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REVIEW

Efficacy of the low FODMAP diet for treating irritable bowel syndrome: the evidence to date

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Abstract: This review summarizes the published clinical studies concerning the management of irritable bowel syndrome (IBS) using restriction of Fermentable Oligosaccharide, Disaccharide, Monosaccharide, and Polyols in the diet (low FODMAP diet). In recent years, the data supporting low FODMAP diet for the management of IBS symptoms have emerged, including several randomized controlled trials, case-control studies, and other observational studies. Unlike most dietary manipulations tried in the past to alleviate gastrointestinal symptoms of IBS, all studies on low FODMAP diet have consistently shown symptomatic benefits in the majority of patients with IBS. However, dietary adherence by the patients and clear dietary intervention led by specialized dietitians appear to be vital for the success of the diet. Up to 86% of patients with IBS find improvement in overall gastrointestinal symptoms as well as individual symptoms such as abdominal pain, bloating, constipation, diarrhea, abdominal distention, and flatulence following the diet. FODMAP restriction reduces the osmotic load and gas production in the distal small bowel and the proximal colon, providing symptomatic relief in patients with IBS. Long-term health effects of a low FODMAP diet are not known; however, stringent FODMAP restriction is not recommended owing to risks of inadequate nutrient intake and potential adverse effects from altered gut microbiota. In conclusion, the evidence to date strongly supports the efficacy of a low FODMAP diet in the treatment of IBS. Further studies are required to understand any potential adverse effects of long-term restriction of FODMAPs.

Keywords: irritable bowel syndrome, low FODMAP diet, gastrointestinal symptoms

What is irritable bowel syndrome?

Irritable bowel syndrome (IBS) is a chronic gastrointestinal (GI) disorder characterized by symptoms of abdominal pain, bloating, and altered bowel habit such as constipation, diarrhea, or both.[1] It is the most common GI condition seen by general practitioners[2] and accounts for up to 50% of patients seen in gastroenterology clinics.[3] IBS is a clinical diagnosis and is made using symptom-based criteria such as Rome III criteria[4] (the current gold standard for IBS diagnosis [Table 1]) in addition to the exclusion of any organic disease.[5] Although the exact cause of IBS is unknown, there are increasing insights concerning the possible etiology and pathophysiology of IBS. These include heightened pain sensitivity or visceral hypersensitivity,[6,7] abnormal gut motility,[8] small intestinal bacterial overgrowth,[9] low-grade intestinal inflammation,[10] psychosocial factors,[11] and dysregulated gut–brain axis.[12,13] Thus, IBS appears to be a multifactorial, albeit incompletely understood, disorder.

The global IBS prevalence is 10%–20% depending on the diagnostic criteria used and the geographic region.[14] The varying prevalence of IBS among countries may be

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Table 1 Rome III diagnostic criteria for irritable bowel syndrome[4]

Recurrent abdominal pain or discomfort[a] at least 3 days per month in the last 3 months[b] associated with two or more of the following:

1. Improvement with defecation
2. Onset associated with a change in frequency of stool
3. Onset associated with a change in form (appearance) of stool

Notes: [a]Discomfort is an uncomfortable sensation not described as pain. [b]Criteria fulfilled for the last 3 months with symptom onset of at least 6 months prior to diagnosis. Reprinted from *Gastroenterology*, 130(5), Longstreth GF, Thompson WG, Chey WD, Houghton LA, Mearin F, Spiller RC, Functional bowel disorders, 1480–1491, Copyright (2006), with permission from Elsevier.

due to variable application of the diagnostic criteria, demographic differences, and other factors such as health care utilization, health beliefs, or diet.[14,15] IBS is also more common in women than in men and in individuals below the age of 50 years.[14] IBS can be subclassified into IBS with diarrhea (IBS-D), IBS with constipation (IBS-C), mixed IBS (IBS-M), or unsubtyped (IBS-U) based on their predominant bowel pattern.[4] IBS is associated with high health care costs[16,17] as well as impaired quality of life (QoL), compared to the general population.[18–20] The QoL also compares poorly with other chronic conditions such as gastroesophageal reflux disease, diabetes mellitus, and end-stage renal disease.[18]

The main treatment goal for clinicians treating patients with IBS is to alleviate global GI symptoms; however, because of the multiple symptoms described by patients with IBS, this is often challenging. While an effective physician–patient relationship is considered the cornerstone for effective treatment,[21] a combination of pharmaceutical and nonpharmaceutical approaches are now considered. However, the traditional pharmacological treatments such as bulking agents, anticholinergics, antispasmodics, and antidiarrheals often do not provide adequate symptomatic relief in patients with IBS if used alone.[22,23] A more holistic approach using nonpharmacological therapies such as dietary manipulation, exercise, cognitive-behavioral therapy, and hypnotherapy seems to provide further benefits in these patients.[24] The "Diet as a therapy for IBS" section discusses some of the dietary manipulations aimed at improving the global symptoms of IBS.

