Nutrition in Clinical Practice

Extending Our Knowledge of Fermentable, Short-Chain Carbohydrates for Managing Gastrointestinal Symptoms

Jacqueline S. Barrett Nutr Clin Pract published online 24 April 2013 DOI: 10.1177/0884533613485790

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Extending Our Knowledge of Fermentable, Short-Chain Carbohydrates for Managing Gastrointestinal Symptoms

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Abstract



Nutrition in Clinical Practice Volume XX Number X Month 2013 1–7 © 2013 American Society for Parenteral and Enteral Nutrition DOI: 10.1177/0884533613485790 ncp.sagepub.com hosted at online.sagepub.com



The Monash University low FODMAP (fermentable oligosaccharides, disaccharides, monosaccharides, and polyols) diet is now accepted as an effective strategy for managing symptoms of irritable bowel syndrome (IBS) in Australia, with interest expanding across the world. These poorly absorbed, short-chain carbohydrates have been shown to induce IBS symptoms of diarrhea, bloating, abdominal pain, and flatus due to their poor absorption, osmotic activity, and rapid fermentation. Four clinical trials have been published to date, all with significant symptomatic response to the low FODMAP diet. Up to 86% of patients with IBS have achieved relief of overall gastrointestinal symptoms and, more specifically, bloating, flatus, abdominal pain, and altered bowel habit from the approach. This review provides an overview of the low FODMAP diet and summarizes the research to date, emerging concepts, and limitations. FODMAPs are known to be beneficial to bowel health; the importance of this and how this should be considered in the clinical management of IBS is also discussed. A clinical management flowchart is provided to assist nutrition professionals in the use of this approach. (*Nutr Clin Pract.* XXXX;xx:xx-xx)

Keywords

carbohydrates; irritable bowel syndrome; gastrointestinal diseases; abdominal pain; diarrhea; diet therapy; FODMAP

Irritable bowel syndrome (IBS) is the most common gastrointestinal (GI) disorder, affecting 5%–27% of Western society.¹⁻⁴ GI symptoms, including abdominal pain, bloating, distension, excessive wind, and altered bowel habit, characterize this condition when anatomical abnormalities and inflammation have been excluded. IBS treatments used in clinical practice include pharmaceuticals (such as antispasmodics, stool softeners) and fiber supplements. Prebiotics, probiotics, and hypnotherapy are among a few therapies more recently investigated. Diet has received much attention because the food we eat and the path it follows through the GI tract suggests a strong relationship with IBS symptoms to patients, clinicians, and researchers alike.

The success of dietary manipulation for IBS symptom management varies. High-fiber diets seem the most logical approach to improve bowel function, but clinical trials reveal conflicting results depending on the type and dosage of fiber given.⁵⁻⁷ Dietary fat,^{8,9} caffeine,¹⁰ and alcohol¹¹ have also been pursued as potential triggers, with physiological mechanisms suggesting they may play a role, but inconsistencies in improvements have been seen when these are restricted. Most commonly, elimination diets have been used to identify food sensitivities for IBS. There are several key issues with elimination diets. First, many rely on the diagnosis of food hypersensitivity via IgE or IgG tests.¹²⁻¹⁷ There is controversy over these tests. Ligaarden and colleagues¹⁴ demonstrated that a similar proportion of healthy controls and patients with IBS had positive IgG tests to yeast and foods, concluding IgG tests to be of little use in IBS management. In 1 study that did show benefit

by restricting IgG-positive foods, the benefit was only 10% greater than control.¹⁷ There is no consistent evidence that patients with IBS suffer from food allergy, nor is there documented evidence that food intolerance picked up by such investigations plays a role in IBS symptoms.¹⁸ Second, the structure and restrictions in place during an elimination diet vary considerably depending on the clinician or research group. Elimination diets range from a simple restriction of dairy and wheat products to those with a positive IgE or IgG test, extending to elimination of all natural and artificial food chemicals such as salicylates and benzoates.¹⁹ There is minimal published evidence for the use of an elimination diet for IBS, which is further diluted by the varying types of elimination diets used.

