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Diet Low in FODMAPs Reduces Symptoms of Irritable Bowel Syndrome as Well as Traditional Dietary Advice: A Randomized Controlled Trial

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BACKGROUND & AIMS: A diet with reduced content of fermentable short-chain carbohydrates (fermentable oligo-, di-, monosaccharides, and polyols [FODMAPs]) has been reported to be effective in the treatment of patients with irritable bowel syndrome (IBS). However, there is no evidence of its superiority to traditional dietary advice for these patients. We compared the effects of a diet low in FODMAPs with traditional dietary advice in a randomized controlled trial of patients with IBS. **METHODS:** We performed a multi-center, parallel, single-blind study of 75 patients who met Rome III criteria for IBS and were enrolled at gastroenterology outpatient clinics in Sweden. Subjects were randomly assigned to groups that ate specific diets for 4 weeks—a diet low in FODMAPs (n = 38) or a diet frequently recommended for patients with IBS (ie, a regular meal pattern; avoidance of large meals; and reduced intake of fat, insoluble fibers, caffeine, and gas-producing foods, such as beans, cabbage, and onions), with greater emphasis on how and when to eat rather than on what foods to ingest (n = 37). Symptom severity was assessed using the IBS Symptom Severity Scale, and patients completed a 4-day food diary before and at the end of the intervention. **RESULTS:** A total of 67 patients completed the dietary intervention (33 completed the diet low in FODMAPs, 34 completed the traditional IBS diet). The severity of IBS symptoms was reduced in both groups during the intervention ($P < .0001$ in both groups before vs at the end of the 4-week diet), without a significant difference between the groups ($P = .62$). At the end of the 4-week diet period, 19 patients (50%) in the low-FODMAP group had reductions in IBS severity scores ≥50 compared with baseline vs 17 patients (46%) in the traditional IBS diet group ($P = .72$). Food diaries demonstrated good adherence to the dietary advice. **CONCLUSIONS:** A diet low in FODMAPs reduces IBS symptoms as well as traditional IBS dietary advice. Combining elements from these 2 strategies might further reduce symptoms of IBS. ClinicalTrials.gov ID NCT02107625.

Keywords: Gastrointestinal Symptoms; Food; Carbohydrates; Colon.

Irritable bowel syndrome (IBS) is a functional gastrointestinal (GI) disorder that affects 10%–20% of the population[1] and is characterized by abdominal discomfort or pain, in combination with altered bowel habit.[2] The pathophysiology is only partly understood, with abnormal GI motility, altered brain–gut communication, visceral hypersensitivity, low-grade inflammation, and psychosocial factors being potential contributory factors.[3] As a consequence of the poor understanding of factors underlying symptom generation in IBS, few effective treatment alternatives are currently available, even though development of new treatment alternatives is ongoing.[4] In addition, work productivity and quality of life are reduced in this large group of patients,[5–7] which leads to substantial costs for the society.[8]

Food is a central and recurrent issue that concerns patients with IBS.[9–11] The majority of IBS patients regard food items to be important triggers of their GI symptoms,[12–16] but despite the fact that a large proportion of IBS patients exclude certain foods to reduce symptoms, their nutritional intake seems to be adequate and comparable with the diet in the general population.[17,18] Based on the clear subjective association between food intake and worsening of GI symptoms in IBS,[13,16] many different dietary approaches to reduce IBS symptoms have been attempted over the years, but few controlled trials exist. In fact, current recommendations are based mainly on physiological effects of dietary constituents rather than on evidence from controlled clinical trials.[9,19] One approach that has been widely tested is to increase the dietary fiber intake, which has proven to be beneficial for some IBS patients, but also to worsen symptoms in others.[20–23] Different exclusion diets have been tried with varying and inconsistent results,[24–26] and current recommendations discourage their widespread use.[9,19,27] It can also be beneficial for patients with IBS to reduce fat intake, as IBS patients often report that fatty foods worsen their GI symptoms,[12,16] but so far no controlled clinical trials exist to support that fat reduction leads to diminished symptom severity in IBS. Recently, excluding gluten has been advocated to reduce

Abbreviations used in this paper: FODMAPs, fermentable oligosaccharides, disaccharides, monosaccharides and polyols; GI, gastrointestinal; IBS, irritable bowel syndrome; IBS-SSS, IBS Symptom Severity Scale.

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symptoms in patients with symptoms compatible with IBS, but this is also controversial.[28]

Recent evidence suggests that intake of fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs) can trigger GI symptoms in patients with IBS.[29–31] These carbohydrates are poorly absorbed in the small intestine and can pass unabsorbed to the colon, where they increase luminal water through osmotic activity and induce gas production due to fermentation by colonic bacteria. This in turn can cause luminal distension and lead to GI symptoms in susceptible individuals.[32] However, the effects of FODMAPs on microbiota, immune function, and gut barrier might also be involved in GI symptom generation. There are clinical trials supporting that reduction of FODMAPs is beneficial for IBS patients,[33–35] but so far no randomized controlled trial has demonstrated that a low-FODMAP diet is superior to the traditional dietetic practice that has been used for patients with IBS, which is to encourage a regular meal pattern and "healthy eating"; avoid large meals; reduce intake of fat; discourage excessive fiber intake, especially insoluble fibers; reduce caffeine; and avoid gas-producing foods, such as beans, cabbage, and onions.[36] How well these approaches work in the clinical setting, by providing patients with dietary advice relative to the effect in previous studies in standardized settings where all meals have been prepared for the patients,[30,31,33] is largely unknown.