Diet as a therapy for IBS

Nearly two-thirds of patients with IBS perceive their GI symptoms to be food-related.[25] Incompletely absorbed carbohydrates (found in foods such as lactose found in dairy products, beans, onion, cabbage, apples, and wheat) as well as fatty foods, coffee, alcohol, and spicy foods have all been found to trigger or aggravate GI symptoms.[25,26]

Many early studies focused on strict exclusion or elimination diets followed by food rechallenge to investigate the role of food intolerance in patients with IBS. For example, 25 consecutive patients diagnosed with IBS-D were asked to limit their diets to a single meat, a single fruit, and distilled or spring water for 1 week.[27] Fourteen (67%) of those who completed the diet were symptom free.[27] Six out of 14 patients then underwent a randomized double-blind food challenge in which participants were fed a liquidized preparation of either a test food (believed to provoke symptoms) or a control food via a nasogastric tube, and food intolerance was confirmed.[27] McKee et al[28] repeated the dietary limitation component of this study including other subtypes of IBS and found that only 6/40 (15%) patients with IBS had symptomatic improvement (mostly in IBS-D). In another study, nearly half (91/189) of a cohort of female patients with IBS experienced symptomatic improvement after 3 weeks of a strict exclusion diet without dairy products, cereals, citrus fruits, potatoes, tea, coffee, alcohol, additives, and preservatives, while the remainder (98/189) found no improvement.[29] Parker et al[30] described a similar but nutritionally adequate exclusion diet where alternative foods to those that were being excluded were suggested to participants. However, only 39 of 96 (41%) patients with IBS who completed the 2-week exclusion diet improved.[30] The variability in responses to these exclusion diets is likely due to differences in study protocols including duration of exclusion diet, the types of foods excluded, as well as the subtypes of IBS participants recruited in the study. Well-designed randomized control trials have been lacking when it comes to the investigation of many such exclusion diets. However, designing controlled dietary intervention studies is difficult, particularly with regard to blinding study participants. Given that placebo response rates in IBS trials may be as high as 40%,[31] difficulties in blinding can be a significant source of bias.

Lactose malabsorption resulting from lactase deficiency is known to cause abdominal pain, flatulence, and loose bowel motions. Hypolactasia or lactase deficiency is generally due to primary or secondary deficiency since congenital lactase deficiency at birth is extremely rare.[32] Approximately 70% of the world population have primary lactose deficiency resulting from loss of lactase activity, which begins between the ages of 2 and 6 years,[33] whereas secondary lactase deficiency often occurs as a result of GI illness such as viral gastroenteritis or celiac disease.[32] Some studies have investigated the role of low lactose diet in the management of IBS with mixed results. In one study, 27% of 122 patients with IBS were found to have lactose malabsorption with positive lactose hydrogen

breath test; however, only nine (39%) had improvement in their symptoms following the low lactose diet.[34] In contrast, Böhmer et al[35] found a marked reduction in symptoms with a lactose-restricted diet in patients with IBS with lactose malabsorption (24%) diagnosed with a hydrogen breath test, but no improvement in patients with IBS who tested negative for lactose malabsorption. Therefore, although conflicting, the results concerning lactose malabsorption and restriction suggest that lactose restriction should be tried in patients with IBS in whom lactose malabsorption is proven but that other dietary restrictions may also be required.

Probiotics, a food supplement of a single live microbe or mix of microbes with beneficial properties, is another dietary treatment that has been studied extensively in both IBS and also many other conditions. A systematic review and meta-analysis of 14 randomized control trials of probiotics in patients with IBS found a modest improvement in overall symptoms with probiotic use for several weeks (odds ratio, 1.6;95% confidence interval, 1.2–2.2).[36] However, given that each probiotic may have different characteristics, including variable effects on cytokines, host microbiota, and other potential targets, it is likely that the effects will be specific to each probiotic rather than the entire class.

In fiber supplementation studies, soluble fiber (psyllium)[37] but not insoluble fiber (bran)[37,38] was found to be effective in the management of patients with IBS. In fact, bran supplementation led to worsened symptoms in 55% of the patients.[38] A small study of 13 overweight or obese participants with IBS-D who completed the study found significant improvement in their stool consistency, pain, and QoL with a very low-carbohydrate diet (20 g carbohydrates/d);[39] however, larger studies including patients with normal body mass index are needed to confirm these results.

