Effect of adjuvant oral immunoglobulin therapy on the illness of children with rotavirus enteritis

Hong Jiang

Pediatrics Department, Ziyang First People’s Hospital in Sichuan Province, Ziyang, Sichuan Province, 641300

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ABSTRACT

Objective: To investigate the effect of adjuvant oral immunoglobulin therapy on the illness of children with rotavirus enteritis. Methods: A total of 170 children with rotavirus enteritis who were treated in the hospital between May 2016 and December 2017 were divided into control group (n=85) and immunoglobulin group (n=85) by random number table method. Control group received clinical routine therapy for rotavirus enteritis, immunoglobulin group received the oral immunoglobulin combined with routine therapy, and the treatment lasted for 7d. The differences in the contents of inflammatory factors, immunoglobulins and complements in serum as well as the levels of intestinal flora count in feces sample tissue were compared between the two groups before and after treatment. Results: Before treatment, the differences in the contents of inflammatory factors, immunoglobulins and complements in serum as well as the levels of intestinal flora count in feces samples were not statistically significant between the two groups of patients. After 7d of treatment, inflammatory factors IL-2, IL-6, IL-15 and TNF-α contents in serum of immunoglobulin group were lower than those of control group; IgG, IgA, IgM, C3 and C4 contents were higher than those of control group; bifidobacterium and lactobacillus count levels in feces samples were higher than those of control group whereas E. coli count level was lower than that of control group. Conclusion: Adjuvant oral immunoglobulin therapy can help to relieve the inflammatory response, enhance the immune function and balance the intestinal flora distribution in children with rotavirus enteritis.

1. Introduction

Rotavirus enteritis is the most common viral enteritis in children in our country, which is mostly caused by group A rotavirus and occurs frequently in the autumn[1,2]. The course of the disease is usually self-limited, but the symptoms of the weak are more serious, and it may develop into chronic symptomatic diarrhea in those with immune dysfunction, which can directly affect the growth and development of children. To enhance the children's immunity is a reliable way to enhance the antiviral ability, alleviate the illness and shorten the course of disease, and the immunoglobulin, as immune agent, has been successfully applied in the adjuvant treatment of a variety of infectious diseases[3,4]. In the study, adjuvant immunoglobulin therapy was added on the basis of conventional treatment, and its application value was discussed from inflammation, immune function and intestinal flora distribution in order to provide clinical reference for subsequent treatment of such infants.

2. Information and methods

2.1 General information

A total of 170 children with rotavirus enteritis who were treated in the hospital between May 2016 and December 2017 were chosen as the research subjects and divided into control group (n=85) and
immunoglobulin group \((n=85)\) by random number table method. There were 43 males and 42 females in the control group, and they were 2-9 years old; there were 44 males and 41 females in the immunoglobulin group, and they were 1-10 years old. There was no statistically significant difference in gender and age distribution between the two groups, and the follow-up study was approved by the ethics committee.

2.2 Inclusion and exclusion criteria

Inclusion criteria: (1) in accordance with the diagnostic criteria for rotavirus enteritis; (2) without history of rotavirus enteritis within 6 months prior to admission; (3) whose family members signed the informed consent. Exclusion criteria: (1) combined with severe autoimmune diseases; (2) combined with pneumonia and other systemic infectious diseases; (3) combined with severe congenital diseases such as congenital heart disease.

2.3 Therapy

Control group received clinical routine therapy for rotavirus enteritis, including antivirus, fluid infusion, regulating electrolyte and acid-base balance, nutritional support, etc.

Children accept immunoglobulin oral immunoglobulin group with conventional therapy, specific as follows: 400 mg/kg intravenous immunoglobulin was dissolved in double volume of 5% glucose liquid, which was administered by intravenous drip, at 20 drops/min at first, then at 50 drops/min after 15 min and at 200 mg/kg after that, 1 time/d, for 7 d.

2.4 Observation indexes

Before treatment and after 7 d of treatment, peripheral blood specimens were obtained from two groups of children to separate and obtain the upper serum for test, and enzyme-linked immunosorbent assay method was used to detect the contents of inflammatory factors interleukin-2 (IL-2), interleukin-6 (IL-6), interleukin-15 (IL-15) and tumor necrosis factor \(\alpha\) (TNF-\(\alpha\)). The serum contents of immunoglobulin IgG, IgA and IgM as well as complement C3 and C4 were detected by scattering turbidity. The feces samples were obtained from two groups of children at the same point in time to determine the intestinal flora counts, including bifidobacterium, lactobacillus and E. coli.

2.5 Statistical methods

Inflammatory factor, immunoglobulin and complement contents as well as intestinal flora count levels all belonged to measurement data and were input in software SPSS 24.0 to calculate the statistic \(P\) by \(t\) test, and \(P<0.05\) was set as the standard of statistical significance in the differences.

