Effects of dermatophagoides farinae drops combined with pidotimod on inflammatory response and immune response in children with allergic rhinitis combined with asthma

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ABSTRACT

Objective: To investigate the effects of dermatophagoides farinae drops combined with pidotimod on inflammatory response and immune response in children with allergic rhinitis combined with asthma. Methods: A total of 118 children with allergic rhinitis combined with asthma who were treated in our hospital between December 2014 and May 2017 were selected as the research subjects and divided into the control group (n=59) and the dermatophagoides farinae drops group (n=59) by random number table method. Control group received both conventional therapy and pidotimod therapy, and dermatophagoides farinae drops group received both conventional therapy and dermatophagoides farinae drops combined with pidotimod therapy. The differences in inflammatory factor, cellular immunity index and humoral immunity index levels were compared between the two groups before treatment (T0), after 3 months of treatment (T1), after 6 months of treatment (T2) and after 12 months of treatment (T3). Results: At T0, inflammatory factor, cellular immunity index and humoral immunity index levels were not significantly different between the two groups. At T1, T2 and T3, serum inflammatory factor IL-2 contents of dermatophagoides farinae drops group were higher than those of control group at the corresponding time points whereas IL-4, IL-5, IL-9 and IL-18 contents were lower than those of control group at the corresponding time points; peripheral blood cellular immunity indexes CD3+, CD4+, CD8+ and CD4+/CD8+ levels were higher than those of control group at the corresponding time points; serum humoral immunity indexes IgA, IgM and IgG contents were higher than those of control group at the corresponding time points whereas IgE contents were lower than those of control group at the corresponding time points. Conclusion: Dermatophagoides farinae drops combined with pidotimod therapy can effectively reduce the inflammatory response degree and optimize the cellular and humoral immune function of the children with allergic rhinitis combined with asthma.

1. Introduction

Both allergic rhinitis and asthma are common respiratory diseases in clinical practice. In recent years, the incidence of them has been increasing year by year due to the deterioration of air quality and other reasons. The two diseases often occur in the same patient, and children are more likely to develop allergic rhinitis and asthma because their immune system is not fully developed[1,2]. When allergic rhinitis and asthma occur in the same individual, they are more difficult to treat and cause more physical and mental damage to the patients, and some patients even show growth retardation[3]. Pidotimod is a common drug for clinical treatment of allergic rhinitis combined with asthma. As an immunomodulator, it can promote non-specific and specific immune system and has been proved to be able to reduce the acute attack of allergic rhinitis combined with asthma to a certain extent[4]. Dermatophagoides farinae drops are the etiological treatment drug for allergic diseases, and the long-term regular use can fundamentally alleviate the condition of allergic rhinitis, asthma and other diseases and...
2. Information and methods

2.1. Inclusion and exclusion criteria

Inclusion criteria: (1) meeting the diagnostic criteria for clinical allergic rhinitis and asthma; (2) without history of dermatophagoides farinae drops therapy; (3) with informed consent from the family. Exclusion criteria: (1) associated with pneumonia and other airway disorders; (2) combined with severe autoimmunity diseases, such as idiopathic thrombocytopenic purpura; (3) with interrupted treatment due to severe drug allergy during treatment; (4) with severe drug complications during treatment.

2.2 Case information

A total of 118 children with allergic rhinitis combined with asthma who were treated in our hospital between December 2014 and May 2017 were chosen as research subjects and divided into the control group (n=59) and the dermatophagoides farinae drops group (n=59) by random number table method. In the control group, there were 31 males and 28 females who were 2-11 years old; in the dermatophagoides farinae drops group, there were 30 males and 29 females who were 3-14 years old. The differences in gender and age distribution were not significant between groups, and the follow-up research plan was reviewed and approved by the hospital ethics committee.

2.3 Therapeutic regimen

Both groups received routine symptomatic treatment for patients with clinical allergic rhinitis combined with asthma. Control group received both conventional treatment and pidotimod therapy, which was as follows: pidotimod oral solution, 0.4 g/ time, 2 times/d for continuous 1 week. It was then adjusted to once/d and taken before breakfast for a total of 4 weeks. Dermatophagoides farinae drops group received both conventional treatment and dermatophagoides farinae drops combined with pidotimod therapy, which was as follows: Week 1: Changdi No. 1 (protein concentration 1 μg/mL) 2 mL; Week 2: Changdi No. 2 (protein concentration 10 μg/mL, 1, 2, 3, 4, 6, 8, 10 drops successively on d1-d7); Week 3-4: Changdi No. 3 (protein concentration100 μg/mL, 1, 2, 3, 4, 6, 8, 10 drops successively on d1-d7); Week 4 - Week 5: Changdi No. 4 (protein concentration 333 μg/mL), 3 drops/time, 1 time/d; Week 6-1 year: Changdi No. 5 (protein concentration 1 000 μg/mL), 2 drops/time, 1 time/d.

