-4 content was lower than that of control group (*P*<0.05), shown in Table 3.

### 4. Discussion

Clinical treatment of children with recurrent respiratory tract infection is related to children's growth and development, the long-term incidence of cardiovascular diseases and so on, anti-infection, antitussive and other conventional treatment help to relieve the illness, but the disease still progresses in some patients and even leads to adverse outcomes[6-8]. Previous studies have shown that the immune function of children with recurrent respiratory tract infection is generally lower than that of normal children, and it is suspected that the abnormal immune function is the important cause of recurrent respiratory tract infection in children. Pidotimod is a synthetic dipeptide with high purity, which is a kind of immunostimulant, and can stimulate the nonspecific immunity, cellular immunity and humoral immunity, enhance the phagocytosis and killing effect of a variety of cells on pathogenic bacteria, and ultimately exert significant antibacterial and antiviral effect[9-11]. Given the immune dysfunction in children with recurrent respiratory tract infection, many clinical scholars recommend adding pidotimod to their treatment, and the effect of the adjuvant drug therapy on the children’s infection status and immune function was explored so as to lay a foundation for future treatment of similar disease.

Inflammatory mediators are highly consistent with the severity of infection status in children, and their serum levels can objectively reflect the disease of children with recurrent respiratory tract infection and determine the effectiveness of clinical therapy[12,13]. TNF-α is a typical pro-inflammatory factor that can induce mononuclear/macrophages to produce and aggregate, make them synthesize and secrete more inflammatory factors, and form inflammatory cascade reactions. PCT is a kind of high-profile new inflammatory mediator at present, also known as “late inflammatory factor”, the content increases in the case of apparent infection, and the specific content is positively related with infection severity[14,15]. In the study, the serum levels of these inflammatory mediators of two groups of children were detected, and it was found that compared with those before treatment, serum TNF-α and PCT contents of both groups of patients decreased after treatment, indicating that both therapies can reduce the patient's infection symptoms; further compared with those of control group, serum TNF-α and PCT contents of observation group were lower, confirming that adjuvant pidotimod therapy can more effectively inhibit the production of inflammatory mediators, which is the direct evidence that it lowers infection status.

Acute phase proteins are a class of proteins whose contents in the blood significantly change in the case of inflammation, infection, tumor and other cases in the body, include CRP, PAB, TRF, etc, and are the important parts for breeding mechanism, and their contents are positively correlated with the body inflammation or damage[16-18]. In the study, the differences in serum levels of above-mentioned acute phase proteins were compared between two groups of children, and it was found that compared with those before treatment, serum CRP, PAB and TRF contents of both groups of patients decreased after treatment, explaining that both therapies can reduce the inflammation and infection in the body; further compared with those of control group, serum CRP, PAB and TRF contents of observation group were lower, proving that the adjuvant pidotimod therapy is more effective in inhibiting the inflammation and infection of the body.

Immunocompromise is considered to be one of the important causes of recurrent respiratory tract infection, and the cellular immune dysfunction plays an important role. Th1 and Th2 cells are the most important CD4+ T lymphocyte subsets, the Th1/Th2 system is in balance under physiological state, and the pathogen infection can cause dominant Th2 response and abate Th1 response, resulting in infection spread and poor prognosis[19]. Th1 cells mainly secrete IFN-γ, Th2 cells mainly secrete IL-4, and the ratio of IFN-γ/IL-4 reduces in infection status[20,21]. In this study, the differences in serum levels of Th1/Th2 cytokines were compared between the two
groups of patients, and it was found that compared with those before treatment, serum IFN-γ and IFN-γ/IL-4 levels of both groups increased while IL-4 levels decreased after treatment, indicating that both therapies could help reverse Th1/Th2 system imbalance; further compared with those of control group, serum IFN-γ and IFN-γ/IL-4 levels of observation group were higher while IL-4 level was lower after treatment, confirming that adjuvant pidotimod therapy can be more effective in optimizing Th1/Th2 cellular immune balance, and this is also the important internal mechanism for it to suppress the infection status.

Pidotimod combined with conventional drug therapy can effectively control the infection symptoms in children with recurrent respiratory tract infection, and its efficacy is directly related to optimizing Th1/Th2 cellular immune balance state.

References