Effect of bifidobacterium enteral nutrition on intestinal flora and systemic inflammatory stress in patients with severe stroke

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Objective: To study the effect of bifidobacterium enteral nutrition on intestinal flora and systemic inflammatory stress in patients with severe stroke. Methods: Patients with severe stroke who were treated in our hospital between March 2015 and July 2017 were selected and randomly divided into the observation group who accepted bifidobacterium enteral nutrition and the control group who accepted conventional enteral nutrition, and the contents of intestinal flora in feces as well as the contents of intestinal mucosal barrier markers, inflammatory response indexes, stress response indexes in serum were determined. Results: D-lactic acid, DAO, PCT, Claudin-4, TNF-α, IL-1β, Hcy, sICAM1, NE, Cor and MDA contents in serum of both groups 14 days after treatment were lower than those before treatment whereas T-AOC contents were higher than those before treatment, and bifidobacterium, lactobacillus and bacteroides contents in feces as well as T-AOC content in serum of observation group 14 d after treatment were higher than those of control group whereas enterococcus and enterobacter contents in feces as well as D-lactic acid, DAO, PCT, Claudin-4, TNF-α, IL-1β, Hcy, sICAM1, NE, Cor and MDA contents in serum were lower than those of control group. Conclusion: Bifidobacterium enteral nutrition is able to improve the intestinal flora and inhibit the systemic inflammatory stress in patients with severe stroke.

1. Introduction

Stroke is a common neurological cerebrovascular disease that will cause nerve injury and lead to clinical symptoms of sensory and movement dysfunction, there will be dysphagia, disturbance of consciousness and other circumstances in patients with severe stroke, so patients cannot eat independently, and the parenteral nutrition or enteral nutrition is needed for nutrition support[1]. Parenteral nutrition is easy to operate and the nutrients can directly enter into the blood circulation and be used by the body, but long-term parenteral nutrition can cause the digestive tract to lose food stimulus and increase the risk of intestinal mucosal barrier function injury; enteral nutrition is used to supplement nutrients through jejunal nutrition tube, which can maintain the integrity of intestinal mucosal barrier function under the condition of ensuring the supply of nutrients[2]. Intestinal flora is involved in the formation of the intestinal mucosal barrier, and the neurotransmitter and gastrointestinal hormone secretion disorder in the course of stroke can cause flora disorder and ectopia, which will result in the excessive activation of systemic inflammatory and stress response[3]. Bifidobacterium is the important probiotic bacteria in the intestines, and the bifidobacterium supplementation by enteral nutrition tube may help maintain intestinal flora balance, and then correct the systemic inflammatory stress response caused by flora disorder. In the following studies, we specifically analyzed the effects of bifidobacterium enteral nutrition on intestinal flora and systemic inflammatory stress in patients with severe stroke.

2. Case information and research methods

2.1 Clinical case information

Patients with severe stroke who were treated in our hospital between March 2015 and July 2017 were selected, all patients were diagnosed with severe stroke and received enteral nutrition support, a total of 84 cases were selected, and the random number table method was used to divide them into the observation group who
accepted bifidobacterium enteral nutrition and the control group who accepted routine enteral nutrition. 42 cases in each group. Control group were given Ruixian for enteral nutrition therapy, the dosage was 200 mL on the first day, increased at the rate of 1/4 every day until it reached 400 mL and maintained there for 14 d, there were 25 men and 17 women, and they were 39-62 years old; on the basis of Ruixian enteral nutrition therapy, observation group were treated with bifidobacterium, 3 tablets each time and 1 time every day, there were 28 men and 14 women, and they were 41-61 years old. There was no significant difference in the general data between the two groups (P>0.05).

2.2 Research methods

2.2.1 Detection methods of intestinal flora in feces

14 d after treatment, right amount of feces tissue was collected, 1 g was weighed, diluted with 5 mL of distilled water and inoculated in culture medium to determine the number of bifidobacterium, lactobacillus, bacteroides, enterococcus and enterobacter.