A double-blind, randomized, placebo-controlled rechallenge trial of gluten in patients with IBS resulted in significantly worse overall symptoms of pain, bloating, and stool consistency in the gluten group (who received gluten-containing foods) compared to the placebo group.[40] Interestingly, a subsequent double-blinded crossover trial in subjects with nonceliac gluten sensitivity (NCGS) and IBS without celiac disease performed by the same group found no evidence of specific or dose-dependent effects of gluten, while improvements in symptoms were seen with a diet low in fermentable carbohydrates (Fermentable Oligosaccharide, Disaccharide, Monosaccharide, and Polyols [FODMAPs]).[41] This study[41] suggests that the carbohydrate component (fructans and galacto-oligosaccharides) of the wheat as opposed to the gluten may be responsible for the IBS symptoms experienced by patients with NCGS and IBS. Thus, it may be that a combination of incompletely absorbed carbohydrates may be responsible for eliciting many symptoms of IBS rather than one specific food or food component.

The low FODMAP diet

FODMAPs are a group of carbohydrates that are poorly absorbed in the small intestine and subsequently fermented in the small or large intestine.[42] These poorly absorbed short-chain carbohydrates include fructose and lactose (in patients who malabsorb these with impaired enzyme activity or transport mechanisms), fructans, galacto-oligosaccharides, and polyols or sugar alcohols. Table 2 lists representative examples of common foods that are known to be high in FODMAPs and examples of suitable low FODMAP alternatives. The implementation of low FODMAP diet is beyond the scope of this paper, but it is covered in detail elsewhere.[43,44]

How does a low FODMAP diet work in IBS?

Not all FODMAPs exacerbate abdominal symptoms in patients with IBS. The presence and degree of abdominal symptoms in a given individual depends on the degree of malabsorption experienced by the individual. There are two main mechanisms responsible for the induction of symptoms in patients with IBS by FODMAPs. First, FODMAPs are poorly absorbed by the small intestine and are osmotically active, leading to net secretion of fluid into the small intestine. This may distend the small intestine, leading to abdominal symptoms, in addition to increasing water delivered to the colon. In a study of ileostomates,[45] intestinal output was increased by 22% with high consumption of FODMAPs within meals secondary to an increased osmotic load. In addition, a recent magnetic resonance imaging study has shown an abnormal accumulation of fluid in the small intestine of patients with IBS following ingestion of an unabsorbed carbohydrate, lactulose, as well as provoking significantly more symptoms compared to healthy controls.[46] These results support the underlying mechanism leading to diarrhea experienced by some patients with IBS. Second, FODMAPs are rapidly fermented by the colonic microbiota, leading to colonic distention from gas production, with associated pain and bloating. A reduction in breath hydrogen production, which measures the degree of gas produced by the microbiota, in both healthy and IBS subjects with a low FODMAP diet has been shown in a recent study, suggesting reduced fermentation and gas production with restriction of poorly absorbed carbohydrates.[47] Subsequently, there was an

Table 2 Examples of food high in FODMAPs and suitable low FODMAP alternatives

Types of sugars	High FODMAPs food	Low FODMAP alternatives
Oligosaccharides	FOS Grains: wheat-, rye-, and barley-based products Vegetables: onion, garlic, artichokes, leeks, beetroot, and savoy cabbage Fruits: watermelon, peaches, persimmon, prunes, nectarines and most dried fruit GOS Legumes: red kidney beans, baked beans, and soya beans Vegetables: beetroot and peas	Fruit: banana, most berries (except boysenberries and blackberries), grapes, lemon, lime, mandarin, orange, kiwi fruit, pineapple, passion fruit, and rhubarb Vegetables: capsicum, bok choy, green beans, parsnip, silverbeet, cucumber, carrots, celery, eggplant, lettuce, potatoes, yams, tomatoes, and zucchini Grains: wheat-free grains/flour, gluten-free bread or cereal products, and quinoa
Disaccharides	Lactose Dairy products: cows/goat milk, and yoghurt	Dairy products: lactose-free, almond or rice-based milk, yoghurt and ice cream, hard cheese, feta and cottage cheese
Monosaccharides	Fructose (in excess of glucose) Fruits: apples, pears, watermelon, mango, cherries, boysenberries and fruit juice from high-fructose foods Honey Sweeteners: high-fructose corn syrup Vegetable: asparagus and snap peas	Fruit: banana, grapes, honeydew, melon, kiwifruit, lemon, lime, mandarin, orange, passionfruit, paw paw, and most berries (except boysenberries and blackberries) Sweeteners: maple syrup and golden syrup
Polyols	Sorbitol Fruit: apples, pears, avocado, apricots, blackberries, nectarines, peaches, plums, prunes, and watermelon Mannitol Vegetables: sweet potato, mushrooms, cauliflower, and snow peas	Sweeteners: Maple syrup, and sugar (sucrose) Fruits: banana, grape, honeydew, melon, kiwifruit, lemon, mandarin, orange, passionfruit, and paw paw

