Effect of glutamine enteral nutrition on the postoperative nutrition status and immune function in elderly patients with gastrointestinal tumor

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ABSTRACT

Objective: To explore the clinical efficacy of glutamine enteral nutrition in the treatment of gastrointestinal tumor in elderly patients and the effect in improving the nutrition and immunity. Methods: A total of 92 elderly patients with gastrointestinal tumor who were admitted in our hospital from June, 2014 to March, 2016 were included in the study and randomized into the control group (n=46) and the treatment group (n=46). The patients in the two groups were given adjuvant chemotherapy 2 weeks after operation and routine enteral nutrition 1 d after operation. On the basis of routine enteral nutrition, the patients in the treatment group were given glutamine granules for intensive treatment. The patients in the two groups were continuously given 10 d nutrition support. The gastrointestinal function recovery and intestinal mucosal barrier recovery before and after operation in the observation group were compared. The levels of related nutrition and immune indicators before and after operation in the observation group were compared. Results: The first exhaust and first defecation time after operation in the treatment group was significantly shortened when compared with the control group. When compared with before operation, L/M and plasma DAO level 1 d and 10 d after operation in the control group were significantly elevated. L/M and plasma DAO level 1 d after operation in the treatment group were significantly elevated, while those 10 d after operation were significantly reduced when compared with before operation. L/M and plasma DAO level 1 d and 10 d after operation in the treatment group were significantly lower than those in the control group. The serum TP, Alb, PA, and TRF levels 1 d and 10 d after operation in the two groups were significantly elevated when compared with before operation, and those in the treatment group were significantly higher than those in the control group. When compared with before operation, the plasma IgA and IgG levels, CD4+, and CD4+/CD8+ 1 d after operation in the two groups were significantly reduced, while CD8 was significantly elevated. The plasma IgA and IgG levels, CD4+, and CD4+/CD8+ 10 d after operation in the two groups were significantly elevated when compared with 1 d after operation, while CD8 was significantly reduced. Moreover, the plasma IgA and IgG levels, CD4+, and CD4+/CD8+ 10 d after operation in the treatment group were significantly higher than those in the control group or when compared with before operation. Conclusions: Glutamine enteral nutrition in the treatment of gastrointestinal tumor in elderly patients can effectively improve the postoperative intestinal mucosal barrier function, promote the postoperative gastrointestinal function recovery, correct malnutrition, and enhance the humoral immunity and cellular immunity function, with efficacy significantly superior to that by the routine enteral nutrition.

1. Introduction

The gastrointestinal tumor is one of the common malignant tumors in the clinic, and operation is an effective method in the treatment of gastrointestinal tumor. However, the gastrointestinal tumor patients are usually accompanied by the severe stress reaction shortly after operation, especially in the elderly patients. The damaged immunological barrier after operation is easy to induce infection, aggravate the condition, and even one of the most important factors for developing death[1-3]. The postoperative enteral nutrition can significantly reduce the intestinal permeability, stabilize the...
intestinal mucosal structure, prevent the bacterial translocation, and regulate the postoperative nutrition status[4]. Glutamine is one of the essential amino acids, and is also the important nutrient substance for repairing the intestinal mucosa[5]. The study is aimed to explore the clinical efficacy of glutamine enteral nutrition in the treatment of gastrointestinal tumor in elderly patients and the effect in improving the nutrition and immunity.

2. Materials and methods

2.1. Clinical materials

A total of 92 elderly patients with gastrointestinal tumor who were admitted in our hospital from June, 2014 to March, 2016 were included in the study, and confirmed by the pathological examination. Inclusion criteria: (1) those who were aged more than 60 years old; (2) those who had obvious operation indications and could accept the radical operation; (3) those who could endure the operation and were willing to accept the operation; (4) those who needed adjuvant chemotherapy after operation; (5) those who had no extensive abdominal metastasis; (6) those who had no enteral nutrition and chemotherapy contraindications; (7) those who had not taken glucocorticoids or immune agents in recent 3 months. Exclusion criteria: (1) those who were accompanied by severe malnutrition and infection before operation; (2) those who could not endure enteral nutrition; (3) those who were accompanied by severe autoimmune diseases; (4) those who were merged with severe heart, liver, and renal dysfunction; (5) those who were merged with severe endocrine disorder or metabolic disease. The informed consents were obtained from all the patients or their relatives.

