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Clinical and Experimental Study on Probiotics in the Treatment of Constipation Type Irritable Bowel Syndrome

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Abstract

Aim: The effects of probiotics on symptoms scores, gastrointestinal hormones and oxidative stress index in constipative Irritable Bowel Syndrome (IBS-C) patients were studied-during the period of 2018.

Methods: 96 patients with IBS-C who had been treated in our hospital previously. The patients in the control group (49) were treated with Mosapride, and the patients in the observation group (47) were treated with Bifidobacterium triple viable enteric-coated capsules on the basis of the control treatment. The clinical efficacy including: clinical symptoms, gastrointestinal hormones, 5-HT and oxidative stress were studied and compared between the two groups.

Results: In the observation group, the clinical efficacy in 29 cases (61.70%) was markedly effective and in 15 cases (31.91%) moderately effective, in comparison the total effective rate was 93.62%in the observation group, and 79.59% in the control group ($P < 0.05$). After treatment, the clinical symptoms score in both two groups decreased significantly. The scores of abdominal distension, abdominal pain, defecation frequency, stool characteristics and defecation difficulty in the observation group were significantly lower than those in the control group ($P < 0.05$). Although the levels of 5-HT, MDA and LPO in both groups decreased significantly after treatment. The levels of 5-HT, MDA and LPO in the observation group were even lower than those in the control group ($P < 0.05$). Similarly, the levels of gastrointestinal hormones in both groups were improved with the respective treatments. However, the MTL level in the observation group was significant higher than that in the control group, and the levels of VIP and S were lower in the observation group than those in the control group ($P < 0.05$).

Conclusion: Bifidobacterium triple viable capsule combined with Mosapride is more effective in the treatment of IBS-C. The combination therapy can better relieve symptoms, and further decreased gastrointestinal hormone levels and reduce oxidative stress response in IBS-C patients. It is therefore highly recommended for clinical application.

Keywords: Constipation Irritable Bowel Syndrome; Clinical Study; Experimental Study; Probiotics

Introduction

Irritable Bowel Syndrome (IBS) is a common clinical intestinal dysfunction syndrome, and its clinical manifestations include recurrent abdominal pain, abdominal distension, and changes in defecation habits, which seriously affects the quality of life of patients [1]. Constipation-type Irritable Bowel Syndrome (IBS-C) is a common type of IBS, and its pathogenesis is related to gastrointestinal motility disorders, mental factors, visceral paraesthesia, intestinal micro ecological disorders and other factors [2]. Currently, there is no specific drug for effective treatment of IBS-C, and the main treatment strategy is to induce diarrhoea, stimulate intestinal peristalsis, and regulate intestinal visceral sensation, although this treatment strategy can alleviate the clinical symptoms of the IBS-C patients in the short term, the long-term efficacy is difficult to achieve [3]. Moxabelil is a commonly used gastrointestinal motility drug in clinical practice, which activates the cholinergic 5-hydroxytryptamine 4 receptor in the gastrointestinal wall muscles, releasing a large amount of acetylcholine, thereby promoting gastrointestinal peristalsis, and acceleratings gastrointestinal emption [4]. Liyang Qin reported that Moxabelil may have a curative effect for IBS-C [5]. In recent years, studies have found that IBS is associated with intestinal flora, suggesting that probiotics may benefit for the treatment of IBS [6].

Therefore, In this study, the effects of combined probiotics regimen on symptom score, gastrointestinal hormones and oxidative stress indexes of patients with IBS-C weresdudied.

Patients and Methods

Subjects

96 The patients (96) with IBS-C who had been treated in our hospital from January to December 2018 were selected.

Inclusion criteria: 1) patients were diagnosed with Roman type Ⅲ standards; 2) over 18 years of age; 3) the patient had not used any gastrointestinal dynamic drugs, antibiotics or probiotics within a month; 4) patients did not have other digestive tract disease; 5) Patient I fully understood and signed informed consent form.

