Protective effect of perioperative recombinant human growth hormone application on intestinal mucosal barrier function in patients with intestinal obstruction and the assessment of immune inflammatory response

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ABSTRACT

Objective: To study the protective effect of perioperative recombinant human growth hormone (r-hGH) application on intestinal mucosal barrier function in patients with intestinal obstruction and the influence on the immune inflammatory response. Methods: 60 patients with intestinal obstruction who underwent surgical treatment in our hospital between February 2013 and July 2016 were selected as the research subjects and divided into the control group (n=34) who received conventional surgical treatment and the observation group (n=26) who received surgery combined with perioperative r-hGH treatment. The serum levels of intestinal mucosal barrier indexes, immunoglobulin and inflammatory response indicators were compared between two groups of patients before and after treatment. Results: Before treatment, differences in serum levels of intestinal mucosal barrier indexes, immunoglobulin and inflammatory response indicators were not statistically significant between the two groups of patients. After treatment, serum intestinal mucosal barrier indexes Endotoxin, D-Lactate and DAO levels in observation group were lower than those in control group, immunoglobulin IgA, IgM and IgG levels were higher than those in control group, and inflammatory response indicators IL-1, IL-6, PCT and TNF-α levels were lower than those in control group patients. Conclusion: Perioperative r-hGH application in patients with intestinal obstruction can protect the intestinal mucosal barrier, also optimize the humoral immunity and suppress the systemic inflammatory response.

1. Introduction

Intestinal obstruction is a kind of intestinal content passage disorder, it is one of the most common clinical acute abdomen diseases, it progresses rapidly, and the mortality is high in the old and infirm[1,2]. Surgical separation of adhered bowel or direct resection of the obstructed part is currently the main method to cure intestinal abnormality, but there is still a significant postoperative intestinal mucosal barrier dysfunction in a large part of patients, which further leads to internal environment disturbance and influences the recovery of disease and the prognosis of patients. Recombinant human growth hormone (r-hGH) is produced by recombinant DNA technology, which has multiple functions such as activating the immune system, promoting tissue organ cell regeneration and regulating central nervous function, and has become a common drug to optimize patients’ body state after surgical treatment[3,4]. In the following studies, the protective effect of perioperative r-hGH application on intestinal mucosal barrier in patients with intestinal obstruction and the influence on the immune inflammatory response were analyzed.
2. Information and methods

2.1 Case information

A total of 60 patients with intestinal obstruction who underwent surgical treatment in our hospital between February 2013 and July 2016 were selected as the research subjects, and the patients or family members signed the consent form. After the therapies were reviewed, the enrolled patients were divided into the control group (n=34) who received conventional surgical treatment and the observation group (n=26) who received surgery combined with perioperative r-hGH treatment. Control group included 18 male cases and 15 female cases that were 38-80 years old; observation group included 15 male cases and 11 female cases that were 40-78 years old. The gender and age distribution of the two groups were not significant (P>0.05), and the study was approved by the hospital ethics committee.

2.2 Inclusion and exclusion criteria

Inclusion criteria: (1) B ultrasound indicated intestinal obstruction; (2) associated with clinical criteria such as typical persistent severe abdominal pain and vomiting; (3) without the history of intestinal obstruction or gastrointestinal surgery. Exclusion criteria: (1) with intestinal tumor-induced obstruction; (2) associated with chronic intestinal disorders such as Crohn's disease and ulcerative colitis; (3) associated with systemic infectious diseases; (4) associated with autoimmune deficiency disease.

2.3 Therapy

Control group of patients received conventional surgery for intestinal obstruction, the observation group of patients received perioperative r-hGH treatment, and it was as follows: 0.1 IU/kg r-hGH (Anhui Anke Biotechnology (Group) Co., Ltd., approved by S20093033), by subcutaneous injection 1 d before operation, 1 time/d. From 1d after operation, subcutaneous injection of r-hGH 0.1 IU/kg began, 0.1 IU/kg, 1 time/d, for consecutive 7 d.

2.4 Observation indexes

2.4.1 Intestinal mucosal barrier function indexes

Before treatment and after treatment (7 d after operation), fasting cubital venous blood was extracted from the two groups of patients, anti-coagulated and centrifuged at 2 500 r/min for 10 min to get supernatant. Improved perchloric acid method was used for determining the contents of serum endotoxin, enzyme-linked immunosorbent assay (ELISA) was used to determine serum the content of D-Lactate, and o-dianisidine reagent method was used to determine serum diamine oxidase (DAO) content.

