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Dietary fructose intolerance, fructan intolerance and FODMAPs

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Abstract

Dietary intolerances to fructose, fructans and FODMAPs (**F**ermentable **O**ligosaccharides, **D**isaccharides, **M**onosaccharides **A**nd **P**olyols) are common, yet poorly recognized and managed. Over the last decade, they have come to the forefront because of new knowledge on the mechanisms and treatment of these conditions. Patients with these problems often present with unexplained bloating, belching, distension, gas, abdominal pain or diarrhea. Here, we have examined the most up-to-date research on these food-related intolerances, discussed controversies, and have provided some guidelines for the dietary management of these conditions. Breath testing for carbohydrate intolerance appears to be standardized and essential for the diagnosis and management of these conditions, especially in the Western population. While current research shows that the FODMAP diet may be effective in treating irritable bowel syndrome, additional research is needed to identify more foods items that are high in FODMAPs, and to assess the long-term efficacy and safety of dietary interventions.

Keywords

Fructose intolerance; fructose malabsorption; fructan intolerance; breath testing; FODMAPS; irritable bowel syndrome; diet

INTRODUCTION

Malabsorption and intolerance to carbohydrates are common problems frequently encountered in the gastrointestinal (GI) and primary care clinics, but is poorly recognized and managed. Their exact prevalence is unknown. These intolerances frequently lead to unexplained GI symptoms such as abdominal bloating, gas, flatulence, pain, distension, nausea and diarrhea. Often, patients with such GI symptoms and especially those with alarm symptoms will undergo investigations to rule out organic disorders that may include endoscopy, imaging studies, blood and stool tests. When these tests are negative, then they are likely to have functional GI disorders that may include functional dyspepsia, functional bloating and irritable bowel syndrome (IBS) etc. which are frequently overlapped.

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Conflict of Interest

Satish S. C. Rao declares no conflict of interest. Amy Fedewa is employed by Georgia Regents Medical Center.

Compliance with Ethics Guidelines

Human and Animal Rights and Informed Consent

This article does not contain any studies with human or animal subjects performed by any of the authors

IBS is estimated to affect 5 to 30% of the world's population and approximately 10 to 15% of population in the US [1]. Research suggests that these disorders have a negative impact on the quality of life to a similar extent to chronic diseases including gastroesophageal reflux disease or asthma [2]. Self-reported food intolerance among subjects with high symptom burden has a great negative impact on their quality of life [3]. Approximately 60–80% of patients with IBS believe that their symptoms are diet-related, of which three-quarters is related to incompletely absorbed carbohydrates [3, 4]. In addition, the advice patients receive regarding diet varies enormously. Thus, there is a large unmet need for a clear diagnosis of the underlying problem(s) as well as consistent and effective advice on dietary treatments.

In this review, we focus on dietary fructose and fructan intolerances, both which are poorly recognized until recently and also discuss the role of dietary interventions including low FODMAPs in patients with unexplained GI symptoms.

FRUCTOSE INTOLERANCE

Fructose is a 6-carbon monosaccharide molecule that is naturally present in a variety of foods. Foods high in fructose can include certain fruits, vegetables and honey but it is also produced enzymatically from corn as high fructose corn syrup (HFCS), which is commonly found in many food sweeteners and soft drinks (Table 1). According to the US Department of Agriculture (USDA), HFCS consumption has increased for more than 1000% between 1970 and 1990 [5], with an annual consumption of fructose to have risen from less than a ton in 1966 to 8.8 million tons in 2003 [6]. It is possible that a rise in fructose consumption in the US population has resulted in a rise in fructose malabsorption and intolerance [7]. Both conditions are pretty much often unrecognized and this has resulted in mislabeling of many patients as having IBS especially in those with diarrhea-predominant symptoms. One study has estimated that up to one third of patients with suspected IBS had fructose malabsorption and dietary fructose intolerance (DFI) [8].