Notes: Data from Monash University. Low FODMAP Diet Application. Available at: http://www.med.monash.edu/cecs/gastro/fodmap/. Android version accessed August 26, 2015.[72]

Abbreviations: FODMAP, fermentable oligosaccharide, disaccharide, monosaccharide, and polyols; FOS, fructo-oligosaccharides; GOS, galacto-oligosaccharides.

improvement of GI symptoms in the patients with IBS on a low FODMAP diet.[47] Thus, the study supports the hypothesis that rapid fermentation of undigested, unabsorbed FODMAPs in the colon results in distention of the large bowel, bloating, and abdominal pain from excess gas production.

Clinical studies of low FODMAP diet and IBS

Studies on the effect of dietary restriction of FODMAPs in patients with IBS have shown consistent results supporting the efficacy of the low FODMAP diet in improving overall GI symptoms of adult patients with IBS (Tables 3 and 4). However, as noted earlier, designing and implementing a prospective placebo-controlled dietary intervention study are extremely difficult. In the field of a low FODMAP diet in the treatment of IBS symptoms, many studies are retrospective[48,49] or prospective and uncontrolled,[47–53] making the studies potentially subject to bias and confounding. To date, there have been two controlled trials[49,54] and six randomized controlled trials[47,55–59] evaluating low FODMAP diet in patients with IBS. These studies, and others described in Tables 3 and 4 were conducted in Australia (four), Norway (two), Denmark (two), New Zealand (one), Switzerland (one), Sweden (one), and the UK (two).

The majority of studies comprised a small number of participants (fewer than 100),[47,48,50,52,54,56–58,60] and two of the studies[50,51] had poor study completion or response rates (<50%). The average age of IBS participants ranged from 35 to 50 years and, as one might expect with an IBS cohort, a large proportion of the participants were female (66%–87%) in all studies.[47–54,56–60] The common primary outcome measure was changes in GI symptoms (overall and/or individual symptoms); however, the use of scoring scales varied considerably with a few studies using validated questionnaires.[49,50,54,56] While not all studies assessed for dietary intake, the dietary assessment methodologies included food frequency questionnaire,[49,50] food diaries,[47,55,56,58] and other unspecified methods.[53] Dietary advice on a low FODMAP diet was mostly delivered by a specialized or trained dietitian, with the exception of two studies where a registered nurse had provided the dietary guidance.[49,50] Not all studies provided the list of foods allowed in the low FODMAP diet; however, two studies[49,50] allowed peeled apples, pears, and milk as part of the low FODMAP diet, which is not consistent

Table 3 Observational studies of low FODMAP diet in adults with IBS

Study	Study design	Participants recruited for the study	Inclusion and exclusion criteria	Dietary intervention	Outcome measures	Key results
Observational studies						
Shepherd and Gibson[48]	Retrospective study Follow-up telephone interview 2–40 months after dietary intervention (median 14 months)	62 consecutive patients with IBS and fructose malabsorption Median age 50 years 76% female	IBS (Rome II criteria) Positive fructose breath hydrogen test. Excluded celiac disease, IBD, and patients with known lactose malabsorption	1-hour dietitian-delivered advice: • avoidance of high free fructose foods in excess of glucose and high fructan foods • positive food choices • sample meal plan • coingestion of free glucose with fructose • avoiding foods rich in polyols	Dietary adherence Barriers to adherence Strategies used by patients Self-assessment of IBS symptoms using a –10 to 10 scale	48 (77%) adhered to the diet 46 (74%) responded positively in all abdominal symptoms Improvement in symptoms was significantly better in those adherent to the diet
Staudacher et al[54]	Nonrandomized, controlled study Questionnaire 2–6 months after dietary manipulation	82 consecutive patients with IBS Mean age 38 years 71% female	IBS diagnosis based on NICE criteria	Dietitian-led advice 39 – standard dietary advice (NICE guidelines) 43 – low FODMAP dietary advice: • suitable/unsuitable foods • meal plans • recipes adapted for the UK setting	Validated IBS Global Improvement Scale (7-point Likert scale) Four statements on satisfaction with symptom response and dietary advice	Overall symptom improvement greater in low FODMAP (86%) than standard diet (49%) group Greater benefits were seen in low FODMAP group for bloating, abdominal pain, and flatulence
Ostgaard et al[49]	Retrospective, case-control study Dietary guidance was given 2 years before the study Questionnaires sent by mail	63 patients with IBS without dietary guidance, 70 with dietary guidance, and 42 healthy controls Mean age 36 years 85% female	IBS diagnosis (Rome III criteria) Excluded organic GI disease, clinically significant systemic diseases, pregnant or lactating women, and abdominal surgeries, except appendectomy, Cesarean, and hysterectomy	Nurse-delivered dietary advice Two 1-hour sessions covering FODMAP avoidance	Validated MoBa FFQ SF-NDI IBS-QoL Validated Birmingham IBS Symptom scores (5-point Likert scale)	114 patients (65%) completed study (35 controls, 36 unguided, 43 guided patients with IBS) In guided patients with IBS, significant reduction in abdominal pain, but no significant differences in the total score or diarrhea/constipation Significant QoL improvement of guided patients with IBS compared to unguided patients
Mazzawi et al[50]	Prospective uncontrolled study Questionnaires before and 3–9 months after dietary intervention (median 4 months)	46 patients with IBS Mean age 35 years 76% female	IBS (Rome III criteria) Excluded organic GI disease, clinically significant systemic disease, pregnant or lactating, drug abuse, serious psychiatric diseases, abdominal surgeries, except appendectomy, cesarean section, and hysterectomy	Registered nurse with special training and experience. Three 45-minute sessions on dietary management	Validated Birmingham IBS symptom score IBS-QoL questionnaire SF-NDI Validated MoBa FFQ	17 (37%) completed study Reduced total IBS symptoms scores and significantly improved quality life following dietary guidance Significant improvement in abdominal pain, diarrhea, but not constipation Dietary guidance also resulted in adequate intakes of vitamins and minerals

