Clinical study on the efficacy of mesalazine and live combined Bacillus subtilis and Enterococcus faecium enteric-coated capsules in the treatment of ulcerative colitis

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ABSTRACT

Objective: To explore the clinical efficacy of mesalazine and live combined Bacillus subtilis and Enterococcus faecium enteric-coated capsules in the treatment of ulcerative colitis (UC).

Methods: A total of 70 patients with UC who were admitted in our hospital from January, 2015 to January, 2016 were included in the study and randomized into the observation group and the control group. The patients in the control group were given mesalazine, 1 g/time, 4 times a day. On this basis, the patients in the observation group were given live combined Bacillus subtilis and Enterococcus faecium enteric-coated capsules, 0.42 g/time, 3 times/d, taken with warm water half an hour after meal. Four-week treatment was regarded as one course. The levels of IL-6, IL-8, and IL-10 before and after treatment were determined. The change of Sutherland index was detected, and the efficacy was estimated.

Results: The serum IL-6 and IL-8 levels after treatment in the two groups were significantly reduced, IL-10 level was significantly elevated when compared with before treatment, and those in the observation group were significantly superior to those in the control group. Sutherland index after treatment in the observation group was significantly lower than that in the control group. The total effective rate in the observation group (97.14%) was significantly higher than that in the control group (80.00%).

Conclusions: Mesalazine and live combined Bacillus subtilis and Enterococcus faecium enteric-coated capsules in the treatment of UC can effectively regulate the cytokine level, correct the intestinal flora disturbance, and improve the intestinal environment, with a satisfying clinical effect.

1. Introduction

Ulcerative colitis (UC), a non-specific inflammatory bowel disease, can invade the distal colonic mucosa and submucosa, progress inversely to the proximal end, and spread to the terminal end and the whole colon[1], with main clinical manifestations of bloody purulent stool, abdominal pain, diarrhea, tenesmus, and fatigue, and is characterized by long course and repeated attack[2]. With the acceleration of life rhythm and the alteration of living habits, the morbidity of UC is gradually increasing in recent years, which can severely affect the living qualities[3]. The pathogenesis of UC is not yet clarified. Numerous studies show that UC is associated with heredity, immunoregulation, intestinal flora disturbance, and infection. In recent years, the clinical studies demonstrate that the intestinal flora imbalance plays a vital role in the pathogenesis of UC, while probiotics can adhere to the surface of intestinal mucosa to resist the digestion of gastric acid and entero-enzymes, regulate the intestinal immune response, and alter the balance between the intestinal microflora to reach the goal of treating UC[4,5]. The study is aimed to explore the clinical efficacy of mesalazine and live combined Bacillus subtilis and Enterococcus faecium enteric-coated capsules in the treatment of UC.

2. Materials and methods

2.1. General materials
A total of 70 patients with UC who were admitted in our hospital from January, 2015 to January, 2016 were included in the study and randomized into the observation group and the control group. The patients were in accordance with the diagnostic criteria of UC in the Consensus Opinion of Diagnosis and Treatment Standard of Chinese Inflammatory Bowel Disease[6]. In the observation group, there were 35 cases, among which 17 were male, and 18 were female; aged from 22 to 63 years old, with an average age of (41.3±3.5) years old; course from 0.5 to 10 years, with an average course of (4.7±3.6) years; 8 were mild, 12 were moderate, and 15 were severe. In the control group, there were 35 cases, among which 16 were male, and 19 were female; aged from 21 to 64 years old, with an average age of (42.1±3.2) years old; course from 0.5 to 10 years, with an average course of (4.6±3.7) years; 7 were mild, 13 were moderate, and 15 were severe. The comparison of the general materials between the two groups was not statistically significant (P>0.05).

2.2. Inclusion and exclusion criteria

Inclusion criteria: (1) those who were in accordance with the related diagnostic criteria of UC; (2) those who were confirmed by the colonoscope and pathological examination; (3) those who had normal heart, liver, and kidney functions; (4) those who had no allergy or contraindications to related drugs; (5) those who had signed the informed consents. Exclusion criteria: (1) those who had infectious colitis, ischemic enteritis, Crohn’s disease, and colon cancer; (2) those who were merged with intestinal perforation and intestinal obstruction; (3) those who were pregnant or during the lactation period.