Exclusion criteria: 1) patients were allergic to experimental drugs; 2) patients were suffering any internal secretion, druging and nervous constipation problems; 3) patients were pregnant or lactating or having mental illness; 4) patients were having any serious primary diseases.

96 patients were divided into control group (n=49) and observation group (n=47) on random number table basis. In the control group, there were 24 males and 25 females, at an average age of 44.82± 5.39 years with an average history of disease of 18.27± 2.57 months. In the observation group, there were 23 males and 24 females, with an average age of 44.75± 5.32 years with an average history of disease of 18.32± 2.64 months. There was no significant statistics difference between the two groups ($P > 0.05$).

Methods

Patients in the control group were treated with moxapride, moxapride (specifications: 5mg; National drug approval number H19990317; Manufacturer: lunanbet pharmaceutical co., LTD.) oral administration, 5mg each time, 3 times a day; Observation group were treated with Mosapride combined with Bifidobacterium triplex viable enteric capsules (size: 210mg; Approval number: national drug approval code S10950032; Manufacturer: Shanghai xinyi pharmaceutical co., LTD.) orally, 420mg each time, 3 times a day. Both groups were treated for 8 weeks.

Observation indicators

Clinical efficacy: Excellent: the clinical symptoms of abdominal pain and abdominal distension disappeared, fecal properties restored to normal, and the interval between defecation was 2d; Effective: the clinical symptoms and fecal traits of the patients were significantly improved, and the interval between defecation became less than 3ds; Invalid: no improvements in clinical symptoms, fecal traits, defecation interval (> 3ds) were found. Total effectiveness = excellent+ effectiveness

Improvement of symptom: To evaluate the clinical symptoms between the two groups of patients, a 4-grade scoring method (0~3 points) were used. The higher the score means the more serious symptoms of the patients, including abdominal distension and pain, defecation frequency, stool characteristics and defecation difficulty.

The levels of 5-Hydroxytryptamine (5-HT), Malondialdehyde (MDA) were measured using Enzyme Linked Immunosorbent Assay (ELISA). 5-HT and MDA Kit from Biological Technology co., LTD of Shanghai ELISA,10-66-892and 10-67296; lipid peroxide (LPO) by Barbituric acid method from Biologic Institute of Nanjing Jiancheng

The levels of gastrointestinal hormones including motilin (MTL), Vasoactive Intestinal Peptide (VIP) and Somatostatin (SS) were studied using ELISA.

Statistical methods

SPSS21.0 was used for statistical analysis. The obtained data were using a t tested by t test, the count data were analysed by chi-square test, and the rank sum test was used for grade data. $P < 0.05$ indicated statistically significant difference.

Results

Comparison of clinical efficacy between the two groups

In observation group, there were 29 cases (61.70%) showing significant therapeutic effect, 15 cases (31.91%) showing moderate therapeutic effect, and the total effective rate reached 93.62%, while the total effective rate in control group was 79.59% ($P < 0.05$), as shown in Table 1.

Group	Cases	Excellent	Effective	Ineffective	Total effective
control	49	21(42.85)	18(36.73	10(20.41)	39(79.59)
Observation	47	29(61.70)	15(31.91)	3(6.38)	44(93.62)
Z/χ^2 value	-	2.184			4.374
P value	-	0.029			0.036

Table 1: comparison of clinical efficacy between the two groups [n (%)].

Comparison of clinical symptom scores between the two groups

The clinical symptom scores of the two groups were similar before treatment ($P > 0.05$), Although thru clinic symptom cores in both groups were significantly decreased after respective treatment in both groups. The scores of abdominal distension and pain, frequency of defecation, stool traits and defecation difficulty in the observation group were significantly lower than those in the control group ($P < 0.05$), as shown in Table 2.

