Probiotic Fermented Milk Containing Dietary Fiber Has Additive Effects in IBS with Constipation Compared to Plain Probiotic Fermented Milk

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Background/Aims: Although controversial, probiotics and dietary fiber are commonly used for patients with irritable bowel syndrome (IBS). We evaluated the effects of multistrain probiotics on the symptoms of IBS to determine whether the addition of dietary fiber had an additive effect on constipation-predominant IBS. **Methods:** A total of 142 participants who met the Rome III criteria were recruited and randomized into a control group or a test group. Participants in the control group received multistrain probiotic fermented milk with *Streptococcus thermophilus*, *Lactobacillus acidophilus* and *Bifidobacterium infantis*; the participants in the test group received the same probiotic fermented milk mixed with dietary fiber such as sea tangle extracts, radish extracts and glasswort extracts. The patients were treated for four weeks. **Results:** Most of the symptoms of IBS, with the exception of flatulence, stool consistency, and frequency of defecation, significantly improved in both groups. In the analysis of IBS subtypes, especially constipation-predominant IBS, the frequency and duration of defecation and straining at stool were improved more in the test group than in the control group. **Conclusions:** Dietary fiber had additive benefits for the symptoms of constipation, especially in constipation-predominant IBS. (*Gut Liver* 2011;5:22-28)

Key Words: Constipation; Dietary fiber; Irritable bowel syndrome; Probiotic fermented milk

INTRODUCTION

Irritable bowel syndrome (IBS) is a functional bowel disorders characterized by symptoms of abdominal pain or discomfort associated with disturbed bowel movements; approximately 10-

20% of the population is estimated to have IBS.^{1,2} The pathogenesis of IBS has not been clearly defined, but current evidence suggests that altered gut motility, visceral hypersensitivity, dysregulation of the brain-gut axis, abnormal fermentation, and immune activation are involved in this disorder.²⁻⁴ Thus probiotics are good candidates for controlling the symptoms associated with IBS, where treatment safety is paramount in this nonlethal disorder. Lactobacilli, Bifidobacteria, and Streptococci are among the most commonly studied probiotics in IBS; they have demonstrated efficacy in patients with IBS.⁵⁻¹⁵ However, the benefits of one given species or organism have not been shown to be better than other species or organisms.

Dietary fiber is commonly used in the treatment of patients with IBS. The proposed mechanism of action of fiber, in the treatment of IBS and constipation, is the acceleration of oro-anal transit and a decrease in the intra-colon pressures.^{16,17} Despite a large number of trials, each with design limitations, the benefits remain unproven and patient tolerance can be a problem. However, there may be a limited role for the careful use of dietary fiber or bulking agents, in the management of some patients with IBS, especially in those with the constipation dominant form.¹⁸

Therefore, in this study, we evaluated the effects of *Streptococcus thermophilus*, *Lactobacillus acidophilus* and *Bifidobacterium infantis* in patients with IBS, and evaluated whether supplementary dietary fiber had an additive effect in patients with constipation-predominant IBS.

MATERIALS AND METHODS

1. Participants

Ethical approval for this study was granted by the Institu-

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tional Review Board of Samsung Medical Center, Seoul, Korea on 25 June, 2008. All participating patients provided informed consent. Volunteers between 18 and 70 years of age who met the Rome III criteria via interview were recruited by direct advertisement at the hospital. The exclusion criteria were severe liver, lung, renal, hematological, or a major psychiatric disorder, and history of abdominal surgery, except for appendectomy or hysterectomy. In addition, patients more than 50 years of age who had not had sigmoidoscopy or colonoscopy, during the previous five years, patients who used antipsychotic or anticholinergic medications within the prior month, patients with abnormal results of thyroid function test, blood counts, and serum chemistry, patients who are pregnant or lactating, and patients already receiving medication for IBS were excluded from the study. A total of 142 participants were recruited and randomized (stratified by age and gender) to the test group (n=71) or the control group (n=71).