Therefore, the aim of the study was to perform a randomized controlled trial to compare the effect on IBS symptoms of a low-FODMAP diet compared with traditional dietary advice in outpatients with IBS in a setting resembling standard clinical practice and to perform this study in a single-blinded fashion.

Materials and Methods

Subjects

For this multi-center, parallel, randomized, controlled, single-blind, comparative trial, we recruited adult patients (18−70 years of age) meeting Rome III criteria for IBS[2] from the gastroenterology outpatient clinics of Sahlgrenska University Hospital, Gothenburg; Karolinska University Hospital, Stockholm; and Sabbatsbergs Hospital, Stockholm. In Gothenburg, patients were also recruited through advertisement in the local newspaper. Exclusion criteria were presence of a severe cardiac, liver, neurologic, or psychiatric disease or a GI disease other than IBS (eg, inflammatory bowel disease, celiac disease) that could explain the current symptoms. The patients were also not allowed to be following a diet that excessively restricts certain nutrients before entering the study (eg, low in FODMAPs, gluten-free, vegan diet). A lactose-reduced diet was allowed, as long as they agreed to keep this intake consistent during the study period if not advised to reduce lactose further (ie, if they were randomized to the low-FODMAP diet). The patients should also be willing to change their current food intake to participate in the study. The use of probiotic products was allowed, but patients who consumed probiotic products were instructed to continue with an unaltered intake during the study period. IBS medications, including antidepressants, were allowed, provided that they used them on a regular basis and were on a stable dose for at least 1 month before inclusion. Subjects were studied between September 2013 and March 2014. All patients were given study-specific verbal and written information before giving their written consent to participate in the study. The study protocol was approved by the Regional Ethical Review Boards in Gothenburg and Stockholm, Sweden.

Study Design

Figure 1 provides a schematic drawing of the study design.

Visit 1: Screening. At this visit, the patients received verbal and written information about the study and gave informed consent. Patients were informed that the aim was to compare 2 different diets with potential benefits for patients by alleviation of IBS symptoms, but also that none of the diets were intended to cure IBS or expected to remove all symptoms, and that no existing evidence shows that one of the diets should be superior to the other. No detailed information about the composition of the diets was revealed at this stage, and the term *FODMAPs* was not used. During the subsequent 10 days, the participants completed a daily stool diary based on the Bristol Stool Form scale for IBS subtyping[2] and bowel habit assessment, and a food diary was administered in which the participants recorded their food intake during 4 days (Wednesday through Sunday) before the second visit, to capture their habitual diet (see Supplementary Material for more details).

Visit 2 (Day 0): Randomization. Ten days after the screening visit, patients returned to the research unit and the IBS Symptom Severity Scale (IBS-SSS)[37] (see Supplementary Material for more details) was completed by the patient on site. An IBS-SSS $\geq$175 (ie, moderate to severe symptoms) was necessary to be randomized. In addition, inclusion and exclusion criteria were reviewed again, including dietary habits, and if the patients were found to be eligible for randomization, a computer-generated web-based randomization program provided by an external contact research organization was used to determine which diet each patient should be assigned. The participants were randomized to follow 1 of 2 different diets (diet A or diet B), both with the intention to alleviate symptoms related to IBS. Patients were, according to instructions by a dietitian, advised to eat a low-FODMAP diet (diet A) or to eat according to traditional IBS dietary advice (diet B), and to follow these diets during the coming 4 weeks, before returning for the final study visit. Participants were only informed about diet A or diet B, and received no information of the "other" diet, and again, the term *FODMAPs* was not used.

Patients received thorough verbal instructions about the dietary advice from 1 of the 3 study dietitians (LB, TL, and LC) together with a brochure specifically produced for this study, with written instructions about the diet, including careful instructions about food items to avoid and/or reduce and alternatives to these food items. In order to have conformity among the dietitians and to assure that they gave similar

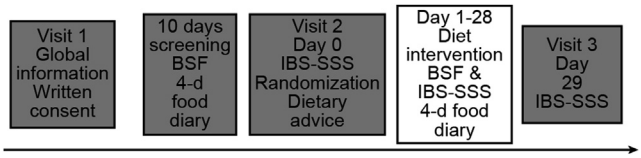

Figure 1. Schematic drawing of the study design, for details see text.

advice, a 1-day meeting with the dietitians was held before study start, where the content of verbal and written information at the randomization visit was agreed upon. All of the dietitians had previous experience working with IBS patients and thorough knowledge about FODMAPs and general IBS dietary advice. Before leaving the research unit, the patients completed baseline questionnaires, Hospital Anxiety and Depression scale,[38] Visceral Sensitivity Index,[39] Multidimensional Fatigue Inventory-20,[40] The Patient Health Questionnaire-15[41] (used as potential predictors for symptom response; see Supplementary Material for more details), and received 4 booklets, 1 for each intervention week, with the questionnaires and diaries that the patients were supposed to complete during the intervention period—Bristol Stool Form daily, IBS-SSS day 14 and the food diary for 4 days (Wednesday through Saturday) during the last week of the 4-week intervention period.

Visit 3 (Day 29): End of Treatment Period. At this visit, the completed questionnaires were collected by the study dietitian, including the 4-day food diary completed during the last week of the intervention period, and the patients completed a final IBS-SSS questionnaire at the site. Compliance with the dietary advice was discussed with the patient and potential adverse events during the intervention period were verbally assessed.

