Journal of Gastroenterology and Hepatology

JGHF

doi:10.1111/jgh.14051

GASTROENTEROLOGY

Low fermentable oligo-di-mono-saccharides and polyols diet *versus* general dietary advice in patients with diarrhea-predominant irritable bowel syndrome: A randomized controlled trial

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Key words
abdominal pain, carbohydrates, irritable bowel syndrome, low FODMAP diet.

Accepted for publication 11 November 2017.

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Declaration of conflict of interest: The authors declare that they have no conflict of interest.
Author contribution: M. J. Z, V. B., and M. Z. have substantial contributions to the conception and design of the work. V. B. and M. Z. have contributions to the acquisition, analysis, and interpretation of data for the study. V. B. has contributions to drafting the work. M. J. Z. revised the manuscript for important intellectual content. M. J. Z. conducted final approval of the version to the published. V. B. was accountable for all aspects of the work. All authors read and approved the final manuscript.
Financial support: The present study was supported by a grant from Vice Chancellor for Research, Kerman University of Medical Sciences, Kerman, Iran.
Guarantor of the article: Vahideh Behrouz.
Clinical trial registration number: www.irct.ir: IRCT2017093033308N1.

Abstract

Background and Aim: Recent evidence indicates that new approach of the diet with low fermentable oligo-di-mono-saccharides and polyols (FODMAPs) may have an effective role in management of the patients with irritable bowel syndrome (IBS). We compared the results of low FODMAP diet with current dietary treatment, general dietary advices (GDA), on the clinical response in patients with diarrhea subtype of IBS (IBS-D).
Methods: In this randomized, controlled, single-blind trial, we included 110 patients with IBS-D in two intervention groups. Participants were randomly assigned to the low FODMAP diet (n = 55) and GDA (n = 55) for 6 weeks after a 10-day screening period. Gastrointestinal symptoms and bowel habit status were evaluated using a symptom severity scoring system and Bristol stool form scale pre-intervention and post-intervention. Patients completed 3-day food diary before and after the intervention.
Results: Of 110 patients, 101 completed the dietary interventions. At the baseline, the nutrient intake, severity of symptoms, and demographic data were similar between two groups. After 6 weeks, the low FODMAP diet improves significantly overall gastrointestinal symptoms scores, stool frequency, and consistency *versus* GDA group ($P < 0.001$, $P < 0.001$, and $P = 0.003$, respectively). Compared with the baseline, both intervention groups expressed a significant reduction in overall scores of symptom severity scoring system, abdominal pain, distension, consistency, and frequency, but this reduction is greater in low FODMAP diet group.
Conclusions: Both low FODMAP diet and GDA in patients with IBS-D led to adequate improvement of gastrointestinal symptoms for 6 weeks. However, the low FODMAP diet has greater benefits in IBS improvement.

Introduction

Irritable bowel syndrome (IBS) is a functional, chronic, and highly prevalent gastrointestinal (GI) illness with uncertain etiology and without effective therapy. Prevalence of IBS is observed in 10–25% of population, and it is twice as common in women as men.[1–3] Directly or indirectly, IBS has a significant impact on the health-care costs. In addition to the economic burden on IBS patients, there is a significant decrease on quality of life (QOL).[1,4,5] Current guidelines for IBS treatment recommended a multidisciplinary treatment. In fact, treatment includes a variety of medical sciences such as gastroenterology, psychology, nutrition, and pharmacology.[1,6] Nutrition can have a major effect on well-being in IBS. The majority of patients have noted the certain foods aggravate the symptoms of disease. Hence, dietary management is recommended as part of first-line treatment of IBS.[7,8] Based on the clear relationship between food intakes and worsening of symptoms in IBS, many different dietary attitudes have

been expressed to improve the symptoms of IBS in recent years, for example, restricting of many dietary component (e.g. fatty foods, foods containing gluten, caffeine, dairy, alcohol, spicy food, and gas-producing food such as beans, cabbage, and onions). But it has been proven that these recommendations are often ineffective for IBS sufferers. In fact, current standard dietary advices are not based on evidence from controlled clinical trials and offer general dietary advices (GDA) for the management of disease.[9,10] A new approach suggests that intake of fermentable oligo-di-mono-saccharides and polyols (FODMAPs) can aggravate the GI symptoms of IBS. FODMAPs are poorly absorbed by the small intestine and including short chain oligosaccharide polymers of fructose (fructans) and galacto-oligosaccharides (stachyose and raffinose), disaccharides (lactose), monosaccharides (fructose), and sugar alcohols (polyols), such as sorbitol, mannitol, xylitol, and maltitol. These sugars have osmotic effects and drag water into the intestine via osmosis. Also, they serve as food for bacteria in the colon, generate gases, and finally can cause the sensation of abdominal pain, bloating, and other GI symptoms that are commonly experienced by IBS sufferers. So low FODMAPs diet can be considered a new treatment for IBS.[6,11,12] For the first time, FODMAPs restriction could satisfy 74% of patients with IBS when removed fructose in a period of 2–40 months.[13] Then, in a clinical trial, fructose and fructan administration aggravated GI symptoms of IBS.[14] So, based on observation and considering that the number of clinical trials to determine the efficacy of low FODMAPs diet on IBS sufferers is very low, the necessity of this study can be justified. The objective of the present randomized, controlled, single-blinded study was to compare the effect of low FODMAPs diet with GDA on QOL and clinical symptoms in patients with diarrhea subtype of IBS (IBS-D).

