Original Article

Effect of Probiotic Administration Immediately and 1 Month after Colonoscopy in Diarrhea-predominant Irritable Bowel Syndrome Patients

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Abstract

Background: Irritable bowel syndrome (IBS) is one of the most common disorders among young adults. Various studies have demonstrated that the use of probiotics can reduce the overall symptom of IBS, and thus, our aim was to evaluate the efficacy of probiotic products in the reduction of IBS syndrome after colonoscopy. **Materials and Methods:** Our patients were divided among three groups, including immediate probiotic users, start use of probiotics 1 month after colonoscopy, and placebo group. All the patients were interviewed for having common IBS symptoms (stool consistency and frequency, gas, abdominal pain, and flatulence) at baseline, 3rd month of follow-up, and 6th month of follow-up. **Results:** The mean reduction in abdominal pain was 3.05 ± 1.21, 3.86 ± 0.94, and 3.82 ± 0.63 in the control group, immediate probiotic users, and 1 month after colonoscopy, respectively ($P < 0.001$). The symptoms of the disease, such as stool consistency, the frequency of defecation, and flatulence (except gas) in the first quarter, in the two treatment groups were significantly improved more than in the control group ($P < 0.05$). In contrast, the frequency of defecation was not significantly different in the treatment group receiving the probiotics month after colonoscopy compared to the placebo users ($P > 0.05$). **Conclusion:** According to our results, the use of probiotics had the beneficial effect on IBS symptoms. Furthermore, it can be said that reductions in symptoms and pain in the two treatment groups were not significantly different, but after 6 months of treatment, the effect of probiotics in patients who immediately use it after colonoscopy was more visible and more stable.

Keywords: *Clinical trial, irritable bowel syndrome, probiotics, symptoms of disease*

Introduction

Irritable bowel syndrome (IBS) is a gastrointestinal (GI) tract disorder with high worldwide incidence. There is not any specific age conflicted by the disorder, but the most common age of affection is observed in young adult.[1] Females are more at risk of affection than men by 2:1 in the western countries. Many factors are in association with IBS such as unsuitable quality of life, having high mental stress as well as many pathophysiological factors, which lead to the imposition of considerable health costs on different societies.[2-4]

Some factors such as psychological aspects,[5,6] genetics,[7] and food[8] are known to have an antecedent role in IBS. It has been reported that microbiota has a noticeable role in the pathogenesis of IBS.[9] Everybody has a specific microbiota due to his diet, infection and antibiotic use, mode of birth, age, and kind of feeding.[10] There are a variety of heterogeneous abnormalities seen in IBS patients, and also, the diversity of bacterial species was reported to be reduced during disease phase.[11] Microbiome analyses have revealed dysbiosis; however, the microbial pattern was not consistent in patients with IBS. Some measures can be done to reach balance of the gut microbiome such as using of prebiotics, antibiotics, specific diets, probiotics, and microbial transplantation for restoring balance in bacterial flora.[12]

Probiotics are live microorganisms using in dietary as supplemental products. They have the beneficial effect on gut microenvironment by enhancing the defense through production of strong barrier in intestinal, making better mobility, releasing bacteriocidins, the effect on immune system, which leads to producing anti-inflammatory agents and immune regulation, and preventing of pathogens for adhesion to the gut epithelium.[13] Many

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studies have shown that uses of probiotics were useful in IBS symptoms such as abdominal pain.[14] Nevertheless, it cannot say confidentially that uses of probiotics are universally recommended in IBS patients because of many factors, including subtypes of IBS (IBS-D, IBS-C, and IBS-M), heterogeneity, and different outcomes due to the use of various stains, dosing of probiotics, and therapy duration;[13] although in practice, NICE in the United Kingdom recommends that the use of probiotics according to manufacturer's orders at least for 4 months would be beneficial for IBS patients if any adverse effect be in control and therapeutic efficacy be monitored carefully.[15]

Colonoscopy is the normal procedure for the treatment and diagnosis of colon lesions. This approach needs bowel preparation to visualize the colonic mucosa better. During the preparation, a change of gut microbiota is happening due to the evacuation of bowel. Recent studies have focused on using of supplementary materials, which help to return the intestine and colon to normal conditions.[16] Various studies have examined the beneficial effect of probiotics in gut microbiota,[17,18] but no study has evaluated the impact of using of probiotics initiated at different times after the colonoscopy. On the other hand, after 1 month from colonoscopy, we still observed that IBS-D patients had complained about manifestations and had postcolonoscopy symptoms; hence, we examined the effect of probiotics on diarrhea-predominant IBS (IBS-D) patients who just undergone colonoscopy for symptoms of stool consistency, stool frequency, producing gas, abdominal pain, and flatulence in comparison with the placebo group immediately and compared it to 1-month delay in the prescription of probiotics after colonoscopy.