In the 1980s and 1990s, research demonstrated that dietary sugars, including fructose (and its chain form fructooligosaccharides) and sorbitol, could induce IBS symptoms with highdose challenges.²⁰⁻²⁶ Dietary restriction of these short-chain carbohydrates appeared successful, providing some support for the use of this type of therapeutic diet for IBS management, but

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Financial disclosure: None declared.

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information on the composition of foods for these carbohydrates was limited.^{27,28}

Introducing the FODMAP Approach: Fermentable Oligosaccharides, Disaccharides, Monosaccharides, and Polyols

In 2005, previous research on fructose, fructooligosaccharides, and lactose was brought together, with further work commenced to build on the suggestion that restricting this group of short-chain carbohydrates may improve IBS symptoms. Fructose, a monosaccharide, was the sugar with the most attention, in addition to its long-chain form, fructooligosaccharides (or fructans).²² Lactose, a disaccharide, was also a well-known contributor in some individuals.²⁹⁻³¹ These 3 short-chain carbohydrates comprised the early stages of the FODMAP approach.³² FODMAP stands for *fermentable oligosaccharides, disaccharides, monosaccharides, and polyols.* The acronym was created to include all short-chain carbohydrates that can be poorly absorbed and are rapidly fermented in the gut as this was the mechanism by which these carbohydrates were thought to induce symptoms.

Initial studies included a retrospective study of the efficacy of the diet, demonstrating that 75% of individuals with IBS had improvement of bloating, abdominal pain, nausea, flatus, diarrhea, and/or constipation when on a diet low in fructose and fructans.³³ Randomized, placebo-controlled rechallenge trials then confirmed the role of these sugars by challenging individuals with IBS and fructose malabsorption to blinded solutions of fructose, fructans, fructose plus fructans, and glucose (placebo).³⁴ Symptom induction was highly significant to all challenge substances with a low placebo effect proving that symptom relief was achieved through restriction of these substances, rather than through elimination of other components.

The Monash University Low FODMAP Diet

Further work by a growing team of gastroenterologists, scientists, nutritionists, and dietitians at Monash University, Eastern Health and Central Clinical Schools, has expanded the approach, developing the Monash University low FODMAP diet.³⁵ The expansion of the diet low in poorly absorbed, shortchain carbohydrates now includes the oligosaccharides fructooligosaccharides (fructans or FOS), found in wheat, rye, onion, and garlic, and galactooligosaccharides (GOS), found in legumes and some nuts; the disaccharide lactose found in milk products; the monosaccharide fructose in apples, pears, watermelon, mango, and asparagus; and the sugar polyols, used as artificial sweeteners and naturally occurring as sorbitol in stone fruits and mannitol in mushrooms and cauliflower. Dietary fiber and resistant starch, although not absorbed in the small intestine, are more slowly fermented, less osmotically active, and therefore unlikely to induce symptoms. Indeed, the low FODMAP diet used in research studies has provided its symptomatic benefits while ensuring adequate intake of resistant starch and dietary fiber.^{36,37} Food lists have changed over time and will continue to be modified as new foods are tested in Australia and internationally.³⁸⁻⁴⁰ Foods that are low in all FODMAPs have been identified to assist dietitians, ensuring their patients understand what is safe to include in the diet (see Table 1 for a list of the richest FODMAP sources and safe alternatives).

The Monash University low FODMAP diet has since been demonstrated to be an effective dietary treatment not only for those with IBS, but there is evidence for its efficacy in 70% of people with quiescent Crohn's disease and ulcerative colitis exhibiting functional symptoms.⁴¹ The existing retrospective study and rechallenge trials are now further supported by international research. Up to 86% of patients with IBS in the United Kingdom had improvement of overall GI symptoms and, more specifically, bloating, borborygmy, and urgency on the low FODMAP diet when compared with a traditional diet for IBS.³⁷ This is achieved after following the low FODMAP diet for just 4 weeks.

