Invited Review

aspen | LEADING THE SCIENCE AND PRACTICE OF CLINICAL NUTRITION
American Society for Parenteral and Enteral Nutrition

Nutrition in Clinical Practice
Volume 33 Number 4
August 2018 468–475

DOI: 10.1002/ncp.10108
wileyonlinelibrary.com
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Dietary Fermentable Oligosaccharides, Disaccharides, Monosaccharides, and Polyols (FODMAPs) and Gastrointestinal Disease

Nimish Vakil, AGAF, FACG, FASGE[1,2]

Abstract

FODMAP is an acronym for fermentable oligosaccharides, disaccharides, monosaccharides, and polyols. Dietary modification of FODMAPs has been shown to have significant effects on the physiology of the gastrointestinal tract and improves symptoms of abdominal pain, distention, and bloating in patients with irritable bowel syndrome. Structured withdrawal and reintroduction of FODMAPs supervised by a dietitian is the optimal practice for dietary FODMAP modification in irritable bowel syndrome. FODMAPs are present in enteral feeding formulas and may have a role in diarrhea and bloating in tube-fed patients. Emerging areas of research include the effects of dietary modification of FODMAPs on the microbiome, micronutrient absorption, and caloric intake. FODMAP dietary modification is an emerging area in other gastrointestinal disorders and is of relevance to all practicing dietitians. (*Nutr Clin Pract.* 2018;33:468–475)

Keywords

disaccharides; enteral nutrition; FODMAP; irritable bowel syndrome; inflammatory bowel diseases; microbiota; monosacccharides; oligosaccharides; polysaccharides; sugar alcohols

Introduction

FODMAP is an acronym for fermentable oligosaccharides, disaccharides, monosaccharides and polyols. FODMAPs are short-chain carbohydrates that have the following 3 characteristics: they are poorly absorbed in the small intestine, they are fermentable, and they are osmotically active. The FODMAP content of foods may be found in Table 1.

Carbohydrates and Their Absorption

Carbohydrates consist of sugars, including monosaccharides and disaccharides; polyols, which are sugar alcohols such as sorbitol and xylitol; and oligosaccharides, which are carbohydrates containing 3–10 monosaccharides found in plants such as onions. Polysaccharides are large chains of monosaccharides. Polysaccharides may be designed for energy storage, such as glycogen or starch or serve a structural function such as cellulose or chitins. A fructan is a polysaccharide made up of fructose. Fructooligosaccharides are fructans with a short chain length. A detailed description of carbohydrates and their absorption may be found elsewhere.[1]

The digestion of carbohydrates begins with the breakdown of complex carbohydrates by salivary and pancreatic amylase into simpler sugars such as dextrin and maltose. Enzymes in the brush border of the small intestine called glucosidases break down the dextrin and maltose further and with other disaccharidases (lactase and sucrase) break sugars down further into monosaccharide units. Lactose is a disaccharide composed of glucose and galactose and is broken down into its component monosaccharides by lactase. In the absence of the lactase enzyme, lactose is carried to the distal small bowel and colon where it is used by bacteria and can cause symptoms of bloating and diarrhea. Glucose, galactose, and fructose are absorbed through the epithelium and are transported by the portal vein to the liver. At low concentrations, glucose is absorbed using a sodium-dependent active transporter. At higher concentrations, a second facilitated transporter becomes active. Galactose is absorbed using the same transporters.

Fructose is an important monosaccharide that is present in a free from in the diet, as a subunit of a disaccharide

From the [1]University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin, USA; and [2]Aurora Health Care, Summit, Wisconsin, USA.

Financial disclosure: None declared.

Conflicts of interests: None declared.

This article originally appeared online on June 5, 2018.

Corresponding Author:
Nimish Vakil, MD, Aurora Summit Medical Center, 36500 Aurora Drive, Summit, WI 53066.
Email: nvakil@wisc.edu

Table 1. High FODMAP Foods by Component.