Intervention Diets

The low-FODMAP diet (diet A) implies a restricted intake of foods containing fermentable oligosaccharides, monosaccharides, disaccharides, and polyols.[32] The patients who were randomized to follow this diet received a pamphlet with detailed information of which foods to avoid (eg, apple, beans, white bread, and milk) and of alternative food items that could be ingested instead (eg, orange, blueberries, lactose-free milk, and 100% spelt bread). More specifically, the patients were instructed to avoid food sources rich in fructans and galactooligosaccharides, such as wheat, rye, barley, onion, and legumes; lactose-containing products; foods with "free fructose" (ie, fructose in excess of glucose), such as apples, pears, watermelon, asparagus, and honey; and food items rich in sorbitol, mannitol, maltitol, and xylitol, such as apricots, peaches, and artificially sweetened products.

The traditional IBS diet (diet B) implies a greater focus on how and when to eat rather than on what foods to ingest. The diet is based on the dietary recommendations from National Institute for Health and Care Excellence and the British Dietetic Association.[19,27] Specifically, the participants were instructed to regularly eat 3 meals and 3 snacks a day, never too much or too little each time, never to be hungry or too full; to eat in peace and quiet and to chew thoroughly; reduce intake of fatty or spicy foods, coffee, alcohol, onions, cabbage, and beans; avoid soft drinks and carbonated beverages, chewing gums, and sweeteners that ends with -ol, and to eat fibers but distribute the intake evenly during the day.

Symptom Assessment

In order to assess the effect of the dietary interventions, all patients in both groups completed the same questionnaires during the intervention period, as detailed in the Supplementary Material:

- IBS-SSS[37] was used to assess the severity of IBS symptoms. The questionnaire was completed on days 0, 14, and 29.
- The patients recorded all bowel movements in a stool diary, based on Bristol Stool Form scale[2] every day during the intervention period (28 days), as well as during the 10-day screening period.

Assessment of Nutrient Intake

All patients completed a 4-day food diary twice (see Supplementary Material for more details) once during the screening period and once during the last week of the 4-week intervention period. Different food items and beverages were entered in DIETIST XP version 3.1 (Kostdata.se, Stockholm, Sweden), and average daily intakes were calculated for energy, macronutrients, monosaccharides, lactose, dietary fibers, and FODMAPs.

Statistical Analysis

The primary end point in this trial was the change in IBS-SSS at the end of the treatment period relative to baseline, and the proportion of responders to the dietary intervention based on the recommended cut-off of a reduction (ie, improvement) in IBS-SSS $\geq$50, which is considered to reflect a clinically meaningful improvement.[37] To plan our sample size, we performed a power calculation based on the ability to detect a difference between the 2 diets in reduction of IBS-SSS of at least 50 with 80% power at $\alpha = .05$, assuming an SD of 70, and this indicated that we would need at least 31 patients in each group. As secondary end points, we analyzed the effect of the dietary interventions on the individual items of IBS-SSS, as well as on bowel habits measured by stool diaries. Adherence to the dietary advice was assessed by comparing dietary intake at baseline with the last week of the intervention period within and between the treatment groups. Potential baseline predictors for being a responder (IBS-SSS reduction $\geq$50 at the end of the intervention period) were also evaluated by comparing baseline variables between responders and nonresponders in the treatment groups. Data are presented as mean (SD) unless otherwise stated. Categorical variables were compared with χ^2 test, and continuous variables were compared with independent-samples and paired-samples t tests, after the normality of the distribution had been demonstrated with Kolmogorov-Smirnoff statistic, and with histograms of the data. Two-tailed P values $<.05$ were considered statistically significant. All patients who were randomized and who received dietary instructions were included in the responder comparisons, where dropouts were considered to be nonresponders (intention to treat analysis), and for comparisons of questionnaire data at the end of the intervention period vs baseline, only patients who completed the intervention were included (per-protocol analysis). All statistical analyses were performed using the SPSS statistical package, version 19.0 (released 2010, IBM Corp, Armonk, NY); data from questionnaires were entered into a database by a person not involved in the study, and data from food diaries were analyzed and entered into a database by one of the dietitians (LB). All authors had access to the study data and reviewed and approved the final manuscript.

Results

Subjects

Eighty-four patients entered the screening period of the study (mean age 42.5 [SD 16.3] years; 66 females) (Sahlgrenska University Hospital, n = 70; Karolinska University Hospital, n = 9; Sabbatsbergs Hospital, n = 5). There were 9 screening failures (mean age 44.0 [SD 17.1] years; 5 females) (Sahlgrenska University Hospital, n = 8; Karolinska University Hospital, n = 0; Sabbatsbergs Hospital, n = 1), which were not randomized because they did not fulfill the randomization criterion of IBS-SSS ≥175 at the randomization visit. Seventy-five patients were randomized—38 to the low-FODMAP diet and 37 to the traditional IBS diet. Eight patients dropped out prematurely during the intervention period due to unspecified adverse effects from the low-FODMAP diet (n = 1) because the diet was too time-consuming, stressful, or demanding to follow (n = 6; 4 in the low-FODMAP group, 2 in the traditional IBS diet group), or factors unrelated to the study (n = 1 in the traditional IBS diet group), which leaves 67 patients for the per-protocol analysis (56 females; mean age 43 [SD 16] years), 33 in the low-FODMAP group and 34 in the traditional IBS diet group (Figure 2). Baseline characteristics in the 2 groups are shown in Table 1 and the groups were similar, except for a tendency toward more severe fatigue in the low-FODMAP group.