Humans have a limited absorptive capacity for fructose since its absorption is an energy independent process and this capacity is quite variable [9, 10]. While glucose is completely absorbed through an active transport mechanism in the small intestine that is facilitated by GLUT-2 and GLUT-5 transporters, fructose is mainly absorbed through carrier-mediated facilitative diffusion and GLUT-5 [10, 11]. A recent study did not show a difference in expression of GLUT-2/-5 transporters in a small number of patients with DFI vs. controls [9]. This suggests other transporters may have been involved as indicated in animal studies with GLUT-8 [12] but confirmation in human studies is needed. Malabsorption of fructose generates an osmotic force which increases water influx into the lumen and then leads to rapid propulsion of bowel contents into the colon, which is then fermented and leads to production of gas [13]. This can result in symptoms including abdominal pain, excessive gas and bloating, especially in patients with visceral hypersensitivity [11].

Breath testing and diagnosis of fructose intolerance

It is important to consider small intestinal bacterial overgrowth (SIBO) as a cause for unexplained GI symptoms, and especially when breath tests for hydrogen (H₂) and methane (CH₄) are positive with glucose and fructose (in the diabetic population). A discussion on SIBO is beyond the scope of this review but if found then this should be treated with antibiotics before considering fructose intolerance.

Breath testing after ingestion of fructose has been widely adopted as a standard method of identifying fructose malabsorption and intolerance. A dose of 25 g of fructose dissolved in a 10% solution is generally accepted as the appropriate dose of fructose for clinical use of H₂

and CH₄ breath testing [14]. A study that compared 3 doses of fructose (15, 25 and 50 g) found that 100% of healthy volunteers could absorb 15 g of fructose, 90% could absorb 25 g of fructose but only 20–30% could absorb 50 g [14]. In pediatrics, appropriate dosage still requires standardization, but a dose of 0.5–1 g/kg with a maximal dose of 10–15 g has been suggested [15]. These tests are by no means perfect, but are the best available tools for diagnosis of fructose intolerance. Presence of malabsorption and reproduction of symptoms during a breath test provides the best objective evidence and symptom correlation for fructose intolerance that can then lead to a firm diagnosis, and this helps avoid the use of empirical or unnecessarily restrictive diets. An example of a positive fructose breath test is shown in Figure 2.

During testing, both H₂ and CH₄ should be analyzed from the breath samples that are collected every 30 minutes for up to 3 hours. A rise in 5 ppm over 3 consecutive measurements or 20 ppm H₂ or 10 ppm (CH₄) or 15 ppm H₂ and CH₄ rise above baseline is regarded as a positive test [14]. One issue associated with this testing is the interpretation of symptoms. Symptoms do not appear to correlate with rises in H₂. Some practitioners use a lack of symptoms during testing as a rationale to exclude fructose intolerance despite significant increases in breath H₂ [16, 17], while others disagree. Symptoms may also lag somewhat. For example, a patient may experience symptoms only after testing ended. These episodes could be related to delayed intestinal transit and should be considered in the interpretation of test results. Patients who experience otherwise unexplained symptoms such as diarrhea or bloating during testing but do not show rises in H₂ are also considered to have fructose malabsorption. In such individuals there is a rapid influx of fluid into the lumen and rapid transport of highly osmotic and unabsorbed fructose across the colon. Consequently, there is less time available for gas production from the fermentation of fructose. Patients are often interested in knowing if their breath test can identify if they have mild or severe intolerance. Unfortunately, there is a lack of studies to support such a categorization in the literature [16, 17].

Dietary treatment for fructose intolerance

Published guidelines for fructose intolerance from the American Dietetic Association (now the Academy for Nutrition and Dietetics) include foods with less than 3 g of fructose per serving, less than 0.5 g of free fructose (defined as fructose in excess of glucose) per 100 g of food and less than 0.5 g of fructan per serving but these guidelines are only arbitrary cut-off values [13]. It is proposed that it is the free fructose which most strongly influences fructose malabsorption, though a meal with high total fructose content could result in symptoms as well. In one study that tested these dietary recommendations, 77% of the 62 patients with IBS were considered adherent to the diet while 74% of all patients responded favorably in all abdominal symptoms [18]. Interestingly, 15% of these patients used supplemental glucose to balance free fructose in their diets and all reported to be symptom free with this strategy [18]. Another study which examined this phenomenon found that when subjects consumed 50 g of free fructose, breath H₂ levels were four times higher when compared to subjects who consumed 50 g of fructose in the form of sucrose [19].