3. Results

3.1 Inflammatory factors

Comparison of serum inflammatory factors IL-2, IL-6, IL-15 and TNF-\(\alpha\) contents between two groups of children was as follows: before treatment, the differences in serum IL-2, IL-6, IL-15 and TNF-\(\alpha\) contents were not statistically significant between the two groups of children \((P>0.05)\). After 7 d of treatment, serum IL-2, IL-6, IL-15 and TNF-\(\alpha\) contents of both groups were lower than those before treatment; serum IL-2, IL-6, IL-15 and TNF-\(\alpha\) contents of immunoglobulin group were lower than those of control group \((P<0.05)\), shown in Table 1.

3.2 Immunoglobulin and complement

Comparison of serum contents of immunoglobulin IgG, IgA and IgM as well as complement C3 and C4 between two groups of children was as follows: before treatment, the differences in serum IgG, IgA, IgM, C3 and C4 contents were not statistically significant between the two groups of children \((P>0.05)\). After 7 d of treatment, serum IgG, IgA, IgM, C3 and C4 contents of both groups

### Table 1.

Comparison of serum inflammatory factor contents between two groups of children before and after treatment (pg/mL).

<table>
<thead>
<tr>
<th>Groups</th>
<th>(n)</th>
<th>IL-2 Before treatment</th>
<th>IL-2 After 7 d of treatment</th>
<th>IL-6 Before treatment</th>
<th>IL-6 After 7 d of treatment</th>
<th>IL-15 Before treatment</th>
<th>IL-15 After 7 d of treatment</th>
<th>TNF-(\alpha) Before treatment</th>
<th>TNF-(\alpha) After 7 d of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>85</td>
<td>15.39±1.76</td>
<td>11.07±1.53*</td>
<td>15.42±1.68</td>
<td>7.49±0.81*</td>
<td>39.42±4.63</td>
<td>21.88±2.69*</td>
<td>20.61±2.85</td>
<td>12.17±1.65</td>
</tr>
<tr>
<td>Immunoglobulin group</td>
<td>85</td>
<td>15.42±1.68</td>
<td>7.49±0.81*</td>
<td>25.69±3.07</td>
<td>11.87±1.56*</td>
<td>39.61±4.57</td>
<td>13.27±1.56*</td>
<td>20.57±2.69</td>
<td>7.09±0.83*</td>
</tr>
<tr>
<td>(t)</td>
<td></td>
<td>0.183</td>
<td>9.193</td>
<td>0.217</td>
<td>8.485</td>
<td>0.330</td>
<td>10.493</td>
<td>0.265</td>
<td>7.498</td>
</tr>
<tr>
<td>(P)</td>
<td></td>
<td>&gt;0.05</td>
<td>&lt;0.05</td>
<td>&gt;0.05</td>
<td>&lt;0.05</td>
<td>&gt;0.05</td>
<td>&lt;0.05</td>
<td>&gt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Note: compared with same group before treatment, \(*P<0.05\).
Comparison of serum complement contents between two groups of children before and after treatment (g/L).

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Before treatment</th>
<th>After 7 d of treatment</th>
<th>t</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>85</td>
<td>5.38±0.59</td>
<td>6.29±0.68</td>
<td>0.291</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Immunoglobulin group</td>
<td>85</td>
<td>5.41±0.56</td>
<td>8.16±0.95</td>
<td>0.48±0.06</td>
<td>0.91±0.11</td>
</tr>
</tbody>
</table>

Note: compared with same group before treatment, \( P < 0.05 \).

Comparison of intestinal flora count in feces samples between two groups of children before and after treatment (Copy/g wet feces).

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Before treatment</th>
<th>After 7 d of treatment</th>
<th>t</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>85</td>
<td>0.67±0.09</td>
<td>0.82±0.09</td>
<td>0.195</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Immunoglobulin group</td>
<td>85</td>
<td>0.68±0.08</td>
<td>0.97±0.13</td>
<td>0.195</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Note: compared with same group before treatment, \( P < 0.05 \).

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

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Before treatment</th>
<th>After 7 d of treatment</th>
<th>t</th>
<th>P</th>
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<tbody>
<tr>
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<td>85</td>
<td>0.67±0.09</td>
<td>0.82±0.09</td>
<td>0.195</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Immunoglobulin group</td>
<td>85</td>
<td>0.68±0.08</td>
<td>0.97±0.13</td>
<td>0.195</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Note: compared with same group before treatment, \( P < 0.05 \).

Comparison of bifidobacterium, lactobacillus and E. coli count levels in feces samples of children before and after treatment.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Before treatment</th>
<th>After 7 d of treatment</th>
<th>t</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>85</td>
<td>7.18±0.92</td>
<td>8.46±0.92</td>
<td>0.318</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Immunoglobulin group</td>
<td>85</td>
<td>7.16±0.85</td>
<td>9.17±0.98</td>
<td>0.318</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Note: compared with same group before treatment, \( P < 0.05 \).

