Controversies and Recent Developments of the Low-FODMAP Diet

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Abstract: The low–fermentable oligo-, di-, and monosaccharide and polyol (FODMAP) diet is a 2-phased intervention, with strict reduction of all slowly absorbed or indigestible short-chain carbohydrates (ie, FODMAPs) followed by reintroduction of specific FODMAPs according to tolerance. The efficacy of the elimination phase of the FODMAP diet is well established, but the success of maintaining this diet has been shown in only a few observational studies. How the efficacy of the low-FODMAP diet compares with that of other therapies has received limited attention, but recent studies have shown this diet to be comparable or superior to diets that address eating style and choice of food as well as to gut hypnotherapy. There has been no comparison between the low-FODMAP diet and the gluten-free diet, which moderately reduces FODMAP intake. Mechanistically, dietary FODMAPs have very limited effects on the consistency of bowel actions but seem to suppress the release of histamine. Neither symptom pattern nor breath hydrogen testing for fructose or polyol malabsorption is a useful predictor of efficacy, but analysis of gut microbiota has potential. As a restrictive diet, the low-FODMAP diet carries risks of nutritional inadequacy and of fostering disordered eating, which has received little attention. Strict FODMAP restriction induces a potentially unfavorable gut microbiota, although the impact of this consequence upon health is unknown. This observation puts additional impetus on the reintroduction of FODMAPs according to tolerance during the maintenance phase of the diet. Studies of the low-FODMAP diet in children are few but do suggest benefit. However, such a strategy should be implemented with care due to the psychological and nutritional risks of a restrictive diet. Clinical wisdom is required in utilizing the low-FODMAP diet.

Since the first description of the concept of fermentable oligo-, di-, and monosaccharides and polyols (FODMAPs),[1] as well as the detailed description of the principles of the low-FODMAP diet for patients with irritable bowel syndrome (IBS),[2] there has been a considerable amount of research across the world to understand

whether this diet works, how it compares to other therapeutic approaches, how best to deliver the diet to patients, how to define predictors and examine risks, and how to determine the mechanism of action of the diet. Controversy has arisen over aspects of efficacy and risks, mainly regarding the effect of the diet in its strictest form on the gut microbiome. This article focuses on controversial issues and recent developments in the application of the low-FODMAP diet, particularly in children.

Efficacy of the Low-FODMAP Diet in Patients With Irritable Bowel Syndrome

The low-FODMAP diet is a 2-phased intervention, with strict reduction of all dietary FODMAPs followed by reintroduction of specific FODMAPs according to tolerance. The efficacy of the elimination phase of the low-FODMAP diet for overall gastrointestinal symptom relief in adult patients with IBS has been seen in randomized, controlled trials; a blinded, randomized, rechallenge study; and observational studies that have been reviewed in detail elsewhere[3,4] as well as in a meta-analysis.[5] These studies have shown that 50% to 86% of patients have a clinically meaningful response to the low-FODMAP diet. In contrast, the success of maintenance (the reintroduction phase of the diet) has been studied less (in only a few observational studies).[6,7] Due to the difficulties of designing an appropriately blinded, randomized, longer-term, interventional study, the evidence base for maintenance will likely remain less solid.

There remains controversy as to whether the low-FODMAP diet has sufficient evidence to be considered a legitimate first-line therapy.[8-10] Several issues have been raised, including inappropriate comparator placebo arms, failed blinding of the diet, short durations of the controlled trials, and the small number of patients in the trials. An additional criticism is that Rome subgroups based upon predominant bowel habit have not been specifically studied. Thus, efficacy has not been related to bowel habit in the published studies. The idea that Rome III criteria define populations with different therapeutic responses might be appropriate for drugs targeting specific pathogenic pathways or symptoms, especially bowel habits, but extrapolating this to studies of the low-FODMAP diet cannot be justified. One reason is that, although satisfaction with stool consistency improves with the low-FODMAP diet, more objective stool consistency (judged by fecal water content or an independent observer's assessment of stool) does not improve with the diet.[11] The use of composite endpoints, such as those mandated by US and European authorities for drug trials in IBS, may not be applicable in this setting. Although many of the

methodologic criticisms have some merit, the weight of the evidence for the diet's efficacy counters the weight of these criticisms. Nevertheless, these criticisms must be kept in mind when considering the quality and strength of the results of the randomized, controlled trials and observational studies.