Patient compliance in the restriction of fructose was only found in slightly more than half of study participants, as shown by Choi et al. but in the compliant group, significant improvements were seen in belching, bloating and abdominal pain as well as all other symptoms within a year [8]. Despite having mild to moderate impact on their quality of life, all of the adherent patients planned to continue the dietary restriction even after study completion [8]. Another study similarly reported significant improvement in symptoms but a lesser impact on lifestyle with restriction of both fructose and fructans in a group of IBS patients with DFI [18].

There are no established protocols or guidelines in the dietary management of fructose malabsorption or intolerance and therefore management depends on the center's experience. At our center, patients with fructose intolerance will undergo firstly, the "elimination phase", where patients are encouraged to follow a diet with approximately 5 g of fructose per day for about 2 weeks (a totally fructose free diet is cumbersome and not usually required). Once patients experience sufficient relief from their intolerance symptoms (usually in 2–6 weeks), they are then encouraged to start a "re-introduction phase" where they reinstate small amounts of slightly higher fructose-containing foods, one at a time, in order to determine exactly how much fructose they can personally tolerate and have a diet that is the least restrictive as possible while still keeping their symptoms under control. The lists of foods that we advise patients to consume and avoid during the elimination and reintroduction phase are found in Table 1. Typically, patients can tolerate 10–15 g of fructose per day.

Alternative treatments

While lactase enzyme tablets are available to help people digest products containing lactose, there is a dearth of such enzyme-based treatments for dietary fructose intolerance. One crossover study reported the use of xylose isomerase (fructosin, which converts fructose to glucose) as an alternative therapy for fructose intolerance. While this product did lead to significant decreases in H₂ excretion (but not elimination of H₂ and CH₄ was not measured), as well as symptoms such as nausea and abdominal pain, it did not reduce bloating [20]. Furthermore, 30% of patients receiving isomerase or placebo showed no rise in H₂, which suggests that some of the subjects may not have been truly fructose intolerant [20]. More research is needed to determine if this compound or others would be an effective treatment for those with fructose intolerance.

FRUCTAN INTOLERANCE

Fructans are oligo- or polysaccharides that include short chains of fructose units with a terminal glucose molecule. Fructans with a 2–9 unit length are referred to as oligofructose and those with >10 units as inulins [21]. The most common structural forms of fructan are inulin, levanare and geraminan. The human body has limited ability to break down these oligo- or polysaccharides in the small bowel and only absorbs 5 – 15% of fructan [22, 23]. The mechanism for malabsorption and intolerance is related to the lack of enzymes to fully hydrolyze glycosidic linkages in the complex polysaccharide, and therefore results in the malabsorbed fructans to be delivered to the colon, which are then fermented [24]. Furthermore, the small molecule of fructans draws more water into the intestine which can result in bloating and diarrhea [24].

The USDA 1994–1996 Continuing Survey of Food Intakes by Individuals showed that the average fructan consumption in the US population was 3.91 g/day [25] but in other populations it may vary between 1 to 20 g [18]. The consumption rate is believed to have increased further by now since fructan-containing diets are very common in the Western diet, as more wheat-based products (breakfast cereals, pasta and bread) are consumed but further epidemiological data are needed. Many foods are high in fructans and examples are shown in Table 2. Although fructose and fructan content of different foods has been estimated [25, 26], additional research is needed in a wider range of newly-introduced items especially inulin-based in the market. Also, the effect of food preparation and cooking on foods containing fructan is unknown and needs to be examined as well.

No standardized test but breath testing is a possibility

At the moment, there is no standardized test for a diagnosis of fructan intolerance. There are only a few studies on absorptive capacity of fructan in humans [27, 28]. A preliminary report suggests that a dose of 7.5 g may be the optimal dose for breath testing of up to 3 hours in fructan intolerance [23]. In this dose-ranging response study, 14 healthy subjects, in a random order, were subjected to 7.5, 10 or 12.5 g of 10% fructan (chicory inulin) solution at weekly interval. Breath samples were collected and assessed for H₂ and CH₄ every 30 min for 5 hours. It was found that the amount of H₂ and CH₄ production correlates with dose of ingested fructan and peak by around 4 hours. A composite index, Fructan Intolerance Index (FII) that is a change of 20 ppm over baseline of H₂ and or CH₄ along with abdominal symptoms during the test was found to best characterize fructan intolerance. More studies are needed to confirm the utility of this test in clinical practice.

