Effects of alanine glutamine on inflammatory, immune, antioxidant and nutritional indicators in colon cancer patients

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ABSTRACT

Objective: To explore the effects of alanine glutamine on inflammatory, immune, antioxidant and nutritional indicators in colon cancer patients. Methods: A total of 126 cases of colon cancer with intestinal obstruction were divided into control group (n=63) and observation group (n=63) from May 2015 to May 2017 in Zhongnan Hospital of Wuhan University and Gezhouba Dam group central hospital, the control group only received parenteral nutrition, while the observation group was treated with parenteral nutrition plus alanine glutamine treatment. The expression levels of nutritional indicators, inflammatory factors, immunity and antioxidant were compared between the two groups. Results: Before and 1 d after treatment, there was no significant difference between the two groups of prealbumin (PA), albumin (ALB), tumor necrosis factor-α (TNF-α), C reactive protein (CRP), interferon-γ (IFN-γ) and immunoglobulin (IgA, IgG, IgM), superoxide dismutase (SOD) and malondialdehyde (MDA). 1 d after treatment, the levels of PA, ALB, IFN-γ, IgA, IgG, IgM and SOD in two groups were significantly lower than before the treatment, and TNF-α, CRP and MDA were significantly higher than before the treatment. On the 7 d after treatment, the levels of PA, ALB, IFN-γ, IgA, IgG, IgM and SOD in two groups were significantly increased compared with the 1 d after treatment, while TNF-α, CRP and MDA were significantly lower than the 1 d after the treatment. On the 7 d after treatment, the levels of PA, ALB, IFN-γ, IgA, IgG, IgM and SOD in two groups were significantly increased compared with the 1 d after treatment, while TNF-α, CRP and MDA were significantly lower than the 1 d after the treatment, the PA, ALB, IFN-γ, IgA, IgG, IgM and SOD levels in the observation group were significantly higher than those in the control group, while TNF-α, CRP and MDA were significantly lower than those of the control group, there was no significant difference in IgA, IgG and IgM levels between the observation group and that before treatment. There was no significant difference in MDA and SOD levels between the control group and that before treatment. Conclusions: Parenteral nutrition support in patients with colon cancer with intestinal obstruction, alanyl glutamine, can significantly improve the nutritional level, reduce the inflammatory response, enhance the immune and antioxidant functions.

1. Introduction

Colon cancer, as a common malignant tumor of the digestive tract, has a high incidence of mortality[1,2]. Its pathogenesis may be closely related to factors such as inflammation, immunity and oxidative stress[3–5]. Intestinal obstruction is a common complication of colon cancer, which easily aggravates the patient's condition and causes an increase in the body’s inflammatory immune response[6]. Nutrition support is one of the main means to promote postoperative rehabilitation of colon cancer patients. At present, the nutritional support mode of colon cancer with intestinal obstruction is mainly conventional nutritional therapy, but the effect of postoperative recovery is not obvious[7]. Alanyl-glutamine is not only a conditionally essential amino acid, but also plays an important role in the pathological state of the body[8,9]. Therefore, this study supports a colon cancer patient by alanyl-glutamine parenteral nutrition, and explores its effects on inflammatory, immune, antioxidant and nutritional indicators of patients, as reported below.
2. Data and methods

2.1 General information

A total of 126 patients with colon cancer and intestinal obstruction admitted to Zhongnan Hospital of Wuhan University and Central Hospital of Gezhouba Group from May 2015 to May 2017 were divided into control group (n=63) and observation group (n=63) according to different treatment methods (n=63). Among them, the observation group 33 males and 30 females, aged 32-69 years, with obstructive symptoms occurring 4.5 h to 10 d, left colon cancer in 28 cases, right colon cancer in 35 cases, TNM staging: stage II in 15 cases, stage III were 26 cases and 22 cases in stage IV. The control group 31 males and 32 females, aged 35-67 years, with obstructive symptoms occurring 5 h to 12 d, left colon cancer in 29 cases, right colon cancer in 34 cases, and TNM staging: stage II in 17 cases, stage III. 23 cases, 23 cases of stage IV. There was no significant difference in the general data (sex, age) between the two groups of colon cancer patients with intestinal obstruction (P>0.05), which was comparable.

Inclusion criteria: colon cancer, CT, X-ray barium enema, etc. diagnosed as colon cancer with intestinal obstruction; age less than 75 years; no evidence of infection before surgery; patient and their families known. Exclusion criteria: parenteral nutrition tolerance; preoperative nutritional malnutrition; multiple organ dysfunction; preoperative evidence to support infection; distant metastasis; second primary cancer; mental disorders.

