Effect of probiotics in combined with alanyl glutamine on gut barrier function in severely ill patients

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ABSTRACT

Objective: To study the protective effect of probiotics in combined with alanyl glutamine (Gln) on gut barrier function in severely ill patients. Methods: A total of 108 critically ill patients with gastrointestinal diseases were included in the study and randomized into the normal PN group (n=36), the probiotics group (n=36), and the combination group (n=36), which were treated by the conventional parenteral nutrition (PN), PN+probiotics, PN+probiotics+Gln, respectively. The actulose/mannitol (L/M) ratio, and serum endotoxin, lactobacillus and gram-negative bacterium concentrations before operation, the 3rd day and the 8th day after operation in the three groups were determined. Results: The L/M ratio and the serum endotoxin concentration the 8th day after operation in the probiotics group were significantly lower than those in the PN group, while those in the combination group were also significantly lower than those in the probiotics group. The lactobacillus concentration in the probiotics was significantly higher than that in the PN group, while that in the combination group were also significantly higher than that in the probiotics group. The comparison of the gram-negative bacterium concentration among the three groups was not statistically significant. Conclusions: The combination of probiotics in combined with Gln in protecting the gut barrier function has a better effect.

1. Introduction

Malnutrition often exists in the surgical critically ill patients, especially in the elderly patients whose elemental status is poor to promote the intestinal mucosal barrier function to be easily destroyed, even leading to multiple organ dysfunction syndrome (MODS)[1]. Alanyl glutamine has been proved to play a vital role in protecting the gut barrier function, and the protective effect of probiotics on gut barrier is receiving much attention, but there is less research on the combination of alanyl glutamine and probiotics in protecting the gut barrier function in the surgical critically ill patients, in reducing the intestinal permeability, in improving the intestinal tract microbial population, and in reducing the endotoxin[2,3]. The study is aimed to observe the protective effect of probiotics in combined with alanyl glutamine (Gln) on gut barrier function in severely ill patients.

2. Materials and methods

2.1. Clinical materials

A total of 108 critically ill patients who were admitted in the Surgical ICU of the First Hospital of Qinhuangdao City from May, 2013 to May, 2014 were included in the study, among which 54 cases were male, and 54 were female. All the included patients had no abnormal heart, liver, kidney, and lung function, and no contraindications of enteral nutrition. The enrolled subjects were randomly divided into the normal PN group (n=36), the probiotics group (n=36), and the combination group (n=36), among which 18 cases were male, and 18 were female in each group. PN group: aged from 30 to 70 years old, with an average age of (54.5±7.2)
years old, APACHE II scores of (15.4±1.8), receiving PN treatment; probiotics group: aged from 28 to 68 years old, with an average age of (53.4±6.8) years old, APACHE II scores of (15.8±1.5), receiving PN+probiotics treatment; combination group: aged from 29 to 69 years old, with an average age of (53.8±6.4) years old, APACHE II scores of (15.6±1.7), receiving PN+probiotics+Gln treatment. The comparison of the clinical materials among the three groups was not statistically significant (P>0.05).

2.2. Treatment methods

The treatment was immediately initiated after the vital signs were stabilized, and the blood sugar disorder, the abnormal acid, base, electrolyte, and hemodynamics were corrected in the three groups. PN group: providing conventional PN treatment; probiotics group: PN + live combined bifidobacterium and lactobacillus (produced by Shuangqi Pharmaceutical Ltd of Inner Mongolia), 4 tablets each time, three times each day; combination group: PN + live combined bifidobacterium and lactobacillus + Gln injection (Trade name: Dortmund, Keren Pharmaceutical Ltd of Sichuan Province); for live combined bifidobacterium and lactobacillus, 4 tablets each time, three times each day, taken with warm water; for Gln injection (20 g), once a day, ivdrip, a continuous treatment for 8 d.

2.3. Observation indicators

The venous blood before operation, the 3rd day, and the 8th day after operation was extracted, respectively. Chromogenic end-point tachypleus amebocyte lysate and the spectrophotometer were used to detect the endotoxin concentration. The high pressure liquid chromatograph of the electrochemical monitor method was used to determine the urine L/M. The fresh faeces specimen was taken and placed in the sodium chloride solution for dilution. The drip method was used for inoculation on the selective medium for qualitative and quantitative analysis.

2.4. Statistical analysis

SAS 9.2 software was used for statistical analysis. The measurement data were expressed as mean±SD, and ANOVA and t test were used.

3. Results

3.1. General condition after treatment

Incision infection occurred in 1 case in the combination group, and diarrhea occurred in 1 case in the probiotics group. No abdominal pain, diarrhea, and incision infection occurred in the rest groups.