The Mechanism of Action of FODMAPs

The mode of action of FODMAPs in inducing symptoms is most likely due to stimulation of mechanoreceptors as a response to luminal distension from a combination of increased luminal water content from the osmotic effect, especially in the small intestine,[12] and from the release of gases, mostly carbon dioxide and hydrogen, from the bacterial fermentation of oligosaccharides and the proportion (if any) of malabsorbed fructose, polyols, and lactose.[3] Such stimulation can lead to ascending messages that might be interpreted as pain or bloating; reflex responses to the diaphragm and anterior abdominal wall, leading to increased abdominal distension; and effects on motility with potential change in bowel habits. Although large doses of FODMAPs (eg, lactulose) can induce diarrhea, the amount needed is usually much greater than that consumed in diet. This is relevant because many researchers believe that a low-FODMAP diet is best for those with diarrhea-predominant IBS (IBS-D). However, this belief is inconsistent with data from randomized, controlled clinical trials, where such patients do not do better than those with constipation-predominant IBS[3-5] and where water content of the stools and gut transit change minimally in response to the diet.[11] The release of short-chain fatty acids (SCFAs) from fermentation of FODMAPs is also likely to influence motility.

Whether alteration of FODMAP intake affects visceral sensitivity has not been directly assessed. However, SCFAs can alter such sensation,[13] and the release of histamine,[14] presumably a neuroinflammatory response that involves mast cell activation, might also change visceral sensitivity. Because alteration of FODMAP intake changes the gut microbiome, other pathogenic mechanisms for modulating symptoms might also play a role. The poorly documented observation that some patients are more sensitive to FODMAP exposure after a period of restriction—much like the transient bloating effect of increasing fiber content—might suggest that adaptation of the microbiota or enteric nervous system might also be important in mechanistic pathways. Thus, although the reduction of luminal distension remains the important mechanism by which FODMAPs induce symptoms, the pathways proximal to this are just starting to be unravelled, and other mechanisms also may well play roles.

Delivery of the Low-FODMAP Diet in Practice

The majority of the data in the published literature on the efficacy of the low-FODMAP diet derive from dietitian-delivered dietary education and sometimes via specially trained nurses.[4] There are no studies in which the diet has been self-taught via information from printed material or the Internet. Especially given the high prevalence of IBS, the shortage of dietitians trained in the use of the low-FODMAP diet and the limited access to reliable FODMAP data represent significant obstacles to its use in clinical practice. Furthermore, teaching patients about the low-FODMAP diet is labor-intensive, with initial appointments typically lasting 1 hour. Whigham and colleagues compared the effectiveness of group education sessions with one-on-one dietetic counseling and found that the proportion of patients with adequate symptom control at follow-up 6 to 10 weeks later did not differ significantly between the groups (P=.895).[15] Although 39% of patients would have preferred individual counseling, the authors suggest that peer support, sharing of experiences, and shorter waiting times make group education sessions worthy of consideration. Similarly, Kinrade and colleagues found group education for low-FODMAP dietary therapy to be a feasible and effective method for promoting symptom control in patients with IBS.[16] The authors surveyed 17 patients upon completion of the 8-week low-FODMAP diet and found that 82% (14/17) reported satisfactory relief of gut symptoms.

Suboptimal dietary advice and inaccurate FODMAP composition data may lead to disappointing responses to the low-FODMAP diet. This highlights the need for training for health care professionals as well as access to accurate and relevant (ie, current and local) FODMAP food composition data. The Monash University Low-FODMAP Diet Smartphone Application has facilitated access to up-to-date FODMAP composition of foods.[17] This application contains detailed and ongoing food analysis for food products from 10 countries across 4 continents.