Dietary management of fructan intolerance

Restricting fructan in dietary intake may reduce symptoms in a variety of GI disorders [16]. It has been estimated that 24% of IBS patients may be sensitive to fructans [3]. In one study, restriction of fructan and fructose in diet was found to reduce symptoms in patients with IBS [27]. The only study to look at fructan independently of other FODMAPs found that patients with unexplained GI symptoms and who were negative for bacterial overgrowth, fructose intolerance, and lactose intolerance showed a significant malabsorption of fructans and were symptomatic during testing indicating intolerance [28]. Clearly, more robust evidence is needed to demonstrate the benefits of fructan restriction in functional GI disorders.

There are no clear guidelines on dietary management in fructan intolerance since there are no robust published data. As with other carbohydrate intolerance, identification and elimination of problematic foods containing fructan is the principle approach. The list in Table 2 is by no means exhaustive since more fructan containing foods have been introduced recently into the market. Furthermore, foods containing higher unit length of fructans (for example rye) may be better tolerated but on the other hand, restricting galactans (for example raffinose and stachyose) may be difficult with vegetarians. In any case, involvement of an interested dietitian is paramount.

WHAT ARE FODMAPS? IS IT JUST HYPE?

FODMAPs (Fermentable Oligosaccharides, Disaccharides, Monosaccharides And Polyols) are a group of short-chain carbohydrates which are poorly absorbed in the GI tract. A list of high FODMAP foods is shown in Table 2. The monosaccharide, fructose and oligosaccharide, fructan as discussed above are all part of FODMAPs. The disaccharide lactose is found in a variety of dairy products. Polyols are sugar alcohols found in certain fruits including peaches and plums. Sugar alcohols such as sorbitol, lactitol and xylitol are also commonly found in sugar free products [29]. At least 70% of polyols are not absorbed in healthy individuals [29]. These highly osmotic substances are rapidly fermented by bacteria. FODMAPs may induce GI symptoms via immune-mediated pathways, luminal distension or through direct action of the FODMAPs themselves [30]. Many patients with IBS have visceral hypersensitivity, which could be triggered by abrupt luminal distension [30]. FODMAPs have an additive effect on symptoms in patients with IBS [19, 31] and therefore, total FODMAPs intake becomes important. However, some people may be more sensitive to some groups of FODMAPs than others. A study by Böhn et al. examining self-reported dietary intolerances in IBS found that 70% of surveyed patients reported sensitivity to foods high in FODMAPs, 49% reported sensitivity to dairy products (high in lactose), 36% were sensitive to beans (galactans) and 23% were sensitive to plums (fructose +

polyols) [3]. The low FODMAPs diet was developed in 2001 to help treat functional gut disorders but its efficacy and safety remains controversial.

Efficacy of low FODMAPs diet

Recent bodies of evidence suggest that low FODMAPs diet appears to be efficacious in improving symptoms in patients with unexplained GI symptoms. The key principle for its success is dietary education. Whilst effective short term, there are practical hurdles regarding such education, and its long term safety or efficacy is not yet known.

A low FODMAPs diet in IBS was shown in a study to be more effective than dietary guidelines [32]. A RCT also showed greater effectiveness of low FODMAPs compared to habitual diet in improving IBS symptoms [33]. Similarly a recent single blinded RCT showed its efficacy in IBS [34]. A summary of these published studies are shown in Table 3. To conclude, there is significant disparity in subject selection, dietary interventions and outcome assessments in some of these studies, and hence definitive conclusions on efficacy of low FODMAPs diet cannot yet be made.

Besides functional diseases, some studies suggest that patients with IBD or patients with an ileostomy may also benefit from a low FODMAP diet. It is also possible that the FODMAP content of food may be linked to diarrhea seen in patients receiving enteral nutrition [36, 37], but more studies are needed despite recent reviews supporting this form of dietary management [38].