2.4 Observation indexes

Before treatment (T0), after 3 months of treatment (T1), after 6 months of treatment (T2) and after 12 months of treatment (T3), 3.0 mL of peripheral blood samples were obtained from the two groups of children respectively, 1.5 mL of them were directly frozen and the other 1.5 mL were used to separate serum, which was cryopreserved. Enzyme-linked immunosorbent assay was used to determine serum contents of interleukin-2 (IL-2), interleukin-4 (IL-4), interleukin-5 (IL-5), interleukin-9 (IL-9) and interleukin-18 (IL-18); flow cytometry was used to measure the levels of cellular immunity indexes in peripheral blood, including CD3+, CD4+, CD8+ and CD4+/CD8+; serum contents of humoral immunity indexes were measured by radioimmunoassay, including immunoglobulin A (IgA), immunoglobulin M (IgM), immunoglobulin G (IgG) and immunoglobulin E (IgE).

2.5 Statistical methods

The specific values of inflammatory factor contents, cellular immunity index levels and humoral immunity index contents were all recorded into SPSS 24.0, and the statistical value P was calculated to determine whether the differences between groups were statistically significant. P<0.05 was set as the criterion of statistical significance in differences.

3. Results

3.1 Inflammatory factors

Comparison of serum inflammatory factors IL-2, IL-4, IL-5, IL-9 and IL-18 contents at different time points was as follows: at T0, serum IL-2, IL-4, IL-5, IL-9 and IL-18 contents were not significantly different between the two groups (P>0.05). At T1, T2 and T3, serum IL-2 contents of both groups were higher than those at T0 whereas IL-4, IL-5, IL-9 and IL-18 contents were lower than those at T0 (P<0.05). At T1, T2 and T3, serum IL-2 contents of dermatophagoides farinae drops group were higher than those of control group at the corresponding time points whereas IL-4, IL-5, IL-9 and IL-18 contents were lower than those of control group at the corresponding time points (P<0.05), shown in Table 1.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>IL-2</th>
<th>IL-4</th>
<th>IL-5</th>
<th>IL-9</th>
<th>IL-18</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>59</td>
<td>T0</td>
<td>30.28±4.11</td>
<td>21.57±2.48</td>
<td>60.17±6.58</td>
<td>15.42±1.91</td>
<td>22.48±2.61</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T1</td>
<td>32.09±3.32</td>
<td>19.26±2.01</td>
<td>51.04±5.75</td>
<td>13.27±1.54</td>
<td>19.03±2.41</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T2</td>
<td>35.17±4.38</td>
<td>15.77±1.95</td>
<td>45.78±5.62</td>
<td>11.01±1.32</td>
<td>15.88±1.72</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T3</td>
<td>37.82±5.12</td>
<td>13.85±1.61</td>
<td>41.20±4.83</td>
<td>10.83±1.41</td>
<td>11.73±1.35</td>
</tr>
<tr>
<td>Dermatophagoides</td>
<td>59</td>
<td>T0</td>
<td>30.21±4.09</td>
<td>21.37±2.61</td>
<td>60.24±6.29</td>
<td>15.37±1.62</td>
<td>22.31±2.49</td>
</tr>
<tr>
<td>farinae drops group</td>
<td></td>
<td>T1</td>
<td>37.66±4.85</td>
<td>15.37±1.82</td>
<td>43.71±5.34</td>
<td>11.09±1.64</td>
<td>14.72±1.59</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T2</td>
<td>42.85±5.09</td>
<td>11.05±1.46</td>
<td>32.85±0.70</td>
<td>8.72±0.97</td>
<td>10.05±1.93</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T3</td>
<td>45.71±6.48</td>
<td>10.14±1.53</td>
<td>23.42±3.20</td>
<td>7.12±0.84</td>
<td>7.57±0.86</td>
</tr>
</tbody>
</table>