(*Continued*)

Table 3 (*Continued*)

Study	Study design	Participants recruited for the study	Inclusion and exclusion criteria	Dietary intervention	Outcome measures	Key results
de Roest et al[51]	Prospective uncontrolled study Questionnaires at baseline and follow-up (mean follow-up of 15.7±9 months) after dietary intervention	192 patients with IBS who had performed lactulose, fructose, and lactose breath testing Mean age 45 years 74% female	IBS diagnosed by a gastroenterologist or a colorectal surgeon Excluded significant GI comorbidities (IBD, celiac disease, significant diverticular disease or bowel resection)	Advice by a trained dietitian: • 1-hour appointment and 30-minute follow-up 6 weeks later • lists of safe and restricted foods • recipes and shopping guide provided • reintroduction of restricted group of carbohydrates at follow-up	GSRS (7-point Likert scale) Assessment of safety and efficacy of the diet by email or post	90 patients with IBS (47%) completed the whole study. Significant improvement reported symptoms at follow-up (44% patients with improvement in abdominal pain, 38% in bloating, 38.5% in constipation, 60% in diarrhea) Significant positive correlation between adherence and improvement in individual GI symptoms
Wilder-Smith et al[53]	Prospective, uncontrolled study Questionnaires at baseline and 4 weeks after dietary intervention	1,372 patients with FGID (212 patients with IBS) who performed fructose and lactose breath testing Mean age 42 years 73% female	Classified into FGID subgroups according to (Rome III) 312 patients with positive fructose and lactose intolerance Excluded organic disease including celiac disease	Experienced dietitian-led advice: • standardized 4-week dietary modification • 1 week of diet low in saccharides and polyols followed by weekly introduction of fructose-, fructan-, inulin-, and lactose-containing food to individual tolerance	A nonstandard questionnaire on abdominal symptoms (10-point Likert scales) Bowel and dietary habits	237 of 312 (76%) patients completed the study Over 80% of patients attained adequate global symptom relief; 93% and 96% of patients with fructose or lactose malabsorption, respectively, 85% adequate relief in patients with diarrhea, 96% with bloating, and 51% with constipation
Pedersen et al[52]	Prospective uncontrolled pilot study Web-based questionnaires completed weekly during control and low FODMAP diet period (6 weeks each)	19 patients with IBS Median age 35 years 81% female	IBS (Rome III criteria) Excluded IBD, celiac disease, GI infection, and positive lactose intolerance gene test, history of food allergy, alarm symptoms, and other significant diseases	6 weeks of habitual diet (control) Dietitian-delivered low FODMAP diet: • 45-minute consultation • 6 weeks on the diet	IBS-SSS IBS-QoL	All 19 patients with IBS completed the study Significant improvement in IBS in control period and following dietary intervention period Low FODMAP diet further reduced symptoms (11 patients [57%] improved to mild IBS severity) Significant IBS-QoL change during low FODMAP diet period

Abbreviations: FODMAP, fermentable oligosaccharide, disaccharide, monosaccharide, and polyols; IBS, irritable bowel syndrome; FM, fructose malabsorption; IBD, inflammatory bowel disease; NICE, National Institute for Health and Clinical Excellence; MoBa FFQ, MoBa Food Frequency Questionnaire; SF-NDI, short-form nepean dyspepsia index; QoL, quality of life; IBS-SSS, irritable bowel syndrome symptom scoring system; GSRS, gastrointestinal symptom rating scale; GI, gastrointestinal; FGID, functional gastrointestinal disorder; ITT, intention to treat; PP, per-protocol.