2. Study design and protocol

The study was designed as part of the Seoul Research and Business Development Program and was a single center, randomized, double-blind study to evaluate the effects of two types of probiotic fermented milk with or without dietary fiber over a period of four weeks. The eligible participants were referred to an investigator who interviewed the participants using a structured questionnaire. Each participant was provided with

a standardized explanation of the questions and definitions of symptoms by an investigator at baseline and after four weeks of treatment. Each fermented milk was provided in a bottle and taken twice daily for four weeks. The questionnaire assessed age, gender, height, body weight, stool consistency, IBS related symptoms such as the severity of the abdominal pain (discomfort), abdominal distension (bloating), urgency, straining, feeling of incomplete evacuation, frequency of flatulence (per day), frequency of defecation (per week), duration of defecation (minute), and improvement of overall IBS symptoms and adverse event during treatment period. Abdominal pain (discomfort), abdominal distension (bloating), urgency, straining, feeling of incomplete evacuation and improvement of overall IBS symptoms were measured using the visual analogue scale (VAS) (0, no symptoms; 2.5, mild; 5, moderate; 7.5, severe; and 10, very severe). The stool consistency was measured with the Bristol Stool Scale (range, 1-7).

We also reinterviewed participants with the same questionnaire at the end of the study. Primary endpoint was the difference of the symptom frequency, duration (defecation) and VAS score from the baseline in each group and between both groups.

3. Product preparation

Each bottle contained either 150 mL of test or control product and was provided by the NamYang Dairy Products, Co., Ltd (Gongju, Korea). The control product contained three strains of *S.*

Table 1. Demographics and Baseline Characteristics of Subjects

	Fiber containing FM (n=70)	Plain FM (n=71)	p-value
Age, yr	33.7±10.2	34.0±8.4	0.885
M:F	17:53	18:53	0.957
BMI, Kg/m ²	20.3±3.4	20.6±3.5	0.883
Subtype of IBS			0.907
Constipation, n (%)	16 (22.9)	18 (25.4)	
Diarrhea, n (%)	20 (28.6)	21 (29.6)	
Mixed, n (%)	34 (48.6)	32 (45.1)	
Abdominal symptoms			
Abdominal pain or discomfort (VAS)	3.7±1.5	3.5±1.5	0.526
Frequency of abdominal pain or discomfort/wk	5.5±4.4	4.9±5.2	0.476
Abdominal distension or bloating (VAS)	5.1±2.3	4.5±2.1	0.146
Flatulence/day	5.0±4.5	5.2±4.3	0.847
Bowel habit			
Defecation frequency/wk	6.9±4.9	7.2±4.9	0.637
Defecation duration, min	8.8±5.4	9.4±6.1	0.559
Urgency (VAS)	3.6±2.2	4.0±2.4	0.272
Straining (VAS)	4.2±2.2	4.0±2.6	0.572
Stool consistency (BSS)	4.2±1.5	4.0±1.5	0.547
Feeling of incomplete evacuation (VAS)	4.1±2.3	4.2±2.2	0.833

BMI, body mass index; IBS, irritable bowel syndrome; FM, fermented milk; VAS, visual analogue scale; BSS, Bristol Stool Scale.

thermophilus, *L. acidophilus*, and *B. infantis* at total of 3.75×10^{12} colony forming units (CFU) per bottle. The test product contained the same strains with added dietary fibers (sea tangle extract powder 0.1%, radish extract 0.25%, glasswort extract 0.15%, in total 3.15 g). Both the test and control products were without flavor and had similar color, texture, and taste.

4. Statistical methods

The sample size was estimated to detect a minimum 20% difference in responders of test group compared to the control group.

About seventy percent of the patients in the control group were estimated to be responders.

It was calculated that 62 patients per group were required to complete the study in order to detect this difference with a 80% power with a two-sided p-value <0.05 . In order to compensate for dropouts, it was planned to recruit 71 per group.