Gastrointestinal Symptoms

The IBS symptom severity was reduced in both groups at the end of the intervention period compared with baseline ($P < .0001$ in both groups) (Figure 3). At day 14, there was already a reduction in the IBS-SSS scores in both groups, and this reached statistical significance in the low-FODMAP group ($P = .002$), with a trend in the same direction in the traditional IBS diet group ($P = .051$). The change in the IBS-SSS scores relative to baseline did not differ between the low-FODMAP and traditional IBS group at day 14 (62 ± 98 vs 23 ± 65; $P = .062$) or day 29 (77 ± 110 vs 65 ± 84; $P = .62$). A similar proportion of patients were defined as responders (IBS-SSS reduction ≥50) in the treatment groups, with 19 responders in the low-FODMAP group (50%) and 17 in the traditional IBS diet group (46%) ($P = .72$). When assessing the effect of the interventions on the individual items of the IBS-SSS score, all items were improved in both groups at day 29 relative to

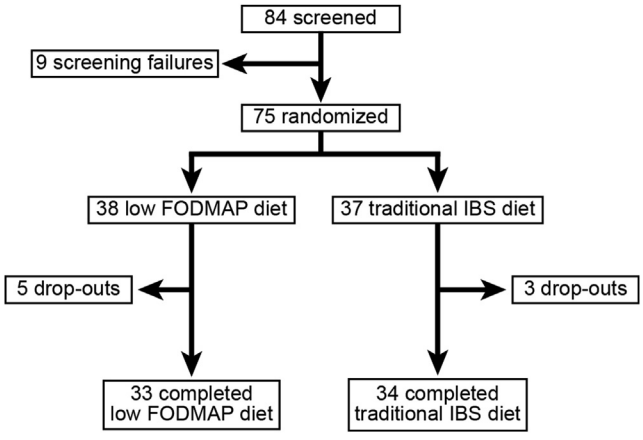

Figure 2. Flow chart demonstrating the number of patients in the different phases of the study, for details see text.

Table 1. Baseline Characteristics of the Randomized Patients

Baseline characteristics	Low-FODMAP diet (n = 38)	Traditional IBS diet (n = 37)	*P* value
Females, n (%)	30 (79)	31 (84)	.59
Age, *y*, mean (range)	44 (18–69)	41 (18–68)	.35
BMI, *kg/m²*, mean ± SD	24.5 ± 3.8	24.2 ± 3.8	.78
Patient Health Questionnaire-15, mean ± SD	12.5 ± 4.5	12.2 ± 4.6	.82
Visceral Sensitivity Index, mean ± SD	40.6 ± 12.6	41.8 ± 16.7	.73
Hospital Anxiety and Depression Scale, mean ± SD			
Anxiety	8.2 ± 4.5	7.0 ± 4.3	.24
Depression	5.1 ± 3.8	3.8 ± 2.9	.10
20-Item Multidimensional Fatigue Inventory, mean ± SD			
General fatigue	*15.2 ± 3.2*	*13.3 ± 3.7*	*.02*
Physical fatigue	*13.4 ± 3.8*	*10.6 ± 4.0*	*.004*
Reduced activity	*12.0 ± 4.5*	*9.2 ± 3.9*	*.005*
Reduced motivation	*9.5 ± 3.8*	*7.7 ± 3.3*	*.04*
Mental fatigue	12.2 ± 3.7	10.7 ± 4.0	.09
Predominant bowel habit, n (%)			.55
Constipation	9 (24)	13 (35)	
Diarrhea	10 (26)	8 (22)	
Mixed/unsubtyped	19 (50)	16 (43)	
IBS-SSS, mean ± SD	318 ± 67	302 ± 64	.35
IBS-SSS, n (%)			.42
Moderate	15 (39)	18 (49)	
Severe	23 (61)	19 (51)	

NOTE. Significant differences are displayed in italic.
BMI, body mass index.

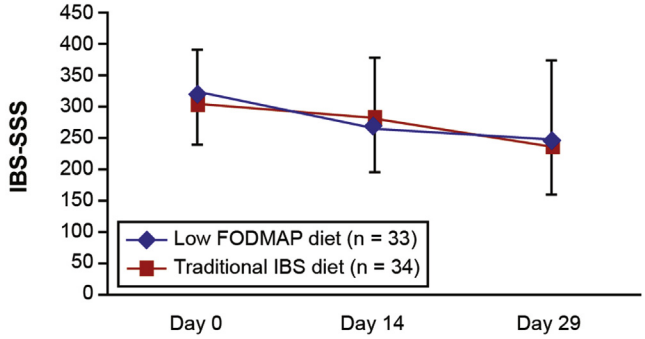

Figure 3. IBS symptom severity (mean ± SD) in patients who completed the intervention. IBS symptom severity measured by IBS-SSS was reduced in both groups at the end of the intervention period (day 29) compared with baseline ($P < .001$ in both groups), whereas at day 14, the reduction in the IBS-SSS reached statistical significance in the low-FODMAP group ($P = .002$), with a trend in the same direction in the traditional IBS diet group ($P = .051$). No differences between the groups were detected.

baseline, and this reached statistical significance for abdominal pain frequency, severity of abdominal distention, and life interference in both groups, and for bowel habit dissatisfaction in the traditional IBS diet group, without significant between-group differences (Table 2). In the low-FODMAP group, the number of bowel movements per day was reduced at the end of the treatment period relative to baseline ($P < .0001$), and no significant effect was seen in the traditional IBS diet group. Mean stool consistency remained unaltered in both groups (Table 2).