The Low-FODMAP Diet Compared to Alternative Therapy

Although the evidence from randomized studies consistently indicates that the low-FODMAP diet is superior to placebo approaches (diet or observation only), it is important to define how its efficacy compares with that of other therapeutic approaches applied in patients with IBS. Although no other dietary therapies have evidence of efficacy from randomized, placebo-controlled studies, the low-FODMAP diet has been compared directly or indirectly with other dietary strategies and

nonpharmacologic approaches that have been directed at IBS in general.

Standard Dietary Advice

There is currently no widely recognized standard for dietary advice for patients with IBS. However, the National Institute for Health and Care Excellence (NICE) from the United Kingdom has published dietary guidelines that cover a variety of aspects, including style of eating and food choice, although the efficacy of these guidelines has not been evaluated in placebo-controlled trials. Three studies have compared a low-FODMAP approach with a local version of the NICE diet. The first, from the United Kingdom, was a nonrandomized comparison performed at a time when skepticism of the low-FODMAP approach was prevailing.[18] The study could arguably be regarded as a competition between 2 approaches. The low-FODMAP approach was superior, with response achieved in 76% of patients compared with 54% of patients who used the NICE diet. In contrast, a recent randomized study from Sweden reported similar responses between the low-FODMAP diet and the traditional IBS diet.[19] The traditional diet included advice regarding style of eating (eg, have regular meals, do not eat too much at once, eat slowly) and advice on food choice (eg, reduce intake of fat, spicy foods, coffee, alcohol, onions, cabbage, and beans; avoid carbonated beverages, chewing gum, and using artificial sweeteners ending with "-ol"). The traditional diet included reduced intake of FODMAPs, although the measured intake somewhat surprisingly revealed only a small reduction of FODMAPs, according to assessment via an unreported database. The low-FODMAP diet mainly impacted lactose intake (which might have minimal relevance in a Swedish cohort) rather than intake of other FOD-MAPs. Both interventions were delivered by dietitians and were equally effective. Thus, 19 of the 33 patients (57%) who completed the low-FODMAP diet and 17 of the 34 patients (50%) who completed the traditional IBS diet met the predefined definition of response at 4 weeks of at least 50% reduction in IBS Symptom Severity Score. However, the response rate of 57% for the low-FODMAP diet was well below the expected rate; rates of 68% to 86% have been reported in previous observational and randomized studies.[3-5] The third study, from the United States, was restricted to patients with IBS-D, and the traditional diet was modified from NICE guidelines in that foods high in FODMAP content were not restricted.[20] Although the primary endpoint (overall satisfaction) was not different between the traditional and low-FODMAP diets, analysis of multiple secondary endpoints, particularly abdominal pain and bloating, showed clear superiority of the low-FODMAP diet.

The traditional IBS diet partly reduces FODMAP intake. Limited evidence suggests that at least 75% of patients can reintroduce FODMAPs and still have good symptom control with only mild FODMAP restriction.[7] This raises the question of whether patients need such a strict elimination phase. This issue was directly assessed in a recent randomized, controlled trial of 87 patients with IBS in whom high- and low-FODMAP rye bread was the only dietary difference.[21] Although some symptoms and breath hydrogen production were reduced with the inclusion of the low-FODMAP bread, the patients did not improve overall. This study provides evidence for a broader change in diet rather than just limiting dietary change to major FODMAP-containing food.

Gut-Directed Hypnotherapy

Gut-directed hypnotherapy has been subject to randomized, controlled trials, which have indicated efficacy broadly in IBS cohorts.[22] A recent randomized clinical trial compared the short- and long-term efficacies of gut-directed hypnotherapy to the low-FODMAP diet and showed similar durable effects for the relief of gastrointestinal symptoms.[7] Seventy-four patients were randomly allocated to receive therapy via hypnotherapy (n=25), diet (n=24), or both (n=25). Clinically significant improvements in overall gastrointestinal symptoms were observed from baseline to week 6 in 72%, 71%, and 73% of patients, respectively. This improvement persisted 6 months posttreatment in 74%, 82%, and 54% of patients, leading the researchers to conclude that gut-directed hypnotherapy showed efficacy in a similar proportion of patients as the low-FODMAP diet but that these modalities did not show evidence of additive effects when used concurrently. Although IBS quality of life was significantly improved across all groups, hypnotherapy resulted in superior improvements in psychological indices. Consequently, when expertise is available to deliver gut-directed hypnotherapy, this modality should certainly be considered as an alternative to dietary management.