Fructose	Lactose	Fructans and Galacto oligo-saccharides	Polyols
Fruits: apples, cherries, figs, mango, pears, watermelon	Cheese: soft cheeses (ricotta, cottage, mozzarella)	Legumes: beans (black, fava, kidney, navy), soy (beans, flour, milk)	Sweetening agents: sorbitol, mannitol, xylitol, isomal
Vegetables: artichokes, asparagus, dried tomatoes and sugar snap peas	Milk: sheep, cow, goat and buffalo	Nuts and grains: wheat, rye, barley, pistachios and cashews, Almonds (>10)	Fruits: nectarines, peaches, pears, blackberries, cherries, plums, prunes, watermelon, lychee
Sweeteners: honey, high fructose corn syrup, agave nectar	Milk products: yogurt, ice-cream, custard, condensed and evaporated milk	Vegetables: garlic, leek, scallion, onion or garlic powder	Sweetners: isomalt, sorbitol, mannitol, xylitol, maltitol, lactitol
Alcohol: sherry, port, rum sweet wines		Fruit: grapefruit, watermelon. Plums, prunes, peaches, figs, dates, currants and banana	Vegetables: cauliflower, celery, snow peas, sweet potato
		Other: teas (oolong, chamomile and fennel), inulin (also appears as chicory root extract), carob	Other: hard candies, toffee, jams and preserves, chewing gum, chocolates, protein powders, baked goods, cough drops and throat lozenges

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

and as a component of the polysaccharide fructan. Fructose consumption has increased in the U.S. diet in recent years. The prevalence of high-fructose corn syrup used as a sweetener in various foods increased from 16% in 1977 to 42% in 1998 and has remained stable at that rate.[2] Fructose is absorbed by 2 transporters GLUT-2 and GLUT-5, which are located in the brush border epithelium of the small intestine. Absorption through the GLUT-2 pathway is facilitated by ingestion of glucose, but the GLUT-5 pathway is independent of glucose coadministration.[3] Approximately half the population cannot tolerate 25 grams of fructose.[4] With the average consumption of fructose ranging from 11–54 grams a day, the increasing use of fructose as a sweetener exposes many patients to high doses of fructose.

An exception to the absorptive mechanisms described previously is the handling of dietary fiber. Fiber is a complex polysaccharide that cannot be absorbed and passes through the gastrointestinal (GI) tract into the stool. Colonic bacteria may metabolize some parts of dietary fiber.

Physiologic Effects of FODMAPs

Effect on intestinal water. The effect of high FODMAP diets has been studied in humans with an ileostomy by examining the fluid effluent from the ileostomy. Other studies have measured intestinal water by using magnetic resonance imaging to quantify intestinal water.[5,6] High FODMAP diets increase intestinal water. This may contribute to pain because of intestinal distention in patients with visceral hypersensitivity and diarrhea as a result of the increased water content of luminal content.[7] Poorly absorbed carbohydrates such as the FODMAPs increase intestinal water by their osmotic activity.[8]

Effects on colonic gas. Passage of undigested or unabsorbed short-chain carbohydrates into the colon provides a substrate for colonic bacteria to produce hydrogen and methane. Studies in healthy individuals and patients with irritable bowel syndrome using magnetic resonance imaging show a significant increase in colonic gas with high FODMAP diets. In patients with irritable bowel syndrome, the increased gas is associated with the development of abdominal symptoms.[9,10] Studies using magnetic resonance imaging show that polysaccharides such as inulin commonly derived from plant products such as chicory root increase colonic gas in both healthy individuals and patients with irritable bowel syndrome and are associated with symptoms in patients with irritable bowel syndrome.[5] A double-blind, placebo-controlled trial of the administration of a fructan (maltodextrin) to children with irritable bowel syndrome showed a significant worsening of bloating, flatulence, and abdominal pain symptoms with fructan exposure.[11]

Effects on short-chain fatty acids and visceral hypersensitivity. In addition to the production of methane and hydrogen, the fermentation of short-chain carbohydrates in the colon results in the production of short-chain fatty acids. An important feature of functional gastrointestinal disorders such as irritable bowel syndrome is the heightened sensitivity of these patients to gut stimulation or distention, a