Dietary Intake

At baseline, both groups had similar intake of nutrients, including the intake of FODMAPs. However, during the last week of the intervention period, clear changes in dietary intake were noted, both within the groups and between the groups (Table 3). Most notably, as predicted, the low-FODMAP group had markedly reduced their intake of FODMAPs, which was seen for all the different groups of FODMAPs, including a reduced total intake of carbohydrates and dietary fiber, which was not seen in the traditional IBS diet group and with significant between-group differences for these food constituents at day 29. Both groups reduced their energy intake during the intervention period, and this reduction was significantly larger in the low-FODMAP group. For intake of protein and fat, no differences between the groups were detected, even though both groups reduced the intake of fat and protein during the intervention period relative to baseline. The number of meals per day was increased in the traditional IBS diet group during the intervention period, and the opposite was seen in the low-FODMAP group, with a significant difference in the number of meals between the groups during the intervention period.

Predictors for Treatment Response

When comparing responders and nonresponders in the 2 treatment groups, responders in the low-FODMAP group had lower intake of FODMAPs already at baseline compared with nonresponders (12.4 ± 7.2 g/d vs 20.6 ± 11.3 g/d; $P = .01$), but at day 29, no difference in the intake of FODMAPs between responders and nonresponders was noted (4.1 ± 4.0 g vs 2.9 ± 1.6 g; $P = .29$). In addition, the responders to the low-FODMAP diet were older and almost exclusively female, and IBS subtype influenced the likelihood of being a responder to the traditional IBS diet (IBS with constipation less likely to respond) (Table 4). In line with this, in the traditional IBS diet group, the reduction in IBS symptom severity was lower after the intervention period in IBS with constipation (19 ± 86) than in IBS with diarrhea (50 ± 56) or the mixed/unsubtyped group (103 ± 81) ($P = .03$). Even though a numerically higher proportion of IBS patients with diarrhea responded favorably to the low-FODMAP diet (70%) compared with IBS with constipation (44%) and IBS mixed/unsubtyped (42%) groups, this did not reach statistical significance ($P = .34$), and no significant differences between IBS subgroups in reduction IBS symptom severity (IBS-SSS) were seen with the low-FODMAP diet (IBS with constipation: 60 ± 152; IBS with diarrhea:70 ± 103; IBS mixed/unsubtyped: 94 ± 87; $P = .76$).

Discussion

In this study, we found that providing dietary advice to patients with IBS in the clinical setting reduces GI symptoms, but without obvious differences between a low-FODMAP diet and traditional IBS dietary advice. The assessment of food diaries demonstrated that it seems possible to give dietary advice and reach the desired effects, for example, reduced intake of FODMAPs, based on careful verbal and written instructions, but that calorie and nutrient intakes need to be monitored thoroughly in order to avoid malnutrition if diets are used long term. A self-initiated reduction of food items rich in FODMAPs seems to imply an increased chance of responding favorably to further reduction of FODMAP content in the diet.

IBS patients often complain of food-related GI symptoms,[13,16] and foods rich in carbohydrates and fat are

Table 2. Irritable Bowel Syndrome Symptoms Symptom Severity Score and Bowel Habit (Bristol Stool Form scale) in the Intervention Groups

	Low-FODMAP diet			Traditional IBS diet			*P* value between intervention groups[a]
	Baseline (n = 33), mean ± SD	Intervention (n = 33), mean ± SD	*P* value within group[a]	Baseline (n = 34), mean ± SD	Intervention (n = 34), mean ± SD	*P* value within group[a]	
IBS-SSS total score	324 ± 69	246 ± 127	*<.001*	302 ± 61	236 ± 78	*<.001*	.62
Abdominal pain intensity	51.8 ± 23.8	42.2 ± 32.6	.07	46.9 ± 23.0	37.6 ± 26.9	.06	.53
Abdominal pain frequency	*57.6 ± 31.4*	*43.6 ± 30.6*	*.008*	*60.6 ± 28.6*	*37.8 ± 26.5*	*<.001*	.33
Abdominal distension	*68.7 ± 21.6*	*45.8 ± 32.8*	*<.001*	*62.4 ± 26.2*	*50.0 ± 31.5*	*.003*	.60
Dissatisfaction of bowel habit	65.9 ± 25.5	58.5 ± 31.2	.22	*63.6 ± 21.5*	*53.4 ± 25.3*	*.01*	.47
Interference on life in general	*72.5 ± 20.7*	*55.9 ± 31.0*	*.001*	*69.9 ± 20.8*	*58.6 ± 24.3*	*.002*	.69
Stool consistency	4.0 ± 1.1	3.9 ± 1.1	.12	3.8 ± 1.1	3.6 ± 1.0	.07	.28
Stool frequency	*1.9 ± 0.8*	*1.5 ± 0.7*	*<.001*	1.6 ± 0.7	1.5 ± 0.6	.15	.64

NOTE. Significant differences are displayed in italic.
[a]Comparisons were made per protocol, that is, in participants who completed the intervention.

Table 3. Dietary Intake in Patients on Low-FODMAP Diet and Patients on Traditional Irritable Bowel Syndrome Diet

