

INTESTINAL FLORAL CHANGES IN PATIENTS WITH IRRITABLE BOWEL SYNDROME AFTER INGESTION OF CLOSTRIDIUM BUTYRICUM PREPARATION

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Chinese Journal of Microbiology, 1999

Abstract

A *Clostridium butyricum* preparation has been used in the treatment of patients with IBS, studying its efficacy in these patients and in changing the gut microbiota. Thirty patients were selected to enter the study, of whom twenty-one were male and nine were female. A fecal microbiota test was performed in treated patients both before treatment and at the end of the study, also using tests on healthy patients that served as quality control. Prior to treatment, the amount of *Bifidobacterium* and *Lactobacillus* in IBS patients decreased, while the amount of potentially pathogenic *Clostridia* increased significantly. After treatment, the number of daily bowel movements decreased from 6.0 ± 5.6 in pre-treatment to 1.7 ± 1.11 ($p < 0.001$) in patients after treatment. The overall response rate was 83.4%. No side effects were observed during treatment. The number of *Bifidobacterium* and *Lactobacillus* increased significantly in IBS patients after treatment with *C. butyricum*, highlighting how *Clostridium butyricum* may be able to regulate the intestinal flora and reverse it in a state of equilibrium, inhibiting putr and inflammatory intestinal bacilli and bacteria pathogens, promoting the growth of beneficial intestinal bacteria such as *bifidobacteria* and *lactobacilli*.

Materials and methods

30 outpatients, including 21 males and 9 females, with a mean age of 32 years (19-56 years) with a mean duration of IBS of 4 to 10 years presenting at least one of the following symptoms were randomly selected: abdominal pain, intestinal swelling with gas, diarrhoea, predominant constipation or alternating diarrhoea. Patients with diarrhea more or less alternating with constipation and no evidence of organic disease who could explain the above symptoms were therefore examined. All subjects were free of chronic liver disease, history of gastrointestinal surgery, diabetes and hyperthyroidism and chronic inflammation of the small intestine.

Endpoint

Stool frequency before and after treatment, nature of stools, improvement of symptoms and clinical signs and time to stop diarrhea, collateral effects, abdominal pain associated with defecation, bloating, change in bowel habits, mucus and foul odor after defecation were examined. In addition, the fecal microbiota was performed to evaluate the presence of pathogenic bacteria, coliform bacteria, *Enterococcus*, *Lactobacilli* and *Bifidobacteria*, and anaerobic diseases.

Treatment

The study involved the administration of a preparation based on *Clostridium butyricum* CBM 588 (Miyarisan Co., Ltd) orally, 1 gram daily for 14 days of treatment.

Results

After treatment with *Clostridium butyricum* CBM 588, diarrhea has been significantly reduced. In fact, the number of diarrheal evacuations decreased by an average of 6.0 ± 5.6 before therapy to 1.7 ± 1.1 after surgery ($p < 0.001$). In 86.4% of cases, diarrhoea begins to improve on the day of initiation of CBM 588 therapy (4.6 ± 2.1 evacuations on average). After treatment with *C. butyricum* the features of stools have been substantially improved. No side effects were found during the entire treatment process.

SYMPTOM	Before therapy (n° cases)	Reduced symptoms (%)	Disappearance of symptoms (%)	Efficacy (%)
Abdominal pain	20	13 (65%)	3 (15%)	80%
Diarrhoea	22	3 (13.6%)	16 (72.7%)	86.3%
Swelling	16	2 (12.5%)	12 (75%)	87.5%
Constipation	9	2 (22.2%)	4 (44.4%)	66.6%
Borborygmi	21	4 (19%)	12 (57.1%)	76.1%
Alternating bowel habits	10	2 (20%)	6 (60%)	80%

Clinical symptoms after treatment with C. butyricum CBM 588

State of the intestinal microbiota

The gut microbiota of patients receiving *C. butyricum* CBM 588 was assessed prior to therapy and at the end of the 14 days of treatment, comparing it with the microbiota of 30 subjects in a healthy

group. Before treatment, in the IBS group the concentration of total anaerobic bacteria showed a significant difference compared to the healthy group. After treatment with CBM 588, *bifidobacteria* and *lactobacilli* increased significantly. With regard to the other bacteria highlighted in the group at the end of treatment, there are basically no significant differences compared to the healthy group, while significant important differences emerged when comparing the microbiota of patients before and after treatment with *C. butyricum*.

BACTERIA	Healthy group (10 ⁿ CFU/g)	Before therapy (10 ⁿ CFU/g)	After therapy (10 ⁿ CFU/g)	<i>p</i> (first treatment vs after treatment)
Coliform	8.34 ± 0.45	9.09 ± 0.49	8.63 ± 0.36	0.001
<i>Enterococcus</i>	4.29 ± 0.24	5.51 ± 0.49	4.26 ± 0.34	<0.001
<i>Lactobacillus</i>	7.79 ± 0.75	6.55 ± 0.98	8.37 ± 0.36	<0.001
<i>Clostridia</i>	4.38 ± 0.51	10.05 ± 1.21	4.41 ± 0.52	<0.001
<i>Bifidobacteria</i>	9.04 ± 0.56	4.79 ± 1.08	9.26 ± 0.41	<0.001
Anaerobic bacteria	12.79 ± 0.51	10.15 ± 0.51	12.47 ± 0.54	<0.001

Discussion

Clostridium butyricum has been used for more than half a century in various countries around the world in case of clinical disorders of gut microbiota associated with acute and chronic diarrhea, irritable bowel syndrome and antibiotic-induced enteritis. Study results confirm that patients with irritable bowel syndrome reported an improvement in several clinical symptoms, with a total effectiveness rate of 83.4%.

As shown by various studies, the fecal colonic microbiota of healthy people is known to be dominated by anaerobic bacteria. It is also known that the genus *Bifidobacterium* is one of the most present and common in normal gut microbiota of humans. As demonstrated in this study, patients with IBS had intestinal dysbiosis characterized by deficiency of *bifidobacteria*, *lactobacilli* and total anaerobic bacteria compared to the healthy group, with an increase, conversely, in those bacteria that are not usually present in the colonic environment, such as the genus *Clostridia*, *Enterococcus* and coliform bacteria. After treatment with *C. butyricum* CBM 588, on the other hand, a normalization of the concentration of all the bacterial genera examined was observed, with an

increase in *bifidobacteria*, *lactobacilli*, total anaerobic bacteria and a reduction in potentially pathogenic coliform bacteria, enterococci and *Clostridia*, with the result of significantly improving clinical symptoms. Therefore, the study showed how *Clostridium butyricum* can inhibit intestinal decomposition bacteria and pathogenic bacteria, while conversely promoting the development of *bifidobacteria* and other bacteria beneficial for the colonic environment, thus restoring a substantially healthy intestinal microbiota.