2.3. Methods

The patients in the control group were given mesalazine (produced by Sunflower Pharmaceutical Industry Co. Ltd., Approval No. H19980148), 1 g/time, 4 times a day. On this basis, the patients in the observation group were given live combined Bacillus subtilis and Enterococcus faecium enteric-coated capsules (produced by Shanghai Xinyi Pharmaceutical Industry Co. Ltd., Approval No. S10950032), 0.42 g/time, 3 times/d, taken with warm water half an hour after meal. One-month treatment was regarded as one course.

2.4. Observation indicators

A volume of 5 mL fasting venous blood before and after treatment was collected, and centrifuged for serum. ELISA was used to detect the serum IL-6, IL-8, and IL-10 levels. The change of Sutherland index was detected, i.e. symptoms relieved: 0-2 scores; mild activity: 3-5 scores; moderate activity: 6-10 scores; severe activity: 11-12 scores. The efficacy was estimated in the following: (1) complete remission: the colonscopy showed that the intestinal mucosa was basically normal, and the symptoms were completely disappeared; (2) effective: the colonscopy showed that the intestinal mucosa had mild inflammation or the pseudopolyp was formed, and the symptoms were basically disappeared; (3) invalid: the colonscopy showed that the intestinal mucosa was not obviously changed, and the symptoms were not improved.

2.4. Statistical analysis

SPSS 18.0 software was used for the statistical analysis. The measurement data were expressed as mean±SD, and t test was used. Chi-square test was used for the enumeration data. P<0.05 was regarded as statistically significant.

3. Results

3.1. Comparison of the serum IL-6, IL-8, and IL-10 levels before and after treatment

The serum IL-6 and IL-8 levels after treatment in the two groups were significantly reduced, IL-10 level was significantly elevated when compared with before treatment, and those in the observation group were significantly superior to those in the control group (P<0.05) (Table 1).

3.2. Sutherland index change before and after treatment

Sutherland index after treatment in the observation group was significantly lower than that in the control group (P<0.05) (Table 2).

Table 1. Comparison of the serum IL-6, IL-8, and IL-10 levels before and after treatment (ng/L).

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>IL-6</th>
<th>IL-8</th>
<th>IL-10</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Before treatment</td>
<td>After treatment</td>
<td>Before treatment</td>
</tr>
<tr>
<td>Observation</td>
<td>35</td>
<td>185.47±28.36</td>
<td>93.71±13.24</td>
<td>293.15±25.13</td>
</tr>
<tr>
<td>Control</td>
<td>35</td>
<td>184.41±30.11</td>
<td>142.43±18.61</td>
<td>292.46±27.92</td>
</tr>
</tbody>
</table>

*P<0.05, when compared with before treatment; #P<0.05, when compared with the control group.

Table 2. Sutherland index change before and after treatment (score).

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Before treatment</th>
<th>After treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>35</td>
<td>7.57±2.12</td>
<td>2.51±1.12</td>
</tr>
<tr>
<td>Control</td>
<td>35</td>
<td>7.62±2.11</td>
<td>5.38±1.31</td>
</tr>
</tbody>
</table>

*P<0.05, when compared with before treatment; †P<0.05, when compared with the control group.
3.3. Comparison of the efficacy

After treatment, in the observation group, 23 (65.71%) were completely relieved, 11 (31.43%) were effective, 1 (2.86%) was invalid, and the total effective rate was 97.14%; while in the control group, 16 (45.71%) were completely relieved, 12 (34.29%) were effective, 7 (20.00%) was invalid, and the total effective rate was 80.00%. The total effective rate in the observation group was significantly higher than that in the control group.

4. Discussion

The pathogenesis of UC is not yet clear, and it is deemed to be closely associated with the mucosal immune injury caused by the intestinal flora imbalance, which can induce an immune response of intestinal mucosa in the susceptible hosts, and a large amount of inflammatory cells aggregated, trigger the release of numerous inflammatory mediators, resulting in intestinal caspase cascade to induce intestinal mucosal injury[8,9].

