Observation of curative effect in antibiotics associated diarrhea children treated by pidotimod and the influence on the inflammation factors and the immune function

Zhao–Yang Yin*, Yao Chen, Ting Zhao

Department of Pediatrics, Central Hospital of Shangluo City, Shaanxi, Shangluo 726000, China

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ABSTRACT

Objective: To explore the curative effect in antibiotics associated diarrhea children treated by pidotimod and the influence on the inflammation factors and the immune function. Methods: A total of 82 cases antibiotic associated diarrhea children were divided into control group and observation group according to random number table method, 41 cases in each group, children in two groups were given conventional treatment, on this basis, children in observation group were with pidotimod treatment, they were treated for 2 weeks, compared the clinical efficacy and immune globulin: IgA, IgG, IgM, T cell subgroup: CD3+, CD4+, CD8+, CD4+/CD8+, and inflammation factors: tumor necrosis factor-α (TNF-α) and interleukin 6 (IL-6). Results: The total effective rate in control group was 75.61%, it was significantly lower than 95.12% in observation group; The levels of CD3+,CD4+,CD4+/CD8+, IgA, IgG after treatment in two groups were significantly rised while the levels of TNF-α, IL-6 were significantly reduced than before treatment, The amplitude of index above in observation group was greater than the control group, the difference were all statistically significant. Conclusion: The curative effect in antibiotics associated diarrhea children treated by pidotimod is obvious, it can reduce inflammation, improve immunity.

1. Introduction

Antibiotic treatment is often used in children with infectious diseases, but the antibiotic use can cause intestinal flora imbalance which may lead to the occurrence of antibiotic associated diarrhea[1,2]. Antibiotic associated diarrhea is one of the most common drug diarrhea in children. In recent years, its morbidity is getting higher and higher with the abuse of broad-spectrum antibiotics[3,4]. Studies have found that in antibiotic associated diarrhea children with intestinal flora imbalance, resulting in low immune function[5,6]. In this study, we used a new type of immune regulator pidotimod to treat antibiotic associated diarrhea in children and we got satisfactory effects, reports as follows.

2. Materials and methods

2.1 General information

A total of 82 cases of children with antibiotic associated diarrhea in the pediatric department of Shangluo Central Hospital from January 2014 to October 2015 were selected as the research objects. All children were selected in accordance with the following conditions: (1) conformed to the diagnostic criteria of antibiotic associated diarrhea; (2) Aged 3 months to 8 years; (3) children’s family informed the consent and voluntary participated the study; (4) excluded other causes of diarrhea; (5) excluded patients with viral enteritis and other inflammatory diseases; (6) excluded children with immune system disease. According to the random number table method, all children were divided into two groups with each 41 cases. In the observation group, male 22 cases, female 19 cases; age from 1 to 6 years old with an average (3.41±1.22) years;
Severity of diarrhea: mild 13 cases, moderate 22 cases and severe 6 cases; Antibiotic associated diarrhea: First generation cephalosporin 18 cases, Third generation cephalosporin 23 cases. In the control group, male 20 cases, female 21 cases; age from 6 months to 5 years old with an average (3.01±1.20) years; Severity of diarrhea: mild 11 cases, moderate 23 cases and severe 7 cases; Antibiotic associated diarrhea: First generation cephalosporin 14 cases, Third generation cephalosporin 27 cases. There was no significant difference in general data between the two groups.

2.2 Treatment methods

Both two groups children were given conventional symptomatic treatment, including anti-diarrheal, anti-inflammatory, nutritional support and the use of Micro-probiotics. On this basis, the observation group were given pidotimod treatment, with oral 400 mg pidotimod, two times a day, both two groups were treated for 2 weeks.

2.3 Evaluation indexes

2.3.1 Clinical curative effect

Markedly effective: the frequency and symptoms of defecation and the accompanied characteristics of the fever with significant improvement; Effective: after the treatment, the frequency and symptoms of defecation and the accompanied characteristics of the fever improved; Invalid: did not appear effect and effective symptoms. Total effective rate: Effect rate add Effective rate.

2.3.2 Immune function indexes

Extracted children’s fasting venous blood before and after treatment, the one way agar diffusion method was used to detect immunoglobulin: IgA, IgG and IgM. Flow cytometry was used to detect the T cell subsets: CD3+, CD4+, CD8+, and calculated CD4+/CD8+ ratio.