Gluten-Free Diet

Wheat is considered to be one of the most common foods that precipitates abdominal pain, bloating, and/or change in bowel habits.[23] An Australian survey of 1184 adults found that 8% avoid wheat or are gluten-free to relieve such symptoms.[24] One of the most controversial debates is which component(s) of wheat are responsible for the clinical effects of protein (primarily gluten) or carbohydrate (primarily FODMAPs),[23] as indigestible oligosaccharides, fructans, and galacto-oligosaccharides coexist with gluten in wheat, rye, and barley.[25] The dilemma from a clinical perspective is which of these 2 evidence-based approaches to recommend: the gluten-free diet (GFD) or low-FODMAP diet.

Although no comparative studies have been performed between the low-FODMAP diet and GFD, an observational report of the benefits of the GFD in patients with IBS-D has indicated response rates similar to those for the low-FODMAP diet (29 of 41 patients; 71%).[26] Twenty-one of the 29 patients reported that they would continue their GFD and, indeed, all reported still following it and experiencing symptom improvement at 18-month follow-up. Likewise, the very low–carbohydrate diet, consisting of 20 g of carbohydrates per day (and reductions of both FODMAPs and gluten), administered for 4 weeks in 13 obese patients with IBS-D reduced stool frequency and consistency and improved pain scores and quality of life.[27] These observations, while impressive, do not help in determining whether the amelioration of symptoms is due to placebo, the absence of gluten, the reduced intake of FODMAPs that coincides with avoidance of gluten-containing cereal products, or another reason.

Only 1 randomized, controlled trial has compared gluten-containing diet to GFD in patients with IBS.[28] In a 4-week study in which 45 patients with IBS-D received gluten-containing diet or GFD, bowel frequency was reduced by less than 1 movement per day on gluten diet, and no changes were observed for stool consistency or ease of passage. The effects on barrier function were assessed in that study by dual sugar permeability tests and the expression of zonula occludens-1, claudin-1, and occludin via immunohistochemistry. Although changes were reported as gluten-mediated increases in permeability for some indices, correction for multiple comparisons negated the statistical significance of any of these. Furthermore, the claim that gluten was responsible was not substantiated.[25] No attention was paid to FODMAPs in this study.

Patients with IBS-like symptoms with or without extraintestinal symptoms in whom celiac disease and wheat allergy have been excluded are referred to as having nonceliac gluten sensitivity (NCGS). Some will have undiagnosed celiac disease.[29] Approximately 1 in 4 have uncontrolled symptoms despite gluten avoidance, and other food intolerances are identified in 65% of patients.[30] This was evident in a randomized, placebo-controlled, crossover, rechallenge study in which all of the 36 patients experienced improvement in gastrointestinal symptoms when placed on a low-FODMAP diet during the run-in period, and none had repeatedly consistent exacerbation of symptoms specifically on ingestion of FODMAP-depleted gluten during the blinded rechallenge phases.[31] One logical interpretation of such data is that the FODMAP reduction associated

with avoidance of wheat, rye, and barley—all high in FODMAPs—led to partial response, and more extensive FODMAP restriction further improved that response. A similar lack of gluten specificity in the induction of symptoms in the vast majority of patients with self-reported NCGS has also been observed in 3 other randomized studies,[32-34] indicating that gluten is seldom the dietary culprit.

For the majority of patients with IBS, it is important to distinguish between gluten or FODMAP intolerance. When clinicians help patients identify trigger food(s) and the quantities that induce symptoms, they are able to minimize dietary restrictions, ensure appropriate substitution of the foods excluded, and optimize dietary variety. Thus, they can minimize the associated risks of the low-FODMAP diet and GFD, namely micronutrient deficiencies, poor dietary fiber, dysbiosis, and disordered eating.[23] To direct dietary management of IBS, it is vital to have a clinical pathway, such as the one suggested by Biesiekierski and colleagues,[30] as well as to adhere to the gold standard of food intolerance testing (ie, food exclusion to achieve symptom resolution followed by gradual food reintroduction and subsequent symptom induction to identify tolerance).[35] This dietary management is only possible with an appropriately qualified dietitian who has knowledge of FODMAP and gluten content of the local food supply.