3.2. Intestinal permeability

The results of the comparison of L/M ratio among the three groups before and after operation were shown in Table 1. The comparison of L/M ratio in the urine before operation and the 3rd day after operation was not statistically significant (P>0.05). The L/M ratio in the probiotics group the 8th day after operation was significantly lower than that in the PN group (P<0.05); while that in the combination group was significantly lower than that in the probiotics group, showing that the intestinal permeability was improved (Table 1).

Table 1. Comparison of L/M ratio among the three groups before and after treatment.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Before operation</th>
<th>The 3rd day after operation</th>
<th>The 8th day after operation</th>
</tr>
</thead>
<tbody>
<tr>
<td>PN group</td>
<td>36</td>
<td>0.122±0.013</td>
<td>0.134±0.024</td>
<td>0.146±0.015</td>
</tr>
<tr>
<td>Probiotics group</td>
<td>36</td>
<td>0.125±0.016</td>
<td>0.116±0.031</td>
<td>0.092±0.043a</td>
</tr>
<tr>
<td>Combination group</td>
<td>36</td>
<td>0.123±0.015</td>
<td>0.103±0.027</td>
<td>0.070±0.025b</td>
</tr>
</tbody>
</table>

a: P<0.05, t=5.914, when compared with PN group; b: P<0.05, t=1.975, when compared with the probiotics group.

3.3. Serum endotoxin

The comparison of the serum endotoxin concentration (ng/L) among the three groups before and after operation was shown in Table 2. The comparison of serum endotoxin concentration among the three groups before operation and the 3rd day after operation was not statistically significant (P>0.05). The endotoxin concentration in the probiotics group the 8th day after operation was significantly lower than that in the PN group (P<0.05); while that in the combination group was significantly lower than that in the probiotics group (Table 2).

Table 2. Comparison of the serum endotoxin concentration (ng/L) among the three groups before and after operation.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Before operation</th>
<th>The 3rd day after operation</th>
<th>The 8th day after operation</th>
</tr>
</thead>
<tbody>
<tr>
<td>PN group</td>
<td>36</td>
<td>0.382±0.016</td>
<td>0.523±0.027</td>
<td>0.446±0.035</td>
</tr>
<tr>
<td>Probiotics group</td>
<td>36</td>
<td>0.376±0.031</td>
<td>0.476±0.012</td>
<td>0.312±0.023a</td>
</tr>
<tr>
<td>Combination group</td>
<td>36</td>
<td>0.387±0.024</td>
<td>0.421±0.019</td>
<td>0.290±0.032b</td>
</tr>
</tbody>
</table>

a: P<0.05, t=11.246, when compared with PN group; b: P<0.05, t=1.996, when compared with the probiotics group.

3.4. Changes of intestinal flora in the faeces before and after operation

The comparison of lactobacillus and gram-negative bacterium concentrations in the faeces among the three groups before and after operation was shown in Table 3. The comparison of the intestinal
flora among the three groups before operation and the 3rd day after operation was not statistically significant ($P>0.05$). The lactobacillus concentration the 8th day after treatment in the probiotics group and the combination group was significantly elevated when compared with the PN group ($P<0.05$), while that in the combination group was significantly higher than that in the probiotics group ($P<0.05$). But the comparison of the gram-negative bacterium concentration among the three groups was not statistically significant ($P>0.05$). CFU was converted into the logarithmic value ($\log_{10}$CFU/g) (Table 3).

### Table 3.
Comparison of lactobacillus and gram-negative bacterium concentrations in the faeces among the three groups before and after operation.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Time</th>
<th>Lactobacillus</th>
<th>Gram-negative bacterium</th>
</tr>
</thead>
<tbody>
<tr>
<td>PN group</td>
<td>Before operation</td>
<td>7.43±0.159</td>
<td>8.25±0.208</td>
</tr>
<tr>
<td></td>
<td>The 3rd day</td>
<td>7.45±0.131</td>
<td>8.41±0.321</td>
</tr>
<tr>
<td></td>
<td>The 8th day</td>
<td>7.52±0.109</td>
<td>8.35±0.428</td>
</tr>
<tr>
<td>Probiotics group</td>
<td>Before operation</td>
<td>7.36±0.269</td>
<td>8.27±0.251</td>
</tr>
<tr>
<td></td>
<td>The 3rd day</td>
<td>7.53±0.211</td>
<td>8.34±0.172</td>
</tr>
<tr>
<td></td>
<td>The 8th day</td>
<td>8.36±0.179a</td>
<td>8.29±0.220c</td>
</tr>
<tr>
<td>Combination group</td>
<td>Before operation</td>
<td>7.38±0.351</td>
<td>8.31±0.219</td>
</tr>
<tr>
<td></td>
<td>The 3rd day</td>
<td>7.85±0.309</td>
<td>8.46±0.371</td>
</tr>
<tr>
<td></td>
<td>The 8th day</td>
<td>9.11±0.411b</td>
<td>8.28±0.348d</td>
</tr>
</tbody>
</table>

Note: *P<0.05, t=17.548, when compared with PN group; b: P<0.05, t=5.639, when compared with the probiotics group; c: P>0.05, t=0.350, when compared with PN group; d: P<0.05, t=0.169, when compared with the probiotics group.