	Low-FODMAP diet			Traditional IBS diet			*P* value between intervention groups[a]
	Baseline (n = 38), mean ± SD	Intervention (n = 33), mean ± SD	*P* value within group[a]	Screen (n = 37), mean ± SD	Intervention (n = 34), mean ± SD	*P* value within group[a]	
Energy, *kcal*	2100 ± 435	1658 ± 365	<.001	2085 ± 446	1889 ± 482	.009	.03
Protein, *g*	90.3 ± 36.6	75.2 ± 16.7	.001	85.3 ± 16.9	77.2 ± 21.9	.03	.67
Fat, *g*	89.1 ± 27.4	68.3 ± 25.5	<.001	90.4 ± 24.8	78.4 ± 24.7	.009	.11
Carbohydrates, *g*	205.0 ± 53.8	159.1 ± 40.6	<.001	200.2 ± 62.7	193.1 ± 57.8	.42	.007
Dietary fiber, *g*	18.2 ± 6.2	15.1 ± 5.6	.001	20.0 ± 7.9	20.2 ± 6.4	.99	.003
Alcohol, *g*	11.2 ± 11.0	9.7 ± 12.9	.05	11.6 ± 13.0	8.9 ± 11.1	.06	.005
Monosaccharides	29.4 ± 16.9	20.0 ± 10.5	.001	27.6 ± 45.5	28.3 ± 11.0	.97	.001
Fructose	14.9 ± 9.9	8.4 ± 4.9	<.001	13.8 ± 8.1	11.6 ± 4.9	.12	.009
Total FODMAPs, *g*	16.6 ± 10.3	3.8 ± 3.3	<.001	15.8 ± 8.4	13.5 ± 8.7	.16	.05
Excess fructose	2.9 ± 5.7	0.9 ± 3.1	.07	3.5 ± 7.2	0.5 ± 1.6	.03	.55
Lactose	10.0 ± 9.3	1.5 ± 1.7	<.001	8.3 ± 5.6	9.3 ± 8.5	.56	.002
GOS	0.4 ± 0.3	0.2 ± 0.2	.001	0.5 ± 0.4	0.4 ± 0.3	.06	<.001
Fructans	2.3 ± 1.0	1.0 ± 0.6	<.001	2.4 ± 1.1	2.3 ± 1.3	.77	<.001
Polyols	1.0 ± 1.5	0.1 ± 0.1	.001	1.1 ± 1.4	1.0 ± 1.1	.61	<.001
No. of meals/d	5.9 ± 1.1	5.5 ± 1.4	.002	5.5 ± 1.1	6.0 ± 0.9	.006	.05
Energy/meal, *kcal*	365 ± 84	321 ± 106	.01	389 ± 83	316 ± 71	<.001	.85
Dietary fiber/meal, *g*	3.2 ± 1.1	3.0 ± 1.3	.18	3.8 ± 1.7	3.4 ± 1.0	.14	.16

GOS, galacto-oligosaccharides.
[a]Comparison made per protocol, that is, in patients who completed the intervention.

considered especially problematic.[16,18] Therefore, many IBS patients ask for dietary advice to improve their symptoms. Recently, reducing intake of food items rich in FODMAPs has shown promise in the management of IBS.[42] A few randomized trials demonstrating the efficacy of a low-FODMAP diet in IBS patients have been published recently.[33,34] However, whether this approach is superior to current dietetic practice is unknown, and concerns about the long-term safety with a low-FODMAP diet have been raised recently[43]; consequently, the usefulness of this strategy in clinical practice remains unclear. Our study is the first to assess the effect of a low-FODMAP diet in a randomized controlled trial with an active comparator, utilizing a setup resembling the use of dietary advice in the clinical setting as far as possible. Previous groundbreaking trials in this area that have validated the concept of a low-FODMAP diet in IBS have used a standard or habitual diet as comparator, without the aim to improve symptoms with this comparative diet,[33,34] or used a nonrandomized, nonblinded study design.[35] Our aim with this study was to have an active comparator to the low-FODMAP diet, that is, the prevailing standard dietary advice based on current knowledge about the association between food and GI physiology and IBS pathophysiology.[9,19,27] We also made this study single blind, that is, we informed the patients that we compared 2 different diets with potential beneficial effects on GI symptoms, without giving these diets specific names that could create bias, but instead used "diet A" and "diet B" in the verbal and written information. The term *FODMAPs* was not used, as we believe that this would have created an unwanted placebo effect in this trial, based on the considerable publicity associated with this diet recently, resulting in high expectations in patients. Further, we also tried to resemble the use of dietary advice in the clinical setting and therefore did not provide meals to the patients in this study, which is, of course, valuable in proof-of-concept studies, but does not provide information about how the concept works in clinical practice. The contact time with a dietitian was also intentionally kept low, as this is what would be realistic in clinical practice, managing a very common patient group, such as IBS. Seeing a dietitian repeatedly would probably enhance the clinical effect, but would not be achievable in clinical settings. Therefore, we believe that our trial provides important results for clinical management of patients with IBS, suggesting that dietary advice is valuable for patients with IBS, but that a low-FODMAP diet does not seem to be superior to standard dietary advice in IBS. Future studies should aim at finetuning these dietary strategies, and potentially combine concepts from both interventions tested in this trial.

The response rate in our trial seems to be somewhat lower compared with previous trials,[33–35] but comparing responder rates between trials is difficult because the reponder definitions differ. In our trial, the 50-point reduction in IBS-SSS was considered to reflect a clinically meaningful improvement,[37] but others have suggested a 50% symptom improvement.[44] Several explanations for this discrepancy in response rates between studies may exist, such as differences in study design, end points, symptom assessment, and contact time with dietitian between studies, an active strategy to reduce the placebo response in our study (by using a single-blinded study design), and the differences in IBS symptom severity (only moderate to severe IBS was included in our trial). When comparing the symptom

Table 4. Potential Predictors for Response to Dietary Interventions—Comparison Between Responders and Nonresponders to Low-FODMAP Diet and Traditional Dietary Advice