2.2. Methods

The patients were randomized into the control group (n=46) and the treatment group (n=46). In the control group, 27 were male, and 19 were female; with an average age of (64±7) years old and average BMI of (20.3±3.9) kg/m2; 19 had gastric carcinoma and 27 had intestinal cancer according to the pathological type; 11 were performed with total gastrectomy, 17 had proximal gastrectomy, and 18 had distal gastrectomy according to the surgical methods. In the treatment group, 26 were male, and 20 were female; with an average age of (63±6) years old and average BMI of (20.5±4.2) kg/m2; 21 had gastric carcinoma and 25 had intestinal cancer according to the pathological type; 12 were performed with total gastrectomy, 19 had proximal gastrectomy, and 15 had distal gastrectomy according to the surgical methods. The comparison of gender, age, BMI, pathological type, and surgical method between the two groups was not statistically significant (P>0.05), and it was comparable. The patients in the two groups were given adjuvant chemotherapy (FOLFOX6 regimen) 2 weeks after operation, 1 time every 2 weeks. The patients in the control group were given routine enteral nutrition 1d after operation. The jejunum needle was punctured into the jejunum about 20 cm under Trier ligament, and extracted from the abdominal wall moving about 2.5 cm. TPF-T (1 500 mL/d) was supplemented 24-48 h after operation. The dose was gradually increased according to the patients’ tolerance degree. Liquid food was replaced 7 d after operation. On the above basis, the patients in the treatment group were given glutamine granules (produced by Chengdu Lisite Pharmaceutical Co. Ltd, Approval No. H20040245, 1.0 g/granule), through the naso-intestinal feeding tube, 30 g/d, for 3 times, i.e. 10 g glutamine granule was added to 100 mL warm water each time. The patients in the two groups were continuously given enteral nutrition for 10 d.

2.3. Observation indicators

(1) The first exhaust and defecation time after operation in the two groups was observed; (2) The spectrophotometric method was used to detect the plasma DAO level before operation, 1 d and 10 d after operation. The morning urine was collected. After urination, the patients were orally administrated with lactulose/mannitol solution (lactulose 10 g, mannitol 5 g) 50 mL, and the urine was collected after 6 h. HPLC was used to detect L/M. (3) A volume of 5 mL fasting venous blood before operation, 1 d and 10 d after operation was collected, and centrifuged for the serum. ELISA was used to detect the serum TP, Alb, PA, and TRF. FCM and radioimmunoassay were used to detect T lymphocyte subsets and immunoglobulin.

2.4. Statistical analysis

SPSS 13.0 software was used for the statistical analysis. The measurement data were expressed as mean ± SD. The paired t test was used for the intra-group comparison, while the independent t test was used for the comparison between the two groups. P<0.05 was regarded as statistically significant.

3. Results

3.1. Comparison of the gastrointestinal function before and after treatment

The first exhaust and defecation time after operation in the treatment group (2.49±0.67) d, (5.11±0.98) d was significantly shortened when compared with the control group (3.46±0.59) d, (6.47±1.01) d (P<0.01).

3.2. Comparison of L/M and plasma DAO level before and after treatment

When compared with before operation, L/M and plasma DAO level 1 d and 10 d after operation in the control group were significantly elevated (P<0.01). L/M and plasma DAO level 1 d after operation in the treatment group were significantly elevated, while those 10 d after operation were significantly reduced (P<0.01) when compared with the control group.