2.4.2 Immunoglobulin and inflammatory response indicators

Before treatment and after treatment (7 d after operation), ELISA was used to determine the content of immunoglobulin A (IgA), immunoglobulin M (IgM) and immunoglobulin G (IgG) as well as the content of inflammatory factors interleukin-1 (IL-1), interleukin-6 (IL-6), procalcitonin (PCT) and tumor necrosis factor (TNF-α).

2.5 Statistical processing

Statistical software was SPSS 20.0 and the statisticians received professional training and passed the exam. Intestinal mucosal barrier function indexes, immunoglobulin, inflammatory response indicators and other measurement data were in terms of mean ± standard deviation, and comparison was by t test. P<0.05 was the standard of statistical significance in differences.

3. Results

3.1 Intestinal mucosal barrier function indexes

Comparison of serum intestinal mucosal barrier function indexes Endotoxin (EU/mL), D-Lactate (μg/mL) and DAO (U/mL) levels between two groups of patients before and after treatment was as follows: before treatment, differences in serum Endotoxin, D-Lactate and DAO levels were not statistically significant between two groups of patients (P>0.05); after treatment, serum Endotoxin, D-Lactate and DAO levels were lower than those before treatment, serum Endotoxin, D-Lactate and DAO levels in observation group were lower than those in control group, and differences in serum intestinal mucosal barrier function indexes were statistically significant within group before and after treatment as well as between groups after treatment (P<0.05), shown in Table 1.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Endotoxin Before treatment</th>
<th>Endotoxin After treatment</th>
<th>D-Lactate Before treatment</th>
<th>D-Lactate After treatment</th>
<th>DAO Before treatment</th>
<th>DAO After treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>34</td>
<td>0.39±0.05</td>
<td>0.28±0.03</td>
<td>22.47±3.21</td>
<td>13.38±1.76</td>
<td>10.16±1.98</td>
<td>7.23±0.85</td>
</tr>
<tr>
<td>Observation group</td>
<td>26</td>
<td>0.38±0.04</td>
<td>0.20±0.03</td>
<td>22.53±3.19</td>
<td>9.26±1.05</td>
<td>10.23±1.87</td>
<td>4.18±0.53</td>
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<tr>
<td>T</td>
<td></td>
<td>0.163</td>
<td>5.893</td>
<td>0.236</td>
<td>9.283</td>
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<td>9.674</td>
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<tr>
<td>P</td>
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<td>&gt;0.05</td>
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</table>

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

Table 2.
Comparison of serum IgA, IgM and IgG levels before and after treatment (g/L).

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>IgA Before treatment</th>
<th>After treatment</th>
<th>IgM Before treatment</th>
<th>After treatment</th>
<th>IgG Before treatment</th>
<th>After treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>34</td>
<td>2.74±0.35</td>
<td>2.98±0.37</td>
<td>5.48±0.74</td>
<td>6.18±0.73</td>
<td>11.23±1.84</td>
<td>12.53±1.54</td>
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<tr>
<td>Observation group</td>
<td>26</td>
<td>2.75±0.31</td>
<td>3.41±0.45</td>
<td>5.79±0.72</td>
<td>7.24±0.85</td>
<td>11.53±1.79</td>
<td>14.18±2.31</td>
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</tbody>
</table>

<table>
<thead>
<tr>
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<td>&gt;0.05</td>
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</table>

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

Table 3.
Comparison of serum inflammatory response indicator levels before and after treatment.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>IL-1 Before treatment</th>
<th>After treatment</th>
<th>IL-6 Before treatment</th>
<th>After treatment</th>
<th>PCT Before treatment</th>
<th>After treatment</th>
<th>TNF-α Before treatment</th>
<th>After treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>34</td>
<td>9.37±0.98</td>
<td>6.13±0.72</td>
<td>17.58±2.14</td>
<td>11.46±1.73</td>
<td>2.18±0.32</td>
<td>1.05±0.14</td>
<td>5.38±0.72</td>
<td>2.74±0.31</td>
</tr>
<tr>
<td>Observation group</td>
<td>26</td>
<td>9.42±0.99</td>
<td>2.75±0.41</td>
<td>17.63±2.09</td>
<td>5.09±0.73</td>
<td>2.21±0.29</td>
<td>0.62±0.08</td>
<td>5.34±0.69</td>
<td>1.53±0.21</td>
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</tr>
</tbody>
</table>

3.2 Immunoglobulin

Comparison of serum immunoglobulin IgA, IgM and IgG levels between two groups of patients before and after treatment was as follows: before treatment, differences in serum IgA, IgM and IgG levels were not statistically significant between two groups of patients (P>0.05); after treatment, serum IgA, IgM and IgG levels in both groups were higher than those before treatment, serum IgA, IgM and IgG levels in observation group were higher than those in control group, and differences in serum IgA, IgM and IgG levels were statistically significant within group before and after treatment as well as between groups after treatment (P<0.05), shown in Table 2.