Predictors of Response

Biomarkers and clinical features that predict both an individual patient's response (or lack of response) to the low-FODMAP diet and sensitivity to specific FODMAP types (ie, fructose in excess of glucose, lactose, sorbitol, mannitol, and oligosaccharides) would enable clinicians to choose the most suitable and least intrusive therapeutic option. To date, there are no data suggesting that symptom patterns accurately foretell issues with FODMAPs in general or with specific FODMAPs.

Breath Hydrogen Testing

Breath hydrogen testing continues to be widely used in clinical practice to direct dietary management despite uncertainties with methodologies, poor reproducibility of results, and interpretative difficulties.[3] The need to restrict each FODMAP is based on whether the specific FODMAP is malabsorbed (ie, breath hydrogen is increased) after ingestion of that sugar and whether this is associated with symptoms. Breath hydrogen testing is of unlikely benefit for oligosaccharides, which are always malabsorbed. Rather, this tool has been applied to lactose to determine the presence of hypolactasia and has also been applied to slowly absorbed FODMAPs

(fructose, sorbitol, and mannitol) to determine whether any of the ingested dose enters the colon. It is with the latter application that controversy exists. The degree of malabsorption depends upon the dose of the FODMAP ingested (eg, 80% of patients will malabsorb a 50-g load of fructose, but only 10% will malabsorb 25 g[36]) and the small intestinal transit time as much as inherently reduced absorptive capacity. The reproducibility of detecting fructose malabsorption is poor,[37] indicating that the results at any one point in time do not reflect underlying absorptive capacity. Furthermore, malabsorption of fructose, mannitol, and sorbitol, as shown by an increase in breath hydrogen, has no relation at all to the induction of gastrointestinal symptoms.[37,38] This is likely due to the distending osmotic effect of the slow absorption of those FODMAPs in the lumen of the small intestine. The other issue with the overuse of breath hydrogen testing in clinical practice is that it tempts clinicians to preferentially diagnose intolerances rather than deal with the real issue that the patient has IBS. Management of IBS is multimodal, and diet is only one strategy. Current recommendations state that the complete low-FODMAP diet be administered without antecedent breath tests and that specific sensitivities be identified in the reintroduction phase of implementing the diet.

Stool Microbiome Analysis

Recently, there has been considerable interest in studying the microbiome and metabolite profiling. One study of a pediatric population assessed whether symptomatic response to the low-FODMAP diet, based upon pain frequency, was predicted by microbiota at baseline.[39] This was a randomized, double-blinded, crossover trial in which children were exposed to diets of high- and low-FODMAP content for 2 days. To define pre-diet predictors of response, patients were divided into responder, nonresponder, and placebo-responder groups on the basis of the frequency of painful episodes during the 2 dietary interventions. Responders, comprising 24%, were found to have increased baseline abundance of taxa such as *Bacteroides*, *Ruminococcus*, and *Faecalibacterium prausnitzii*, which are known to have greater carbohydrate fermentative capacity. This finding is consistent with the hypothesis that efficacy of the low-FODMAP diet relates to reducing intestinal luminal distension and suggests that patients with enriched microbiota with saccharolytic potential may benefit the most from a reduction in dietary fermentable substrates. To date, no such associations have been found in adult patients,[40] and more data are required from parallel-arm trials of longer duration.

Risks of the Low-FODMAP Diet

Although dietary therapies are generally considered to be benign, they, as with all therapies, are not without risks or adverse effects. The low-FODMAP diet is no exception. Although issues of nutritional adequacy always remain a concern for any restrictive diet, 3 issues of great relevance to the use of the low-FODMAP diet in patients with IBS have been identified.