Methods

Participants. Eligible patients referring to gastroenterology care clinic, Afzalipour Hospital, Kerman, Iran, that meeting Rome III criteria for IBS,[15] participated in this study between February and August 2016. The study was explained to all patients, and written informed consent was obtained. Inclusion criteria for participants' enrollment were IBS-D (Bristol stool form scale ≥ 5)[15] and age 20–60 years old. Exclusion criteria were having a confounder medical condition such as celiac disease, inflammatory bowel disease, or presence of cardiovascular, liver, kidney, neurologic diseases, diabetes, and thyroid disorders, consumption of ω-3 fatty acids and other nutritional supplements in the last 3 months, and pregnancy during the study. Referrals with a nutrients restricting diet before entering the study (e.g. gluten free, low FODMAP diet, vegan diet, low carbohydrate, or high protein diet) were excluded. The use of effective drugs against IBS such as drugs affecting GI motility was not allowed, but antidepressants drugs were allowed on a stable dose for the last 3 months before inclusion. Also, the use of products containing probiotic on a regular basis was allowed, but the use of probiotic supplement was not allowed during the study and in the last 3 months before inclusion. In addition, patients with significant changes in the recommended diet were also excluded from study.

The study protocol was approved by the ethics committee of Kerman University of Medical Sciences on human research (no. IR.KMU.REC.1395.98).

Study protocol

Visit 1 (screening). At this visit, the patients received full information on the subject, objectives, and implementation of the study, then signed an informed consent, and completed a demographic questionnaire. Patients were informed that there are two different diets in present study, and both diets are effective in alleviation of IBS symptoms, but none of the diets were not superior to another. Also, dietitians did not express any information about composition of diets in the present study. Then, patients entered into screening period (10 days) for determination of IBS subtype by daily stool diary based on the Bristol stool form scale.[15] In addition, patients completed food record questionnaire (two usual days and one weekend day) in this period.

Visit 2. After screening period, IBS sufferers returned to the gastroenterology care clinic, and dietitians were controlled inclusion and exclusion criteria, again. Daily stool diary was analyzed, and patients with IBS-D entered to study. Then, IBS severity scoring system (IBS-SSS) questionnaire[16] for determination of the IBS severity was completed. Patients were stratified according to their age, gender, and severity of disease. In the present study, participants were randomly allocated into two groups according to the pre-arranged balanced block randomization to receive low FODMAP diet (diet A) or GDA (diet B) for 6 weeks. Also, IBS-QOL questionnaire and hospital anxiety and depression scale (HADS) questionnaire[17] were completed in visit 2. Patients were requested to complete daily stool diary for determination of stool consistency and frequency during the study and food record (two usual days and one weekend day) at the last week of study. The present study was single-blinded study design, and trained dietitians were not blinded.

Visit 3. After 3 weeks, participants were evaluated for adherence to the diet, severity of symptoms by IBS-SSS questionnaire, and difficulties that were encountered during the last 3 weeks.

Visit 4. At the end of study, participants returned to the gastroenterology care clinic again, and dietitians collected daily stool diary and 3-day food record. Also, patients completed clinical end points including IBS-SSS, IBS-QOL, and HADS questionnaires at the clinic. At this visit, dietitians answered to questions and assessed adverse events.

Diets. In present study, all participants met with the specialized dietitians to educate and receive dietary plan in a 45-min one-to-one appointment. The low FODMAP diet (diet A) was supplied less than 0.5 gr per meal fermentable oligosaccharides, monosaccharides, disaccharides, and polyols.[18] The patients who were randomized to diet (A) group received a pamphlet with suitable foods, unsuitable foods, and their substitutes, shopping guide, strategies for eating out, and information about cooking foods without onion and garlic (Table 1).

Table 1 Examples of high FODMAPs food sources (unsuitable foods) and low FODMAPs food sources (suitable foods)