condition termed *visceral hypersensitivity*. Short-chain fatty acids in luminal contents have been shown create visceral hypersensitivity in animal studies.[12,13] Low FODMAP diets are associated with a decrease in liposaccharides (a complex of fat and polysaccharides) in the luminal content of the colon.[11] Intracolonic administration of fecal supernatant from patients with irritable bowel syndrome induces visceral hypersensitivity in rats.[11] Administration of a lipopolysaccharide antagonist blocked the increase and fecal supernatant from healthy individuals, and patients with irritable bowel syndrome on a low FODMAP diet did not have an effect on visceral hypersensitivity.[11] Low FODMAP diets may therefore alter visceral sensitivity by changing the composition of luminal contents (decreasing luminal short-chain fatty acids and liposaccharides). Short-chain fatty acids have a beneficial effect on epithelial function, and therefore concerns remain about the prolonged use of low FODMAP diets on colonic health and the risk of colon cancer.[8] There are a number of limitations with the studies that have been performed to date, including small sample sizes, conflicting results, and difficulties with the measurement of short-chain fatty acids in the ascending colon.[8]

Effect on the microbiome. The gastrointestinal tract harbors a large number of organisms in an ecosystem that is unique for the individual and relatively stable over time.[14] This ecosystem consists of luminal bacteria and bacteria that are adherent to the mucosal surface. The microbiota communicates with wall of the organ and can influence function. The 2 main families or phyla of organisms are Firmicutes and Bateroidetes that together make up 90% of the microbiome.[15] Alterations in the microbiome could change the cross-talk between the bacteria and intestine, altering function and creating symptoms. Diets that differ in FODMAP content have been shown to have an effect on the gut microbiome of the host.[16] In patients with irritable bowel syndrome, symptoms improved on a low FODMAP diet, but concentrations of bifidobacter (a beneficial organism in the colon) decreased.[17,18] A probiotic coadministered with the low FODMAP diet restored bifidobacter concentrations.[15] A small study showed that a 3-week low FODMAP diet when compared with a high FODMAP diet resulted in a higher abundance of Adlercreutzia, a genus that uses hydrogen.[17] Investigation into the effects on the FODMAP diet on the microbiome are in their infancy.

Effect on the metabolome. The metabolome refers to the complete set of small-molecule chemicals found within a biological sample. Within the human body there is an endogenous metabolome and also a food-related metabolome, which is of growing interest. The food metabolome is defined as the part of the human metabolome directly derived from the digestion and biotransformation of foods and their constituents. In a randomized, controlled, single-blind trial, McIntosh et al[19] evaluated the effect of low and high FODMAP diets on the food-related metabolome by measuring histamine, p Hydroxybenzoic acid, and azelaic acid in the urine of patients with irritable bowel syndrome. In patients on a high FODMAP diet, urinary levels of histamine increased significantly, whereas histamine levels dropped in patients randomized to the low FODMAP diet. Histamine is an endogenous amine that is thought to play a role in irritable bowel syndrome and studies blocking histamine have shown a benefit in patients with this disorder.[20] A number of other agents may be involved in the genesis of symptoms in irritable bowel syndrome, but additional research is necessary in this area.

Disease States

Irritable Bowel Syndrome

Irritable bowel syndrome is a common and debilitating medical condition that is associated with abdominal pain, bloating distention, and changes in bowel habit. No single curative treatment exists, and patients often report an association of symptoms with certain foods. A detailed review of the criteria for a diagnosis may be found elsewhere.[21]

Short-term studies (4–6 weeks) on FODMAP restriction in irritable bowel syndrome. Of the patients in various studies, 50%–80% report an improvement of their symptoms on a low FODMAP diet. A recent meta-analysis evaluated 6 randomized controlled trials and 16 nonrandomized trials and reported substantial improvements in abdominal pain, bloating, and overall symptoms with odds ratios ranging from 1.75–1.81.[22] Dietary intervention with low FODMAP dietary education when compared with sham (placebo) dietary intervention has shown a substantial benefit for dietary advice given by a dietitian when compared with placebo with regard to irritable bowel syndrome symptoms.[15]

