RESEARCH ARTICLE

Efficacy of *Bifidobacterium Tetragenous Viable Bacteria* Tablets for Cancer Patients with Functional Constipation

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Abstract

Objective: To investigate the efficacy and side effects of *Bifidobacterium tetragenous viable bacteria* tablets in treating cancer patients with functional constipation during chemotherapy. Methods: A consecutive cohort of 100 cancer patients with functional constipation were divided into two equal groups: patients in the experimental group were given *Bifidobacterium tetragenous viable bacteria* tablets combined with chemotherapy, while patients in the control group received chemotherapy alone. After 4 weeks, the efficacy and side effects in treating functional constipation were evaluated. Results: Constipation in 48 patients in experimental group was controlled (9 returned to normal), with a total response rate of 96%, and 1 patient reported diarrhea (2%). In contrast only 16 patients in the control group demonstrated improvement and 34 were still constipated after chemotherapy, with a response rate of 32%. The difference in response rate was statistically significant (P <0.05). Conclusion: This study suggested that *Bifidobacterium tetragenous viable bacteria* tablets are effective and safe in treating cancer patients with functional constipation during chemotherapy.

Keywords: Functional constipation - *Bifidobacterium tetragenous viable bacteria* tablets - efficacy - cancer patients

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Introduction

Chemotherapy-induced nausea and vomiting (CINV) is a common side effect of chemotherapy for many cancer patients (Botrel TE et al., 2011; Guo-Li Wei et al., 2013). CINV may lead to discontinuation of treatment, decrease quality of life of patients. So, preventing CINV during chemotherapy is important and 5-HT3 receptor antagonists are (5-HT3-RA) widely used as antiemetics in clinical (Claudio Faria et al., 2014). But one side effect of the 5-HT3 receptor antagonists is constipation, because the 5-HT3 receptor antagonists (5-HT3-RA) prevent the gastrointestinal peristalsis, at the same time (Botrel et al., 2011; Faria et al., 2013). The 5-HT3 receptors antagonists affect GI vagal afferents to inhibit the vomiting reflex, gastric distension and delaye gastric emptying (Andrews et al., 1988; Yoshioka et al., 1990; Horn et al., 2004; Badary et al., 2006). 5-HT3 receptor antagonists also decrease small bowel transit, inhibit small bowel secretion, induce constipation in humans (De Boer-Dennert et al., 1997) and delay colonic transit in animal studies (Picard et al., 2002).

The 4 components of bifidobacterium tetragenous viable bacteria tablets are: bifidobacterium infantis, lactobacillus acidophilus, enterococcus faecalis and bacillus cereus (Liu et al., 2013; Dimidi et al., 2014). The mechanism of action is as follows: First, anaerobic bacterias, mainly bifidobacterium, closely integrate the intestinal epithelial cells to form biological barriers and fight against harmful bacteria. Second, these anaerobic bacterias produce organic acid due to fermented sugar, make the PH value decreased and stimulate peristalsis to improve the intestinal fermentation process. Finally changed the microenvironment, and feces easy to be excreted (Abrams et al., 1967; Agrawal et al., 2009).

Materials and Methods

Eligibility

Patients were required to be pathologically diagnosed with cancer and received chemotherapy in Jiangsu Cancer Hospital & Research Institute. Eligibility criteria were as follows: 1. All cases meet the diagnostic criteria for Rome II Chronical functional constipation; 2.Patients all with cancer and without gastrointestinal obstruction or other organic disease; 3. No limit in gender and age; 4.Rarely occurs loose stools without using laxatives. Exclusion criteria: 1. failed to complete four weeks of treatment; 2.Probiotics allergy; 3. Liver or kidney dysfunction; 4. With brain disease or abnormal judging ability; 5. Drug or alcohol abusers; 6. With any serious medical or psychiatric condition (Fedorak et al., 2013; Liu et al., 2013).

Methods

From July to October in 2014, 100 cancer patients who received chemotherapy in Jiangsu Cancer Hospital

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Table 1. The Wexner Score was Calculated as Follow (Range is from 0 to 20)

Stool frequency(times)	
1-2/1-2d	0
2/week	1
1/week	2
>1/wk, <1/month	3
>1/month	4
Pain	
Never	0
Occasionally	1
Sometimes	2
Usually	3
Always	4
Incompleteness	
Never	0
Occasionally	1
Sometimes	2
Usually	3
Always	4
Abdominal pain	
Never	0
Occasionally	1
Sometimes	2
Usually	3
Always	4
Toilet Time(min)	
< 5	0
5-10	1
10-20	2
20-30	3
> 30	4
Assistance forms	
Nothing	0
Stimulant laxatives	1
Finger assistance or enemas	2
Failed attempt defecation in 24h(times)	
0	0
1-3	1
3-6	2
6-9	3
> 9	4
Constipation Duration (years)	
0	0
1-5	1
5-10	2
10-20	3
> 20	4

& Research Institute . And they also meet the diagnostic criteria for Rome II Chronical functional constipation (Agachan F et al., 1996). All patients reported symptoms of dry and hard stools, or bloating, or abdominal pain, or stool obscure and others. No laxative therapy was conducted in 1 month. Before accepted treatment, all patients had a calculation of Wexner score.