Inappropriate Use of the Low-FODMAP Diet

One of the practices that has been observed is the use of the low-FODMAP diet by health professionals as a diagnostic test for IBS (personal observations) in place of using a positive diagnostic approach as outlined, for example, by the Rome Foundation.[41] This is likened to the use of GFD to diagnose gluten sensitivity in the community. Such an application is poor medicine, as any patient with gut symptoms may potentially improve with the reduction of FODMAP intake whether the underlying disorder is functional or primarily organic, such as with inflammatory bowel disease (IBD) as outlined below. As with all therapeutic tools, the low-FODMAP diet should be implemented in the appropriate setting.

Altered Gastrointestinal Microbiota

Fructans and galacto-oligosaccharides have prebiotic actions. Their restriction, in the setting of the low-FODMAP diet, may lead to a reduction in beneficial bacteria. Indeed, 2 studies have shown that a diet very low in FODMAPs carried out over 3 and 4 weeks, respectively, is associated with a reduction in the relative abundance of *Bifidobacteria* in feces.[42,43] This is interesting given that studies have demonstrated reduced *Bifidobacteria* in IBS patients compared with healthy controls[44,45] and that a negative relationship between the fecal abundance of *Bifidobacteria* and pain score in IBS has been reported.[45-47] If dysbiosis is causal in IBS (although there is no direct evidence to support this), then the effect of a strict low-FODMAP diet might be counterproductive. Furthermore, strongly butyrate-producing bacteria are markedly reduced in absolute and relative numbers, and mucus-degrading bacteria are increased with strict reduction of FODMAP intake.[43] These effects, if maintained over the long term, might theoretically carry health implications. However, the clinical significance of such changes remains unknown. It should also be noted that studies have not examined the microbiome of patients with IBS following the reintroduction of high-FODMAP foods to tolerated levels, as adherence to a strict low-FODMAP diet is only recommended for 2 to 6 weeks. Given the greater temporal instability of the microbiota in IBS patients vs healthy controls,[48] as well as a greater instability in response to dietary modification,[49] further work is needed to show the true effect of a diet low in FODMAPs, as delivered in clinical practice, on the microbiome of a person with IBS in the medium to long term.

Disordered Eating

There is some evidence that people with gastrointestinal disorders who undergo dietary change may be at increased risk for disordered eating behaviors. Satherley and colleagues systematically reviewed the evidence concerning disordered eating practices in patients with celiac disease, IBS, and IBD, and found that the prevalence rates (5%-44%) were similar to those found in other dietary-controlled health conditions whereby there is a constant need to monitor food intake.[50] The authors hypothesized that, in patients with good dietary management and disordered eating, gastrointestinal symptoms may create food aversion and cause alterations to eating patterns. These individuals may be anxious and concerned with the preparation of their food and experience anxiety around unfamiliar foods, leading them to self-cater and/or avoid social situations around eating. Such behaviors have recently been linked to orthorexia nervosa, a condition in which people restrict their diet based upon its quality.[51] This condition is associated with symptoms such as an "obsessive focus on food choice, planning, purchase, preparation, and consumption; food regarded primarily as [a] source of health rather than pleasure; [and] exaggerated faith that inclusion or elimination of particular kinds of food can prevent or cure disease or affect daily well-being."[50] These traits can be seen in patients who strongly adhere to dietary management. The limited evidence in this area is concerning, as this condition impacts both the physical and psychological well-being of these patients. Regular screening of eating pathology in gastrointestinal clinics could help facilitate appropriate referrals as well as direct clinicians to recommend alternative therapeutic strategies to patients displaying evidence of disordered eating. Hypnotherapy may be a better option for these individuals with IBS by taking the focus off diet and restrictive eating practices.

The Low-FODMAP Diet in Children With Functional Gastrointestinal Disorders

Approximately 5% of school-aged children have IBS according to the Rome III criteria.[52,53] Childhood IBS has a substantial impact on families and the health care system alike, with reports noting that these children have significantly lower quality of life,[54] increased risks for depressive symptoms, social isolation, and school absenteeism.[55] The average cost of diagnostics is estimated to be $6000 per child.[56] Augmenting this burden of

disease is the fact that childhood cases are likely to persist into adulthood.[57] Although popular belief links food intolerances to symptom generation and children report that certain foods exacerbate symptoms,[5] there have been few controlled trials in pediatric cohorts. However, evidence has recently emerged for consideration of a diet low in FODMAPs when treating children with IBS.