The symptom score was analyzed first for normality of distribution using the Shapiro-Wilk test. If the score was normally distributed, the Student's t-test was used for comparisons between the two groups. Changes in the symptom scores before and after the intervention, for each group, were assessed using the paired t-test. A p-values less than 0.05 were considered statistically significant.

RESULTS

A total of 142 participants were enrolled and randomized (stratified by age and gender) to the test group (fiber containing fermented milk [FM] group; $n=71$) and the control group (plain

FM group; $n=71$). One patient in the test was withdrawn from the study due to exacerbation of abdominal distension on third day. One hundred and forty-one participants (70 in test group and 71 in control group) completed the study. Table 1 shows the demographics and baseline characteristics of the subjects. At the baseline, similar distribution of age, gender, body mass index, and IBS subgroup is noted. The baseline symptom scores for abdominal pain and bowel habit were not different between the both groups.

At week 4, most IBS symptoms except for flatulence, frequency of defecation, and stool consistency significantly improved compared to the baseline in both groups. However, the changes in the symptom scores for the duration of defecation and straining were significantly higher in the test group ($p=0.036$, $p=0.007$; Table 2).

A subgroup analysis of the IBS patients showed that in the constipation-predominant population (Table 3), the frequency of defecation, duration of defecation and straining were significantly more improved in the test group compared to the control group ($p=0.014$, $p<0.001$, $p<0.001$, respectively). The degree of improvement of the symptoms associated with IBS after treatment was also higher in the test group ($p=0.022$). Urgency was significantly improved compared to the baseline only in the control group ($p<0.001$), and there was a significant difference between the two groups ($p=0.036$).

In the diarrhea-predominant IBS population (Table 4), flatulence and frequency of defecation were unaltered from the baseline in the test group and the control group. Straining showed significant improvement from the baseline only in the test group ($p=0.014$). However, there were no significant differ-

Table 2. Changes in Study Parameters after Treatment in All Study Subjects

	Fiber containing FM (n=70)				Plain FM (n=71)				p-value*
	Baseline (mean±SD)	Week 4 (mean±SD)	Δ Week 4	p-value	Baseline (mean±SD)	Week 4 (mean±SD)	Δ Week 4	p-value	
Abdominal symptoms									
Abdominal pain or discomfort (VAS)	3.71±1.51	2.32±1.71	-1.39	<0.001	3.54±1.55	2.14±1.48	-1.40	<0.001	0.977
Frequency of abdominal pain or discomfort/wk	5.52±4.40	3.08±3.13	-2.44	<0.001	4.94±5.26	2.61±2.38	-2.32	<0.001	0.852
Abdominal distension or bloating (VAS)	5.13±2.31	2.82±2.24	-2.30	<0.001	4.58±2.15	2.74±2.16	-1.83	<0.001	0.284
Flatulence/wk	5.09±4.56	4.82±4.73	-0.27	0.062	5.24±4.35	4.56±4.66	-0.68	0.093	0.795
Bowel habit									
Defecation frequency/wk	6.94±4.92	7.46±4.74	0.52	0.433	7.29±4.99	6.53±3.79	-0.76	0.106	0.114
Defecation duration, min	8.85±5.47	4.88±3.48	-3.97	<0.001	9.42±6.12	6.92±5.10	-2.50	<0.001	0.036
Urgency (VAS)	3.64±2.28	2.25±2.09	-1.39	<0.001	4.08±2.47	2.60±2.08	-1.47	<0.001	0.833
Straining (VAS)	4.25±2.22	1.17±2.14	-2.50	<0.001	4.01±2.68	2.82±2.49	-1.19	<0.001	0.007
Stool consistency (BSS)	4.24±1.57	3.99±1.07	-0.25	0.232	4.08±1.53	4.01±1.16	-0.07	0.720	0.520
Feeling of incomplete evacuation (VAS)	4.14±2.36	1.92±2.17	-2.21	<0.001	4.23±2.26	2.28±2.49	-1.93	<0.001	0.517
Improvement of overall IBS symptoms (VAS)		5.78±2.02				5.14±2.02			0.060

FM, fermented milk; VAS, visual analogue scale; BSS, Bristol Stool Scale; IBS, irritable bowel syndrome.