Materials and Methods

In our random double-blind clinical trial study, a total of 105 patients who underwent routine clinical practice colonoscopy for GI symptoms and IBS-D were recruited, according to ROME III, from Al Zahra hospital as one of the referral hospitals from Isfahan, Iran, as well as other private clinics and randomly divided among three groups according to randomly number table: the patients who were received probiotics immediately after colonoscopy, the patients who were received probiotics after 1 month from colonoscopy, and the patients who were received placebo right after colonoscopy (each group consisted of 35 participates). All the patients used the prescribed capsules up to the 6th month after colonoscopy. Informed written consent form was filled by participants. The intervention was approved by Isfahan University of Medical Sciences with the ethical code of "395591" according to the thesis no. ir.mui.rec. 1395.3.591.

Inclusion criteria for patients were being diagnosed as IBS-D patients, undergoing colonoscopy, standard prepared bowel with Pidrolax (polyethylene glycol), not having IBD, active PD, documentary microscopic colitis, and active gallbladder diseases and willing to participate in our trial investigation. Exclusion criteria were age below than 18 years old, not willing to finish the study, lack of proper use of probiotics, stop taking probiotics before the finish the study, not having access to patients for checking the symptoms, any contraindications to colonoscopy, and the recent use of antibiotics or drugs that affect the motility during the past 2 months.

The colonoscopy was performed by Fujinon 2500, Tokyo, Japan. Both patients and biostatistician were blinded from the type of prescribed drug and group categorizing conditions. At the baseline time, the demographic data and clinical and physical signs and symptoms were documented. The prescribed probiotic was Familact™ from Zist Takhmir Co., Tehran, Iran, which includes *Lactobacillus casei, Lactobacillus acidophilus, Lactobacillus rhamnosus*, *Lactobacillus bulgaricus*, *Bifidobacterium breve*, *Bifidobacterium longum*, and *Streptococcus thermophilus* with prebiotic of *Fructooligosaccharides* species (250 mg each capsule, 1×10^9 colony-forming unit). The placebo capsule was also from the same company. Intervention groups used two capsules per day and for placebo groups, and the same condition was prepared.

Demographic and symptom data were collected from patients according to the ROME III diagnostic questionnaire. The symptoms of stool consistency, stool frequency, producing gas, flatulence, and abdominal pain were evaluated in three groups at the entrance into the study, 3 and 6 months after colonoscopy. For all variables, the items that asked in person or by phone calls were stool consistency (at baseline/at 3rd month/at 6th month, which was divided into five categories: hard, partially hard, partially loose, loose, and watery), gas (at 3rd month/at 6th month, which was classified into four items: none, less than before, same as before, and more than before), and abdominal pain and flatulence (at baseline/at 3rd month/at 6th month, which were assessed on a numerical scale from 0 to 10 [visual analog scale]). It should be noted that in the follow-up of treatment, five patients because of not finish the trial and one due to intolerance of abdominal pain (placebo group) were excluded from the study.

The data were analyzed by SPSS (version 20; SPSS Inc., Chicago, Ill., USA), and descriptive and Kolmogorov–Smirnov tests were done to check the normal distribution of data. Furthermore, descriptive statistics such as mean, standard deviation, frequency, and the percentage of frequency and inferential statistics such as independent sample *t*-test, one-way ANOVA and *post hoc* test, and Chi-square test were used and considering the significance level <0.05.

Results

In this study, in the control group, 22 patients were female (64.7%) and 12 patients were male 935.3%) and the

mean age of this group was equal to 35.15 ± 11.20 years; in "probiotic immediately" group, 21 patients were female (63.6%) and 12 patients were male (36.4%) and the mean age of this group was equal to 32.97 ± 10.79 years; and in "probiotic 1 month later" group, 19 patients were female (59.4%) and 13 patients were male (40.6%) and the mean age for this group was equal to 30.41 ± 8.52 years. These three groups statistically showed no difference in terms of age and sex ($P > 0.05$) [Table 1].