Table 1.
Comparison the changes of T cell subsets in two groups before and after treatment.

<table>
<thead>
<tr>
<th>Group</th>
<th>Cases</th>
<th>Time</th>
<th>CD3+(%)</th>
<th>CD4+(%)</th>
<th>CD8+(%)</th>
<th>CD4+/CD8+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>41</td>
<td>Before treatment</td>
<td>47.47±6.05</td>
<td>31.87±3.12</td>
<td>27.87±4.02</td>
<td>1.14±0.21</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>66.01±6.51*</td>
<td>40.23±4.26*</td>
<td>26.49±4.11</td>
<td>1.52±0.23*</td>
</tr>
<tr>
<td>Control</td>
<td>41</td>
<td>Before treatment</td>
<td>46.64±6.12</td>
<td>32.08±3.29</td>
<td>28.09±4.20</td>
<td>1.14±0.20</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>58.28±6.64*</td>
<td>35.27±3.85*</td>
<td>26.79±4.00</td>
<td>1.31±0.24*</td>
</tr>
</tbody>
</table>

Ps: Compared with before treatment, *P<0.05; Compared with the control group after treatment, #P<0.05.

Table 2.
Comparison the changes of immunoglobulin in two groups before and after treatment (g/L).

<table>
<thead>
<tr>
<th>Group</th>
<th>Cases</th>
<th>Time</th>
<th>IgA</th>
<th>IgG</th>
<th>IgM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>41</td>
<td>Before treatment</td>
<td>1.29±0.14</td>
<td>7.02±1.14</td>
<td>1.27±0.12</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>2.20±0.20*</td>
<td>13.62±2.06*</td>
<td>1.33±0.18</td>
</tr>
<tr>
<td>Control</td>
<td>41</td>
<td>Before treatment</td>
<td>1.28±0.15</td>
<td>7.05±1.20</td>
<td>1.29±0.11</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>1.62±0.19*</td>
<td>10.14±2.21</td>
<td>1.31±0.21</td>
</tr>
</tbody>
</table>

Ps: Compared with before treatment, *P<0.05; Compared with the control group after treatment, #P<0.05.

2.3.3 Inflammatory factors

Extracted children’s fasting venous blood before and after treatment, centrifugal separation of serum, the tumor necrosis factor alpha (TNF-α) and interleukin -6 (IL-6) were detected by enzyme linked immunosorbent assay (ELISA).

2.4 Statistical treatment

Using SPSS 20.0 software for statistical analysis, the measurement data were expressed by Mean ± SD and the total effective rate was compared by chi square test, the count data was compared by T test, \( P<0.05 \) was considered the difference to be statistically significant.

3. Results

3.1 Comparison the clinical curative effect of the two groups after treatment

After treatment, in the control group, 20 cases were markedly effective, 11 cases were effective, 10 cases were invalid, the total effective rate was 75.61%; in the observation group: 25 cases were markedly effective, 14 cases were effective, 2 cases were invalid, the total effective rate was 95.12% after treatment; The difference between the two groups was significant (\( P<0.05 \)).

3.2 Comparison the Changes of T cell subsets in two groups before and after treatment

After treatment, both two groups CD3+, CD4+ and CD4+/CD8+ were significantly increased, the difference was statistically significant (\( P<0.05 \)) compared with the group before treatment; After treatment, the CD3+, CD4+ and CD4+/CD8+ in the observation group were \((66.01±6.51\%)\), \((40.23±4.26\%)\) and \((1.52±0.23\%)\) respectively, that was significantly higher than the control group after...
treatment and the difference was statistically significant ($P<0.05$). See table 1.

3.3 Comparison the Changes of immunoglobulin in two groups before and after treatment

After treatment, both two groups IgA and IgG were significantly increased compared with before treatment and the difference was statistically significant ($P<0.05$); After treatment, the IgA and IgG in the observation group were (2.20±0.20) g/L and (13.62±2.06) g/L respectively, that was significantly higher than the control group after treatment ($P<0.05$). See table 2.

3.4 Comparison the changes of inflammatory factors in two groups before and after treatment

After treatment, both two groups TNF-α and IL-6 were significantly decreased compared with before treatment and the difference was statistically significant ($P<0.05$); After treatment, the TNF-α and IL-6 in the observation group were (5.51±1.13) ng/L and (15.26±3.90) ng/L respectively, that was significantly lower than the control group after treatment ($P<0.05$). See table 3.