Grain foods	Vegetables	Fruits	Milk products	Meat and alternatives	Drinks	Other
Unsuitable foods: Biscuits, cakes, crackers, pasta (> 1/2 cup in one meal), wheat bread (> 30 gr in one meal), rye, barley, and wheat flour	Garlic, onion, artichoke, asparagus, beetroot, cabbage, cauliflower, leek, mushrooms, kale, green peppers, lentils, shallot, and leek	Apple, apricot, avocado, raspberry, blackberry, cherry, dates, figs, raisin, grapefruit, mango, plum, watermelon, nectarine, peach, pear, dried fruit, persimmon, and pomegranate	Soft cheeses (e.g. cream, ricotta, and mascarpone), ice cream, yogurt, milk from cows, goats, or sheep, and cream	Sausage, cooked beans, soybean, peas, and processed meats and proteins food	Coconut water, teas (chamomile, fennel, and oolong), sport drinks, soy milk, and apple, pear, and mango juices	Honey, soy sauce, vinegar, tomato paste, vanilla, corn syrup, and foods and chewing gum containing the artificial sweetener (sorbitol, mannitol, maltitol, and xylitol)
Suitable foods: Gluten-free bread, cereals, pastas and crackers without honey, apple/pear juice, brown rice, popcorn, white rice, corn (1/2 cup), potato/tortilla chips, and foods made with corn, rice, oats, potato	Bean sprouts, broccoli (1/2 cup), zucchini, carrot, potato, tomato, pumpkin, common cabbage (1/2 cup), cucumber, eggplant, olive, spinach, lettuce, cinnamon, sweet pepper, radish, saffron, basil, parsley, mint, and spring onion (green part only)	Banana, blueberry, grape, cantaloupe, melon, kiwi, oranges, pineapple, lemon, lime, strawberry, and pomegranate (1/4 cup)	Cheeses (cheddar, colby, parmesan, swiss, cottage, etc.), butter, soft cheeses (feta, mozzarella), lactose free/low lactose dairy, and Greek yogurt	Beef, chicken, deli slices, eggs, fish, lamb, pork, shellfish, turkey, shrimp, nuts (walnut and peanut), and nut butters	Tea, coffee (1 cup) and fruits and vegetable juices (1/2 cup)	Jam, jelly, mayonnaise, sugar, salt, seeds (flax, pumpkin, sesame, and sunflower), and cooking oils

The GDA (diet B) implied dietary recommendations from British Dietetic Association[19] such as limitation of caffeine, alcohol, spicy food, fatty food, and carbonated drinks; to eat small frequency meals; to eat slowly and in peace; and avoidance of chewing gums and sweeteners containing polyols.

Questionnaires. During the 6-week study period, all participants in both groups completed same assessment tools, as described here:

1. IBS-SSS[16] uses a five visual analogue scale to measure abdominal pain, abdominal distension, intestinal transit, and interference with daily life. The overall score of IBS-SSS ranges from 0 to 500. According to this standardized, validated questionnaire, scores of 75–175, 175–300, and > 300 are regarded as mild, moderate, and severe symptoms, respectively. IBS-SSS questionnaire was completed on weeks 0, 3, and 6.
2. IBS-QOL assessed eight subscales of health including dysphoria, interference with activity, body image, health worry, food avoidance, social reaction, and sexual relationships. Each item is graded on a 5-point scale. The total score ranges from 0 to 100, with higher scores reflecting poorer QOL.[20] The IBS-QOL questionnaire was completed at baseline and end of the study.
3. Stool consistency was assessed using the validated Bristol stool form scale.[15] Stool frequency (number of stools per day) was recorded during the intervention and screening period. All bowel movement (stool frequency and consistency) was collected on a daily basis.
4. HADS questionnaire has two subscales with seven items to measure the severity of anxiety and depression. Each item is scored from 0 to 3, and total score between 0-7, 8-10, and 11-21 indicates normal, borderline, and abnormal case, respectively.[17] HADS questionnaire was completed on weeks 0 and 6.
5. Food diary was completed for 3 days (one weekend day and two usual days) during the screening period and during the last week of intervention. Also, researchers assessed adherence to the diet and its possible problems at the end of each week.

Statistical analysis. In our research, the sample size was determined according to abdominal pain frequency as a key variable in a previous study among the subjects with IBS.[8] Considering the confidence level of 95% and 80% power, we needed 50 patients per group. However, we recruited 55 patients per group to account for the possible dropouts.

Collected information by food diaries was analyzed in the NUTRITIONIST 4 software (First Databank Inc., Hearst Corp., San Bruno, CA) modified for Iranian foods. Data from food record questionnaire were entered and analyzed by an expert dietitian. Analysis of data was performed using SPSS 21 for Windows (SPSS Inc., Chicago, IL, USA). Kolmogorov–Smirnov test was used to verify the normal distribution. Categorical variables were analyzed with chi-square test; comparison between the variables was performed by paired samples *t*-test at the beginning and end of the study in each group. To detect differences in continuous variables between the two groups, independent samples *t*-test was used for baseline measures. Continuous data at the end of study were compared between groups using analysis of covariance with baseline measures as a covariate. The tests were two-sided, and *P* value of less than 0.05 was considered significant.

Results

Participants. Two hundred twenty-four patients entered the screening period and assessed for eligibility. Out of the 224 patients, 110 were randomized to low FODMAP group (n = 55) and GDA group (n = 55). In the low FODMAP group, three patients were lost because of noncompliance, and two were lost to follow-up. In GDA group, two patients were excluded because of travel, and two were lost to follow-up. Therefore, the results obtained with 50 patients in the low FODMAP group and 51 patients in the GDA group (Fig. 1). Baseline characteristics in the two groups are shown in Table 2. The groups were similar except for stool consistency (P = 0.038).