	Low-FODMAP diet			Traditional IBS diet		
Variables at baseline	Responders (n = 19)	Nonresponders (n = 19)	*P* value within group[a]	Responders (n = 17)	Nonresponders (n = 20)	*P* value within group[a]
Females, n (%)	18 (95)	12 (63)	.02	16 (94)	15 (75)	.12
Age, *y*, mean ± SD	49 ± 13	39 ± 17	.05	35.9 ± 15.1	44.7 ± 17.7	.12
BMI, kg/m^2, mean ± SD	23.6 ± 2.7	25.5 ± 4.6	.15	24.1 ± 3.7	24.3 ± 4.0	.89
Patient Health Questionnaire-15, mean ± SD	12.5 ± 4.1	12.4 ± 4.9	.93	13.0 ± 3.9	11.6 ± 5.2	.35
Visceral Sensitivity Index, mean ± SD	39.2 ± 14.5	42.0 ± 10.4	.52	40.5 ± 17.8	43.0 ± 16.1	.66
Hospital Anxiety and Depression Scale, mean ± SD						
Anxiety	8.1 ± 4.4	8.4 ± 4.7	.81	7.3 ± 4.9	6.8 ± 3.7	.73
Depression	4.5 ± 3.6	5.6 ± 4.0	.38	3.0 ± 2.9	4.5 ± 2.8	.13
20-Item Multidimensional Fatigue Inventory, mean ± SD						
General fatigue	15.3 ± 3.4	15.1 ± 3.0	.84	12.9 ± 3.6	13.6 ± 3.7	.62
Physical fatigue	13.7 ± 4.1	13.1 ± 3.5	.59	10.1 ± 3.8	11.1 ± 4.3	.47
Reduced activity	11.5 ± 4.0	12.6 ± 5.1	.50	9.3 ± 4.1	9.1 ± 3.9	.85
Reduced motivation	9.5 ± 3.5	9.4 ± 4.3	.92	7.5 ± 3.5	7.9 ± 3.2	.70
Mental fatigue	12.2 ± 3.7	12.3 ± 3.8	.96	10.8 ± 4.1	10.6 ± 4.0	.84
Predominant bowel habit, n (%)						.02
Constipation	4 (21)	5 (26)	.34	2 (12)	11 (55)	
Diarrhea	7 (37)	3 (16)		5 (29)	3 (15)	
Mixed/unsubtyped	8 (42)	11 (58)		10 (59)	6 (30)	
IBS symptom severity (IBS-SSS), n (%)						.13
Moderate	6 (32)	9 (47)	.32	6 (35)	12 (60)	
Severe	13 (68)	10 (53)		11 (65)	8 (40)	
Nutrient intake, mean ± SD						
Energy, *kcal*	2162 ± 406	2038 ± 464	.39	2136 ± 443	2039 ± 455	.52
Protein, *g*	87.4 ± 17.3	93.1 ± 49.4	.64	83.7 ± 14.5	86.7 ± 19.1	.60
Fat, *g*	92.7 ± 22.3	85.6 ± 32.0	.43	94.1 ± 25.4	87.1 ± 24.5	.41
Carbohydrates, *g*	209.9 ± 53.2	200.0 ± 55.4	.58	202.0 ± 69.6	198.6 ± 57.8	.87
Total FODMAPs, *g*	12.4 ± 7.2	20.6 ± 11.3	.01	15.3 ± 9.0	15.7 ± 8.0	.90
Dietary fiber, *g*	19.9 ± 5.8	16.6 ± 6.3	.10	18.1 ± 5.7	21.7 ± 9.3	.18
Alcohol, *g*	14.0 ± 8.5	8.4 ± 12.7	.12	13.3 ± 16.8	10.1 ± 8.6	.48

BMI, body mass index.
[a]Comparison made per protocol, that is, in patients who completed the intervention.

respone, the magnitude of IBS symptom reduction in our study is actually comparable with the trial by Halmos et al.[33]

One aim in the present study was to find predictors for a positive treatment response in the groups. In a previous study, we found that the perceived severity of food intolerance measured as the number of food items that produced GI symptoms, was associated with IBS symptom severity as well as somatic symptoms in general.[12] We therefore hypothesized that GI and non-GI symptom severity, IBS subtype, and potentially dietary intake, might be predictors for symptom response to dietary interventions. The only dietary factor that differed between responders and nonresponders to the dietary interventions in this study was that patients who responded favorably to the low-FODMAP diet already at baseline tended to have lower intake of FODMAPs than the nonresponders, whereas symptom severity and psychological factors did not influence the likelihood of being a responder to any of the diets. This may indicate that these patients had already noticed symptoms after foods rich in FODMAPs and therefore had reduced intake of these food items somewhat, potentially secondary to the presence of carbohydrate malabsorption, which we did not assess in this trial. Therefore, asking the patient about food items that produce GI symptoms or testing for the presence of carbohydrate malabsorption might be helpful when choosing a strategy for the dietary advice given to the patients, but this needs to be evaluated in prospective trials. Future studies should also more clearly investigate the different impacts of individual FODMAPs on symptoms, as all FODMAPs are not created equal in terms of impact on GI physiology.[45] In addition, female as well as older patients were more likely to respond favorably to a low-FODMAP diet.

Deliberately, we decided to include all IBS subtypes, even though it may seem more logical to focus on IBS with diarrhea, where you might expect the most favorable response when intake of carbohydrates are restricted.[32] However, bloating, abdominal pain, and flatulence are the symptoms in which the greatest symptom improvement on a low-FODMAP diet has been found,[34,35] and these symptoms are prominent in all IBS subtypes.[2] Comparative trials have not found a clear difference between the response to a

low-FODMAP diet in IBS with constipation and IBS with diarrhea.[33,35] In line with this, we could not demonstrate a difference in the response between IBS subtypes in the low-FODMAP group, even though admittedly our trial was not powered to detect subgroup differences. Future studies should address differences in response to dietary interventions in IBS subgroups, regarding overall symptom response, as well as differences in the effect on individual symptoms.