Dietary guidelines for the low FODMAPs diet

Although patients often observe some improvement in symptoms within the first week, usually there is progressive increase in efficacy over the first 6 weeks; hence it is recommended that patients who benefit from the diet, strictly adhere for at least 6–8 weeks. Following this period of elimination, patients are encouraged to “challenge” themselves with different groups of FODMAPs, in order to determine which group (s) of FODMAPs they are sensitive to, and then to liberalize the diet as much as possible [29]. The challenge phase can be done either by adding foods high in a particular group of FODMAPs for a day, or by starting with a very small amount of FODMAPs from one group and gradually adding more items into the diet in order to determine the individual tolerance. Most seem to favor the more cautious approach. If there is little efficacy after 8 weeks of elimination, the diet may be discontinued. However, some people who report inadequate symptom improvement with the diet, still report that their symptoms are aggravated when they eat high FODMAP foods [29].

Patients on the low FODMAP diet were found to have altered starch, total sugar, carbohydrates and calcium intake [32]. Also, fiber intake can sometimes be of concern to some patients. Whole grain gluten free breads, other wheat-free whole grains such as brown rice and the inclusion of low FODMAP fruits and vegetables are all encouraged to offset that potential low fiber intake [29]. More studies are needed to determine the nutritional adequacy of the diet. It is also unknown if the change in prebiotic intake in the FODMAP diet would have any negative effects on the intestinal microbiome or if the associated changes in the gut microenvironment could affect health. It appears that it is safe to follow the diet as long as necessary with the assistance of a dietitian [29], and thus can also help to increase compliance [39].

CONCLUSIONS

Dietary fructose and fructan intolerance are common clinical problems that lead to unexplained GI symptoms. Gastroenterologists and dietitians need to be aware of these

conditions and of the tests designed to diagnose these problems. A fructose-restricted diet is an effective treatment option for dietary fructose intolerance, but more studies are needed to examine the long term efficacy and adherence to such diets. Fructan intolerance is a new concept and warrants further studies. The efficacy of dietary restrictions in fructan intolerance is not known. The FODMAP diet seems to be useful in controlling IBS symptoms, but more rigorous studies are needed including the FODMAP content of more foods. Tests to determine tolerance to individual FODMAPs may help to liberalize a patient's diet, though this also calls for additional study.

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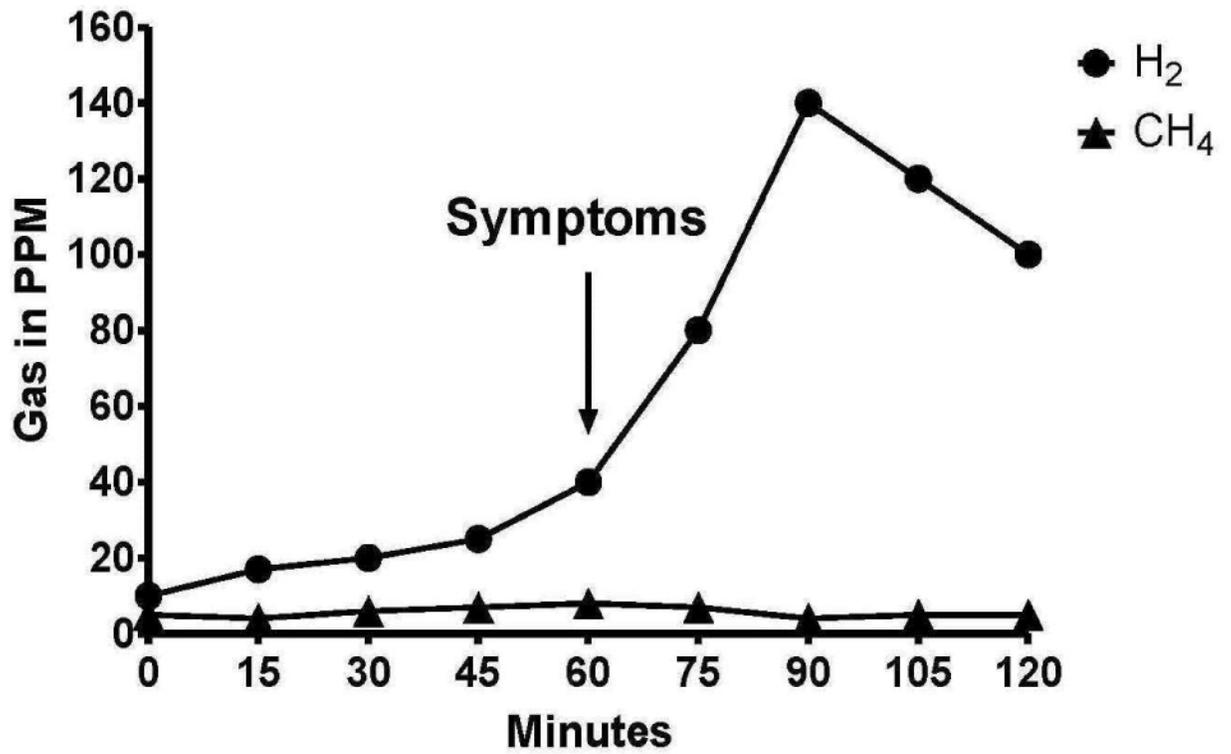