Table 4 Randomized control trials of low FODMAP diet in adults with IBS

Study	Study design	Participants recruited for the study	Inclusion and exclusion criteria	Dietary intervention	Outcome measures	Key results
Interventional studies						
Shepherd et al[57]	Double-blinded, randomized, quadruple arm, placebo-controlled rechallenge trial 2 weeks maximum test period	26 participants with IBS and fructose malabsorption Median 38 years 85% female Previously good GI symptom control while on low FODMAP diet	IBS (Rome II criteria) Excluded celiac disease, IBD, other concomitant serious morbidity or if taking medications potentially influencing GI symptoms	All participants on supplied low FODMAP diet followed by rechallenge of graded doses of fructose, fructans, fructose, and fructan mix or glucose (control) drinks with meals >10-day washout between tests	Mean score of individual symptoms using 100-mm VAS A global symptom question asked at the end of each highest dose consumed for the drinks	Symptoms induced in a dose-dependent manner when drinks containing fructose (70%), fructans (77%), and a combination (79%) were given as opposed to 14% symptom induction in those receiving glucose drink
Ong et al[47]	Randomized, single-blinded, crossover intervention trial 2 days of each diet	15 healthy subjects Mean 23 years 60% female 15 subjects with IBS mean 41 years 87% female	IBS (Rome III criteria) No medically significant comorbidities, not pregnant, and had no prebiotic supplements or antibiotics for >8 weeks prior to the study No prior IBS education	Provided low (9 g/d) and high (50 g/d) FODMAP diet All food matched for total energy, starch, protein, fat, indigestible long-chain CHO Dietary fiber and resistant starch kept constant 7-day washout period before crossover	Breath hydrogen levels A questionnaire consisting of five general GI symptoms Food diaries	All subjects completed the study All symptoms were significantly worsened with high FODMAP diet in patients with IBS Only increased flatus production was reported by healthy volunteers
Staudacher et al[56]	Randomized, control trial 4 weeks of either diet	41 patients with IBS Mean age 35 years 66% female	IBS (Rome III criteria) IBS with bloating and/or diarrhea Excluded other major GI conditions, constipation as predominant IBS symptom, pregnancy, lactation, use of probiotics, prebiotics, lactulose 4 weeks prior to study or changes in IBS meds prior to/during study	An experienced dietitian-led advice: • Low FODMAP diet (19) or control group with habitual diet (22) for 4 weeks • Weekly follow-up via email or telephone	Validated GSRS Stool output Food diaries	All 41 patients were included for ITT and 35 in the PP analysis At follow-up, more patients in the intervention group reported adequate symptom control with ITT (68% vs 23%) and for PP (81% vs 26%)
Halmos et al[55]	Randomized, controlled, single-blind crossover trial 21 days of either diet	45 participants 33 IBS (mean age 41 years, 70% female) 12 healthy individuals (mean age 31 years, 75% female)	IBS (Rome III criteria) Healthy controls without GI symptoms Exclusion of celiac disease, previous abdominal surgery, and significant other diseases No previous dietary or other treatments for IBS and no pharmacological agents	1 week of habitual diet followed by low FODMAP diet (<0.5 g FODMAPs/meal) or typical Australian diet All foods were provided (three meals and three snacks) At least 21 days of washout period	100-mm VAS Fecal assessment Breath hydrogen Food diaries	30 IBS participants (91%) and 8 controls (67%) completed the study 70% IBS subjects had lower overall GI symptom scores on low FODMAP diet compared with typical and subjects' habitual diet Similar results with individual symptoms Minimal or unaltered symptoms in controls

(*Continued*)

Table 4 (*Continued*)