Long-term results of FODMAP restriction on irritable bowel syndrome. The evidence for long-term efficacy of a low FODMAP diet in irritable bowel syndrome is limited in quality and in the number of studies available. A dietary strategy of reducing fructose and fructans was effective in alleviating symptoms in 74% of patients at 14 months.[23] The study was small, and recall bias limits the validity of the observed benefit. A randomized trial comparing gut-directed hypnotherapy with a low FODMAP diet evaluated patients at 6 months and reported that 82% of patients in the diet therapy group had improved symptoms when compared with their baseline. Hypnotherapy achieved similar results, but the numbers of patients in each group were small ($n = 25$).[24] A retrospective study of patients with irritable bowel

syndrome followed for 16 months on a low FODMAP diet suggested that one third of patients continued to adhere to the diet, whereas 84% of patients used a modified low FODMAP diet. Of the patients, 54% used the diet on and off based on symptom severity; 54% of patients reported a partial improvement in symptoms and 32% reported complete resolution.[25] The British Dietetic Association recommends the low FODMAP diet as a second-line strategy with dietary advice to be provided by a dietitian.[26]

Nonceliac gluten sensitivity. Nonceliac gluten sensitivity is a disorder characterized by abdominal symptoms that improve after gluten withdrawal in the absence of celiac disease. This is one of the fastest growing segments of the food industry in North America, and the sale of gluten-free foods is expected to reach $7.5 billion in 2020.[27] In a double-blind crossover trial of patients with irritable bowel syndrome and nonceliac gluten sensitivity, Biesiekierski et al[28] administered a low FODMAP diet for 2 weeks followed by high-gluten (16 g gluten/day), low-gluten (2 g gluten/day and 14 g whey protein/day), or control (16 g whey protein/day) diets for 1 week. In all patients, symptoms improved significantly on a low FODMAP diet and worsened equally when gluten or whey protein was added to the diet, suggesting the lack of a specific effect for gluten in aggravating symptoms. Wheat contains several potential symptom inducers including gluten, fructans, and soluble proteins. Wheat-containing foods are a major source of fructans in the U.S. diet. To determine the effects of gluten compared with fructans, Skodje et al[29] studied patients who did not have celiac disease by diagnostic tests and who were on a self-imposed, gluten-free diet for relief of abdominal symptoms.[29] Participants were randomized in a blinded manner to diets containing gluten (5.7 g), fructans (2.1 g), or placebo concealed in muesli bars for 7 days. After a washout period, patients were re-randomized until every patient received each of the dietary interventions. Symptoms were recorded using validated questionnaires. Symptoms of bloating and overall symptoms of irritable bowel syndrome were substantially worse in patients given fructans, but there was no difference in symptoms between those given placebo or gluten-enriched bars. These data suggest that fructans may be the cause of symptoms in many patients who report gluten sensitivity in the absence of celiac disease. From a clinical standpoint, it is reasonable to treat patients who present with gluten sensitivity and who do not have celiac disease with the structured dietary approach for the low FODMAP diet that is described later because their symptoms may be related to fructans in wheat and they may be sensitive to other FODMAPs as well.

Inflammatory bowel disease. Inflammatory bowel disease (Crohn's disease and ulcerative colitis) is known to be affected by changes in the fecal microbiome, and some patients with these disorders report aggravation of symptoms with certain foods. There are limited data on the FODMAP diet in inflammatory bowel disease. In a small study of patients with quiescent Crohn's disease, a low FODMAP diet was associated with changes in the fecal microbiome when compared with a normal Australian diet.[30] Symptoms of irritable bowel syndrome coexist in patients with inflammatory bowel disease. A recent meta-analysis found that patients with inflammatory bowel disease who were still symptomatic despite adequate control of their disease by objective tests (markers of inflammation or endoscopic evidence of active disease) had significant improvement in abdominal symptoms with a low FODMAP diet.[30,31]

Predicting a Response to the FODMAP Diet

Because of the cost and inconvenience associated with the low FODMAP diet, a number of strategies are being evaluated to determine if a response to the diet can be predicted by diagnostic tests. A recent study suggests that fecal bacterial profiles using a commercially available assay may predict a response to the FODMAP diet in irritable bowel syndrome. Bacterial abundance was higher in nonresponders to the low FODMAP diet when compared with responders.[32,33] In a small recent study, the measurement of volatile organic compounds in stool using a low-cost assay predicted a response to a low FODMAP diet in 100% of patients.[34] Fructose and lactose breath testing are not predictive of a response to a low FODMAP diet.[35]