3.3 Intestinal flora distribution

Comparison of bifidobacterium, lactobacillus and E. coli count levels in feces samples between two groups of children was as follows: before treatment, the differences in bifidobacterium, lactobacillus and E. coli count levels in feces samples were not statistically significant between the two groups of children (\( P > 0.05 \)). After 7 d of treatment, bifidobacterium and lactobacillus count levels in feces samples of both groups were higher than those before treatment whereas E. coli count levels were lower than those before treatment; bifidobacterium and lactobacillus count levels in feces samples of immunoglobulin group were higher than those of control group whereas E. coli count level was lower than that of control group (\( P < 0.05 \)), shown in Table 4.

4. Discussion

Rotavirus enteritis has become the main cause of diarrhea in children. It is usually manifested as yellow watery stool, which is frequent and abundant, and is mostly accompanied by fever[5,6]. The course of diarrhea is mostly self-limited in those with normal immune function, but the immune function of children is not fully developed, and the protracted course of disease easily occurs in the weak and even causes serious complications of other organs. Besides the basic means such as fluid infusion and electrolyte balance regulation, actively enhancing the immune function is a reliable way to accelerate the recovery of children with rotavirus enteritis. In this study, oral immunoglobulin was provided on the basis of conventional treatment, and the effect of the adjuvant therapy on the children's condition was discussed.

The rotavirus infection in children can directly activate the body's inflammatory response and lead to the release of a large number of inflammatory cytokines, and severe cases form inflammatory cascade and aggravate the disease. IL-2 is produced by antigen-activated CD4+T cells, it enhances the killing vitality of NK cells to produce antiviral action, many studies have confirmed that there is high expression of IL-2 in virus infectious disease, and the specific expression is consistent with the illness severity[7,8]. IL-6 is synthesized by activated T cells when the body is stimulated by the virus, which can initiate the inflammatory response caused by the pathogenic bacteria and participate in the immune function damage[9,10]. IL-15 and IL-2 have many similarities in function, they can promote the differentiation and proliferation of B lymphocytes and play an important role in the immune response to resist early pathogen infection, and its content change is the same as that of IL-2[11]. TNF-α is secreted by activated mononuclear macrophages, which can promote the synthesis and secretion of inflammatory factors such as IL-6, further achieve neutrophil chemotaxis and increase vascular permeability[12,13]. The study results showed that serum contents of above inflammatory factors of both groups were declining after treatment, and the decrease in these indexes of immunoglobulin group was more significant, indicating that oral immunoglobulin preparations can further inhibit the systemic inflammatory response and control the disease progression in
children with rotavirus enteritis.

Humoral immune deficiency plays a key role in the occurrence and development of rotavirus enteritis, and IgA, especially the secretory IgA, is the main antibody of anti-infection immunity in local mucosa, and can neutralize rotavirus and reduce its virulence[14,15]; IgG is the main component of serum immunoglobulin, which has multiple functions such as anti-virus, virus neutralization and immune regulation, and plays an important role in the anti-infection of the newborn[16,17]; IgM is the immunoglobulin with the highest molecular weight, which has powerful functions such as sterilization, complement activation and immune regulation[18]. The complement C3 and C4 also play an important role in the humoral immune function, they can enhance the anti-pathogen effect of B lymphocytes, and the C3 and C4 contents mostly decrease in those with immune deficiency[19]. The study results showed that serum IgG, IgA, IgM, C3 and C4 contents of both groups increased after treatment, and the increase in immunoglobulin group was more significant, it shows that oral immunoglobulin therapy on the basis of conventional symptomatic treatment can effectively enhance the children’s humoral immune function, and this is also one of the internal causes of optimization in children's condition.

The viral infections and the increased number of diarrhea can both lead to intestinal flora disorder in children with rotavirus enteritis, the quantity of dominant bacterial community decreases while the quantity of opportunistic pathogen increases, it leads to intestinal mucosal barrier dysfunction, and the pathogenic bacteria enter into the blood via the intestinal mucosa and forms toxemia, which is the main cause of a series of systemic reactions in the children. In this study, the bacterial flora distribution in feces specimens were compared between the two groups of patients, and the result showed that the probiotics bifidobacterium and lactobacillus count levels of both groups increased whereas opportunistic pathogen E. coli count levels decreased after treatment, and the change in above flora count levels in immunoglobulin group was more significant, explaining that adjuvant oral immunoglobulin therapy can be more effective to regulate the intestinal flora distribution and optimize the intestinal function.

To sum up, adjuvant oral immunoglobulin therapy on the basis of symptomatic treatment can effectively reduce the inflammatory response, enhance the humoral immune function and optimize the intestinal flora distribution in children with rotavirus enteritis, it is a reliable way to shorten the course of disease and improve the treatment outcome, and it is worthy of popularization and application in clinical practice in the future.

References