Effect of immune-enhancing enteral nutrition application before radical resection of rectal carcinoma on postoperative immune response level and trauma endurance capacity

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Objective: To study the effect of immune-enhancing enteral nutrition application before radical resection of rectal carcinoma on postoperative immune response level and trauma endurance capacity. Methods: A total of 94 patients who received radical resection of rectal carcinoma in our hospital between May 2013 and October 2015 were selected and randomly divided into EN group and control group, the EN group received preoperative immune-enhancing enteral nutrition preparations, and the control group received routine preoperative nutrition intervention. The same day after operation, peripheral blood mononuclear cells were collected to determine CD69 and HLA-DR levels, and serum was collected to determine the levels of IgM, IgG, inflammatory response indexes and stress response indexes. Results: CD69 and HLA-DR levels in peripheral blood mononuclear cells as well as IgM, IgG, TP, ALB, PA and TF levels in serum of EN group were significantly higher than those of control group, and serum CRP, YKL-40, IL-1β, TNF-α, IL-6, HSP70, ACTH, Cor and HO-1 levels of EN group were significantly lower than those of control group. Conclusion: Immune-enhancing enteral nutrition application before radical resection of rectal carcinoma can improve the immune function and nutritional status, strengthen trauma endurance capacity and relieve postoperative inflammatory response and stress response.

1. Introduction

Rectal carcinoma is one of the common malignant tumors of digestive tract, radical resection is the first choice for clinical treatment, and aided by postoperative chemotherapy, it can achieve ideal 5-year survival rate[1,2]. Most patients with rectal carcinoma have different degree of preoperative malnutrition and immune function decline, and the trauma caused by operation can cause nutrient consumption and inhibit immune response, which increase the occurrence risk of complications such as poor healing of incision, delayed gastrointestinal emptying as well as incision and systemic infection after radical resection of rectal carcinoma[3,4]. In recent years, the perioperative nutritional support in patients with rectal carcinoma has received more and more attention, the preoperative effective enteral nutrition intervention can not only improve the body's nutritional status and immune function, but can also enhance the body's capacity to endure surgical trauma, and it is conducive to the postoperative recovery[5]. Immune-enhancing enteral nutrition preparations contain the immune nutrients such as ω-3 polyunsaturated fatty acids (ω-3 PUFA), glutamine (Gln) and arginine (Arg), and have the outstanding value for improving immune function and enhancing immune response. In the following study, the effect of immune-enhancing enteral nutrition application before radical resection of rectal carcinoma on postoperative immune response level and trauma endurance capacity was analyzed.

2. Subjects and methods

2.1 Research subjects

A total of 94 patients who received radical resection of rectal
carcinoma in our hospital between May 2013 and October 2015 were selected as the research subjects, all patients were diagnosed with rectal cancer by preoperative histopathological examination and conformed to the indications for selective radical resection of rectal carcinoma, and the patients combined with intestinal obstruction and intestinal perforation, those requiring parenteral nutrition support and those receiving preoperative neoadjuvant chemotherapy were ruled out. Random number table was used to divide the included patients into EN group and control group, 47 cases in each group. EN group of patients received preoperative immune-enhancing enteral nutrition preparations, including 31 male cases and 16 female cases that were 42-66 years old; control group of patients received preoperative routine diet and nutrition intervention, including 33 male cases and 14 female cases that were 42-66 years old. The two groups of patients were not significantly different in general information (P>0.05).

2.2 Nutrition intervention methods

Control group of patients received preoperative regular diet and nutrition intervention, ate through the mouth, and orally took intestinal lavage solution 1 d before operation for bowel preparation; EN group of patients received preoperative immune-enhancing enteral nutrition preparations, received same preoperative regular diet and nutrition intervention as control group, ate through the mouth, received additional immune-enhancing enteral nutrition preparations with the dose of 125.52 kJ (30 kcal)/(kg•d) for continuous 3 d on the basis of original diet 3 d before operation, and orally took intestinal lavage solution 1 d before operation for bowel preparation.

2.3 Peripheral blood index detection methods

The same day after operation, 5 mL of peripheral venous blood was collected from the two groups of patients, added in lymphocyte separation medium and centrifuged, the peripheral blood mononuclear cells suspended in the middle were absorbed, washed with PBS twice and centrifuged, the cells were collected, added in protein lysis buffer, fully broken and centrifuged again to collect protein suspension, and then the CD69 and HLA-DR levels per mg total protein were calculated.

2.4 Serum index detection methods

The same day after operation, 5 mL of peripheral venous blood was collected from the two groups of patients and centrifuged to separate serum, and enzyme-linked immunosorbent assay kits were used to determine IgM, IgG, total protein (TP), albumin (ALB), prealbumin (PA), transferrin (TF), CRP, YKL-40, IL-1β, TNF-α, IL-6, HSP70, ACTH, Cor and HO-1 levels.