2.2.2 Detection methods of molecule indexes in serum

Before and after treatment, right amount of peripheral venous blood was collected to separate serum, then enzyme-linked immunosorbent assay kit was used to detect D-lactic acid, DAO, PCT, Claudin-4, TNF-α, IL-1β, Hcy, sICAM1, NE and Cor, and radiimmunoprecipitation kit was used to determine the contents of MDA and T-AOC.

2.3 Statistical methods

The data were input in software SPSS 20.0, the data between two groups were compared by t test and the difference was statistically significant when P<0.05.

3. Results

3.1 The number of intestinal flora in feces

Comparison of intestinal flora bifidobacterium, lactobacillus, bacteroides, enterococcus and enterobacter in feces between the two groups of patients 14 d after treatment was as follows: intestinal flora bifidobacterium, lactobacillus, bacteroides, enterococcus and enterobacter contents in feces of observation group were higher than those of control group whereas enterococcus and enterobacter contents were lower than those of control group.

3.2 Serum intestinal mucosal barrier marker contents

Comparison of serum intestinal mucosal barrier markers D-lactic acid (μg/mL), DAO (U/L), PCT (ng/mL) and Claudin-4 (pg/mL) between the two groups of patients before treatment and 14 days after treatment was as follows: serum D-lactic acid, DAO, PCT and Claudin-4 contents were not were significantly different between the two groups of patients before treatment (P>0.05) whereas serum D-lactic acid, DAO, PCT and Claudin-4 contents were significantly different between the two groups of patients after treatment (P<0.05), and serum D-lactic acid, DAO, PCT and Claudin-4 contents of observation group were lower than those of control group; serum D-lactic acid, DAO, PCT and Claudin-4 contents of both groups were significantly different between before and after treatment (P<0.05), and serum D-lactic acid, DAO, PCT and Claudin-4 contents after treatment were lower than those before treatment.

3.3 Serum inflammatory response index contents

Comparison of serum inflammatory response indexes TNF-α, IL-1β, Hcy and sICAM1 (ng/mL) between the two groups of patients before treatment and 14 d after treatment was as follows: serum TNF-α, IL-1β, Hcy and sICAM1 contents not were significantly different between the two groups of patients before treatment (P>0.05) whereas serum TNF-α, IL-1β, Hcy and sICAM1 contents were significantly different between the two groups of patients after treatment (P<0.05), and serum TNF-α, IL-1β, Hcy and sICAM1 contents of both groups were significantly different between before and after treatment (P<0.05), and serum TNF-α, IL-1β, Hcy and sICAM1 contents after treatment were lower than those before treatment.

Table 1.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Bifidobacterium (×10^9 CFU)</th>
<th>Lactobacillus (×10^9 CFU)</th>
<th>Bacteroides (×10^9 CFU)</th>
<th>Enterococcus (×10^9 CFU)</th>
<th>Enterobacter (×10^9 CFU)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>42</td>
<td>7.82±0.95</td>
<td>6.48±0.82</td>
<td>7.51±0.89</td>
<td>5.33±0.76</td>
<td>7.02±0.89</td>
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<td>Control</td>
<td>42</td>
<td>6.57±0.93</td>
<td>5.22±0.69</td>
<td>5.89±0.75</td>
<td>6.85±0.78</td>
<td>8.71±0.94</td>
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<tr>
<td>t</td>
<td>11.278</td>
<td>&lt;0.05</td>
<td>8.798</td>
<td>9.675</td>
<td>12.374</td>
<td>9.126</td>
</tr>
<tr>
<td>P</td>
<td>0.05</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>