*Comparison between both groups.

Table 3. Changes in Study Parameters after Treatment in the Constipation – Predominant Population

	Fiber containing FM (n=16)				Plain FM (n=18)				p-value*	
	Baseline (mean±SD)	Week 4 (mean±SD)	Δ Week 4	p-value	Baseline (mean±SD)	Week 4 (mean±SD)	Δ Week 4	p-value		
Abdominal symptoms										
Abdominal pain or discomfort (VAS)	4.21±1.98	2.50±2.04	-1.72	0.006	4.08±2.02	2.50±1.91	-1.58	0.002	0.848	
Frequency of abdominal pain of discomfort/wk	6.46±4.52	3.75±2.99	-2.72	0.001	4.80±2.47	3.11±2.05	-1.69	0.014	0.333	
Abdominal distension or bloating (VAS)	5.78±2.53	2.81±2.39	-2.96	<0.001	5.13±2.18	2.77±2.55	-2.36	0.002	0.528	
Flatulence/day	5.25±7.08	5.31±6.79	0.06	0.893	5.77±5.89	5.38±4.24	-0.39	0.468	0.527	
Bowel habit										
Defecation frequency/wk	4.62±2.97	8.59±5.45	3.97	0.007	5.05±2.48	5.58±2.79	0.53	0.336	0.014	
Defecation duration, min	12.25±4.82	4.25±2.15	-8.00	<0.001	12.9±6.88	10.86±6.66	-2.06	0.001	<0.001	
Urgency (VAS)	3.12±1.93	2.81±2.21	-0.31	0.669	4.02±2.29	1.94±1.83	-2.08	<0.001	0.036	
Straining (VAS)	6.25±1.29	0.78±1.05	-5.47	<0.001	5.83±1.17	4.02±2.98	-1.81	0.018	<0.001	
Stool consistency (BSS)	2.50±1.31	4.06±1.23	1.56	0.001	2.55±1.09	3.72±1.44	1.17	0.014	0.516	
Feeling of incomplete evacuation (VAS)	4.84±2.65	1.87±2.81	-2.96	0.002	4.86±2.00	2.50±3.09	-2.36	<0.001	0.506	
Improvement of overall IBS symptoms (VAS)		6.40±1.57				5.27±2.82			0.022	

FM, fermented milk; VAS, visual analogue scale; BSS, Bristol Stool Scale; IBS, irritable bowel syndrome.

*Comparison between both groups.

Table 4. Changes in Study Parameters after Treatment in the Diarrhea – Predominant Population

	Fiber containing FM (n=20)				Plain FM (n=21)				p-value*
	Baseline (mean±SD)	Week 4 (mean±SD)	Δ Week 4	p-value	Baseline (mean±SD)	Week 4 (mean±SD)	Δ Week 4	p-value	
Abdominal symptoms									
Abdominal pain or discomfort (VAS)	3.87±1.51	2.50±1.40	-1.37	0.012	3.69±1.50	2.26±1.56	-1.42	0.001	0.931
Frequency of abdominal pain of discomfort/wk	6.38±5.18	3.90±3.83	-2.47	0.008	6.21±7.75	2.86±3.33	-3.35	0.009	0.545
Abdominal distension or bloating (VAS)	5.38±2.33	3.12±2.27	-2.25	0.009	4.52±2.03	2.61±2.30	-1.90	0.001	0.708
Flatulence/day	5.05±4.06	3.93±4.32	-1.12	0.203	5.90±4.17	5.50±5.70	-0.40	0.629	0.547
Bowel habit									
Defecation frequency/wk	10.78±4.72	8.93±5.14	-1.85	0.074	10.19±6.00	8.45±4.96	-1.73	0.061	0.577
Defecation duration, min	7.40±4.73	4.98±2.91	-2.42	0.006	6.36±4.86	4.60±3.38	-1.76	0.002	0.472
Urgency (VAS)	5.13±2.21	2.62±2.36	-2.50	<0.001	5.48±2.45	3.09±2.07	-2.38	0.001	0.876
Straining (VAS)	2.75±1.79	1.50±1.49	-1.25	0.014	2.74±2.35	1.90±1.75	-0.83	0.130	0.557
Stool consistency (BSS)	5.70±0.97	4.10±1.16	-1.60	<0.001	5.71±0.56	4.38±1.20	-1.33	<0.001	0.538
Feeling of incomplete evacuation (VAS)	3.63±2.36	1.75±1.64	-1.87	0.010	3.81±2.18	2.61±2.30	-1.19	0.038	0.419
Improvement of overall IBS symptoms (VAS)		5.87±2.33				5.11±1.85			0.256