Chumpitazi and colleagues conducted a double-blind, randomized, controlled trial of 52 children with IBS, aged 7 to 17 years.[39] Baseline data were collected over 7 days, after which children were provided for 2 days with either a low-FODMAP diet or a typical American childhood diet, which was moderate in FODMAPs. The children then completed a 5-day washout period before crossing over. Thirty-three children completed both arms of the crossover trial and were found to have significantly fewer daily episodes of abdominal pain during the low-FODMAP intervention compared to typical diet intervention (P<.05) and baseline (P<.01). In adults, the maximal response to lowering FODMAP intake is seen by 7 days.[11] Thus, a longer intervention time frame may have allowed for a greater effect size to emerge.

Poorly Absorbed Carbohydrates and Functional Abdominal Pain

Although studies in children on a diet low in all FOD-MAPs are scarce, certain poorly absorbed carbohydrates—namely lactose, fructose, and sorbitol—have long been implicated in the pathogenesis and treatment of childhood functional gastrointestinal diseases (FGIDs). In 1985, Hyams and Leichtner reported that excessive amounts of apple juice caused chronic nonspecific diarrhea in young children who experienced complete recovery after apple juice was eliminated.[58] This finding highlights how modern nutritional practices can play a key role in the pathogenesis and treatment of FGIDs. Moreover, there should be consideration of whether basic nutritional advice for a diet that is varied and balanced (ie, adequate but not excessive in the amounts of food from each of the 5 food groups) will suffice to restore normal gastrointestinal function. Hyams and Leichtner also reported a rise in breath hydrogen following consumption of apple juice.[58] This observation made carbohydrate malabsorption a focus of research in functional gastrointestinal symptoms in adults and children.

The contribution of fructose, lactose, and/or sorbitol to functional abdominal pain was implicated by several open, uncontrolled studies in children. In a study of 32 children with functional abdominal pain, 28% had a positive hydrogen breath test for fructose malabsorption, and 9 of these patients (81%) reported rapid symptom improvement on a fructose-restricted diet, with abdominal pain and bloating remaining significantly reduced at

2 months after the initial breath test.[59] In another cohort of 222 children with functional abdominal pain, 55% had a positive breath test for fructose malabsorption, and 77% (P<.0001) experienced clinical improvement after 2 months on a low-fructose diet.[60] Wintermeyer and colleagues found that 42% of 117 children had a positive hydrogen breath test for fructose malabsorption.[61] Seventy-five of these children followed a dietitian-administrated low-fructose diet for 4 weeks. Pain frequency and intensity improved significantly within 2 weeks of the dietary initiation. In another retrospective study, in which long-term data were available for 118 children with fructose malabsorption, the vast majority of those placed on a diet reduced in lactose, fructose, and/or sorbitol responded, and family satisfaction was reported as very high.[62]

Whether the improvements in pain in these 4 studies were directly attributed to fructose or indeed to the malabsorption of fructose remains uncertain. First, in the absence of a control treatment group, the benefits may have been purely placebo-related. Second, the nature of the diet was unclear. For example, the authors do not comment on whether fructose in excess of glucose alone was restricted or if fructo-oligosaccharides were also eliminated. Third, the relationship of the efficacy to the presence of fructose malabsorption itself was not evaluable, as no dietary change was reported for those without fructose malabsorption (see below). Finally, restriction of polyols (which coexist in foods such as fruits and juice) may have contributed to these positive results. Nevertheless, the open experience did support the concept that altering intake of poorly absorbed, short-chain carbohydrates may be therapeutically useful.