2.2 Treatment

All patients were fasted from 3 d before surgery to 7 d after surgery. At the same time, the conventional parenteral nutrition support of the two groups was 90-100 kJ/(kg•d), and the proportion of fat in the hot card was 40%-50%. On the basis of this, the observation group was treated with alanyl-glutamine injection (National Medicine Zhunhong H20103031, Wuhan Daan Pharmaceutical Co., Ltd.) for treatment, 100 mL/d, and the control group only gave the balanced amino acid of the same heat card as the observation group.

2.3 Observation indicators

All patients received venous blood 5 mL 1 d before surgery and 7 d after surgery. The automatic biochemical analyzer (purchased from Beckman Coulter) was used to detect nutritional indicators: prealbumin (PA) and albumin (ALB); ELISA detection of inflammation indicators: tumor necrosis factor-α (TNF-α), C-reactive protein (CRP), interferon-γ (IFN-γ) and immunoglobulin: IgA, IgG, IgM; Antioxidant indicators were detected by immunoradiometric assay: superoxide dismutase (SOD) and malondialdehyde (MDA). The above kits were purchased from Shanghai Bangsheng Biotechnology Co., Ltd.

2.4 Statistical methods

The data collected by Zhongnan Hospital of Wuhan University and the Central Hospital of Gezhouba Group were processed and analyzed by SPSS 22.0. The count data were analyzed by chi-square test. The measurement data such as inflammation, immunity, antioxidant and nutritional indicators were expressed by (Mean ± SD). For the test, one-way analysis of variance was used for comparison between groups. P<0.05 was considered statistically significant.

Table 1.
Comparison of nutritional indicators between the two groups (n=63).

<table>
<thead>
<tr>
<th>Group</th>
<th>Time</th>
<th>PA (g/L)</th>
<th>ALB (g/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>Before treatment</td>
<td>215.83±29.17</td>
<td>39.27±3.51</td>
</tr>
<tr>
<td></td>
<td>After treatment 1 d</td>
<td>157.29±18.76</td>
<td>31.38±2.96</td>
</tr>
<tr>
<td></td>
<td>After treatment 7 d</td>
<td>227.95±32.10</td>
<td>45.73±3.95</td>
</tr>
<tr>
<td>Control</td>
<td>Before treatment</td>
<td>212.64±25.83</td>
<td>39.50±3.79</td>
</tr>
<tr>
<td></td>
<td>After treatment 1 d</td>
<td>155.33±18.01</td>
<td>30.72±2.18</td>
</tr>
<tr>
<td></td>
<td>After treatment 7 d</td>
<td>218.50±27.88</td>
<td>42.11±4.10</td>
</tr>
</tbody>
</table>

Note: compared with before treatment *P<0.05; compared with 1 day after treatment **P<0.05; compared with control group after treatment ***P<0.05.

Table 2.
Comparison of inflammatory factors levels between the two groups (n=63).

<table>
<thead>
<tr>
<th>Group</th>
<th>Time</th>
<th>TNF-α (ng/L)</th>
<th>CRP (mg/L)</th>
<th>IFN-γ (ng/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>Before treatment</td>
<td>310.28±63.91</td>
<td>17.07±3.95</td>
<td>8.25±1.06</td>
</tr>
<tr>
<td></td>
<td>After treatment 1 d</td>
<td>378.56±73.33</td>
<td>25.79±5.06</td>
<td>5.58±0.80</td>
</tr>
<tr>
<td></td>
<td>After treatment 7 d</td>
<td>65.79±75.08</td>
<td>17.67±12.19</td>
<td>8.37±1.22</td>
</tr>
<tr>
<td>Control</td>
<td>Before treatment</td>
<td>318.02±65.27</td>
<td>17.67±5.89</td>
<td>8.37±1.22</td>
</tr>
<tr>
<td></td>
<td>After treatment 1 d</td>
<td>380.21±75.62</td>
<td>26.27±5.89</td>
<td>5.50±0.75</td>
</tr>
<tr>
<td></td>
<td>After treatment 7 d</td>
<td>93.70±19.13</td>
<td>9.36±1.90</td>
<td>13.52±3.68</td>
</tr>
</tbody>
</table>

Note: compared with before treatment *P<0.05; compared with 1 d after treatment **P<0.05; compared with control group after treatment ***P<0.05.
### 3. Results

#### 3.1 Nutrition indicators

There was no significant difference in the expression levels of PA and ALB between the two groups before treatment and 1 d after treatment ($P>0.05$). At 1 d after treatment, the expression levels of PA and ALB were significantly lower than those before treatment ($P<0.05$). On the 1st day after treatment, the expression levels of PA and ALB in the observation group were significantly increased compared with the control group ($P<0.05$). See Table 1.