Study	Study design	Participants recruited for the study	Inclusion and exclusion criteria	Dietary intervention	Outcome measures	Key results
Pedersen et al[59]	Randomized, unblinded controlled trial Web-based questionnaires completed weekly during 6 weeks intervention	123 patients with IBS Median age 37 years 73% female	IBS (Rome III criteria) Negative colonoscopy, celiac, and lactose intolerance gene Excluded low BMI <18, alarming symptoms such as weight loss > 5 kg, anemia, fever, colorectal cancer, and other significant disease	6 weeks of: • 42 low FODMAP diet or • 40 normal Danish/Western diet or • 41 normal diet and probiotics (*Lactobaccillus rhamnosis GG*) Low FODMAP diet advice by dietitians Published Australian high FODMAP list used	IBS-SSS IBS-QoL	34 (81%), 37 (92%) and 37 (90%) completed the low FODMAP, normal and probiotic diet, respectively A significant reduction in IBS-SSS in all three groups after 6 weeks from their baseline No significant reduction in IBS score in any groups for IBS-C type and no difference between normal diet and probiotics A significant reduction of IBS-SSS in low FODMAP and probiotic groups compared to normal diet IBS-QoL was statistically improved in all patients from baseline
Böhn et al[58]	Randomized, controlled, single-blind trial 4 weeks of either diet	75 patients with IBS Mean age 43 years 82% female	IBS (Rome III criteria), IBS-SSS ≥175 (moderate-to-severe symptoms) No excessively restrictive diet except low lactose diet. Allowed probiotic products and antidepressants Excluded severe cardiac, liver, neurologic or psychiatric disease, and other GI diseases (IBD, celiac disease)	Advised by experienced dietitians 38 – Diet A (low FODMAP diet) Information on foods to avoid and alternatives. 37 – Diet B (traditional IBS diet advice) Regular meals, healthy eating, avoid large meals, reduce fat intake, etc	IBS-SSS Stool diary 4 days food diary	33 (87%) low FODMAP and 34 (92%) traditional IBS diet group completed the study IBS symptom severity was significantly reduced in both groups compared to baseline; however, the score did not differ between the groups 19 (50%) low FODMAP group and 17 (46%) traditional IBS diet group responded to the interventions

Abbreviations: FODMAP, fermentable oligosaccharide, disaccharide, monosaccharide, and polyols; IBS, irritable bowel syndrome; CHO, carbohydrates; GI, gastrointestinal; GSRS, gastrointestinal symptom rating scale; ITT, intention to treat; PP, per-protocol; VAS, visual analog scale; QoL, quality of life; BMI, body mass index; IBS-SSS, irritable bowel syndrome symptom scoring system; IBS-C, constipation-predominant IBS; IBD, inflammatory bowel disease; VAS, visual analogue scale.

with a low FODMAP diet as it has been described. Since the first low FODMAP diets were described,[48] there have been modifications to the food lists that have been prompted by new scientific data on food composition. However, robust data now exist describing the FODMAP content of commonly consumed foods (Table 2).

Randomized, double-blind, placebo-controlled studies are considered the "gold standard" for an intervention study;[61] however, this is almost impossible to apply in dietary interventions. The more recent study conducted by Halmos et al[55] was a randomized controlled, single-blind crossover study in which 30 IBS and 9 healthy subjects consumed 21 days of low FODMAP diet or the typical Australian diet. The authors were able to address confounding variables by providing all intervention diets that were matched for all nutrients except for the FODMAP content. They found that 70% of IBS subjects (across all four subtypes of IBS) felt better on the low FODMAP diet, whereby the greatest symptom control was achieved and maintained after 7 days on the low FODMAP diet.

Additional evidence supporting FODMAPs as "food triggers" was provided in a randomized, placebo-controlled, rechallenge trial in 25 patients with IBS with fructose malabsorption.[57] In this study, a dose-dependent induction of GI symptoms was seen in the majority of patients with IBS following introduction of fructose (70%), fructans (77%), and fructose and fructans mix (79%) compared to glucose (14%) in liquid forms following a low FODMAP diet. This study also supports cumulative and dose-dependent effects of FODMAPs on inducing GI symptoms in patients with IBS.

Most patients with IBS find the diet easy to adhere to,[51,54] with better symptomatic improvement seen in those with the best adherence.[48,51] A randomized controlled trial conducted by Pedersen et al[59] found that the low FODMAP diet as well as the probiotics had significantly improved the IBS symptom score compared to the normal diet. However, this study was unblinded, and all three groups had a significantly improved symptom score after 6 weeks of intervention and web-based self-monitoring of symptoms compared to the baseline.[59]

Furthermore, the low FODMAP diet has provided symptomatic relief in more patients with IBS compared to a standard dietary advice consisting of healthy eating principles, alteration of insoluble and soluble fibers, and limiting sugar-free foods and foods containing sorbitol (86% and 49%, respectively).[54] A recent single-blinded randomized controlled trial[58] comparing the low FODMAP diet and the traditional dietary advice of regular meal pattern, avoiding or limiting certain foods such as fat, insoluble fiber, caffeine, and "windy vegetables" found reduced severity of symptoms in both groups, but no significant difference between the intervention groups. It was noted, however, the excess fructose intake was significantly lower in the traditional IBS diet group at the end of their study compared to baseline.