Table 1.

Comparison of L/M and plasma DAO level before and after treatment.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>L/M</th>
<th>DAO/(µmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment</td>
<td>46</td>
<td>Before operation</td>
<td>0.19±0.03</td>
<td>1.25±0.10</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 d after operation</td>
<td>0.21±0.02**</td>
<td>1.30±0.09**</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10 d after operation</td>
<td>0.13±0.03**</td>
<td>0.95±0.08**</td>
</tr>
<tr>
<td>Control</td>
<td>46</td>
<td>Before operation</td>
<td>0.17±0.02</td>
<td>1.23±0.07</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 d after operation</td>
<td>0.24±0.02**</td>
<td>1.35±0.08**</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10 d after operation</td>
<td>0.28±0.02**</td>
<td>2.23±0.09**</td>
</tr>
</tbody>
</table>

*P<0.01, when compared with before operation; **P<0.01, when compared with the control group.
with before operation. L/M and plasma DAO level 1 d and 10 d after operation in the treatment group were significantly lower than those in the control group (P<0.01) (Table 2).

### 3.3. Comparison of the nutrition indicators before and after treatment

The serum TP, Alb, PA, and TRF levels 1 d and 10 d after operation in the two groups were significantly elevated when compared with before operation (P<0.05), and those in the treatment group were significantly higher than those in the control group (P<0.05) (Table 2).

### 3.4. Comparison of the immunological indicators before and after treatment

When compared with before operation, the plasma IgA and IgG levels, CD4+, and CD4+/CD8+ 1 d after operation in the two groups were significantly reduced (P<0.05 or P<0.01), while CD8+ was significantly elevated (P<0.05 or P<0.01). The plasma IgA and IgG levels, CD4+, and CD4+/CD8+ 10 d after operation in the two groups were significantly elevated when compared with 1 d after operation, while CD8+ was significantly reduced (P<0.01). Moreover, the plasma IgA and IgG levels, CD4+, and CD4+/CD8+ 10 d after operation in the treatment group were significantly higher than those in the control group or when compared with before operation (P<0.05 or P<0.01), while CD8+ was significantly lower than that in the control group or when compared with before operation (P<0.01) (Table 3).

### 4. Discussion

With the alteration of diet style, the morbidity of gastrointestinal tumor is gradually increased, especially in the elderly patients. Operation is the common means in the treatment of gastrointestinal tumor, but the surgical trauma and application of postoperative adjuvant chemotherapeutics can often cause the postoperative intestinal flora disorder, and intestinal mucosa damage which can promote the intestinal bacterial toxin to run through the intestinal mucosa barrier to release into the blood, and greatly increase the risk of intestinal infection[6,7]. Nausea, vomiting or regurgitation, abdominal distension, and abdominal pain are the common manifestations after operation in elderly patients with gastrointestinal tumor, with immunological dysfunction, and severe malnutrition. The early application of enteral nutrition after operation in patients with gastrointestinal tumor has reached a consensus, but the routine enteral nutrition support can only maintain the nutrition supply, but cannot effectively alleviate the postoperative intestinal mucosa damage, inflammatory reaction, and immunosuppression[8]. Glutamine is the decomposition product of alanyl glutamine, can promote the renewing of intestinal mucosa cells, is also an important nutrient substance to repair the intestine in a stress state, and is the unique energy source of intestinal mucosa cells. In a normal condition, a large amount of glutamine can be synthesized, but in a stress state, the glutamine concentration is obviously reduced, therefore, timely supplementation of glutamine after operation in elderly patients with gastrointestinal tumor is of great importance[9,10]. The results in the study showed that the first exhaust and defecation time after operation in the treatment group was significantly reduced, which is similar to the results reported by Ji et al[11], indicating that glutamine enteral nutrition can accelerate the postoperative gastric dynamics and gastric emptying in elderly patients with gastrointestinal tumor, and promote the gastrointestinal function recovery. Due to the deficiency of glutamine after operation in elderly patients with gastrointestinal tumor, the digestive juice is largely secreted, and there is a lack of food stimulation, resulting in an obviously increased intestinal mucosa permeability, intestinal flora disorder, and intestinal mucosa damage, finally leading to intestinal barrier dysfunction, and reduced immunity; therefore, the intestinal mucosa barrier function recovery is an important reference evidence to evaluate the postoperative recovery in elderly patients with gastrointestinal tumor[10]. L/M and DAO are the most visual indicators to reflect the increasement of intestinal mucosa permeability; moreover, DAO can directly reflect the intestinal mucosa epithelial cell damage and repair, and both can be used to evaluate the integrity of intestinal mucosa barrier. It is reported that[13] early administration of glutamine enteral nutrition after operation is more suitable for the physiological requirement, can regulate and maintain the normal intestinal mucosa permeability and villous length, and positively prevent the intestinal mucosa damage. The results in the study showed that when compared with before operation, L/M and plasma DAO level l d and 10 d