#### 3.2 Inflammatory factors

There was no significant difference in the expression levels of TNF-α, CRP and IFN-γ between the two groups before treatment and 1 d after treatment ($P>0.05$). On the 1st day after treatment, the expression levels of TNF-α and CRP were significantly increased compared with those before treatment, while the expression level of IFN-γ was significantly lower than that before treatment ($P<0.05$). On the 7th day after treatment, the expression levels of TNF-α and CRP were significantly lower than those before treatment and 1 d after treatment, while the expression level of IFN-γ was significantly increased compared with the control group ($P<0.05$). See Table 2.

#### 3.3 Immune indicators

There was no significant difference in the expression levels of IgA, IgG and IgM between the two groups before treatment and 1 d after treatment ($P>0.05$). The expression levels of IgA, IgG and IgM in the two groups were significantly lower than those before treatment ($P<0.05$). On the 7th day after treatment, the expression levels of IgA, IgG and IgM in the two groups were significantly higher than those on the 1st day after treatment ($P<0.05$). There was no significant difference between the observation group and the treatment group ($P>0.05$), and the control group was significantly lower than before treatment ($P<0.05$), while the observation group was significantly increased compared with the control group ($P<0.05$). See Table 3.

#### 3.4 Antioxidant index

There was no significant difference in the expression levels of SOD and MDA between the two groups before treatment and 1 d after treatment ($P>0.05$). On the 1st day after treatment, the expression level of SOD in the two groups was significantly lower than that before treatment ($P<0.05$), and the expression level of MDA was significantly higher than that before treatment ($P<0.05$). At 7 d after treatment, the expression level of SOD in the observation group was 1 d after treatment. And significantly increased before treatment ($P<0.05$), MDA expression level was significantly lower than 1 d after treatment and before treatment ($P<0.05$). SOD expression level of control group was significantly increased compared with 1 d after treatment ($P<0.05$), The expression level of MDA was significantly lower than that at 1 d after treatment ($P<0.05$), and the difference was not significant than before treatment ($P>0.05$). The expression

### Table 3.

Comparison of two groups of immune indicators ($n=63$).

<table>
<thead>
<tr>
<th>Group</th>
<th>Time</th>
<th>IgA (g/L)</th>
<th>IgG (g/L)</th>
<th>IgM (g/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>Before treatment</td>
<td>2.78±0.79</td>
<td>14.02±3.06</td>
<td>1.35±0.58</td>
</tr>
<tr>
<td></td>
<td>After treatment 1 d</td>
<td>1.96±0.51$^a$</td>
<td>9.95±1.76$^b$</td>
<td>0.97±0.26$^c$</td>
</tr>
<tr>
<td></td>
<td>After treatment 7 d</td>
<td>2.83±0.86$^a$</td>
<td>14.77±2.81$^b$</td>
<td>1.43±0.56$^c$</td>
</tr>
<tr>
<td>Control</td>
<td>Before treatment</td>
<td>2.64±0.81</td>
<td>14.53±3.28</td>
<td>1.38±0.52</td>
</tr>
<tr>
<td></td>
<td>After treatment 1 d</td>
<td>1.92±0.53$^a$</td>
<td>9.87±1.80$^b$</td>
<td>0.95±0.22$^c$</td>
</tr>
<tr>
<td></td>
<td>After treatment 7 d</td>
<td>2.27±0.69$^a$</td>
<td>11.52±1.89$^b$</td>
<td>1.19±0.38$^c$</td>
</tr>
</tbody>
</table>

*Note: compared with before treatment $P<0.05$; compared with 1 d after treatment $P<0.05$; compared with control group after treatment $P<0.05$.*

### Table 4.

Comparison of two groups of antioxidant indicators ($n=63$).

<table>
<thead>
<tr>
<th>Group</th>
<th>Time</th>
<th>SOD (nU/mL)</th>
<th>MDA (mmol/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>Before treatment</td>
<td>100.25±6.72</td>
<td>4.61±0.82</td>
</tr>
<tr>
<td></td>
<td>After treatment 1 d</td>
<td>92.30±6.28$^a$</td>
<td>5.13±1.06$^b$</td>
</tr>
<tr>
<td></td>
<td>After treatment 7 d</td>
<td>102.69±7.33$^{abc}$</td>
<td>4.25±0.76$^{bc}$</td>
</tr>
<tr>
<td>Control</td>
<td>Before treatment</td>
<td>98.71±6.93</td>
<td>4.65±0.73</td>
</tr>
<tr>
<td></td>
<td>After treatment 1 d</td>
<td>91.57±6.07$^a$</td>
<td>5.37±1.18$^b$</td>
</tr>
<tr>
<td></td>
<td>After treatment 7 d</td>
<td>97.43±0.69$^a$</td>
<td>4.53±0.95$^b$</td>
</tr>
</tbody>
</table>

*Note: compared with before treatment $P<0.05$; compared with 1 d after treatment $P<0.05$; compared with control group after treatment $P<0.05$.*
level of SOD in the observation group was significantly higher than that in the control group ($P<0.05$). The expression level of MDA was significantly lower than that of the control group ($P<0.05$). See Table 4.