Nutritional data. At the beginning of the study, both intervention groups had similar intake of energy, nutrients, and FODMAPs (Table 3). However, the low FODMAP group had reduced the intake of FODMAPs including monosaccharides and polyols as predicted after 6 weeks of intervention. Also, there is a significance between group differences for FODMAP at the end of the study. The intake of energy and carbohydrate reduced in both groups at week 6, in which this reduction of carbohydrate was significantly larger in the low FODMAP group. Fat consumption decreased within GDA group during study and between groups at the end of study.

Gastrointestinal data. The total scores of IBS-SSS, the scores for individual item (abdominal pain intensity, abdominal pain frequency, abdominal distension, dissatisfaction of intestinal

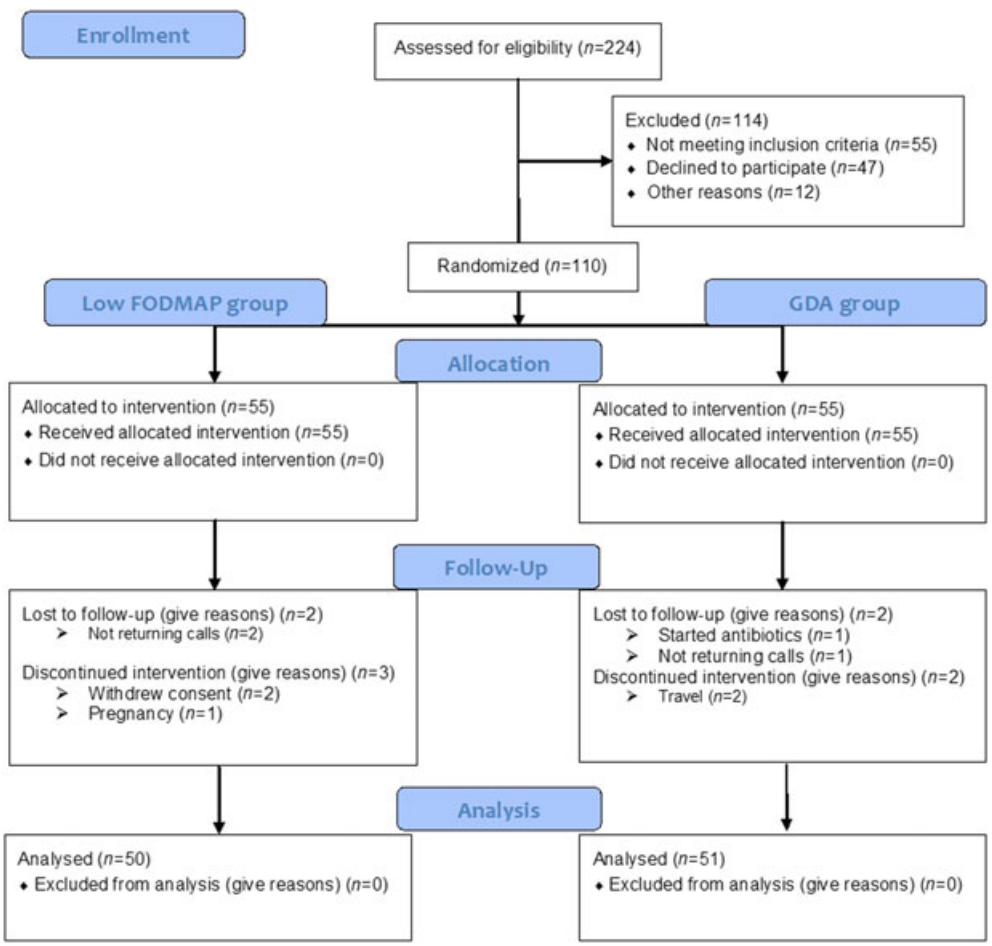

Figure 1 Consolidated Standards of Reporting Trials flow diagram. GDA, general dietary advices.

Table 2 Baseline characteristics of patients with irritable bowel syndrome

Baseline characteristics	Low FODMAP group (n = 50)	GDA group (n = 51)	P value
Age (years)†	37.60 ± 11.09	37.43 ± 13.27	ns
Gender, n (%)‡			ns
Male	26 (52%)	24 (47.05%)	
Female	24 (48%)	27 (52.94%)	
BMI (kg/m^2)†	25.13 ± 4.61	24.36 ± 5.21	ns
HADS†			
Depression	9.05 ± 3.84	7.90 ± 3.12	ns
Anxiety	11.13 ± 4.61	10.18 ± 3.93	ns
IBS-SSS, n (%)‡			ns
Mild (< 175)	11(22%)	11 (22%)	
Moderate (175–300)	20 (40%)	25 (49%)	
Severe (> 300)	19 (38%)	15 (29%)	
QOL†	51.03 ± 17.48	50.30 ± 16.81	ns
Stool frequency	3.29 ± 0.87	3.30 ± 0.77	ns
Stool consistency	5.92 ± 0.45	5.67 ± 0.61	0.038

†Data compared by independent sample t-test.

‡Data are reported by n (percentage of total); the chi-square test was used.