Mechanism of Action

The mechanism of action of these carbohydrates has been extensively studied using the ileostomy model and breath hydrogen and methane testing. The ileostomy model is used in nutrition research, in which patients with an end-ileostomy consume known amounts of a dietary component of interest, which is then measured in the effluent to calculate the degree of absorption in the small intestine. Breath hydrogen and methane testing is used in research and in clinical practice to measure an individual's ability to absorb a test carbohydrate. It involves the individual consuming a low FODMAP, low-fiber diet the day prior to testing and an overnight fast, with a baseline breath sample taken at the commencement of the test. A test solution is then consumed (eg, fructose), with further breath samples collected at regular intervals for up to 3 hours. These tests are a reliable measure of malabsorption.⁴²⁻⁴⁶ Levels of breath hydrogen and methane are detected only if the test sugar is malabsorbed and fermented by intestinal microflora.

The collection of FODMAP carbohydrates shares several key features. First, they all have the potential for malabsorption. Fructose is absorbed in the small intestine via 2 pathways: (1) high-capacity, facilitated transport using the GLUT2 transporter that absorbs fructose in the presence of glucose, and (2) low-capacity facultative transport that occurs via GLUT5. This latter pathway is downregulated in some individuals, giving rise to the potential for malabsorption of fructose. As such, fructose can still be ingested and absorbed in these individuals as long as glucose is present to prompt the GLUT2 pathway of absorption.⁴⁷ This has been clearly demonstrated by breath

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 Table 1. Food Sources of FODMAPs and Alternative Food

 Choices.³⁵

FODMAPs, fermentable oligosaccharides, disaccharides, monosaccharides, and polyols.

testing, with fructose malabsorption detected and then corrected by the addition of an equivalent concentration of glucose.^{48,49} The prevalence of fructose malabsorption has also been studied, demonstrating that 34% of healthy people malabsorb fructose compared with 45% of those with functional GI disorders (FGID) and increasing to 78% of those with ileal Crohn's disease.⁴³

Malabsorption of lactose is well documented. It most commonly occurs when production of lactose enzyme is insufficient, as digestion and absorption of lactose require breakdown of the disaccharide into its monosaccharide units. This occurs in certain ethnicities (eg, Asian and Mediterranean) and with increasing age.^{29,43,50} It has been well documented that most people can tolerate a small amount of lactose, and a dairy-free diet is not usually required.⁵¹ Lactose malabsorption prevalence has also been examined, demonstrating 16% prevalence in healthy whites compared with 23% with FGID and up to 38% of individuals with IBD.⁴³

Malabsorption of the remaining FODMAP carbohydrates is even more common. Breath testing studies for sorbitol and mannitol yield 60% prevalence in healthy individuals.⁵² The oligosaccharides, fructans and GOS, are poorly absorbed in everyone.^{22,53-56} Their chains of fructose and galactose, respectively, are not broken down due to the absence of the respective human enzymes capable of this. Eventually, the undigested carbohydrates are fermented by intestinal microflora, resulting in various gases and IBS symptoms.

Mechanism studies have been completed using the Monash University low FODMAP diet approach. The ileostomy model confirmed poor absorption of these carbohydrates with significant proportions of ingested fructans and sorbitol recovered in the effluent.⁵⁷ Ileostomy output and water content were significantly increased on a high FODMAP diet, with FODMAP recovery closely correlated to water content of the effluent. This confirms the osmotic effect of these carbohydrates, the likely cause of diarrhea in IBS that occurs due to their small molecular size and poor absorption in the small bowel. This osmotic effect has also been well documented for mannitol.58 Breath hydrogen analysis in those with IBS and healthy participants has highlighted the fermentative effect of these carbohydrates. A high FODMAP diet increases breath hydrogen production across the day, reflective of fermentation patterns occurring in the large intestine and consequent symptoms of bloating, flatus, and abdominal pain in those with IBS.³⁶