An unwanted and somewhat surprising finding in this trial is the low-calorie intake in both groups after receiving dietary advice, more or less irrespective of which diet the patient was randomized to follow. We hypothesize that even though patients were not advised to reduce calorie intake, receiving detailed dietary advice where you should limit intake of certain food constituents may result in this unwanted effect. In the short term, this should not be harmful, but a lesson from this trial is that calorie and nutrient intakes need to be supervised in order to avoid malnutrition if long-term dietary changes are initiated. However, one should be aware of the well-known limitations with food diaries and the risk of underestimation of actual food intake.[46] As quality control, food diaries are useful, and in our study it was reassuring to note that patients in the low-FODMAP group substantially reduced the FODMAP content, whereas this was not the case in the traditional IBS diet group.

To conclude, this is the first trial using an active comparator to a low-FODMAP diet in a randomized, controlled, single-blinded trial, with the attempt to resemble clinical practice. Both a low-FODMAP diet and a traditional IBS diet improved IBS symptoms, without any clear differences between the 2 strategies. Future studies should aim to further improve strategies for providing dietary advice to patients with IBS, potentially combining elements from different strategies and ideally customizing dietary advice for different patient populations. Monitoring calorie and nutrient intakes in patients who follow dietary advice seems to be important.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Gastroenterology* at www.gastrojournal.org, and at http://dx.doi.org/10.1053/j.gastro.2015.07.054.

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Conflicts of interest
The authors disclose no conflicts.

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Supplementary Material

Symptom Assessment

In order to assess the effect of the dietary interventions, all patients in both groups completed the same questionnaires during the intervention period, as detailed here:

- IBS-SSS[1] was used to assess the severity of IBS symptoms. The overall IBS-SSS ranges from 0 to 500. A higher score implicates more severe symptoms. The questionnaire has the following items: abdominal pain intensity, abdominal pain frequency, abdominal distension, dissatisfaction with bowel habits, and influence of IBS on life in general ("life interference"). For some of the analyses, the patients were divided into 3 severity groups by use of the accepted cut-off values: <175, mild IBS; 175−300, moderate IBS; >300 severe IBS. The questionnaire was completed on days 0, 14, and 29.
- The patients recorded all bowel movements in a stool diary, based on Bristol Stool Form scale[2] every day during the intervention period (28 days), as well as during the 10-day screening period, to record stool frequency (number of stools per day), mean stool consistency on a 7-point scale and to determine the IBS subtype, that is, IBS with constipation, IBS with diarrhea, or IBS with mixed bowel habits or unsubtyped IBS, where the 2 latter groups were combined into 1 group (IBS mixed/unsubtyped).[2]

Baseline Assessment—Predictors

The following questionnaires were assessed at the second visit (baseline) and were used to evaluate predictors for treatment response and to characterize our patient sample:

- Hospital Anxiety and Depression scale[3] is a 14-item questionnaire used to measure the severity of anxiety and depression on 2 subscales with 7 items each. Each item is scored between 0 and 3, with higher scores indicating more severe symptoms and with a total score range per subscale of 0−21.
- Visceral Sensitivity Index[4] measures GI-specific anxiety, the cognitive, affective, and behavioral response to fear of GI symptoms, and the context in which these occur. The questionnaire contains 15 items scored 0−5, rendering a total score between 0 and 75, with higher score indicating more severe GI-specific anxiety.
- Multidimensional Fatigue Inventory-20[5] assesses the severity of general fatigue, physical fatigue, reduced activity, reduced motivation, and mental fatigue. Each dimension contains 4 questions, with a range of scores between 4 and 20, and a higher score indicates more severe fatigue.
- The Patient Health Questionnaire-15[6] is a 15-item questionnaire used to define the severity of somatic symptoms (0−2). The maximum total score is 28 for men (excluding the question on menstrual problems) and 30 for women.

Assessment of Nutrient Intake

All patients completed a food diary twice, once during the screening period and once during the last week of the 4-week intervention period, for 4 days (Wednesday through Saturday). The diary included details about cooking methods, ingredients, brands of foods (if appropriate), time points for meals, and quantity consumed in grams or household measurements. Patients were given written instructions to enable accurate completion of the food record. At the first occasion, patients were instructed to consume their usual diet. At the second occasion (during the last week of the dietary intervention period), patients were instructed to eat according to instructions and record the food diary accordingly. Different food items and beverages were entered in DIETIST XP version 3.1 (Kostdata.se, Stockholm, Sweden), which converts food items into nutrients and energy amounts. Composite foods (eg, casseroles) were split into ingredients (food items). DIETIST XP software covers around 1600 foods and 52 nutrients. DIETIST XP is designed to estimate macronutrients and micronutrients and energy intake. From the 2 × 4-day food records, average daily intakes were calculated for energy, macronutrients, monosaccharides, lactose, dietary fibers, and FODMAPs. All nutrients in the software DIETIST XP are based on food composition data from the National Food Administration in Sweden, except for the FODMAPs, which were calculated using a new Swedish database for content of lactose, fructose, galacto-oligosaccharides, fructans, and polyols in foods used in Swedish diets (Liljebo et al, manuscript in preparation). As an approximation of fructose in excess of glucose, which was used when calculating the total FODMAP content,[7] we used data for fructose and total monosaccharide content from the food diaries, as glucose is the dominating monosaccharide in food together with fructose.[8] If there were no excess of fructose, that is, if the glucose content was higher than the fructose content, a value of 0 was used for the calculation of the total FODMAPs content.

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