The examination of efficacy of probiotic on patients with IBS-D after colonoscopy indicated that at baseline, there was no difference among three groups in terms of stool consistency, frequency of defecation, and gas ($P > 0.05$), but after 3-month follow-up, the groups taking probiotics showed a significant improvement compared to control group in terms of stool consistency and frequency of defecation ($P < 0.05$).

A 6-month follow-up showed a significant increase in stool consistency only in probiotic immediately group compared to control group ($P < 0.05$) while there was no significant difference between probiotic 1-month later group and control group in terms of stool consistency and stool frequency ($P > 0.05$). Therefore, maybe it can be stated that prescription of probiotics immediately after colonoscopy for 3 and 6 months would be efficacious in stool consistency and gas, but it would show its efficacy in stool frequency in the first 3 months and delayed prescription of probiotics would be efficacious only in stool consistency and only in the first 3 months [Tables 2-4].

On the other side, at baseline, there was no significant difference among three groups in terms of abdominal pain and flatulence ($P > 0.05$), however, after 3-month follow-up, there was a significant difference between both groups treated by probiotics in terms of the severity of flatulence and abdominal pain ($P < 0.05$). Furthermore, after 6-month follow-up, only in probiotic immediately group, the decrease in abdominal pain severity was seen ($P > 0.05$). There was no significant difference between probiotic 1-month later group and control group in this term ($P > 0.05$), while by passing time (6 months), the significant improvement in all the three groups was observed in terms of abdominal pain and the flatulence [Figures 1 and 2].

Table 1: Main characteristics of patients in three groups as a baseline for comparison

Characteristics	Placebo (*n*=34), *n* (%)	Probiotics immediately (*n*=33), *n* (%)	Probiotics 1 month later (*n*=32), *n* (%)	*P*
Gender				
Female	22 (64.7)	21 (63.6)	19 (59.4)	0.895
Male	12 (35.3)	12 (36.4)	13 (40.6)	
Age (year)	35.15±11.20	32.97±10.79	30.41±8.52	0.177

Table 2: Frequency distribution of stool consistency in three groups

Variables	Placebo (*n*=34), *n* (%)	Probiotics immediately (*n*=33), *n* (%)	Probiotics 1 month later (*n*=32), *n* (%)	P_1	P_2	P_3
Stool consistency at baseline						
Hard	0 (0)	1 (3)	1 (3.1)	0.510	0.072	0.712
Partially hard	0 (0)	1 (3)	2 (6.3)			
Partially loose	7 (20.6)	10 (30.3)	13 (40.6)			
Loose	20 (58.8)	16 (48.5)	14 (43.8)			
Watery	7 (20.6)	5 (15.2)	2 (6.3)			
Stool consistency at 3 months						
Hard	0 (0)	2 (6.1)	1 (3.1)	0.004	0.026	0.845
Partially hard	1 (2.9)	7 (21.2)	6 (18.8)			
Partially loose	14 (41.2)	15 (45.5)	15 (46.9)			
Loose	10 (29.4)	9 (27.3)	9 (28.1)			
Watery	9 (26.5)	0 (0)	1 (3.1)			
Stool consistency at 6 months						
Hard	0 (0)	2 (6.1)	1 (3.1)	0.610	0.210	0.202
Partially hard	4 (11.8)	13 (39.4)	10 (31.3)			
Partially loose	19 (55.9)	16 (48.5)	13 (40.6)			
Loose	10 (29.4)	2 (6.1)	8 (25)			
Watery	1 (2.9)	0 (0)	0 (0)			
P_4	0.051	<0.001	0.064			

P_1: The significance level of the comparison placebo with probiotics immediately, P_2: The significance level of the comparison placebo with probiotics 1 month later, P_3: The significance level of the comparison probiotics immediately with probiotics 1 month later, P_4: The significance level of the comparison follow-up treatment in each group

Table 3: Frequency distribution of defecation frequency in three groups

Variables	Placebo (n=34), n (%)	Probiotics immediately (n=33), n (%)	Probiotics 1 month later (n=32), n (%)	P_1	P_2	P_3
Stool frequency at baseline (times)						
≤3	3 (8.8)	1 (3)	0 (0)	0.687	0.266	0.774
3-5	12 (35.3)	13 (39.4)	14 (43.8)			
5-7	11 (32.4)	13 (39.4)	13 (40.6)			
>7	8 (23.5)	6 (18.2)	5 (15.6)			
Stool frequency at 3 months (times)						
≤3	5 (14.7)	14 (42.4)	16 (50)	0.045	0.012	0.279
3-5	20 (58.8)	14 (42.4)	8 (25)			
5-7	7 (20.6)	5 (15.2)	6 (18.8)			
>7	2 (5.9)	0 (0)	2 (6.3)			
Stool frequency at 6 months (times)						
≤3	8 (23.5)	9 (27.3)	10 (31.3)	0.227	0.231	0.938
3-5	17 (50)	14 (42.4)	13 (40.6)			
5-7	6 (17.6)	10 (30.3)	9 (28.1)			
>7	3 (8.8)	0 (0)	0 (0)			
P_4	0.006	<0.001	<0.001			