BMI, body mass index; FOODMAP, fermentable oligo-di-mono-saccharides and polyols; GDA, general dietary advices; HADS, hospital anxiety and depression scale; IBS-SSS, irritable bowel syndrome–severity symptom scale; ns, not significant; QOL, quality of life.

transit, and interference of daily life), and bowel habit status (stool frequency and consistency) are shown in Table 4. The value of these variables had a significant reduction in both groups at the end of the study compared with the baseline ($P < 0.001$ in both groups). The individual item of IBS-SSS scores (abdominal pain intensity, abdominal pain frequency, abdominal distension, dissatisfaction of intestinal transit, and interference of daily life) and bowel habit status (stool consistency and stool frequency) decreased significantly in low FODMAP group compared with the GDA group ($P = 0.001$, $P = 0.017$, $P < 0.001$, $P = 0.001$, and $P = 0.005$, respectively, for individual item of IBS-SSS and $P = 0.003$ and $P < 0.001$, respectively, for bowel habit status). Comparisons of total scores of IBS-SSS through the three moments of assessment between groups showed significant relief in low FODMAP group relative to GDA group (Fig. 2).

Quality of life. There was no difference in the score of QOL between groups at the baseline (Table 2). The QOL score decreased in both intervention groups (-7.3 ± 8.78, $P < 0.001$ in low FODMAP group and -5.35 ± 9.19, $P = 0.001$ in GDA group) at week 6. With adjustment of baseline QOL value, there was not seen significant difference between groups at the end of the study ($P = 0.332$).

Discussion

The present study demonstrated that adherence to low FODMAP diet among the patients with IBS for 6 weeks had beneficial effects on GI symptoms (abdominal pain intensity, abdominal pain frequency, abdominal distension, and bowel habit status); however, it did not influence QOL compared with the GDA group. In our study, the assessment of food record questionnaire showed that FODMAP restriction via dietary advice (suitable and unsuitable foods) can reduce the amount of FODMAP in daily intakes without significant change in calorie intake. But in the long time use, it needs to be monitored because of the possibility of malnutrition.

Currently, GDA is used for improvement of IBS symptoms, which are effective in the management of IBS, but these advices should be examined for their effectiveness in high-quality evidence.[21] There is a growing popularity for the new concept of a low FODMAP diet in IBS, although diet adherence may be problematic for patients with IBS.[22] Few studies have investigated the effects of low FODMAP diet on severity of GI symptoms in IBS patients.[3,8,18,23] The present study compared this concept with GDA to investigate which one of the diets is superior in management of IBS. Also, this randomized, controlled trial was single blind; dieticians were aware of type of the patient's diet (diet A or diet B) to be able to counsel patients about their diet and possible complications. In our study, the advice time with dieticians was 20 min at the first meeting, and diets were trained to patients. In addition, considering our study design as clinical practice, the

Table 3 Dietary intake during the baseline and end of the study in intervention groups

Parameter	Low FODMAP group			GDA group			P** (Week 0)	P*** (Week 6)
	Week 0	Week 6	P*	Week 0	Week 6	P*		
Energy (kcal)	2388.8 ± 542.5	2037.05 ± 379.6	0.03	2417.1 ± 706.5	2185.1 ± 422.09	0.04	ns	ns
Protein (gr)	101.9 ± 35.4	97.67 ± 29.78	ns	94.5 ± 29.01	89.21 ± 20.67	ns	ns	ns
Fat (gr)	69.96 ± 28.10	65.16 ± 17.2	ns	71.62 ± 24.20	51.36 ± 14.59	< 0.001	ns	0.04
Carbohydrates (gr)	342.95 ± 101.8	266.07 ± 61.8	< 0.001	384.07 ± 115.7	360.9 ± 73.7	0.04	ns	< 0.001
Dietary fiber (gr)	15.26 ± 6.54	13.97 ± 4.73	ns	15.95 ± 6.07	14.58 ± 5.89	ns	ns	ns
Soluble fiber (gr)	2.67 ± 0.89	2.26 ± 0.64	ns	2.89 ± 1.05	2.56 ± 0.91	ns	ns	ns
Insoluble fiber (gr)	12.41 ± 5.8	11.85 ± 6.3	ns	13.06 ± 5.04	12.39 ± 4.6	ns	ns	ns
Fructose (gr)	14.26 ± 9.98	7.31 ± 6.4	< 0.001	13.74 ± 8.8	11.73 ± 8.2	ns	ns	0.009
Lactose (gr)	10.28 ± 7.3	2.69 ± 1.8	< 0.001	11.78 ± 9.8	9.7 ± 3.2	ns	ns	< 0.001
Polyols (gr)	1.31 ± 0.8	0.57 ± 0.9	0.003	0.99 ± 1.3	1.03 ± 1.1	ns	ns	0.001

Data are reported as mean ± SD and compared by independent sample t-test.

P* indicates within group, P** between groups at week 0, and P*** between groups at week 6.

FOODMAP, fermentable oligo-di-mono-saccharides and polyols; GDA, general dietary advices; ns, not significant.