Group	Time	Distension pain	Frequency	Caracter	Difficulty
Control	Before	2.68±0.41	2.72±0.44	2.83±0.47	2.78±0.43
	After	1.47±0.32*	1.52±0.36*	1.58±0.39*	1.49±0.33*
Observation	Before	2.65±0.42	2.73±0.42	2.82±0.45	0.79±0.44
	After	0.38±0.15*#	0.41±0.18*#	0.42±0.14*#	0.39±0.16*#
Compared with before treatment, *P < 0.05; Compared with the control group, #P < 0.05					

Table 2: comparison of clinical symptom scores between the two groups (±s).

Comparison of 5-HT and oxidative stress indexes between the two groups

The levels of 5-ht, MDA and LPO in the two groups were similar before treatment ($P > 0.05$), however the above indicators were significantly decreased after respective treatment in both groups. Interestingly, the levels of these indicators in observation group were significantly lower than those in the control group ($P < 0.05$), as shown in Table 3.

Group 5-ht	Time	5-HT(pg/mL)	MDA(nmol/L)	LPO(nmol/L)
Control	Before	1815.49±197.53	4.61±0.64	18.37±2.59
	After	1638.51±171.58*	3.37±0.43*	12.74±2.02*
Observation	Before	1817.82±195.36	4.63±0.65	18.41±2.62
	After	1402.47±152.93*#	2.38±0.24*#	8.15±1.36*#
Compared with before treatment, *P < 0.05; Compared with the control group, #P < 0.05				

Table 3: comparison of 5-ht and oxidative stress levels between the two groups (±s).

Comparison of gastrointestinal hormone levels between the two groups

The gastrointestinal hormone levels between the two groups were similar before treatment ($P > 0.05$), and these gastrointestinal hormone levels of the two groups were substantially improved after their respective treatment. By comparison the MTL level of the observation group was significantly higher than that of the control group, however the VIP and SS levels of the observation group were significantly lower than those of the control group ($P < 0.05$), as shown in Table 4.

Groups	Time	MTL	VIP	SS
Control	Before	141.26±27.94	42.48±6.03	22.15±3.97
	After	185.38±33.25*	36.27±4.81*	17.68±3.14*
Observation	Before	142.03±27.89	42.54±6.07	22.19±3.95
	After	235.16±39.37*#	30.41±3.69*#	12.03±2.61*#
compared with before treatment, *P < 0.05; Compared with the control group, #P < 0.05				

Table 4: comparison of gastrointestinal hormone levels between the two groups (s, pg/mL).

Discussion

IBS is clinically divided into diarrhoea type, constipation type, mixed type and unshaped type. Although it is a benign disease, the patient has no gastrointestinal organic lesions, it is difficult to cure. Long-term recurrence rate is high, chronic malnutrition, anaemia and other complications seriously affect the quality of patients.

The results of this study demonstrated that the total effective rate of the observation group was 93.62%.In comparison ,the total effective rate of the control group was 75.59% ($P < 0.05$). After respective treatment, the scores of abdominal distension, abdominal pain, defecation frequency, stool character and defecation difficulty in the observation group were significantly lower than those in the control group ($P < 0.05$).Intestinal floras are beneficial in maintaining the normal function of gastrointestinal tract, help digestion and absorption, prevent the invasion of pathogenic microorganisms, and affect the proliferation and

differentiation of intestinal epithelial cells and the regulation of intestinal immune response [7-8]. According to examination of the beneficial floras in patients with IBS, It was noted that the beneficial floras lactobacillus and Bifidobacterium present a decreasing trend, and imbalance of intestinal floras exists. some potentially harmful bacilli overgrow [9-10]. It was also demonstrated that oral administration of Bifidobacterium trifecta live bacteria capsules can supplement beneficial intestinal bacteria such as Bifidobacterium, lactobacillus and enterococcus faecal is, allowing them to multiply in the intestinal tract, thereby improving the intestinal micro ecological environment and maintaining the normal intestinal function [11]. Bifidobacterium trifecta viable capsules can also competitively inhibit the cloning and invasion of pathogenic bacteria, promote the recovery of normal intestinal flora, rebuild the biological barrier of intestinal flora, and improve the function of the intestinal tract immune barrier [12]. Acetic acid and lactic acid, metabolites of Bifidobacterium trifecta capsules bacterial, can reduce intestinal pH, accelerate intestinal peristalsis, and promote digestion, decomposition and absorption of food in the intestines [13-14].