3.3 Inflammatory response indicators

Comparison of serum inflammatory response indicators IL-1 (pg/mL), IL-6 (pg/mL), PCT (μg/L) and TNF-α (ng/mL) levels between two groups of patients before and after treatment was as follows: before treatment, differences in serum IL-1, IL-6, PCT and TNF-α levels were not statistically significant between two groups of patients (P>0.05); after treatment, serum IL-1, IL-6, PCT and TNF-α levels in both groups were significantly lower than those before treatment, serum IL-1, IL-6, PCT and TNF-α levels in observation group were significantly lower than those in control group, and differences in above serum inflammatory response indicators were statistically significant within group before and after treatment as well as between groups after treatment (P<0.05), shown in Table 3.

4. Discussion

Intestinal obstruction is one of the most common clinical acute abdomen diseases and also the disease with high emergency mortality rate, and early clarifying the cause of disease and implementing emergency operation is the best way to save patients' life[5,6]. Those with longer time of intestinal obstruction attack are possible to develop intestinal wall ischemia, perforation and necrosis, there is severe water electrolyte and acid-base balance disorder in the body, some patients may receive surgery to remove the diseased bowel, but severe intestinal mucosal barrier dysfunction will be left behind after operation, which directly affects the patients' rehabilitation[7]. r-hGH is a common multifunctional drug that is currently used to optimize the overall state of surgical patients and accelerate postoperative recovery. At present, the value of perioperative r-hGH application for intestinal obstruction has not been reported. In this study, r-hGH was used during the perioperative period of the intestinal obstruction, and its application value was specifically analyzed.

Numerous studies have shown that r-hGH can promote the intestinal cell proliferation and repair, increase the intestinal absorption and utilization of nutrients, and finally optimize the intestinal mucosal barrier function[8,9]. Endotoxin is splitted from the gram-negative bacteria thallus, D-Lactate is produced by the metabolism of intestinal bacteria, they massively shift into the circulating blood in the case of intestinal mucosal barrier function injury, and so their serum levels are the sensitive indicators to judge the intestinal mucosal barrier function[10,11]. DAO is produced when polyamine catabolic enzymes decompose the intestinal bacteria, it can enhance the Endotoxin damage to intestinal mucosa, it can be secreted into the blood and form high blood DAO disease in the case of intestinal mucosal barrier dysfunction, and it is a sign of intestinal dysfunction[12,13]. In the study, serum levels of above intestinal mucosal barrier function indexes were compared between the two
groups of patients, and it was found that serum Endotoxin, D-Lactate and DAO levels in observation group were lower than those in control group after treatment, confirming that r-hGH can protect the intestinal mucosal barrier.

Intestinal obstruction can lead to local and systemic intestinal inflammatory response, and long time of obstruction and vomiting can lead to loss of body fluids and nutrients, which can all lead to decline in the immune function. The humoral immune system is significantly affected by intestinal obstruction, and the patients are mainly characterized by the decreased levels of IgA, IgM and IgG[14,15]. In the study, perioperative immune globulin levels were compared between the two groups of patients, and it was found that after treatment, serum IgA, IgM and IgG levels in both groups were higher than those before treatment, which may be associated with the relief of obstruction and the remission of internal environmental disturbance; serum IgA, IgM and IgG levels in observation group were higher than those in control group after operation, confirming that the r-hGH therapy could improve the postoperative immune function of patients with intestinal obstruction and promote their recovery. After intestinal obstruction, intestinal mucosal barrier dysfunction as well as water electrolyte and acid-base imbalance is directly related to systemic inflammatory state, the release of IL-1, IL-6, PCT, TNF-α and other pro-inflammatory mediators can aggravate the intestinal mucosa edema, and a variety of bacteria and toxins permeate into the blood, cause bacteremia/toxaemia, and affect patients’ postoperative rehabilitation and overall prognosis[16,17]. In the study, perioperative inflammatory mediator levels in two groups of patients were analyzed, and the result showed that after treatment, serum IL-1, IL-6, PCT and TNF-α levels in both groups were lower than those before treatment, serum IL-1, IL-6, PCT and TNF-α levels in observation group were significantly lower than those in control group, it confirms that the perioperative r-hGH treatment can reduce the postoperative inflammatory response in patients with intestinal obstruction, and this is also one of the important mechanisms for it to optimize the intestinal mucosal barrier function.

Perioperative r-hGH therapy for patients with intestinal obstruction can effectively protect the intestinal mucosal barrier function, enhance the humoral immunity and inhibit the systemic inflammatory response, it is an effective way to optimize the outcomes of patients with intestinal obstruction, and it is worthy of popularization and application in clinical practice in the future.

References