Table 4 Gastrointestinal symptoms (IBS-SSS and bowel habit) in patients with irritable bowel syndrome

Parameter	Low FODMAP group				GDA group						
	Week 0 (M1)	Week 3 (M2)	Week 6 (M3)	*P**	Week 0 (M1)	Week 3 (M2)	Week 6 (M3)	*P**	*P*** (M2–M1)	*P*** (M3–M2)	*P*** (M3–M1)
Total scores of IBS-SSS	263.75 ± 91.25	187.63 ± 82.89	108 ± 63.82	< 0.001†	252.5 ± 85.51	202 ± 76.03	149.75 ± 51.39	< 0.001	0.068	< 0.001	< 0.001
Abdominal pain intensity	48.38 ± 29.57	34.13 ± 20.53	16.13 ± 13.13	< 0.001	47.38 ± 33.03	34.88 ± 24.21	25.88 ± 21.11	< 0.001	0.642	< 0.001	0.001
Abdominal pain frequency	37.38 ± 31.63	24.5 ± 24.17	13.25 ± 14.21	< 0.001†	32 ± 28.75	24.5 ± 22.41	16.75 ± 17.74	< 0.001†	0.154	0.068	0.017
Abdominal distension	60.50 ± 26.98	43 ± 23.88	26.25 ± 18.35	< 0.001	58.75 ± 27.09	47.5 ± 21.33	36.88 ± 15.83	< 0.001	0.035	0.002	< 0.001
Dissatisfaction of intestinal transit	69.75 ± 23.03	50.5 ± 17.53	31.75 ± 17.37	< 0.001	62.38 ± 21.36	50.5 ± 19.47	39.25 ± 16.23	< 0.001	0.190	0.007	0.001
Interference of daily life	48.63 ± 26.62	35 ± 20.87	20.13 ± 18.55	< 0.001†	52.25 ± 27.19	43 ± 24.51	31.25 ± 18.56	< 0.001	0.089	0.029	0.005
Bowel habit status	Week 0	Week 6	Difference	*P**	Week 0	Week 6	Difference	*P**		*P***	
Stool consistency	5.92 ± 0.45	4.3 ± 0.5	−1.62 ± 0.51	< 0.001	5.67 ± 0.61	4.61 ± 0.69	−1.05 ± 0.79	< 0.001		0.003	
Stool frequency	3.29 ± 0.87	1.91 ± 0.56	−1.37 ± 0.62	< 0.001	3.3 ± 0.77	2.6 ± 0.96	−0.7 ± 0.88	< 0.001		< 0.001	

Values are reported as mean ± SD.
*P** is obtained from the paired samples *t*-test for comparison of data between the beginning and end of the study and *P*** obtained from analysis of covariance test adjusted for the baseline values between studied groups.
†Obtained from the Wilcoxon test for nonparametric data.
FODMAP, fermentable oligo-di-mono-saccharides and polyols; GDA, general dietary advices; M1, moment 1; M2, moment 2; M3, moment 3.

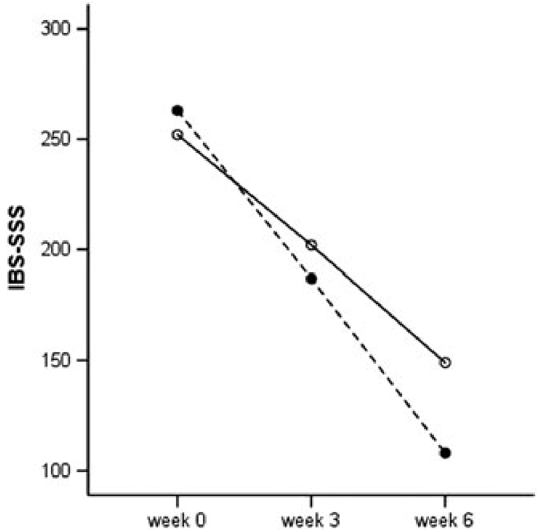

Figure 2 The comparison of the changes of total scores of irritable bowel syndrome–severity scoring system (IBS-SSS) (mean ± SD) through the three moments of assessment between groups. Repeated time variance analysis showed that time × group effect was significant ($P = 0.01$). The differences of the total scores of IBS-SSS in the low fermentable oligo-di-mono-saccharides and polyols (FODMAP) group compared with general dietary advices (GDA) group were 11.25 for week 0, 14.37 for week 3, and 41.75 for week 6. At week 6, the total scores of IBS-SSS decreased significantly in the low FODMAP group relative to GDA group ($P = 0.002$). Intervention groups: - -, Low FODMAP diet; —, GDA.

low FODMAP diet was presented as suitable and unsuitable foods, not as a meal. The diet adherence in both groups depends on patient motivation and study dieticians follow-up. IBS sufferers are well aware that GI symptoms can depend on foods, beverages, and eating habits; hence, they have a high affinity to their diet. One way for evaluation of low FODMAP diet adherence is breath tests. Hydrogen and methane breath tests consider as a marker of colonic fermentation. So breath hydrogen/methane production is lower during low FODMAP diet.[10]