2.5 Statistical methods

SPSS 21.0 software was used to statistically process data, measurement data analysis between groups was by t test and P<0.05 indicated statistical significance in differences.

3. Results

3.1 Postoperative immune response indexes of two groups of patients

The same day after operation, analysis of immune response indexes CD69 (ng/mg total protein), HLA-DR (ng/mg total protein), IgM (mg/L) and IgG (mg/L) levels between two groups of patients was as follows: CD69 and HLA-DR levels in peripheral blood mononuclear cells as well as IgM and IgG levels in serum of EN group were significantly higher than those of control group. Differences in CD69 and HLA-DR levels in peripheral blood mononuclear cells as well as IgM and IgG levels in serum were statistically significant between PE group and control group on the same day after operation (P<0.05).

Table 1. Comparison of immune response indexes between two groups of patients after operation.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Peripheral blood mononuclear cells</th>
<th>Serum samples</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CD69 (ng/mg total protein)</td>
<td>IgM (mg/L)</td>
</tr>
<tr>
<td></td>
<td>HLA-DR (ng/mg total protein)</td>
<td>IgG (mg/L)</td>
</tr>
<tr>
<td>EN</td>
<td>1.89±0.22</td>
<td>1.71±0.20</td>
</tr>
<tr>
<td>Control</td>
<td>1.03±0.13</td>
<td>1.32±0.18</td>
</tr>
<tr>
<td>T</td>
<td>8.375</td>
<td>6.328</td>
</tr>
<tr>
<td>P</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

3.2 Postoperative nutritional status indexes of two groups of patients

The same day after operation, analysis of serum nutritional status indexes TP, ALB, PA and TF levels between two groups of patients was as follows: serum TP, ALB, PA and TF levels of EN group were significantly higher than those of control group. Differences in serum TP, ALB, PA and TF levels were statistically significant between PE group and control group on the same day after operation (P<0.05).

Table 2. Comparison of nutritional status indexes between two groups of patients after operation (g/L).

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>TP</th>
<th>ALB</th>
<th>PA</th>
</tr>
</thead>
<tbody>
<tr>
<td>EN</td>
<td>47</td>
<td>53.41±6.41</td>
<td>33.15±4.25</td>
<td>0.29±0.04</td>
</tr>
<tr>
<td>Control</td>
<td>47</td>
<td>48.37±5.57</td>
<td>28.93±3.57</td>
<td>0.22±0.03</td>
</tr>
<tr>
<td>T</td>
<td></td>
<td>7.182</td>
<td>6.586</td>
<td>6.118</td>
</tr>
<tr>
<td>P</td>
<td></td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

3.3 Postoperative inflammatory response indexes of two groups of patients
The same day after operation, analysis of serum inflammatory response indexes CRP (μg/mL), YKL-40 (pg/mL), IL-1β (pg/mL), TNF-α (pg/mL) and IL-6 (pg/mL) levels between two groups of patients was as follows: serum CRP, YKL-40, IL-1β, TNF-α and IL-6 levels of EN group were significantly lower than those of control group. Differences in serum CRP, YKL-40, IL-1β, TNF-α and IL-6 levels were statistically significant between PE group and control group on the same day after operation (P<0.05).

Table 3.
Comparison of inflammatory response indexes between two groups of patients after operation.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>CRP</th>
<th>YKL-40</th>
<th>IL-1β</th>
<th>TNF-α</th>
<th>IL-6</th>
</tr>
</thead>
<tbody>
<tr>
<td>EN</td>
<td>47</td>
<td>8.39±0.93</td>
<td>4.18±0.56</td>
<td>10.35±1.47</td>
<td>34.51±4.68</td>
<td>22.14±3.25</td>
</tr>
<tr>
<td>Control</td>
<td>47</td>
<td>14.52±1.78</td>
<td>9.45±1.05</td>
<td>17.68±2.84</td>
<td>59.24±7.24</td>
<td>39.47±5.12</td>
</tr>
<tr>
<td>T</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td></td>
</tr>
</tbody>
</table>

3.4 Postoperative stress response indexes of two groups of patients

The same day after operation, analysis of serum stress response indexes HSP70 (ng/mL), ACTH (pmol/L), Cor (nmol/L) and HO-1 (U/L) levels between two groups of patients was as follows: serum HSP70, ACTH, Cor and HO-1 levels of EN group were significantly lower than those of control group. Differences in serum HSP70, ACTH, Cor and HO-1 levels were statistically significant between PE group and control group on the same day after operation (P<0.05).