Instructing Patients on the FODMAP Diet

The management of a FODMAP diet in clinical practice has been proposed as consisting of the following 4 stages (Figure 1): (a) initial dietitian visit for FODMAP restriction, (b) 4–6 week dietitian visit for FODMAP reintroduction and (c) elective third visit for FODMAP personalization, and (d) long-term follow-up of irritable bowel syndrome and nutrition status.[36] During the first visit, there is a detailed dietary assessment including an evaluation of dietary preferences and foods known to cause symptoms. A nutrition assessment is also useful as some patients may lose weight on the FODMAP diet and the long-term nutrition consequences await definition. A description of the FODMAP diet, the association of FODMAPs with symptoms, and the results of FODMAP withdrawal are provided along with counseling on FODMAP restriction. Table 1 provides a list of common foods containing FODMAPs. The initial phase of management consists of removal of all the potential sources of FODMAPs to reduce their concentration in the diet below the threshold of symptom generation. It is important to emphasize to the patient that the diet is not permanent but compliance with the initial phase is important to determine if the patient is going to be a responder to dietary intervention. The importance of

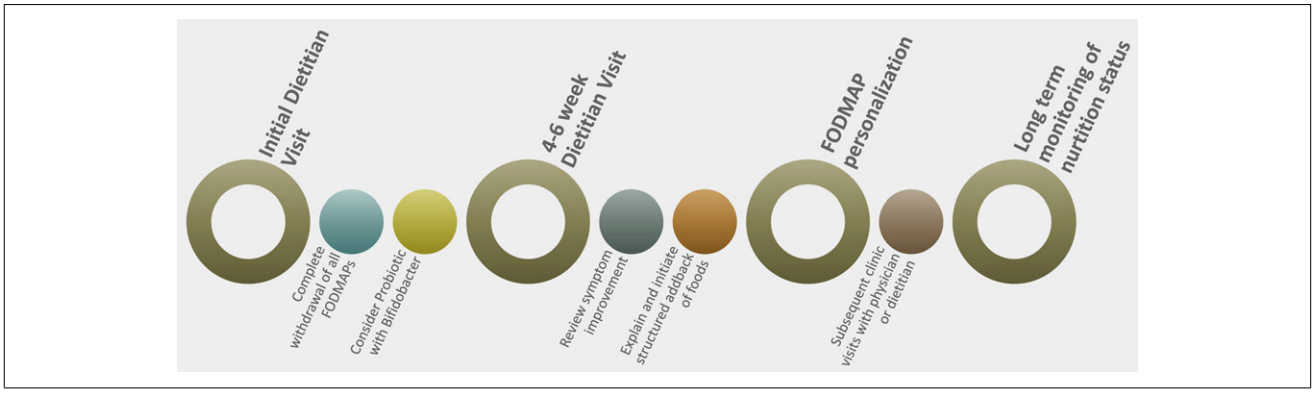

Figure 1. Timeline for fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAP) intervention.

fructans in wheat (as opposed to gluten sensitivity) should be explained. Some patients need a discussion of other diets that they may have tried with varying benefits. A number of diets are described in books and on the internet, including the specific carbohydrate diet, the paleo diet, and the Candida diet. Some of these diets restrict FODMAPs and can result in symptom improvement, but the scientific basis for these diets is inadequate and there is no structured mechanism to reintroduce foods into the diet. Our approach to the first visit for dietary intervention has evolved from giving the patient a handout (which was ineffective) to a structured hour-long visit when the patient meets with the dietitian and the gastroenterologist. The existing therapeutic relationship with the physician is an important part of the management of irritable bowel syndrome and can be used to reassure the patient that they can follow the diet and to enhance compliance with diet therapy.[37,38] Patients frequently ask questions regarding the use of alcohol. Alcohol can cause gastrointestinal symptoms by itself. Beer is low in FODMAPs despite its origins in barley and rye because the fermentation process destroys many fructans. Rum and fortified wines such as sherry and port contain high amounts of fructose and are forbidden in the initial phase. Dry wines (defined as <4 g of sugar per liter) are safe during the initial phase and include varietals such as sauvignon blanc, albarino, and chardonnay in the recommended dose of 150 mL. Whiskey, vodka, and gin are low FODMAP alcohols in a dose of 30 mL per day. The major risk of FODMAP exposure comes from the mixers used with these drinks, such as tonic water and soda. Exercise enthusiasts need to be made aware of chicory root in energy bars, which often cause distress during exercise because of their high fructan content (Table 1). The duration of the initial restrictive phase is in a state of evolution because of the effects of the low FODMAP diet on the microbiota. Randomized controlled trials have generally restricted FODMAPs for 6 weeks or longer, but recent descriptions of a reduction in bifidobacter in the colon have prompted many groups to reevaluate the duration of complete FODMAP withdrawal. A 4-week period of complete FODMAP withdrawal is considered adequate.[35] Supplementing with a probiotic containing bifidobacter has been shown to be effective in replenishing the microbiome and should be discussed with the patient.