Note: vs. same group at T0, P<0.05; vs. control group at T1, P<0.05; vs. control group at T2, P<0.05; vs. control group at T3, P<0.05.
Table 2.
Comparison of peripheral blood cellular immunity index levels at different time points.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>CD3⁺</th>
<th>CD4⁺</th>
<th>CD8⁺</th>
<th>CD4⁺/CD8⁺</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>59</td>
<td>T0</td>
<td>30.8(±3.79)</td>
<td>21.75±2.85</td>
<td>17.49±2.45</td>
<td>1.15±0.12</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T1</td>
<td>36.22±6.05</td>
<td>30.61±3.94</td>
<td>20.58±2.61</td>
<td>1.23±0.15</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T2</td>
<td>39.71±4.37</td>
<td>38.72±4.81</td>
<td>25.72±3.09</td>
<td>1.28±0.16</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T3</td>
<td>43.85±5.18</td>
<td>46.08±5.18</td>
<td>31.66±3.54</td>
<td>1.29±0.17</td>
</tr>
<tr>
<td>Dermatophagoides</td>
<td>59</td>
<td>T0</td>
<td>30.67±3.54</td>
<td>21.67±2.91</td>
<td>17.53±2.38</td>
<td>1.14±0.16</td>
</tr>
<tr>
<td>farinae drops group</td>
<td></td>
<td>T1</td>
<td>41.19±5.37</td>
<td>35.8±4.19</td>
<td>24.71±2.58</td>
<td>1.31±0.16</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T2</td>
<td>48.65±5.09</td>
<td>43.22±5.09</td>
<td>32.58±0.09</td>
<td>1.37±0.19</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T3</td>
<td>52.77±6.09</td>
<td>51.87±6.50</td>
<td>39.77±6.65</td>
<td>1.43±0.16</td>
</tr>
</tbody>
</table>

Note: vs. same group at T0, *P<0.05; vs. control group at T1, *P<0.05; vs. control group at T2, *P<0.05; vs. control group at T3, *P<0.05.

Table 3.
Comparison of serum humoral immunity index contents at different time points (g/L).

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>IgA</th>
<th>IgM</th>
<th>IgG</th>
<th>IgE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>59</td>
<td>T0</td>
<td>1.74±0.21</td>
<td>1.01±0.13</td>
<td>9.16±0.95</td>
<td>485.28±51.77</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T1</td>
<td>1.89±0.25</td>
<td>1.11±0.14</td>
<td>9.54±0.98</td>
<td>440.17±43.82</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T2</td>
<td>1.97±0.23</td>
<td>1.18±0.15</td>
<td>9.82±0.10</td>
<td>392.65±43.87</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T3</td>
<td>2.05±0.27</td>
<td>1.19±0.14</td>
<td>9.98±0.10</td>
<td>371.04±42.44</td>
</tr>
<tr>
<td>Dermatophagoides farinae</td>
<td>59</td>
<td>T0</td>
<td>1.73±0.19</td>
<td>1.02±0.12</td>
<td>9.14±0.93</td>
<td>482.74±50.82</td>
</tr>
<tr>
<td>drops group</td>
<td></td>
<td>T1</td>
<td>2.08±0.24</td>
<td>1.20±0.17</td>
<td>9.94±0.10</td>
<td>392.64±45.21</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T2</td>
<td>2.18±0.26</td>
<td>1.28±0.15</td>
<td>10.31±0.27</td>
<td>319.35±35.72</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T3</td>
<td>2.27±0.25</td>
<td>1.29±0.16</td>
<td>10.75±1.48</td>
<td>274.36±35.91</td>
</tr>
</tbody>
</table>

Note: vs. same group at T0, *P<0.05; vs. control group at T1, *P<0.05; vs. control group at T2, *P<0.05; vs. control group at T3, *P<0.05.

3.2 Cellular immunity indexes

Comparison of peripheral blood cellular immunity indexes CD3⁺, CD4⁺, CD8⁺ and CD4⁺/CD8⁺ levels at different time points was as follows: at T0, peripheral blood CD3⁺, CD4⁺, CD8⁺ and CD4⁺/CD8⁺ levels were not significantly different between the two groups (*P>0.05). At T1, T2 and T3, peripheral blood CD3⁺, CD4⁺, CD8⁺ and CD4⁺/CD8⁺ levels of both groups were higher than those at T0 (*P<0.05). At T1, T2 and T3, peripheral blood CD3⁺, CD4⁺, CD8⁺ and CD4⁺/CD8⁺ levels of dermatophagoides farinae drops group were higher than those of control group at the corresponding time points (*P<0.05), shown in Table 2.