Table 4.
Comparison of stress response indexes between two groups of patients after operation.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>HSP70</th>
<th>ACTH</th>
<th>Cor</th>
<th>HO-1</th>
</tr>
</thead>
<tbody>
<tr>
<td>EN</td>
<td>47</td>
<td>83.51±9.35</td>
<td>8.58±0.93</td>
<td>103.58±13.58</td>
<td>34.12±3.85</td>
</tr>
<tr>
<td>Control</td>
<td>47</td>
<td>146.41±17.68</td>
<td>15.22±1.85</td>
<td>186.42±21.35</td>
<td>64.83±8.23</td>
</tr>
<tr>
<td>T</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

4. Discussion

Radical resection of rectal carcinoma is the first choice for clinical treatment of rectal cancer, and it can effectively remove tumor lesions and prolong patients’ survival time. Nonetheless, the surgery causes great trauma and requires postoperative fasting, and therefore, the postoperative enteral nutrition support is a normal support treatment after radical resection of rectal cancer. Influenced by reduced intake, tumor consumption, mental stress and other factors, patients with rectal cancer already have poor nutritional status and suppressed immune function before operation, which will reduce the patients’ endurance capacity to radical resection and affect postoperative rehabilitation[8,9]. In recent years, nutritional intervention before radical resection of rectal cancer has received more and more attention. Immune-enhancing enteral nutrition preparations are the newly developed enteral nutrition preparations that contain ω-3 PUFA, Gln, Arg and other immune nutrients and have outstanding value for improving the immune function and enhancing the immune response. ω-3 PUFA is a kind of essential fatty acid that has a wide range of biological effects in the body. On the one hand, ω-3 PUFA can induce the differentiation and maturation of T lymphocytes and adjust the proportion of CD4+T cells and CD8+T cells so as to enhance the cellular immune response of the body; on the other hand, ω-3 PUFA has inhibiting effect on a variety of biological actions of malignant tumor cells, and can reduce the tumor load and reduce the nutrient consumption of malignant tumor to a certain extent[10]. Gln is the most abundant amino acid in the body that can not only adjust the intestinal mucosa function and keep normal intestinal barrier function, but can also enhance the immune response function of lymphocytes and mononuclear macrophages; Arg is the essential amino acid in the body and has promoting effect on the differentiation and maturation of CD4+T cells and NK cells[11].

Study has shown that immune-enhancing enteral nutrition can reduce the nutritional risk in patients after radical resection of rectal cancer, and can also reduce the incidence of postoperative complications[12]. In the study, serum protein metabolism indexes were analyzed to reflect the postoperative nutritional status, and the results showed that serum TP, ALB, PA and TF levels of EN group were significantly higher than those of control group. It confirms from the perspective of protein metabolism that immune-enhancing enteral nutrition can improve the nutritional status of patients with radical resection of rectal cancer. The nutrients in immune-enhancing enteral nutrition preparations can not only improve the nutritional status, but also have regulating effect on the immune response process. In order to define the effect of immune-enhancing enteral nutrition preparations on the postoperative immune response in patients with rectal cancer, postoperative cellular immunity and humoral immunity indexes of two groups of patients were analyzed in the study. CD69 is the molecule first expressed on the cell membrane surface during T cell activation and proliferation, it has stimulative effect on T cell subset Th1 differentiation and maturation, and it can enhance antitumor immune response[13]; HLA-DR is a type of MHC-II molecule that is involved in antigen presented and induces cytotoxic T cell differentiation. IgG and IgM are the important proteins that mediate the humoral immune response, and both surgical trauma and nutrient consumption will influence the synthesis and secretion of IgG and IgM[14]. The analysis of the results showed that CD69 and HLA-DR levels in peripheral blood mononuclear cells as well as IgM and IgG levels in serum of EN group were significantly higher than those of control group. This means that immune-enhancing enteral nutrition can improve the cellular immune response and humoral immune response after radical resection of rectal cancer.

Intraoperative stretching and resection scope of radical resection...
of rectal cancer is broad and the trauma extent is big, so good preoperative nutritional status and immune function can enhance the body’s capacity to endure surgical trauma. The trauma caused by surgery can directly activate the body’s inflammatory response and stress response, and evaluating postoperative inflammatory response and stress response can reflect the trauma caused by surgery, and then reflect the body’s trauma endurance capacity. During the activation of inflammatory response, CRP, YKL-40, IL-1β, TNF-α, IL-6 and other inflammatory mediators are massively synthesized and secreted. CRP is mainly from the liver cells, YKL-40 is mainly from neutrophils, and IL-1β, TNF-α and IL-6 are mainly from mononuclear macrophages[15,16]. In the study, analysis of the above inflammatory response indexes showed that serum CRP, YKL-40, IL-1β, TNF-α and IL-6 levels of EN group were significantly lower than those of control group. During the activation of stress response, the massively secreted HSP70 can stabilize protein metabolism and enhance the body’s ability to resist traumatic stimuli, and the activation of the hypothalamus-adrenocortical axis will increase trophicity and trauma endurance capacity, and thus relieve postoperative inflammatory response and stress response.

To sum up, it is believed that immune-enhancing enteral nutrition application before radical resection of rectal carcinoma can improve the cellular immune response and humoral immune response, increase trophicity and trauma endurance capacity, and thus relieve postoperative inflammatory response and stress response.

References