### Table 2.
Comparison of the nutrition indicators before and after treatment (g/L).

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>TP (g/L)</th>
<th>Al (g/L)</th>
<th>PA (g/L)</th>
<th>TRF (g/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment</td>
<td>46</td>
<td>Before operation</td>
<td>60.22±5.03</td>
<td>30.01±2.36</td>
<td>228.47±20.95</td>
<td>1.83±0.20</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 d after operation</td>
<td>65.31±4.91</td>
<td>34.47±2.51</td>
<td>271.06±22.44</td>
<td>2.51±0.19</td>
</tr>
<tr>
<td>Control</td>
<td>46</td>
<td>Before operation</td>
<td>60.39±5.02</td>
<td>30.07±2.27</td>
<td>223.14±21.38</td>
<td>1.81±0.16</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 d after operation</td>
<td>62.68±4.93</td>
<td>31.09±2.43</td>
<td>235.19±21.02</td>
<td>1.94±0.20</td>
</tr>
</tbody>
</table>

*P<0.05, **P<0.01, when compared with before operation; "P<0.05, ""P<0.01, when compared with teh control group.

### Table 3.
Comparison of the immunological indicators before and after treatment.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>IgA (g/L)</th>
<th>IgG (g/L)</th>
<th>CD4+ (%)</th>
<th>CD8+ (%)</th>
<th>CD4+/CD8+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment</td>
<td>46</td>
<td>Before operation</td>
<td>2.31±0.85</td>
<td>11.70±2.35</td>
<td>39.66±2.89</td>
<td>22.89±4.02</td>
<td>1.73±0.36</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 d after operation</td>
<td>1.92±0.67</td>
<td>10.11±1.98</td>
<td>33.17±3.45</td>
<td>24.81±3.68</td>
<td>1.42±0.35</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10 d after operation</td>
<td>2.92±0.84</td>
<td>12.67±2.06</td>
<td>45.18±3.58</td>
<td>19.73±4.06</td>
<td>2.25±0.41</td>
</tr>
<tr>
<td>Control</td>
<td>46</td>
<td>Before operation</td>
<td>2.29±0.80</td>
<td>11.62±2.50</td>
<td>39.64±3.31</td>
<td>23.34±3.40</td>
<td>1.74±0.31</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 d after operation</td>
<td>1.65±0.79</td>
<td>9.73±1.99</td>
<td>32.74±3.03</td>
<td>25.27±4.01</td>
<td>1.36±0.33</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10 d after operation</td>
<td>2.13±0.87</td>
<td>11.54±2.4</td>
<td>40.58±3.77</td>
<td>22.39±3.62</td>
<td>1.81±0.40</td>
</tr>
</tbody>
</table>