Figure 1. A significant rise in H₂ but not CH₄ after an oral dose of 25 g of fructose in a patient with fructose malabsorption or intolerance. There is reproduction of symptoms that correlated with the significant rise in H₂

Table 1

Suggested list of high fructose foods and low fructose alternatives that may be effective during the “elimination phase”

Category	Low fructose alternatives	High fructose foods
Fruits	Avocado, cranberries, lime, lemon cantaloupe, pineapple, strawberries, mandarin orange, bananas.	All fruits not on the allowed list, especially juices, dried fruits (such as prunes, raisins or dates) and fruits canned in juice or syrup.
Vegetables	Bamboo shoots, beets, bok choy, carrots, celery, chives, green pepper, kale, parsnip, plum tomato, radish, rhubarb, spinach, sweet potato, turnip greens, white potato, winter squash. Allowed vegetables that are more likely to give you gas: Brussels sprouts, cabbage, cauliflower, lettuce.	Artichoke, asparagus, broccoli, chutney, leeks, mushrooms, okra, onions, peas, red pepper, shallots, tomato paste, tomato products (canned tomatoes, ketchup).
Grains and Cereals	Buckwheat flour, corn chips, cornmeal, corn tortillas, gluten free breads, crackers and pastas without added HFCS, grits, oatmeal, popcorn without HFCS, quinoa, rice, rye breads without added HFCS, soba noodles and all other flours made from allowed grains.	Foods with wheat as a major ingredient (wheat bread, pasta, couscous), grains with added dried fruit, grains with added HFCS.
Meats	Plain unprocessed meats of any type (beef, chicken, fish, eggs etc.) Legumes, tofu (note that these tend to be more gas forming and may need to be avoided), nut butters that do not contain HFCS.	Marinated or processed meats containing restricted ingredients.
Dairy Products	Milk, cheese, yogurt, soy milk, rice milk, almond milk without added HFCS.	Any product with HFCS. Be especially careful with yogurts, and flavored milks.

HFCS; high fructose corn syrup

Table 2

Sources of high FODMAPs and low FODMAPs alternatives

	High FODMAPs	Low FODMAPs
Fructans	Wheat including bread, pasta, couscous etc., onions, shallots, scallions, garlic, barley, Brussels sprouts, cabbage, broccoli, pistachio, artichoke, inulin or chickory root	Fruits Oranges, unsweetened cranberries, strawberries, cantaloupe, lemon, lime
Galactans	Soy milk, soy protein isolate, miso, veggie-burgers, dried beans and peas, lentils, butter/lima beans, humus, large amount (more than 1 cup per day) of coffee	Vegetables Peas, celery, carrots, plum tomato, spinach, lettuce, green peppers, green beans, bean sprouts, turnip, turnip green, cucumber
Lactose	Soft cheeses including ricotta, cottage and cream cheese, milk, cream, yoghurt, butter, ice-cream	Dairy Hard cheeses including cheddar, Swiss and parmesan. Lactose-free unsweetened yoghurt, lactose-free milk
Polyols	Artificial sweeteners (xylitol, sorbitol etc.), apples, plums, cherries, pear, cauliflower, sweet corn, snow peas, mushrooms	Meats All plain unprocessed meats, peanut butter (not sweetened with high fructose corn syrup), eggs, small amounts of almonds and walnuts, tofu
		Grains Rice (all varieties), gluten and rye-free bread, oats, corn, oat rice, buckwheat or quinoa cereals, corn tortilla, grits, popcorn, potato, quinoa