Table 3. Comparison the changes of inflammatory factors in two groups before and after treatment (ng/L).

<table>
<thead>
<tr>
<th>Group</th>
<th>Cases</th>
<th>Time</th>
<th>TNF-α</th>
<th>IL-6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>41</td>
<td>Before treatment</td>
<td>12.11±2.02</td>
<td>36.11±4.80</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>5.51±1.13*</td>
<td>15.26±3.90*</td>
</tr>
<tr>
<td>Control</td>
<td>41</td>
<td>Before treatment</td>
<td>11.46±1.84</td>
<td>34.57±4.45</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>7.89±1.24</td>
<td>22.18±4.27*</td>
</tr>
</tbody>
</table>

Ps: Compared with before treatment, *$P<0.05$; Compared with the control group after treatment, **$P<0.05$.

4. Discussions

Children are in the stage of physical development, their immune function is low and susceptible to external pathogens infection and thus the emergence of infectious diseases[7,8]. Antibiotics, especially the beta-lactam antibiotic kill bacteria and at the same time will kill the intestinal normal flora, the beneficial bacteria reduce, Gram-negative bacteria and other harmful bacteria proliferate, causing intestinal flora imbalance. Meanwhile, the endotoxin produced in great quantities, causing intestinal inflammatory response, intestinal mucosa damage, intestinal function disorder and antibiotic associated diarrhea[9,10]. In addition, intestinal flora imbalance will lead to the decreased immunity of children, reduce the ability to resist infection, delaying the time of primary infectious disease cure and exacerbate the risk of antibiotic associated diarrhea[11,12].

Children often use anti-diarrheal, anti-inflammatory and nutritional support for antibiotic associated diarrhea treatment, the probiotics treatment has gradually been widely used in the prevention and treatment of antibiotic associated diarrhea in recent years[13,14]. By oral administration of probiotics, it can change the structure of intestinal flora, form new balance of intestinal flora system, inhibit the proliferation of pathogenic bacteria, increase the number of probiotics, thereby reducing the content of endotoxin which released by pathogenic bacteria, alleviating intestinal injury and effectively alleviate the clinical symptoms. In addition, parts of probiotics can secrete some antibiotics that can play a certain antibacterial effect[15,16]. Recent studies have found that antibiotic associated diarrhea children with intestinal flora imbalance, which resulting in low immune function[5,6]. On the basis of routine treatment of antibiotic associated diarrhea in children, we used a new type of immune modulator pidotimod, and we found that the total effective rate in the observation group was 95.12%, significantly higher than 75.61% that in the control group; In addition, after treatment, both two groups’ CD3+, CD4+, CD4+/CD8+, IgA and IgG were significantly higher than those before treatment, and those in the observation group was higher than those in the control group and the difference was significant. The results showed that pidotimod had significantly effect in the treatment of children with antibiotic associated diarrhea and could improve the immunity of children.

Pidotimod is an immune enhancer, by chemical synthesis, it can promote the proliferation of lymphocytes and neutrophile granulocytes, enhance the phagocytic activity of macrophages and neutrophils, so as to strengthen the ability of removing pathogenic bacteria, effectively inhibit and kill pathogens[17]; it also can activate the body’s natural killer cells, enhance the cell killing function, and inhibit Th2 cell function, restore the balance of Th1/Th2, and improve the immune function[18]; Pidotimod can significantly increase the protective effect of respiratory secretion type IgA synthesis and meanwhile affect the humoral and cellular immunity[19].

Inflammation exists in children with antibiotic associated diarrhea, mainly due to intestinal microFlora imbalance, it caused the endotoxin release and intestinal mucosal injury aggravate, and causing intestinal inflammation. IL-6 and TNF-α are the main inflammatory cytokines, which are regulated by the body's own immune. We also found that after treatment, both the two groups’ TNF-α and IL-6 were significantly lower than those before treatment, and those in the observation group was lower than those in the control group and the difference was significant. The results showed that pidotimod could also reduce inflammation in children with antibiotic associated diarrhea, the reasons may be that pidotimod could enhance immune function, restore intestinal bacteria balance, thereby reducing the bacteria endotoxin release and intestinal injury, so the intestinal barrier is repaired and the
inflammation is controlled[20,21].

In summary, our results found that pidotimod combined conventional treatment can significantly improve the clinical efficacy, reduce the inflammatory response and improve the body’s immunity for children with antibiotic associated diarrhea.

References