*P<0.05, **P<0.01, when compared with before operation; \"P<0.01; \"\"P<0.01, when compared with 1 d after operation; P<0.05, when compared with the control group.
after operation in the control group were significantly elevated ($P<0.01$); L/M and plasma DAO level 1 d after operation in the treatment group were significantly elevated, while those 10 d after operation were significantly reduced ($P<0.01$) when compared with before operation; L/M and plasma DAO level 1 d and 10 d after operation in the treatment group were significantly lower than those in the control group ($P<0.01$), indicating that glutamine enteral nutrition can effectively promote the renewing of intestinal epithelial cells, increase the tight junction of intestinal mucosa cells, reduce the intestinal mucosa permeability, and recover the intestinal mucosa barrier function, with more significant effect than the routine nutrition, which can be explained by that due to the essential component of intestinal mucosa cells, glutamine is of great significance in maintaining the integrity of intestinal mucosa structure.

Operation can remove most tumor lesions in elderly patients with gastrointestinal tumor and prevent the tumor cell diffusion, but due to the tumor consumption, nutrition intake insufficiency, and function degeneration, it is easy to cause severe malnutrition and reduction of immune function. Moreover, due to the effect of surgical stress, the inhibition of normal tissue function will also further aggravate the malnutrition and immune disorder, which can affect the prognosis. The intestinal mucosa is involved in the absorption of nutrient substances; therefore, the enteral nutrition support can contribute to guarantee the intestinal mucosa structure and function, enhance the digestive immune function, improve the intestinal mucosa and liver blood supply, and promote the nutrition absorption.[14] The results in the study showed that the serum TP, Alb, PA, and TRF levels 1 d and 10 d after operation in the two groups were significantly elevated when compared with before operation ($P<0.05$), and those in the treatment group were significantly higher than those in the control group ($P<0.05$), indicating that glutamine enteral nutrition can significantly improve the postoperative nutrition status in elderly patients with gastrointestinal tumor, and gradually correct the malnutrition, with significant effect superior to that by the routine enteral nutrition. The reduction of CD4$^+$ and CD4$^+/CD8^+$ is the main manifestation of postoperative immunological dysfunction in elderly patients with gastrointestinal tumor. Glutamic acid in the glutamine can provide the nitrogen source, promote the synthesis of intestinal smooth muscle cell protein, maintain the secretion and proliferation of lymphocytes, and significantly regulate the immunological function. Meanwhile, the up-regulation of cellular immune function can promote B cell activation, and secrete the immunoglobulin (IgG, IgM, and IgA) in order to enhance the humoral immunity.[15] The results in the study showed that when compared with before operation, the plasma IgA and IgG levels, CD4$^+$, and CD4$^+/CD8^+$ 1d after operation in the two groups were significantly reduced ($P<0.05$ or $P<0.01$), while CD8$^+$ was significantly elevated ($P<0.05$ or $P<0.01$); the plasma IgA and IgG levels, CD4$^+$, and CD4$^+/CD8^+$ 10 d after operation in the two groups were significantly elevated when compared with 1 d after operation, while CD8$^+$ was significantly reduced ($P<0.01$); moreover, the plasma IgA and IgG levels, CD4$^+$, and CD4$^+/CD8^+$ 10 d after operation in the treatment group were significantly higher than those in the control group or when compared with before operation ($P<0.05$ or $P<0.01$), while CD8$^+$ was significantly lower than that in the control group or when compared with before operation ($P<0.01$), which is similar to the results reported by Dong et al.[16], indicating that glutamine can significantly enhance the humoral immunity and cellular immunity in elderly patients with gastrointestinal tumor, strengthen the body resistance, and contribute to improve the prognosis. In conclusion, glutamine enteral nutrition in the treatment of gastrointestinal tumor in elderly patients can effectively improve the postoperative intestinal mucosal barrier function, correct malnutrition, and enhance the humoral immunity and cellular immunity function; therefore, it deserves to be widely recommended in the clinic.

References