Table 3

A summary of clinical trials of low FODMAPs diet

Ref #	Design	Study population	Intervention	Time	Outcome measures	Symptom improvement	Compliance	Additional Outcomes
32	Non-randomized, retrospective observational	IBS patients; standard diet group=39, low FODMAP group=43	Low FODMAP or NICE dietary guidelines (fiber, probiotics, exclusion diets), breath tests.	2-6 m	Change in symptoms (7-point Likert scale) and diet satisfaction (5-point Likert scale).	Composite symptom score improved in 86% vs. 49% (low FODMAP vs. standard group) ($P<0.001$).	84% of low FODMAP group assessed; 64% adhered strictly. 30% ~ 50% of the time.	Satisfaction= 76% vs. 54% (low FODMAP vs. standard group, $P=0.038$).
27	Double blind, randomized placebo controlled quadruple-armed	IBS (12 IBS-D, 5 IBS-C and 8 IBS-M) with FM; responded to low FODMAP diet for 3 months	Patients received 3 doses of either fructans (7.14, or 19 g/3 days), fructose (14,28,50 g/3 days), fructans + fructose or glucose (7.14,20g/8 days)	22 w	Daily symptom assessments and adherence to diet through daily food diaries	70% on fructose, 77% on fructans and 79% on fructose + fructans had symptom relapse (gas, bloating, pain) compared to 14% on glucose ($P<0.001$)	Diet adherence was > 95%.	Higher doses of fructose and/or fructans associated with more severe symptoms ($P<0.01$) but not with glucose.
33	Non-randomized prospective observational	90 IBS patients referred for lactose and fructose breath testing	All received high and low FODMAPs lists, recipes, reintroduction of restricted foods guidelines and consultation with dietitian.	Mean total 15.7 m	GI symptom questionnaire (7 point Likert) at baseline and 6 weeks. Adherence and opinion of diet.	Improvement ($P<0.05$) in all symptoms except feeling full, burping and passage of mucus.	76% adherent 50% of the time or more.	Satisfied= 77%; easy to follow diet= 50%. Presence of FM strongly associated with efficacy.
34	Randomized controlled single-blind crossover	30 IBS patients (10 IBS-D, 13 IBS-C, 5 IBS-M and 2 IBS-U) vs. 8 healthy controls	Average of 3.05 g FODMAP/day. Control diet = average of 23.7 g FODMAP per day.	21 d per diet	Daily food records and symptoms; differences in individual & overall symptoms. King's stool chart & fecal water content.	Improvement in 70% of patients, including 70% with FM, 60% without FM and 75% no prior breath test. Pain, bloating and dissatisfaction with stool consistency improved ($P<0.001$) especially IBS-D.	Adherent= at least 17/21 days (80%); control diet=100%; low FODMAP diet= 80%.	None.
35	Randomized single-blind crossover study	15 IBS patients (4 IBS-D, 8 IBS-C, 2 IBS-M, 2 IBS-U) vs. 15 healthy controls	Low (9 g) or high (50 g) FODMAP for 2 days. Breath samples collected on day 2 of study.	2 d per diet	Breath H ₂ , CH ₄ and symptoms measured on a Likert 0 to 3 scale	Abdominal pain, bloating, gas, heartburn, nausea and lethargy reduced in IBS patients when on low FODMAP diet. Gas lower in healthy patients on the low FODMAP diet.	Not assessed.	AUC for H ₂ (not CH ₄) higher with high vs. low FODMAP diet in both normal and IBS.

Ref#: references, IBS-D, C, M; irritable bowel syndrome-diarrhea, constipation and mixed type, FM; fructose malabsorption, H₂; hydrogen, CH₄; methane, AUC; area under the curve