### 4. Discussion

The intestinal tract is the most complicated and important organ in the human body. The intestinal mucosal barrier is composed of the ecological barrier, the mechanical barrier, the immunological barrier, and the chemical barrier, and is also the biggest barrier to prevent the shifting of the bacteria and endotoxin in the gut lumen[4,5]. If there is a lack of intestinal mucosal protein, stress injury, ischemia, and reperfusion injury can destroy the intestinal mucosal barrier to cause the bacterial translocation and endotoxemia, and multiple organ failure will occur in a serious condition. It is reported that[7] the surgical critically ill patients are imposed restrictions on diet and given catharsis 3 d before operation, which can cause the atrophy of intestinal mucosa and the reduction of intestinal barrier function. In addition, the operative wound and the postoperative stress reaction can further cause the destruction of intestinal microecological balance to accelerate the dysbacteriosis and bacterial translocation. Therefore, how to maintain the intestinal barrier function after traumatic stress becomes a difficult problem in the nutritional therapy.

Gln is an essential amino acid in the human body and is a main energy source of the gastrointestinal mucosal cells. Some researches demonstrate that[8] Gln can not only enhance the immunoglobulin level in the intestinal mucosa, promote the secretion of gastrointestinal hormones, prevent the atrophy of intestinal mucosa, but also maintain the intestinal mucosal tissue structure, repair the intestinal mucosal injury, improve the intestinal permeability, and block the bacterial and endotoxin translocation. The microecology is a new emerging life science developed in recent years. The probiotics, as a kind of microecological modulator, which has a protective effect on intestinal barrier function, are receiving more and more attention. Probiotics refer to the flora beneficial to the human body. Bifidobacterium and lactobacillus are the most common probiotics in the intestinal tract[9]. Some researches demonstrate that[9-11] probiotics can adjust the intestinal flora, inhibit the growth of pathogenic bacteria, decrease the postoperative intestinal bacteria and endotoxin translocation, reduce the occurrence of infection, regulate the immune response, and treat food allergy and inflammatory bowel disease.

In the study, probiotics and Gln are used to protect the intestinal mucosal barrier function. The results in the study showed that by taking the purely PN treatment before operation, the 3rd and 8th day after operation, the serum endotoxin concentration was still ascending, and the intestinal permeability was still increasing, thus the intestinal barrier function could not be effectively protected. In combined with probiotics, the difference before operation and the 3rd day after operation was not statistically significant, but on the 8th day after operation, the L/M ratio in the urine and the serum endotoxin concentration in the probiotics group were significantly reduced when compared with the PN group, showing that probiotics can contribute to improve the intestinal permeability and reduce the endotoxin translocation, which is probably associated with the increasing number of lactobacillus, the reduced destroying degree of intestinal barrier, the repaired mechanical barrier, and the inhibition of the growth of gram-negative bacteria after the application of probiotics, which is also verified by detecting CFU in the faeces. In the combination group, the synergistic effect of Gln and probiotics can provide the energy for the intestinal mucosal cells and improve the diversity of intestinal flora. Before operation, the 3rd day and 8th day after operation, the L/M ratio in the urine and serum endotoxin concentration in the probiotics group were significantly reduced when compared with the PN group, showing that probiotics can contribute to improve the intestinal permeability and reduce the endotoxin translocation, which is probably associated with the increasing number of lactobacillus, the reduced destroying degree of intestinal barrier, the repaired mechanical barrier, and the inhibition of the growth of gram-negative bacteria after the application of probiotics.
increase the number of lactobacillus, inhibit the growth of gram-negative bacteria, improve the constitution of intestinal flora, repair the damaged intestinal ecological barrier, reduce the intestinal permeability and the endotoxin concentration, repair the damaged intestinal mechanical barrier, and reduce the intestinal bacteria translocation. But the number of gram-negative bacteria was not significantly reduced, whether on this basis, given other nutrient substances, such as probiotics, to reduce the number of gram-negative bacteria in order to indeed improve the diversity of the intestinal flora and enhance the immunity, which is required a further study.

References