Limitations of low FODMAP diet include lack of clear cutoff levels for FODMAP content in foods and nonavailability of information on FODMAP content on food packages. However, research is being carried out to compile a comprehensive nutrient composition database for FODMAPs. Because the diet is fairly complex, advice should be given by a specialized dietitian trained in the area with appropriate resources, and food intake should be monitored for nutritional adequacy. Compliance may be a factor; nonetheless, the low FODMAP diet does not appear to alleviate GI symptoms of every IBS subject. Furthermore, the health effects of long-term low FODMAP diet are unknown. Human intestinal microbiota plays a critical role in health and disease. Although inulin-type fructans and galacto-oligosaccharides are FODMAPs, the ingestion of which may be associated with abdominal symptoms, they are also prebiotics, stimulating the growth of beneficial bacteria.[62] Studies have shown reduced total bacterial abundance[60] and reduced concentration of bifidobacteria[56] following a low FODMAP diet, suggesting potential adverse health effects of the diet. Generally, the strict low FODMAP diet is not recommended to be followed long term. Reintroduction or rechallenge of FODMAP foods is recommended based on individual tolerance.[63]

There are few low FODMAP dietary intervention studies conducted in children (not included in Tables 3 and 4). Until recently, these studies have focused on lactose malabsorption only.[64,65] More recently, a pilot study[66] and a randomized study[67] have shown reduction in abdominal pain frequency in children between 7 and 17 years of age with the low FODMAP diet. The results from these studies have also suggested that a difference in the microbiome composition at baseline may determine responders and nonresponders to the low FODMAP diet. Specifically, the responders had bacteria with greater saccharolytic capacity (such as genera Sporobacter and Subdoligranulum[66] and *Bacteroids*, *Ruminococcaceae*, and *Faecalibacterium prausnitzii*)[67] at baseline to break down sugars than those who did not respond to the diet. Hence, reduction in GI symptoms in children with IBS was seen with the low FODMAP diet likely due to decrease in osmotic load and gas production from fermentation.

In general, nearly all of the studies have used the Rome diagnostic criteria to select patients with IBS, which have resulted in a predominance of female subjects mostly between the ages of 30 and 50 years. The design of the studies varied

largely in terms of duration and the delivery of dietary intervention as well as symptom scoring tools or scales used. In all studies, however, improvements in overall GI symptoms were evident with those following a low FODMAP diet. Although the results are not consistent, significant improvements in diarrhea and constipation were seen in most studies. However, standardized dietary interventions and outcome measures were not used and are required to allow robust comparison in future studies. Finally, the first meta-analysis published in 2015[68] supports the efficacy of the diet in the treatment of functional GI symptoms including IBS.

Low FODMAP diet in other diseases

There are some studies in which low FODMAP diet has been applied to improve other lower GI disorders. For example, functional gut symptoms or IBS-type symptoms are common in patients with inflammatory bowel disease (IBD), with a greater prevalence seen in Crohn's disease than in patients with ulcerative colitis.[69] Gearry et al[70] have demonstrated that restriction in FODMAPs improved overall abdominal symptoms as well as abdominal pain, bloating, wind, and diarrhea in patients with IBD in a retrospective study. Similarly, reduction in dietary FODMAPs intake improved stool output and consistency in patients with ulcerative colitis following ileorectal anastomosis or ileal pouch formation and colectomy.[71] Both of these studies have shown improvement with good adherence to the diet. As mentioned earlier in this review, significant improvements in GI symptoms were also seen in NCGS subjects with IBS[41] and in all other types of patients with functional GI disorder.[69]

Future directions

Standardized dietary intervention in low FODMAP diet intervention studies and the use of validated symptom scales as predefined primary outcomes are essential to ensure that the results may be generalizable across larger and more diverse populations. Furthermore, modifications of the low FODMAP diet to individual tolerance should be considered in order to test the true efficacy of low FODMAP diet in long-term management of IBS. Finally, the long-term effect of a low FODMAP diet on the colonic health, particularly the microbiome, requires further investigation.

Conclusion

In summary, the evidence to date indicates that restriction of FODMAPs is an effective dietary intervention for reducing IBS symptoms. There are now well-designed clinical trials to support the efficacy of low FODMAP diet with alleviation of GI symptoms in majority of patients with IBS. More studies are required to assess long-term efficacy of low FODMAP diet following food rechallenge and to ascertain any adverse outcomes from effects on the gut microbiota.

Disclosure

The authors report no conflicts of interest in this work.

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