4. Discussion

Colon cancer is a common malignant tumor disease, and long-term morbidity can cause the patient's body to be in a state of severe malnutrition[10], and colon cancer with intestinal obstruction can cause further disorders of the body's functions[11]. In addition, colon cancer patients with intestinal obstruction, postoperative infection, immunosuppression, oxidative stress and other factors can lead to accelerated catabolism, further aggravate the body's malnutrition, and even have a certain impact on the prognosis of patients[12]. Therefore, it is necessary for patients with colon cancer and intestinal obstruction to have nutritional intensive support during the perioperative period. At present, the nutritional support for its perioperative period is mainly conventional nutritional support, but it cannot effectively regulate the related pathological mechanisms such as immune function, inflammatory response and oxidative stress[13].

Alanine-glutamine belongs to a kind of essential amino acid, which not only helps the kidney to synthesize ammonia, but also promotes the synthesis of glutathione in the liver[14]. When the body is in a stress pathological state, the body's alanine-glutamine is consumed in large quantities. Therefore, by replenishing exogenous alanine-glutamine, the body protein synthesis can be accelerated, the negative nitrogen balance can be adjusted, and then the improvement of the role of patient nutrition levels can be achieved[15,16]. The results of this study showed that the expression levels of PA and ALB in the two groups were significantly lower than those before treatment, suggesting that the state of malnutrition was further aggravated after surgery; 7 d after treatment, the expression levels of PA and ALB were higher. There was a significant increase before treatment and 1 day after treatment. The expression levels of PA and ALB in the observation group were significantly higher than those in the control group, suggesting that both nutritional support methods can improve the inflammatory response in patients, and the effect of alanine-glutamine on patients is more significant. The mechanism of action may be that alanine-glutamine can accelerate the synthesis of protein, alleviate the atrophy of intestinal mucosa, inhibit the migration of bacteria and endotoxin, and thus reduce the inflammatory response of patients. Through the analysis of immune indicators, the results of this study showed that the expression levels of IgA, IgG and IgM were significantly lower than those before treatment 1 d after treatment, suggesting that the immunosuppressive effect of patients was further aggravated after surgery, the two nutritional support methods were not significant in improving the early immune function of patients. The mechanism of action may be related to the shorter treatment time and slower recovery of immune function. At 7 d after treatment, the expression levels of IgA, IgG and IgM in the two groups were significantly increased compared with 1 d after treatment, while the observation group was significantly increased compared with the control group, suggesting that both nutritional support methods can regulate the immune function of patients, among which alanine-Glutamine nutritional support has a more significant effect on the improvement of immune function in patients, and its mechanism may be related to alanine-glutamine significantly improving the inflammatory response and enhancing nutritional levels in patients.

After surgical treatment of colon cancer and intestinal obstruction, there are different degrees of stress damage during perioperative period[19-22]. SOD is an important free radical scavenger to protect the body cells from damage. MDA is a lipid peroxidation product that can indirectly show the degree of cellular damage. Through the analysis of anti-oxidation index, the results of this study showed that the expression level of SOD in the two groups was significantly lower than that before treatment, and the expression level of MDA
was significantly increased compared with that before treatment, suggesting that the oxidative stress reaction was further aggravated after surgery. At 7 d after treatment, the expression level of SOD in the two groups increased compared with 1 d after treatment. The expression of MDA was significantly lower than that at 1 d after treatment, and the changes of SOD and MDA expression levels in the observation group were more significant than those in the control group, suggesting that both nutritional support methods can alleviate the oxidative stress response of patients. The alanine-glutamine nutrition support has a more significant effect on the antioxidant effect of patients, and its mechanism may be related to alanine-glutamine significantly improving the patient's inflammatory response and immune function.

In summary, colon cancer patients with intestinal obstruction in the perioperative period with alanyl-glutamine parenteral nutrition support, can significantly improve the state of malnutrition, reduce inflammation, enhance immunity and antioxidant function.

References