Table 2.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>D-lactic acid (ug/mL)</th>
<th>DAO (U/L)</th>
<th>PCT (ng/mL)</th>
<th>Claudin-4 (pg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>42</td>
<td>Before</td>
<td>15.82±2.25</td>
<td>20.35±3.28</td>
<td>11.38±1.57</td>
<td>136±19.3</td>
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<td></td>
<td></td>
<td>After</td>
<td>8.33±1.03</td>
<td>11.28±1.47</td>
<td>4.77±0.61</td>
<td>70.3±9.3</td>
</tr>
<tr>
<td>Control</td>
<td>42</td>
<td>Before</td>
<td>15.47±2.03</td>
<td>20.18±3.05</td>
<td>11.89±1.93</td>
<td>140±17.8</td>
</tr>
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<td></td>
<td></td>
<td>After</td>
<td>12.14±1.78</td>
<td>15.75±2.35</td>
<td>7.03±0.94</td>
<td>98.4±11.5</td>
</tr>
</tbody>
</table>

* comparison between two groups after treatment, P<0.05; † comparison between before and after treatment within group, P<0.05. Zhen Tan et al./ Journal of Hainan Medical University 2018; 24(6): 29-32
than those before treatment. Whereas T-AOC contents were higher and serum NE, Cor, and MDA contents after treatment were lower than those before treatment. In the above research, we analyzed the change of intestinal flora after enteral nutrition therapy, and the results showed that enterococcus and enterobacter contents were lower than those of control group. It indicates that bifidobacterium enteral nutrition can improve the intestinal flora, increase the number of probiotics and decrease the number of pathogenic bacteria.

Comparison of serum stress response indexes between the two groups of patients. *(P<0.05; α=0.05)*

### 3.4 Serum stress response index contents

Comparison of serum stress response indexes (NE ng/mL, Cor ng/mL, MDA nmol/mL, T-AOC U/mL) between the two groups of patients before treatment and 14 d after treatment was as follows: serum NE, Cor, MDA and T-AOC contents were not significantly different between the two groups of patients before treatment (P>0.05) whereas serum NE, Cor, MDA and T-AOC contents were significantly different between the two groups of patients after treatment (P<0.05) and serum NE, Cor and MDA contents of observation group were lower than those of control group whereas T-AOC content was higher than that of control group; serum NE, Cor, MDA and T-AOC contents of both groups were significantly different between before and after treatment (P<0.05), and serum NE, Cor and MDA contents after treatment were lower than those before treatment whereas T-AOC contents were higher than those before treatment.

### 4. Discussion

The intestinal tract is where the microorganisms gather in the human body, the total number of bacteria in the intestines is more than 39 trillion under physiological conditions and the vast majority of the bacteria are bifidobacterium, lactobacillus, bacteroides and other probiotics, which play the roles such as nutrition metabolism, immune regulation and antagonism of pathogenic bacteria breeding; under the pathological conditions, the mass breeding of pathogenic bacteria can cause the disorder and ectopia of the bacteria, which can lead to the activation of systemic inflammatory and stress response[4]. In the course of stroke, especially severe stroke, the neurological damage can cause the secretion of gastrointestinal hormones and neurotransmitters to change, which will affect the function of intestinal mucosa and cause the disorder of intestinal flora. Most patients with severe stroke need enteral nutrition support, which can not only provide the nutrients necessary for the body, but can also protect the intestinal mucosa and prevent the happening of intestinal flora disturbance to a certain extent[5,6]. Bifidobacterium is an important probiotic in the intestinal tract, and the bifidobacterium supplementation via enteral nutrition can enhance the function of probiotics and maintain the balance of bacteria in the intestinal tract[7]. In the above research, we analyzed the change of intestinal flora after enteral nutrition therapy, and the results showed that bifidobacterium, lactobacillus and bacteroides contents in feces of observation group were higher than those of control group whereas enterococcus and enterobacter contents were lower than those of control group. It indicates that bifidobacterium enteral nutrition can improve the intestinal flora, increase the number of probiotics and decrease the number of pathogenic bacteria.