We focused on a subgroup of patients with diarrhea predominantly (IBS-D) in our study. A low FODMAP diet can reduce osmotic fluid transit into the gut and aggravate the constipation (IBS-C); thus, we thought that IBS-D patients could respond better to the low FODMAP diet. But on the other hand, our suggestion is to be considered all subtypes of IBS in future studies, and response to diet should be compared in each subtype of IBS. One previous low FODMAP dietary advice trial reported that 52% of patients with low FODMAP diet *versus* 41% of the patients with standard dietary advices had adequate relief in IBS-D symptoms. This trial demonstrated the low FODMAP diet has greater improvement in individual IBS-D symptoms, particularly pain and bloating, compared with the standard dietary advices.[9]

The assessment of nutritional data from our study shows calorie intake decreased in both intervention groups after 6 weeks, despite the fact that we did not recommend the low-calorie diet to patients. This finding is in line with Eswaran *et al.*[9] study. This result can relate to limitation of specified unsuitable foods intake in low

FODMAP group and some advices in GDA group, which leads to lower calorie intake.

We found that following a low FODMAP diet improves significantly GI symptoms (abdominal pain, bloating, and bowel movement) *versus* GDA group. Although the GDA group has shown a significant reduction in GI symptoms after 6 weeks, but the reduction is greater in low FODMAP diet group. Our results are consistent with a number of previous studies,[7,9,21,23,24] which have reported superiority of low FODMAP diet compared with typical dietary advices or standard diet. Inconsistently with our study, Böhn *et al*.[8] demonstrated the low FODMAP diet reduces IBS symptoms severity as well as traditional dietary advices. Also, bowel habit status, both stool frequency and stool consistency, had statistically significant improvement after 6 weeks of restriction on the FODMAP intake *versus* adherence to the GDA. This finding is controversial in studies.[7–9,18] These differences in the results of trials between the low FODMAP diet and GDA/standard diet were characterized by some explanations. First, we included patients that have IBS-D subtype (IBS with diarrhea), while some previous studies have been performed on all subtypes of IBS. Second, the IBS sufferers were informed of their disease at least for more than 6 months in present study and probably adhered to the GDA; hence, they wanted to know which foods are suitable/unsuitable for the GI symptoms. Dietitians did not restrict FODMAP from diet of patients in GDA group and only advised to limit consumption of foods that contribute to the deterioration of their symptoms. Other potential justifications for this discrepancy in results of the aforementioned studies include differences in the studied population such as cultural issues, genetics, gut microbiota, food habits, and differences in study design such as duration of intervention and sample size.

Notably, low FODMAP diet is a novel issue in Iran; and in our study, the booklet of low FODMAP foods is prepared according to Iranian culture. In addition, low FODMAP diet adherence may be considered hard; but our dieticians did not report it as a problem in research. However, the efficiency of low FODMAP diet needs to be investigated in the clinical practice as well as research in more studies.

The present study has several limitations. Our study results are not generalizable to other subtypes of IBS (IBS-C and IBS-M). Initially, we thought that low FODMAP diet decreased bowel movement and worsened constipation. So this condition can create a bias in the results of the study. However, recent studies have reported that low FODMAP diet can improve GI symptoms and bowel habits in IBS-C.[7,21] Also, dieticians knew about the intervention group of patients and were not blind; thus, the present study was performed as single-blinded fashion. Another limitation is that low FODMAP diet was not provided as meals, preparation of diet based on suitable/unsuitable foods can cause less compliance relative to meals. We tried to restrict this limitation through regular follow-up of the diet by dieticians. On the other hand, education of low FODMAP diet based on suitable/unsuitable foods makes a similar setting to the clinical practice. Stool collection is useful to examine the gut microbiota and to determine the exact stool consistency.

In conclusion, this randomized, controlled, single-blind trial showed that both low FODMAP diet and GDA in patients with IBS-D led to adequate improvement of GI symptoms for 6 weeks. But the low FODMAP diet has greater benefits in reduction of IBS symptoms. Furthermore, we suggest that this diet strategy can be used in combination with other methods as a first-line treatment. However, the efficacy and safety of low FODMAP diet needs to be evaluated for a longer intervention period and in more future studies.

Acknowledgment

Thanks are extended to Vice Chancellor for Research (KMU, Kerman, Iran) for their assistance in this project.