Structured Reintroduction

There is substantial evidence from randomized controlled trials for the FODMAP withdrawal phase, but little structured evidence on the best method to reintroduce foods or the order in which they should be reintroduced. Individual centers have developed their own strategies for the structured addition of foods back to the diet. Our technique is illustrated in Table 2, and the instructions provided to the patient are summarized in Figure 2. We typically schedule a 30-minute dietitian visit to explain the strategy of gradual dose escalation of foods shown in Table 2. A daily symptom chart is provided to the patient, and symptoms are recorded every day. For example, with lactose addition, a half cup is ingested on Monday, 1 cup on Tuesday, and 1½ cups on Wednesday. If the patient develops symptoms on Monday, the experiment is stopped for that week and lactose is listed as a substance the patient cannot tolerate. If the patient is able to tolerate lactose, the experiment is ended on Wednesday. From Thursday–Sunday, the patient returns to the low FODMAP diet that was prescribed for the preceding 4 weeks. On Monday, the next agent on the list is tried using the same protocol. At the end of the structured reintroduction, the patient will know the foods that cannot be tolerated even in low doses. Other foods may be tolerated but in limited amounts, and some foods may generate no symptoms at all. Based on these responses, a diet for long-term use that avoids some foods, limits others, and permits others is crafted for the patient. Symptoms are recorded every day, and it is immediately apparent to the patient whether lactose can be tolerated and at what dose. The strategy is repeated in subsequent weeks until complete. A recent study showed that patients who were

Table 2. Structured FODMAP Reintroduction Plan.

Challenge week	What to eat on challenge days
Week 1: lactose	½ cup milk or ¾ cup plain yogurt (without sweeteners or other FODMAPs)
Week 2: fructose	½ mango or 1–2 tablespoons of honey
Week 3: polyols-sorbitol	Blackberries 3–10 or ¼ avocado
Week 4: polyols-mannitol	1/3 cup cauliflower or ¾ cup sweet potato
Week 5: fructans-wheat	2 slices of whole wheat bread or 1 cup cooked pasta
Week 6: fructans-onion	1 tablespoon diced onion
Week 7: fructans-garlic	1 clove of garlic
Week 8: galacto oligo-saccharides	½ cup kidney beans, black beans, or thawed peas or 15–25 almonds

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

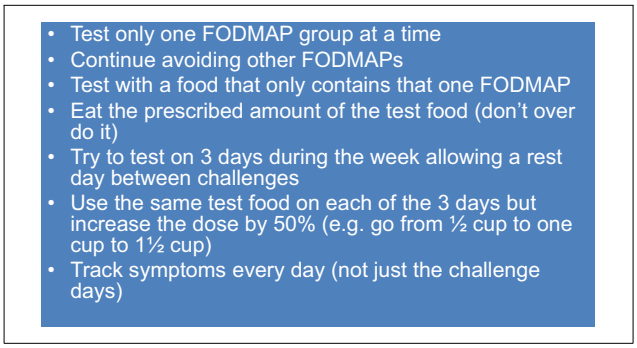

Figure 2. Principles of food reintroduction for patients. FODMAP, fermentable oligosaccharides, disaccharides, monosaccharides, and polyols.

initially treated with a low FODMAP diet and were then allowed to liberalize their diet using a structured approach were able to maintain the symptom improvement seen in the highly restrictive phase and were able to increase the amount of fiber in the diet. Interestingly, the microbiome was not affected in these patients.[39]

Patient Support

Some patients welcome support tools and applications that help them to choose low FODMAP foods. Table 3 lists resources that our patients have found useful in helping them navigate the FODMAP diet. They include an app that can be used on mobile devices to identify the FODMAP content of foods, charts that identify low and high FODMAP-containing foods, recipes, and support from others on the same journey.