Some researches demonstrate that the cytokine imbalance is a key factor for developing non-specific inflammation in UC patients, with insufficient anti-inflammatory cytokine secretion and elevated pro-inflammatory cytokines[10]. IL-6, a cytokine produce by various cellular reactions, can activate and promote the neutrophils aggregated in the inflammatory sites, delay the cell apoptosis, and release the oxygen radicals. IL-6 is a key cytokine for initiating anti-inflammatory reaction, and has a strong inflammatory activity, whose level can be greatly elevated when there is a bacterial infection, and the over expression can usually cause the intestinal environment disturbance[11]. IL-8, an important determining factor for neutrophil mediating, can activate the inflammatory cells to be aggregated in the intestinal mucosa, induce the inflammatory reaction, and play an important role in the occurrence and development of UC[12]. IL-6 and IL-8, as pro-inflammatory cytokines, can mediate the pathological injury of intestinal mucosa, induce the inflammatory reaction, and play an important role in the occurrence and development of UC[13]. IL-10, a multi-functional negative-regulatory factor, can inhibit the chemotaxis of macrophages and neutrophils, and is acknowledged to be the anti-inflammatory cytokine[14]. It is reported that the serum IL-10 level is significantly reduced in the active UC patients, is lower in severe patients, and can be elevated in the remission period. Some scholars argue that the intestinal mucosa immune injury caused by intestinal flora imbalance plays a vital role in the occurrence and development of UC. The number of Bacillus acidilactici and Bifidobacterium bifidum in UC patients at the active phase is significantly lower than that in the normal individuals, and the above flora at the recovery phase are recovered to the normal levels; therefore, based on the anti-inflammation, improvement of intestinal flora imbalance should be added to the treatment of UC[16]. Mesalazine can inhibit the synthesis and release of leukotriene and prostaglandin, suppress the activity of POD, block the amplification effect of leukocytes which can produce the inflammatory mediators, restrain the intestinal mucosal inflammation, and promote the improvement of intestinal inflammation[17]. The live combined Bacillus subtilis and Enterococcus faecium enteric-coated capsules, including Bacillus subtilis and Enterococcus faecium two probiotics, can release the viable bacteria after disintegration by passing the gastric acid barrier, which can plant and colonize in the intestinal tract to form an appropriate environment for the growth of normal superior microflora and recover the intestinal protection barrier, thus, the intestinal immune ability is strengthened[18]. The combination of the above viable bacteria can promote the improvement of intestinal flora imbalance in UC patients, prevent the planting and invading of pathogenic bacteria, and accelerate the recovery of intestinal barrier function[4].

On the above basis, the patients are given appropriate nursing and health education through recognizing, believing, and behavior to promote the recovery. The specific measures are listed in the following[19]: (1) psychological counseling: Due to the long disease course, most UC patients are nervous and have heavy hesitates; therefore, psychological nursing should be taken in order to stabilize their emotions; (2) diet nursing: During the acute period, the patients are given diet free and no irritable food. During the remission period, the patients are given adequate calories, high quality proteins, and food rich in vitamins in order to reduce the disease activity index and maintain the clinical remission; (3) medication nursing: A medication is guided, the necessity of medication and the probable adverse reactions are introduced in order to coordinate the treatment; (4) anal skin nursing: Due to long-term diarrhea, a daily nursing function should be performed in order to prevent the skin erosion.

The results in the study showed that the serum IL-6 and IL-8 levels after treatment in the two groups were significantly reduced, IL-10 level was significantly elevated when compared with before treatment, and those in the observation group were significantly superior to those in the control group (P<0.05); Sutherland index after treatment in the observation group was significantly lower than that in the control group (P<0.05); the total effective rate in the observation group (97.14%) was significantly higher than that in the control group (80.00%) (P<0.05), indicating that mesalazine and live combined Bacillus subtilis and Enterococcus faecium enteric-coated capsules in the treatment of UC has a significant clinical efficacy, superior to that by pure mesalazine.

In conclusion, mesalazine and live combined Bacillus subtilis and Enterococcus faecium enteric-coated capsules in the treatment of UC can effectively regulate the cytokine level, correct the intestinal flora disturbance, and improve the intestinal environment, with a satisfying clinical effect.
References