With the osmotic nature of FODMAPs contributing to diarrhea and the fermentation by-products contributing to symptoms of gas distension, the improvements to constipation-predominant IBS seen by the FODMAP approach need further exploration. Methane production during fermentation of FODMAPs seems to be a viable option. There is a clear relationship between the intestinal microbiota, particularly methane production, delayed intestinal motility, and constipation-predominant IBS.⁵⁹ Methane production has been shown to correlate with degree of constipation and stool form.^{60,61} It is therefore suspected that the low FODMAP diet

would reduce methane production and in turn correct delayed motility in some individuals. Further work is required to confirm this hypothesis.

New and Emerging FODMAP Concepts

The success of the low FODMAP diet in improving IBS symptoms has led to consideration of these carbohydrates as triggers in other clinical situations. The high incidence of diarrhea in those receiving enteral feeding may be partly explained by the FODMAP content of the feeds.⁶² Fructose, FOS, and GOS are frequently used as ingredients in commercial enteral formula. Retrospective audit of enteral feeding–associated diarrhea is highly suggestive of FODMAP composition of feeds,⁶³ with further prospective studies warranted.

Infantile colic is a condition characterized by infant irritability, fussing, and crying. It usually occurs in the first 6 months of life, with long hours of crying and difficulties settling these infants, resulting in a very difficult time for the mother or carer. Some of the behaviors of infants with colic suggest GI distress may be a key feature. Two pilot trials have now been conducted by Monash University (unpublished) with a 100% success rate⁶⁴; breastfeeding mothers switching to a low FODMAP diet report significant improvement in colic-related symptoms of their infant. The mechanism is unclear, but it certainly holds promise for mothers of infants with colic.

Limitations of the Diet

Effect on Gut Microflora

As previously described, FODMAPs are poorly absorbed in health as well as in IBS. Fermentation patterns are similar; however, healthy people do not report the degree of discomfort seen in IBS. This suggests malabsorption of FODMAPs is part of normal digestion. Fructose malabsorption has been referred to as a condition or disorder, but it is commonly seen in healthy individuals. In the presence of symptoms, however, knowledge of whether an individual malabsorbs certain FODMAPs provides an opportunity for therapy.

Both patients with IBS and healthy volunteers produce the same levels of hydrogen gases to a standard amount of FODMAP carbohydrate. However, symptoms are extreme in those with IBS. This was first seen in the 1970s, when barostat studies induced symptoms in patients with IBS, but not healthy individuals, despite both groups receiving the same volume of distension.⁶⁵ Patients with IBS demonstrate hypersensitivity to luminal distension.⁶⁶⁻⁶⁹ They also have altered microflora that may result in differences in fermentation gas type (eg, methane vs hydrogen) and volume.⁷⁰⁻⁷⁴ These differences in patients with IBS are likely the reason for their symptoms. Malabsorption of FODMAPs provides an osmotic effect and fermentable carbohydrate to the IBS bowel. Restricting FODMAPs does not treat IBS, but it does provide a therapeutic strategy to manage symptoms.

In healthy individuals, FODMAPs are malabsorbed. This provides many benefits: natural laxation due to their osmotic effect, a prebiotic effect, and fermentation by-products, including short-chain fatty acids (SCFAs).⁵⁴ SCFAs such as butyrate are suggested to protect against colon cancer.⁷⁵ Diets supplemented with FOS, GOS, and inulin, a long-chain fructooligo-saccharide, have a prebiotic effect, encouraging the growth of bifidobacteria and reducing *Escherichia coli, Bacteroides* spp, and *Clostridium* spp.⁷⁶ This is important, given bifidobacteria are often low in IBS. As such, FODMAPs are important to bowel health, and intake should be encouraged.