Long-Term Monitoring of Nutrition Status

The effects the modified personalized FODMAP diet on the gut microbiome are being actively studied as is the benefit of adding probiotics. There is little information from carefully conducted trials regarding the long-term nutrition impact of the FODMAP diet. In one study, iron intake was unaffected, but calcium intake decreased and overall caloric intake declined in some patients.[14,40] In our experience, some patients lose a small amount of weight in the initial 4–6 weeks of dietary FODMAP restriction. Some patients choose to follow a very restricted diet, and future research will help determine if micronutrient deficiencies occur when these diets are administered long term. Monitoring for micronutrient deficiencies should be individualized based on the degree of dietary restriction.

FODMAPs in Enteral Feeding

FODMAPs may be important in enteral feeding. Diarrhea is a commonly encountered problem with enteral feeding in clinical practice. The FODMAP content of the enteral feeding solution may play a role in the genesis of symptoms. A retrospective study of patients with diarrhea caused by enteral feeding in Australia suggested that a longer hospital stay and a longer duration of enteral feeding were risk factors for diarrhea. Formula FODMAP levels in that study ranged from 10.6–36.5 g/day. A low FODMAP enteral formula was associated with a 5-fold reduction in diarrhea rates.[41] In a randomized, controlled trial of a low, moderate, and high FODMAP enteral feeds in Korea, Yoon et al[42] demonstrated a significant reduction in diarrhea and improvement in nutrition parameters and clinical outcome in patients randomized to the low FODMAP enteral feeding formula. Quantifying FODMAPs in enteral formulas has proven difficult because of the interference with in vitro assays of fructans and raffinose caused by the maltodextrin content of the formula.[43] At the present time, there is no comprehensive list of low FODMAP-containing enteral formulas in the United States, and the FODMAP content of Australian enteral feeding formulas described by Halmos et al[41] may not apply to North America. Some enteral feeding formulas contain fructose and others contain inulin, and these are likely to have a high FODMAP content. Controversy persists regarding the use of fiber supplements in enteral tube feeding, and this debate has recently been summarized elsewhere.[44] It should be noted that many enteral feeding formulas supplemented

Table 3. Resources for Patients Being Started on the FODMAP Diet.

Resource	Cost	Link	Comment
Monash University Mobile App	$12.99	Apple and android app stores	Links to an extensive database of FODMAP containing foods
Low FODMAP recipes & support group	Free	https://www.facebook.com/groups/743558315679493/	Recipes and support group
Low FODMAP foods	Variable	https://www.fodyfoods.com http://trueselffoods.com	Sites for low FODMAP foods including energy bars
Reintroducing FODMAPs book	$17.99	https://reintroducingfodmaps.com/	A book on FODMAP reintroduction of patients who need additional information
A little bit yummy	Free	https://app.alittlebityummy.com/meal-plan/	Multiple FODMAP resources
FODMAP cookbooks	Variable	Online book stores	FODMAP Cookbooks written by registered dietitians
Low and high FODMAP checklists	Free	http://www.katescarlata.com/low fodmapdietchecklists/	Checklist for low and high FODMAP containing foods

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

with fiber have another FODMAP added to the solution (fructo-oligosaccharides).[43] Further work is urgently needed in this area.

Future Directions With FODMAP and Dietary Therapy

Future research is directed at test strategies to determine who will benefit from the low FODMAP diet. We need more data on the long-term outcome of treatment with the low FODMAP diet and its effects on the microbiome and the nutrition status of the individual. An important area of research is in food science. The development of enzymes that break down fructans in food could help enormous numbers of people who currently purchase gluten-free products at substantial cost.

Acknowledgments

I am grateful to Amanda Motl, RD, for the care of our patients and for the information on the reintroduction phase of FODMAP dietary therapy.

Statement of Authorship

N. Vakil contributed to conception/design of the research; N. Vakil contributed to acquisition, analysis, or interpretation of the data; N. Vakil drafted the manuscript; Nimish Vakil critically revised the manuscript; and N. Vakil agree to be fully accountable for ensuring the integrity and accuracy of the work.

Supplementary Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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