FM, fermented milk; VAS, visual analogue scale; BSS, Bristol Stool Scale; IBS, irritable bowel syndrome.

*Comparison between both groups.

ences in the changes of the symptom scores from the baseline to after treatment between the two groups. Also in the mixed type population, there were no significant differences between the both groups (Table 5). During the four-week study, all of the patients reported that they had complied with intervention, defined by taking more than 80% of the allocated products. There were no adverse events reported during study.

DISCUSSION

Several clinical studies have demonstrated the efficacy of probiotics for the treatment of patients with IBS. Lactobacillus, Bifidobacteria, and Streptococci have been among the most commonly studied probiotics. Most of the preparations provided daily doses in the range 10^6 – 10^{10} CFU. However, the benefits have been reported to differ among given species, in different

Table 5. Changes in Study Parameters after Treatment in Mixed Type Population

	Fiber containing FM (n=34)				Plain FM (n=32)				p-value*	
	Baseline (mean±SD)	Week 4 (mean±SD)	Δ Week 4	p-value	Baseline (mean±SD)	Week 4 (mean±SD)	Δ Week 4	p-value		
Abdominal symptoms										
Abdominal pain or discomfort (VAS)	3.38±1.21	2.13±1.76	-1.25	<0.001	3.15±1.20	1.86±1.10	-1.28	<0.001	0.933	
Frequency of abdominal pain of discomfort/wk	4.57±3.72	2.28±2.58	-2.29	<0.001	4.17±4.33	2.17±1.74	-2.00	0.005	0.741	
Abdominal distension or bloating (VAS)	4.67±2.17	2.65±2.21	-2.03	<0.001	4.30±2.22	2.81±1.88	-1.48	<0.001	0.355	
Flatulence/day	5.04±3.35	3.99±3.78	-1.06	0.037	4.50±3.40	3.47±4.02	-1.03	0.123	0.970	
Bowel habit										
Defecation frequency/wk	5.76±4.58	6.06±3.78	0.29	0.762	6.64±4.55	6.45±3.35	-0.19	0.699	0.663	
Defecation duration, min	8.10±5.63	5.12±4.26	-2.99	<0.001	9.47±5.47	6.23±3.73	-3.23	0.001	0.827	
Urgency (VAS)	3.01±2.11	1.76±1.80	-1.25	0.004	3.20±2.22	2.66±2.19	-0.55	0.128	0.201	
Straining (VAS)	4.19±2.11	2.35±2.53	-1.84	<0.001	3.83±2.84	2.73±2.41	-1.09	0.036	0.279	
Stool consistency (BSS)	4.21±1.04	3.89±0.95	-0.32	0.125	3.86±1.13	3.94±0.91	0.06	0.757	0.184	
Feeling of incomplete evacuation (VAS)	4.12±2.21	2.06±2.17	-2.06	<0.001	4.14±2.43	1.95±2.27	-2.19	<0.001	0.828	
Improvement of overall IBS symptoms (VAS)		5.44±2.00				5.08±1.62			0.421	

FM, fermented milk; VAS, visual analogue scale; BSS, Bristol Stool Scale; IBS, irritable bowel syndrome.