References

1 Whigham L, Joyce T, Harper G *et al*. Clinical effectiveness and economic costs of group versus one-to-one education for short-chain fermentable carbohydrate restriction (low FODMAP diet) in the management of irritable bowel syndrome. *J. Hum. Nutr. Diet.* 2015; **28**: 687–96.
2 Nanayakkara WS, Skidmore PM, O'Brien L, Wilkinson TJ, Gearry RB. Efficacy of the low FODMAP diet for treating irritable bowel syndrome: the evidence to date. *Clin. Exp. Gastroenterol.* 2016; **9**: 131–42.
3 Ong DK, Mitchell SB, Barrett JS *et al*. Manipulation of dietary short chain carbohydrates alters the pattern of gas production and genesis of symptoms in irritable bowel syndrome. *J. Gastroenterol. Hepatol.* 2010; **25**: 1366–73.
4 Pedersen N, Andersen NN, Vegh Z *et al*. Ehealth: low FODMAP diet vs *Lactobacillus rhamnosus* GG in irritable bowel syndrome. *World J. Gastroenterol.* 2014; **20**: 16215–26.
5 Rao SS, Yu S, Fedewa A. Systematic review: dietary fibre and FODMAP-restricted diet in the management of constipation and irritable bowel syndrome. *Aliment. Pharmacol. Ther.* 2015; **41**: 1256–70.
6 Shepherd SJ, Halmos E, Glance S. The role of FODMAPs in irritable bowel syndrome. *Curr. Opin. Clin. Nutr. Metab. Care* 2014; **17**: 605–9.
7 Halmos EP, Power VA, Shepherd SJ, Gibson PR, Muir JG. A diet low in FODMAPs reduces symptoms of irritable bowel syndrome. *Gastroenterology* 2014; **146**: 67–75.
8 Bohn L, Storsrud S, Liljebo T *et al*. Diet low in FODMAPs reduces symptoms of irritable bowel syndrome as well as traditional dietary advice: a randomized controlled trial. *Gastroenterology* 2015; **149**: 1399–407.
9 Eswaran SL, Chey WD, Han-Markey T, Ball S, Jackson K. A randomized controlled trial comparing the low FODMAP diet vs. modified NICE guidelines in US adults with IBS-D. *Am. J. Gastroenterol.* 2016; **111**: 1824–32.
10 Laatikainen R, Koskenpato J, Hongisto SM *et al*. Randomised clinical trial: low-FODMAP rye bread vs. regular rye bread to relieve the symptoms of irritable bowel syndrome. *Alim. Pharmacol. Ther.* 2016; **44**: 460–70.
11 Marum AP, Moreira C, Saraiva F, Tomas-Carus P, Sousa-Guerreiro C. A low fermentable oligo-di-mono saccharides and polyols (FODMAP) diet reduced pain and improved daily life in fibromyalgia patients. *Scand. J. Pain* 2016; **13**: 166–72.
12 Marsh A, Eslick EM, Eslick GD. Does a diet low in FODMAPs reduce symptoms associated with functional gastrointestinal disorders? A comprehensive systematic review and meta-analysis. *Eur. J. Nutr.* 2016; **55**: 897–906.
13 Shepherd SJ, Gibson PR. Fructose malabsorption and symptoms of irritable bowel syndrome: guidelines for effective dietary management. *J. Am. Diet. Assoc.* 2006; **106**: 1631–9.

14 Shepherd SJ, Parker FC, Muir JG, Gibson PR. Dietary triggers of abdominal symptoms in patients with irritable bowel syndrome: randomized placebo-controlled evidence. *Clin. Gastroenterol. Hepatol.* 2008; **6**: 765–71.
15 Longstreth GF, Thompson WG, Chey WD, Houghton LA, Mearin F, Spiller RC. Functional bowel disorders. *Gastroenterology* 2006; **130**: 1480–91.
16 Francis CY, Morris J, Whorwell PJ. The irritable bowel severity scoring system: a simple method of monitoring irritable bowel syndrome and its progress. *Alim. Pharmacol. Ther.* 1997; **11**: 395–402.
17 Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta. Psychiatr. Scand.* 1983; **67**: 361–70.
18 Perez y Lopez N, Torres-Lopez E, Zamarripa-Dorsey F. Clinical response in Mexican patients with irritable bowel syndrome treated with a low diet low in fermentable carbohydrates (FODMAP). *Rev. Gastroenterol. Mex.* 2015; **80**: 180–5.
19 McKenzie YA, Bowyer RK, Leach H *et al*. British Dietetic Association systematic review and evidence-based practice guidelines for the dietary management of irritable bowel syndrome in adults (2016 update). *J. Hum. Nutr. Diet.* 2016; **29**: 549–75.
20 Wong RK, Drossman DA. Quality of life measures in irritable bowel syndrome. *Expert Rev. Gastroenterol. Hepatol.* 2010; **4**: 277–84.
21 Staudacher HM, Whelan K, Irving PM, Lomer MC. Comparison of symptom response following advice for a diet low in fermentable carbohydrates (FODMAPs) versus standard dietary advice in patients with irritable bowel syndrome. *J. Hum. Nutr. Diet.* 2011; **24**: 487–95.
22 Molina-Infante J, Serra J, Fernandez-Banares F, Mearin F. The low-FODMAP diet for irritable bowel syndrome: lights and shadows. *Gastroenterol. Hepatol.* 2016; **39**: 55–65.
23 de Roest RH, Dobbs BR, Chapman BA *et al*. The low FODMAP diet improves gastrointestinal symptoms in patients with irritable bowel syndrome: a prospective study. *Int. J. Clin. Pract.* 2013; **67**: 895–903.
24 Staudacher HM, Lomer MC, Anderson JL *et al*. Fermentable carbohydrate restriction reduces luminal bifidobacteria and gastrointestinal symptoms in patients with irritable bowel syndrome. *J. Nutr.* 2012; **142**: 1510–8.