3.3 Humoral immunity indexes

Comparison of serum humoral immunity indexes IgA, IgM, IgG and IgE contents at different time points was as follows: at T0, serum IgA, IgM, IgG and IgE contents were not significantly different between the two groups (*P>0.05). At T1, T2 and T3, serum IgA, IgM and IgG contents of both groups were higher than those at T0 whereas IgE contents were lower than those at T0 (*P<0.05). At T1, T2 and T3, serum IgA, IgM and IgG contents of dermatophagoides farinae drops group were higher than those of control group at the corresponding time points whereas IgE contents were lower than those of control group at the corresponding time points (*P<0.05), shown in Table 3.

4. Discussion

Allergic rhinitis and asthma are two diseases with very similar causes. Studies have found that the probability of asthma in patients with allergic rhinitis is about ten times higher than that in normal people. Children have relatively weaker immune function than adults, so they have higher probability of allergic rhinitis combined with asthma. Allergic rhinitis combined with asthma is more difficult to treat than single disease. Although symptomatic treatment, pidotimod and other immune enhancers can alleviate the disease to a certain extent, they are not radical treatment measures. Dermatophagoides farinae drops are immunotherapy preparations and belong to the category of sublingual immunotherapy (SLIT), their essential component is the dermatophagoides farinae vaccine, and they can stimulate the body to produce an immune response to allergens and eventually produce desensitization effect[7,8]. In this paper, dermatophagoides farinae drops combined with pidotimod were used for the treatment of allergic rhinitis combined with asthma, and the effect of the therapeutic regimen on children’s condition was discussed.

Allergic rhinitis and asthma are both essentially chronic inflammatory diseases. Repeated attacks can cause children to be in the systemic inflammatory response state. Various inflammatory factors are abnormally synthesized and released into blood, which further aggravates the sensitivity of the body and leads to continuous allergic reactions. IL-2 is an important cytokine secreted by Th1 cells, which can induce the proliferation of T lymphocytes and the production of immunoglobulin by B lymphocytes, and play an important role in anti-infection, anti-tumor and other cellular immunity[9,10]. The content of IL-2 decreases significantly in the children with allergic rhinitis and asthma, which was a sign of the inhibition of Th1 cell function. IL-4 and IL-5 are secreted by Th2 cells. The hyperfunction of Th1 cells in children with allergic diseases leads to abnormal secretion of IL-4 and IL-5[11,12]. IL-9 can synergize with IL-4 and induce the production of relevant antibodies, and the airway responsiveness is mostly higher in children with high IL-9 content in circulating blood[13]. IL-18 can specifically up-regulate IgE synthesis, activate Th2 cells, etc, and the content of IL-18 increases with the aggravation of the variant disease[14,15]. The
results in the paper showed that compared with those of control group, serum IL-2 contents of dermatophagoides farinae drops group were higher at the corresponding time points after treatment whereas IL-4, IL-5, IL-9 and IL-18 contents were lower, which proves that the dermatophagoides farinae drops group combined with pidotimod treatment is more effective in inhibiting the systemic inflammatory response of children with allergic rhinitis combined with asthma.

The inhibition of cellular immune function is one of the important reasons for the occurrence of allergic rhinitis, asthma and other allergic diseases, which is specifically manifested as the decreased levels of CD3+, CD4+, CD8+ and other T lymphocytes, and eventually leads to the imbalance of CD4+/CD8+ ratio[16,17]. In this paper, the result showed that compared with those of control group, peripheral blood CD3+, CD4+, CD8+ and CD4+/CD8+ levels of dermatophagoides farinae drops group were higher at the corresponding time points after treatment, this confirms that the dermatophagoides farinae drops combined with pidotimod can more effectively enhance the cellular immune function, and this is also one of the evidences of controlled condition in children with allergic rhinitis combined with asthma. Humoral immunity is also involved in the occurrence and development of allergic diseases, IgE is a typical allergic reaction marker, and its content is highly positively correlated with disease severity[18,19]; immunoglobulin such as IgA, IgM, and IgG are immune factors with protective effects, and the reduction of their expression can lead to immunocompromise and increase the probability of pathogenic bacteria infection[20,21]. The results in the study showed that compared with those of control group, serum IgA, IgM and IgG contents of dermatophagoides farinae drops group were higher at the corresponding time points after treatment whereas IgE contents were lower, which confirms that dermatophagoides farinae drops combined with pidotimod treatment could more effectively balance the children’s humoral immune function and enhance their ability to resist pathogenic bacteria.

Dermatophagoides farinae drops combined with pidotimod can effectively inhibit the degree of inflammatory response, regulate cellular and humoral immune function and ultimately optimize the condition of children with allergic rhinitis combined with asthma. Therefore, it is worthy to be popularized and applied in future clinical practice.

References