*Comparison between both groups.

clinical studies and by the IBS subtypes.^{5-15,19-23} Some organisms exhibit immunomodulatory effects and limited abnormal fermentation in the colon.^{24,25} Others have anti-inflammatory effects²⁶ or enhance the mucosal defense against luminal bacteria by preventing bacterial adherence to the epithelial cell surface, eliminating bacterial translocation and decreasing the increased intestinal permeability.²⁷ Rousseaux *et al.*²² reported that *Lactobacillus* NCFM induced, through the NF-κB pathway, MOR1 and CB2 expression, which contributed to the modulation and restoration of the normal perception of visceral pain. Sinn *et al.*⁹ demonstrated reduction of abdominal pain or discomfort among patients receiving a daily dose of 2×10^9 cfu of *L. acidophilus*-SDC 2012,2013 over four weeks. Agrawal *et al.*¹³ reported that it was necessary to select an organism or a mixture of probiotics that exhibit the properties most suitable for the particular expected health benefit or physiological effect.

In the randomized controlled trial of composite probiotics, Kim *et al.*⁶ identified that VSL#3 reduced flatulence and retarded colonic transit without altering bowel function in patients with IBS and bloating. In another study with composite probiotics, Hong *et al.*⁷ reported that composite probiotics containing *Bifidobacterium bifidum* BGN4, *Bifidobacterium lactis* AD011, *Lactobacillus acidophilus* AD031 and *Lactobacillus casei* IBS041 were safe and effective, especially in patients who excreted mainly normal or loose stool. In this study, the probiotic fermented milk contained three strains of *S. thermophilus*, *L. acidophilus*, and *B. infantis* at total of 3.75×10^{12} cfu. Because previous reports with probiotics didn't show consistent results in patients with constipations, we designed this study. Our results showed that both probiotic fermented milks improved most IBS

symptoms except for flatulence, frequency of defecation, and stool consistency in all study subjects.

Increased dietary fiber is frequently recommended for irritable bowel syndrome. Although dietary fiber does not appear to be useful as the sole treatment for IBS, fiber appears to play a role in the management of some patients with IBS, especially if constipation is the dominant concern.¹⁶⁻¹⁸ The two types of fiber, soluble and insoluble, have different effects on global IBS related symptoms. Insoluble fiber is probably no better than placebo. However, soluble fiber showed favourable results in IBS related constipation.²⁸ For our study, we used sea tangle extract powder, radish extract, glasswort extract which mostly composed of soluble fiber. The subgroup analysis of IBS showed that even with the improvement of most symptoms associated with IBS, in each group, there were no significant differences between the two groups in the diarrhea-predominant subtype and mixed type. However, in fiber containing fermented milk group of the constipation-predominant subtype we observed a significant improvement in the frequency of defecation, duration of defecation, straining, and an overall improvement of the symptoms associated with IBS. It seems to be due to main mechanism of action of fiber, which accelerates oro-anal transit and decrease the intra-colon pressures.¹⁸ Although for urgency there was a little difference between subtypes, in the constipation predominant subtype only fermented milk group showed significant improvement differently from other subtypes. Kim *et al.*⁶ reported that VSL#3 had no effect in urgency in which didn't analyze as subtypes. It suggested that the effect of fiber and probiotics was different among the given organisms and IBS subtypes. The possible mechanism for explaining the difference need to

be investigated further. Considering that in other clinical trials, it is not uncommon to have placebo effects as high as 50%,²⁹ this study has the limitation of no placebo group. Nevertheless, it is noteworthy that dietary fiber such as sea tangle, radish and glasswort had additive effects on the symptoms of constipation, especially in the constipation-predominant IBS.

In conclusion, plain probiotic fermented milk and probiotic fermented milk containing dietary fiber were safe and effective. Especially probiotic fermented milk containing dietary fiber was more effective in patients with the constipation-predominant IBS.

This study is the first trial evaluating this preparation (combination of three lactic acid bacteria strains and dietary fiber). Further investigation is needed with a placebo group to determine the optimal daily dose of probiotics and dietary fiber as well as the duration of treatment.

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