Intestinal probiotics participate in the formation of intestinal mucosal barrier, and the balance of intestinal flora can ensure the normal function of the intestinal mucosal epithelial cells and villous cells, and help to maintain the integrity of the intestinal mucosal barrier. D-lactic acid is the anaerobic fermentation product of the intestinal bacteria, which is increasingly generated and released into the blood circulation during flora disorder; DAO is a catalytic enzyme that participates in the material metabolism in intestinal mucosal villous cells, and the damage of intestinal mucosal barrier can result in the rupture of villous cells and the increase of DAO release[8]; PCT is a sensitive indicator of bacterial infection, and the ectopic intestinal pathogens after intestinal mucosal barrier damage can stimulate the synthesis and secretion of PCT[9]; Claudin-4 is an occludin that is involved in the tight junction formation between intestinal mucosal epithelial cells, and the destruction of the mucosal barrier is accompanied by the large release of Claudin-4. The analysis of the change in intestinal mucosal barrier markers before and after enteral nutrition therapy showed that serum D-lactic acid, DAO, PCT and Claudin-4 contents of both groups after treatment were lower than those before treatment and serum D-lactic acid, DAO, PCT and Claudin-4 contents of observation group after treatment were lower than those of control group. This indicates that enteral nutrition intervention can improve the intestinal mucosal barrier function and the addition of bifidobacterium can further reduce the damage of intestinal mucosal barrier in stroke.

The disordered and ectopic intestinal flora in patients with stroke can be combined with pattern recognition receptors to initiate the inflammatory response and increase the release of various inflammatory molecules, which will aggravate the neural function damage[10,11]. TNF-α and IL-1β are cytokines with pro-inflammatory activity, which mediate the cascade activation process of inflammatory response[12,13]; Hcy is an amino acid with damage effect, and it is massively released in the process of inflammation and can cause damage to endothelial function, which increases the microcirculation permeability in brain tissue and promotes the local accumulation of injury molecules[14]; ICAM1 is a cytokine that mediates the intercellular adhesion, which can promote the
adhesion and aggregation of white blood cells and oxygen free radicals to the cerebrovascular endothelial cells, and then aggravate the cerebral injury[15]. The analysis of the change in inflammatory response indexes before and after enteral nutrition treatment in the study showed that serum TNF-α, IL-1β, Hcy and sICAM1 contents of both groups after treatment were lower than those before treatment and serum TNF-α, IL-1β, Hcy and sICAM1 contents of observation group after treatment were lower than those of control group. This shows that enteral nutrition interventions can reduce the release of inflammatory molecules and inhibit the activation of inflammatory responses, and adding bifidobacteria can further reduce the activation of inflammatory responses in stroke.

The ectopic intestinal flora and the hyperactive inflammatory response are both strong stressors for the body, which can significantly activate the stress response and change the formation of a variety of stress products[16]. NE and Cor are the hormones secreted by the adrenal gland, the former is derived from the adrenal medulla, the latter is derived from the adrenal cortex, and both are massively secreted during the stress response[17,18]; MDA is the lipid peroxidation product in the process of stress reaction, which can not only reflect the degree of stress, but also reflect the degree of peroxidative damage of tissue[19]; T-AOC is the index to evaluate the total antioxidant capacity of the body, and the over-enhanced stress response can increase the consumption of antioxidant enzymes and weaken the antioxidant capacity[20]. The analysis of the change in stress response indexes before and after enteral nutrition treatment in the study showed that serum NE, Cor and MDA contents of both groups after treatment were lower than those before treatment whereas T-AOC contents were higher than those before treatment, and serum NE, Cor and MDA contents of observation group after treatment were lower than those of control group whereas T-AOC content was higher than that of control group. This means that enteral nutrition intervention can reduce the release of stress products and enhance the antioxidant and anti-stress capacity, and adding bifidobacterium can further reduce the activation of stress response in the course of stroke.

Bifidobacterium therapy on the basis of routine enteral nutrition can improve the intestinal flora, increase the number of probiotics and decrease the number of pathogenic bacteria in patients with severe stroke, which can restrain the activation systemic inflammatory stress response in the course of the disease.

References