P_1: The significance level of the comparison placebo with probiotics immediately, P_2: The significance level of the comparison placebo with probiotics 1 month later, P_3: The significance level of the comparison probiotics immediately with probiotics 1 month later, P_4: The significance level of the comparison follow-up treatment in each group

Table 4: Frequency distribution of gas in three groups

Variables	Placebo (n=34), n (%)	Probiotics immediately (n=33), n (%)	Probiotics 1 month later (n=32), n (%)	P_1	P_2	P_3
Gas at 3 months						
None	2 (5.9)	2 (6.1)	3 (9.4)	0.192	0.957	0.167
Less than before	8 (23.5)	16 (48.5)	7 (21.9)			
Same as before	19 (55.9)	12 (36.4)	17 (53.1)			
More than before	5 (14.7)	3 (9.1)	5 (15.6)			
Gas at 6 months						
None	3 (8.8)	4 (12.1)	3 (9.4)	0.039	0.351	0.540
Less than before	10 (29.4)	20 (60.6)	15 (46.9)			
Same as before	15 (44.1)	7 (21.2)	12 (37.5)			
More than before	6 (17.6)	2 (6.1)	2 (6.3)			
P_4	0.564	0.201	0.059			

P_1: The significance level of the comparison placebo with probiotics immediately, P_2: The significance level of the comparison placebo with probiotics 1 month later, P_3: The significance level of the comparison probiotics immediately with probiotics 1 month later, P_4: The significance level of the comparison follow-up treatment in each group

Discussion

In this study, probiotics were used immediately after colonoscopy in one group and also with 1-month delay after colonoscopy in another group and compared both groups in terms of commonly reported complications with controls. Then, we followed up our IBS-D patients 6 months after colonoscopy to check the efficacy of probiotic to alleviate the symptoms of IBS among them. Divided groups were same in terms of baseline (gender and age) characteristics. At baseline, all the patients reported the same diarrhea symptom, and most of the stool consistencies were partially loose, loose, or watery. At the 3rd month, our results revealed that probiotics had a beneficial effect on stool consistency compared to the placebo group; however, there was not any difference between two groups of probiotic users. At the end of follow-up, the best outcome was observed in immediately probiotic users. Likewise, Dapoigny *et al*. reported that complaint of diarrhea in the probiotic users' patients was significantly reduced.[19]

On the other hand, evaluations on stool frequency demonstrated that at the baseline, all the patients had high stool frequency, but after 3 months, the stool frequency was decreased noticeably in immediate and 1-month later probiotic users compared to the placebo group. At the 6th month of follow-up, although in three groups, the stool frequency was considerably fewer, probiotic users had a better stool frequency outcome. Similarly, in the

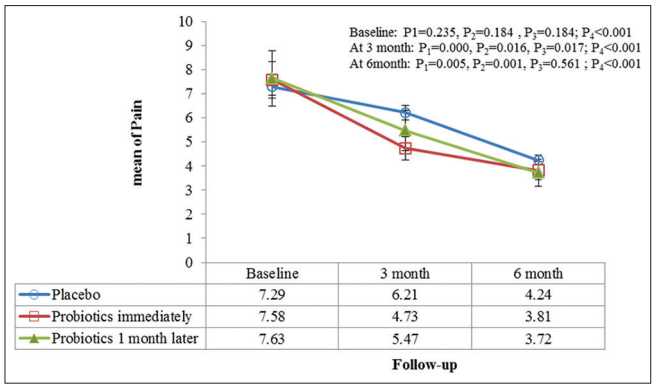

Figure 1: The linear graph based on the average of abdominal pain of all three groups. P_1: The significance level of the comparison placebo with probiotics immediately. P_2: The significance level of the comparison placebo with probiotics 1 month later. P_3: The significance level of the comparison probiotics immediately with probiotics 1 month later. P_4: The significance level of the comparison follow-up treatment in each group