What does this mean for the application of the low FODMAP diet for IBS? Recent work in the United Kingdom has examined the effect of the low FODMAP diet on gut microbiota.⁷⁷ Thirty-five patients with IBS were randomized to their habitual diet or the low FODMAP diet. Stool samples demonstrated that the low FODMAP diet lowered luminal bifidobacteria after 4 weeks. Longer term follow-up has not been examined, and it may be that the bacterial profile returns to normal after several months on the diet, as shown by other dietary changes that affect microbiota.⁷⁸ It may also be that this diet does have a negative impact on microbiota and that a complementary therapy, such as probiotic or prebiotic supplementation, should be considered for people following a long-term low FODMAP diet.

Fiber and Constipation

One of the most important factors to consider in the dietary management of IBS is fiber intake. It is well established that adequate fiber is required for gut health and function. The low FODMAP diet restricts many high-fiber foods, including certain fruits, vegetables, and wheat and rye products. Despite this, research has shown stool consistency improve for patients with diarrhea- and constipation-predominant IBS.33 The mechanism by which constipation improves on the low FODMAP diet may be related to methane production as discussed previously. In clinical practice, it is noted that a proportion of patients with constipation-predominant IBS have an exacerbation of constipation while following the diet. For these patients, ensuring they are choosing high-fiber alternative fruit and vegetable options, as well as choosing high-fiber grains and cereal (eg, oats), is paramount to the success of the diet. Fiber supplementation may be warranted in some individuals, but it is important to avoid those that are highly fermented (eg, wheat bran) as they may exacerbate symptoms. Oat or rice bran supplementation may be better tolerated.

Clinical Management

The Monash University low FODMAP diet has significantly changed the clinical management of IBS in Australia. This is summarized in Figure 1. Dietitian assessment of a patient with confirmed IBS (negative screen for alarm signals suggestive of alternative or additional GI disease) should include notation of



Figure 1. Clinical management flowchart for IBS. FODMAPs, fermentable oligosaccharides, disaccharides, monosaccharides, and polyols; IBS, irritable bowel syndrome.

FODMAP intake and other potential dietary factors that may contribute to symptoms, discussions of the individual's suspect food triggers (although it should be highlighted that the timing of symptoms can vary and suspect food triggers may not always be correct), and assessment of lifestyle factors that may affect IBS symptoms (eg, meal patterns, exercise). Patients can then be educated on the Monash University low FODMAP diet approach, including discussions on breath testing if available to the patient. For those who choose to forgo breath testing, the individuals' tolerance to each of the FODMAP carbohydrates can be tested after an initial dietary trial of approximately 4 weeks. This involves education by the dietitian on the reintroduction of foods that contain only 1 FODMAP carbohydrate (ie, honey for fructose, milk for lactose, apricots for sorbitol, mushrooms for mannitol). Each test is done one at a time, each for several days to assess tolerance. Garlic as a minor ingredient and small amounts of legumes should be trialed to increase fructan and GOS intake, considering their benefits on luminal microflora. For those who choose to undertake breath testing, fructose and lactose are most commonly tested. Fructans and GOS are never tested as we all malabsorb these carbohydrates.

Any FODMAP carbohydrates that have negative breath test outcomes can be immediately reintroduced into the diet, avoiding unnecessary restrictions. Further testing of small amounts of FODMAP carbohydrates should be encouraged long term.

Summary

IBS is the most common GI complaint seen by general practitioners and gastroenterologists, yet until now, most therapies have failed. The Monash University low FODMAP diet has appreciably changed the management of IBS. The evidence is now sufficient to confirm the efficacy of this approach for IBS symptom management. The role of a dietitian in implementing the diet is paramount. The diet needs to be individualized and testing of tolerance should be structured to work toward a less strict version of the diet long term. A potential negative side effect of the FODMAP approach on intestinal microflora may be alleviated by the inclusion of small amounts of fermentable carbohydrates. This should be encouraged. In December 2012, Monash University released the first evidence-based iPhone application for practitioners and patients following the low FODMAP diet. This will improve access to accurate, up-todate information for people already following the diet, and it is hoped that it will spark interest by more practitioners around the world as more patients experience symptom relief from this dietary approach.

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