All patients were divided into two groups. All patients received chemotherapy. Patients in experimental group took 4 bifidobacterium tetragenous viable bacteria tablets (Siliankang®), 3 times per day and continued for 4 weeks as one cycle (Siliankang®, made by Hangzhou Longda New-Tech Bio-pharmaceutical Co., Ltd.). While patients in control group received chemotherapy only. Defecation frequency, stool changes, defecation difficulty, associated symptoms and adverse reactions of patients were recorded.

Table 2. Patient Characteristics (n = 100)

	Experimental group	Control group
Age (years)		
Median	62.1	60.1
Range	62.1±10.9	60.1±9.9
Number of patients (%)		
Sex		
Female	15	17
Male	35	33
Wexner Score(0-30)		
0-10	37	35
11-20	13	15
21-30	0	0
Types of cancer		
Gastric cancer	11	11
Colorectal cancer	4	8

Table 3. Effective Rate of Both Groups

Group	n	Markedly	Effective	Invalid	Total effective rate
Experimental Group	50	9(18%)	39(78%)	2(4%)	96%*
Control Group	50	4(8%)	12(24%)	34(68%)	32%*

After 4 weeks, efficacy and side effects were evaluated.

Efficacy criteria was previously determined (Agachan et al., 1996): 1. Markedly: Stool return to normal and the frequency once per day after treatment; 2. Effective: Stool character improved and the frequency become more than 3 times per week after treatment; 3.Invalid: No improvement in frequency and character of stool, after treatment.

All data were analysed by SPSS13.0 statistical software, measurement data with the mean ± standard deviation ($x \pm s$) and t test. Count data using χ^2 test, and $P < 0.05$ was considered statistically significance.

Results

Before chemotherapy, the Wexner Scores of two group were evaluated. The score of control group was 9.3 ± 2.4, and of experimental group was 9.2 ± 2.5. Difference between two groups was not statistically significant ($P > 0.05$). All Patients received chemotherapy regimens, eg., CHOP regimen in patients with lymphoma, fluoropyrimidine-based chemotherapy regimen in patients with Colorectal cancer, TP regimen in patients with lung cancer, etc.

After treated for 4 weeks, 48 patients in experimental group got better (9 cases returned to normal), but 2 worse. The total effective rate was 96%, and 1 case reported diarrhea (2%) ; 16 patients in control group got improvement and 34 cases still constipated. The total effective rate 32%. Difference efficiency between the two groups was statistically significant ($P < 0.05$). Experimental group had higher effective rate than the control group (Table 2) .

Discussion

Some complications, eg., functional constipation, could occur during chemotherapy for patients with cancer, and abdominal distension, abdominal pain, defecation discomfort could caused by functional constipation.

These compilations make patients spook and harm the quality of life.

A large number of bacteria were inhabited in the normal intestine, most of which are the anaerobic bacteriums. Bifidobacterium is an important kind of physiological bacterium. (Sabikhi et al., 2013; Xu et al., 2013). It has effects of anti-infection, anti-tumor, enhancing immunity, synthesizing multivitamins, promoting the absorption of nutrients, removing toxins and runchang catharsis (Tabbers et al., 2011; Sabikhi et al., 2013). Bifidobacterium can ferment oligosaccharides to produce acetic acid and lactose, stimulate peristalsis, push the stool continuously and finally excreted. After cancer patients were treated by chemotherapy, some factors acted in vivo destroyed the intestinal microorganisms of cancer patients (De Paula et al., 2008; Blokhina et al., 2011; Zhan et al., 2012). The number of bifidobacteriums and other anaerobic bacteria drops, oligosaccharides accumulated in the intestine due to the short of bifidobacteriu (Agrawal et al., 2009; Lu et al., 2013). And the symptoms, eg., abdominal distension, abdominal pain, defecation discomfort, etc. occur.

Currently, no standardized treatment is available for cancer patients with functional constipation. Treatment is mainly focused on adjusting diet, training bowel habit, or medications as lubricants and cathartic (El-Salhy et al., 2008; Wu et al., 2013). But effects of these treatment are unsatisfactory, and the medications are associated with a series of side effects, eg., harming the intestinal wall, causing water and electrolyte disorders after long-term used, etc.

In this research, after treated with bifidobacterium tet agenous viable bacteria tablets for 4 weeks, patients in experimental group had higher effective rate than those in control group, no significant adverse reactions were detected. In conclusion, our result suggests that bifidobacterium tetragenous viable bacteria tablets is effective for treating cancer patients with functional constipation, and is safe and well tolerated. However, further randomized clinical trials should be conducted to evaluate the efficacy and toxicity and be compared with other regimens.

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