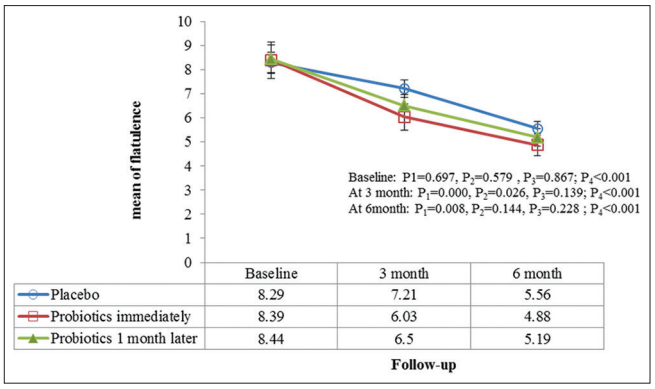

Figure 2: The linear graph based on the average of flatulence of all three groups. P_1: The significance level of the comparison placebo with probiotics immediately. P_2: The significance level of the comparison placebo with probiotics 1 month later. P_3: The significance level of the comparison probiotics immediately with probiotics 1 month later. P_4: The significance level of the comparison follow-up treatment in each group

comprehensive study on 362 primary care IBS patients, it has been found that the use of probiotics decreased the stool frequency significantly compared to the placebo group.[20] In addition, another multicenter, randomized, double-blind, controlled trial showed the same beneficial effect of probiotics on stool frequency over 6 weeks fewer than three times per week.[21]

Producing gas in all the patients after passing of 3 months from treatment did not show the significant difference, and at the 6th month after the trial, the only superiority among three groups was seen in immediate probiotic users compared to the placebo group. The overall reducing gas trend was seen for 6 months of follow-up among three groups; however, it was not statistically significant. In agreement with our results, Lasser *et al*. reported that quantity of intestinal gas was not different between IBS and control participants.[22] The bacteria in the colons are the main source of gas production in the colon through fermentation of undigested food, and it seems that IBS patients are more sensitive to dysbiosis and its consequent effects than the healthy people.[23] However, we believe that larger clinical trials should be designed to find the exact role of gut flora and their function to tolerate the pain and discomfort condition caused by producing intestinal gasses in the IBS patients.

The mean of pain in our 6 months of follow-up demonstrated that all the three groups had a significant reduction in abdominal pain; however, pain reduction in the placebo group was considerably lower than in the immediate and 1 month after colonoscopy probiotic users' groups. In other words, probiotic was beneficial for patients in terms of pain. Other studies have proven the positive effect of probiotic materials on the decrease of pain.[24,25] Abdominal pain is one of the most common symptoms among IBS patients. The recent studies believe that abdominal pain can be mediated by peripheral, spinal, or central brain–gut axis pathways. Brain imaging studies have shown that stress and negative emotion plays a pivotal role in the severity of the pain symptom. Another hypothesis suggested that immune cells have an important role in the pathophysiology of pain in IBS due to anxiety or stress, which triggers central nervous system to command releasing some mediated materials and/or triggers the pain neurological receptors in the intestine. Pathogens and consequence postinfection in IBS patients are other factors, which trigger immune system and further immune-to-brain communication, which results in the induction of abdominal pain in IBS.[26]

Flatulence in all the patients was high at the baseline. Like the abdominal assessment, flatulence symptom in three groups was reduced after 6 months of colonoscopy. The best outcome belonged to probiotic users. Other clinical trials stated the same outcome in probiotic users.[27-29] Excessive produced intestinal gas due to IBS disease condition leads to two types of abdominal symptoms: gas evacuation and retention. In both situations, most of the time, patients complain about flatulence. Overgrowth of colonic bacteria is thought to be the main reason of high level generated gas. Gas evacuation and impaired function of gas absorption lead to bloating and further flatulence in IBS patients.[30]

Conclusion

Our results showed the beneficial effect of probiotics on symptoms of IBS, including stool consistency and frequency, production of gas, abdominal pain, and flatulence. According to better influence of immediate using of probiotics in the reduction of abdominal pain and flatulence, we believe that the use of probiotics as food supplement right after colonoscopy can help out the patients better although it needs to be stated that the use of optimum dose and different microorganisms may have various outcomes; therefore, our recommendation is to investigate about different doses in larger studies to find the best treatment approach with optimum effects.

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Conflicts of interest

There are no conflicts of interest.

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