Gastrointestinal hormones are involved in the regulation of gastrointestinal motility, and the changes of gastrointestinal function may be related to the abnormal changes of gastrointestinal hormones. It is well known that MTL is secreted by endocrine cells, which can accelerate the transport of water and electrolytes in the gastrointestinal tract. When the serum MTL level is increased, the transport speed of water and electrolyte in the body will be significantly accelerated, which is manifested as IBS-D. When the serum MTL level is reduced, the normal movement of gastrointestinal tract is inhibited, which is manifested as IBS-C [15]. VIP is distributed in the nervous system and gastrointestinal tract of the body, and is involved in the regulation process of neurosecretion, and in relaxing gastrointestinal smooth muscle [16]. SS can inhibit intestinal absorption of nutrients, electrolytes and water, inhibit the movement of bile duct and gastrointestine, inhibit the synthesis of gastric acid and the secretion of gastrointestinal hormones [17].

Reducing SS level can reduce SS inhibition of gastrointestinal motor function, as shown in patients with IBC-C, accelerate the transport of nutrients, water and electrolytes, and also reduce the inhibition of MTL and other motility hormones [18]. As showed that serum levels of VIP and SS in patients with IBS-C were higher than those in the control group. VIP may play a role through local neurotransmitter or paracrine to inhibit intestinal peristalsis, and SS also plays an inhibitory effect on gastrointestinal tract, leading to constipation.

The results of this study showed that MTL in observation group was significantly higher than that in control group after respective treatment, and the levels of VIP and SS in observation group were significantly lower than those in control group, indicating that Bifidobacterium trifecta viable capsules could significantly improve the gastrointestinal hormones in patients with IBS-C and alleviate their clinical symptoms.5-HT is an important neurotransmitter in the brain-gut axis. The level of 5-HT in patients with IBS-C is significantly higher than that in normal people. 5-HT can bind with intestinal receptors that causes changes in intestinal perception, secretion, movement and other functions, 5-HTcan also induced high sensitivity of visceral afferent nerve and intestinal nerve system, resulting in abdominal pain, abdominal distension and other symptoms [19]. Oxidative stress refers to a state in which the generation of total oxygen-containing compounds in the body exceeds the defense capacity of the antioxidant system. Excessive production of oxygen-containing compounds in the body or the decline of the body's scavenging ability will lead to oxidative stress in the body and cause tissue and cell damage [20]. It was found that IBS-C patients are accompanied by obvious changes in the state of oxidative stress. Excessive oxygen free radicals in the body can cause dysfunction of intestinal mucosal barrier. Therefore, reducing the levels of 5-HT and the oxidative stress of patients have positive clinical significance for the treatment of IBS-C. Since both LPO and MDA can reflect the oxidative stress state of the body, the levels of MDA and LPO were used to evaluated the oxidative stress state of the patients in this study. The results showed that the levels of 5-HT, MDA and LPO in the observation group were significantly lower than n those in the control group after treatment, Indicating that Bifidobacterium trifecta capsules could meaningfully improve the level of 5-HT and the state of oxidative stress in patients with IBS-C.

Conclusions

Our study demonstrated that combination of Bifidobacterium triplex live bacteria capsule and moxapride has a significant effect on the treatment of IBS-C. This combination regimen can significantly improve the clinical symptoms and gastrointestinal hormone levels of patients, reduce the plasma level of 5-HT, and the oxidative stress. Probiotics is worthy of clinical application especially for the patients of IBS-C.

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Authors Contribution

Zeli Gao designed the research strategy, performed the literature search, analysed the data and drafted the paper, Jieru Ji and Xiaotong He collected the clinical materials.

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