Breath Hydrogen Testing in Children

The aforementioned studies in children assume a positive breath hydrogen test to be a predictor of response to the elimination diet. However, the diagnostic value of the fructose breath hydrogen test is questionable in children. First, the capacity to absorb fructose increases with age up to 10 years. This has significant implications for the performance and interpretation of tests in younger children.[63] Second, as outlined above, studies in adults have shown the results of breath hydrogen tests not to be reproducible.[37] Furthermore, a negative breath test result does not exclude a positive response to fructose restriction. In a blinded, randomized, controlled trial involving 103 children with functional abdominal pain, response to a low-fructose diet was not predicted by a positive fructose breath hydrogen test or by abdominal pain during the test.[64] Finally, a diagnosis of lactose, fructose, and/or sorbitol malabsorption by positive breath hydrogen test leads to the child being labeled with a specific food intolerance

Table. Select Key Points Involving Dietary Manipulation in Children With Functional Gastrointestinal Symptoms

A diagnosis of functional gastrointestinal disorder should be made and the symptoms managed, rather than subjecting children to breath hydrogen tests to provide labels of specific food intolerances.
Children with IBS should initially be advised to • normalize eating by having regular balanced meals and snacks, eating a variety of foods from each of the 5 food groups in adequate but not excessive amounts, and being encouraged to drink water • attempt to open bowels regularly, as children may confuse abdominal pain with the sensation of an imminent bowel movement (which may require dialogue with their school to ensure that toilets are readily available for use during class time, not just during recess and lunch)
In children with ongoing IBS symptoms, a low-FODMAP diet is worth considering but only • under the expert supervision of a specialized dietitian • when the risk of eating disorders is low • when feeding difficulties, such as food refusal and selective eating, are minimal, and, therefore, appropriate low-FODMAP substitute foods will be accepted
If a low-FODMAP diet is successful, a reintroduction program should be instituted, ideally after ≤6 weeks, to minimize restriction according to tolerance to • improve the ability of the child to cope psychosocially • further avoid nutritional compromise • minimize the impact of reduced dietary prebiotics on gut microbiota
If unsuccessful, FODMAP restriction should not be continued.
Any child following a diet with some level of FODMAP restriction should be re-evaluated at regular intervals (eg, every 3 to 6 months) to • monitor nutritional adequacy and growth • screen for disordered eating • ensure that FODMAP restrictions are regularly rechallenged, with high-FODMAP foods reintroduced according to tolerance. Because the capacity to absorb fructose is reduced in young children, tolerance levels may change (ie, increase) as children grow older.

FODMAP, fermentable oligosaccharide, disaccharide, monosaccharide, and polyol; IBS, irritable bowel syndrome.

and may overshadow and distract from the more pertinent diagnosis of IBS. Malabsorption of lactose, fructose, and/or sorbitol has similar frequency in patients with IBS as in healthy subjects.[65] While visceral hypersensitivity in IBS may make this malabsorption relevant to symptom management, unnecessary diagnostic testing may reduce acceptance and distract from a functional diagnosis, namely IBS.[66]

It is established that children under the age of 10 years have a reduced capacity to absorb fructose. It would be important to assess whether young children with IBS are consuming a high-FODMAP diet with excessive amounts of fruit/fruit products, dairy/dairy products, and wheat/wheat products. Furthermore, it would also be important to assess whether normalizing—that is, limiting portions of fruit, dairy, and wheat to reduce dietary intake of FODMAPs—results in symptom resolution.

Dietary Approach in Children With Functional Gastrointestinal Symptoms

Providing evidence-based guidelines for managing functional gastrointestinal symptoms in children is not possible given the number and generally low quality of the published literature. Some guidance in a suggested approach is provided in the Table.

Conclusion

The low-FODMAP diet has a substantial evidence base for efficacy in the management of abdominal symptoms in adult patients with IBS. It has changed paradigms of management and is now being applied in children with IBS and in IBD patients with presumed functional gut symptoms. However, the low-FODMAP diet has been subject to abuse and misinterpretations. It should be applied in appropriate situations with proper education, preferably by a health professional trained in its delivery. Awareness of the risks of the low-FODMAP diet—and indeed any restrictive diet—is paramount, particularly with regard to the impact on nutritional adequacy and promotion of disordered eating in those who are vulnerable. Because of the many gaps in our knowledge and understanding, continuing research into the low-FODMAP diet and other dietary approaches for functional gastrointestinal symptoms is needed.

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