GAVIN PUBLISHERS

Journal of Digestive Diseases and Hepatology

Biesiekierski JR and MasuyI. J Dig Dis Hepatol2017: JDDH-130.

Review Article

The FODMAP Approach: Recent Evidence and Remaining Questions

Jessica R Biesiekierski*, Imke Masuy

Translational Research Center for Gastrointestinal Disorders, University of Leuven, Leuven, Belgium

***Corresponding author:** Jessica Biesiekierski, Translational Research Center for Gastrointestinal Disorders (TARGID), University of Leuven, Campus Gasthuisberg, O&N1, box 701, Herestraat 49, 3000 Leuven, Belgium, Tel: +321630470; Fax: +3216345939 ; E-mail: jessica.biesiekierski@kuleuven.be

Citation: Biesiekierski JR, Masuy I (2017) The FODMAP Approach: Recent Evidence and Remaining Questions. J Dig Dis Hepatol2017: JDDH-130.

Received Date: 16 February, 2017; **Accepted Date:** 03 April, 2017; **Published Date:** 10 April, 2017

Abstract

A group of fermentable oligo-, di-, mono-saccharides and polyols (FODMAPs) found in many dietary components, including grains, vegetables and fruit can precipitate or exacerbate symptoms of irritable bowel syndrome. High-quality evidence, including prospective studies and randomised controlled trials from a variety of countries supports the efficacy of a diet low in FODMAP intake for reducing gastrointestinal symptoms in irritable bowel syndrome. More recent evidence has focused on identifying and understanding predictors of response and how to individualise the diet. As with any restrictive diet, implementation should be undertaken under the guidance of a health care professional to ensure nutritional adequacy and that the re-introduction process is undertaken.

Keywords: Dietary factors, FODMAPs, irritable bowel syndrome

Introduction

The low Fermentable Oligo-, Di-, and Monosaccharide and Polyol (FODMAP) diet is a therapeutic approach for patients with Irritable Bowel Syndrome (IBS) [1]. There is considerable research supporting the concept and principles of the low FODMAP diet, however as with any restrictive diets, it must be implemented with care. Although the efficacy of the diet has been supported by research from across the world, there remain unanswered questions and areas of controversy in the application of the low FODMAP diet. This review will focus on some of the recent developments in the low FODMAP approach and will highlight the gaps in our knowledge.

Dietary Triggers in IBS

IBS is defined by the Rome IV criteria as recurrent abdominal pain associated with defecation or a change in bowel habits [2]. Despite the high prevalence (10% to 25% globally) [3], IBS pathophysiology remains incompletely understood, but is thought to be heterogeneous and multifactorial. Known pathophysiological abnormalities include visceral hypersensitivity, abnormal gastrointestinal (GI) motility, altered permeability, inflammation and altered gut-brain interactions. Additionally, meal challenge tests consistently show that nutrients exacerbate symptom severity in IBS [4]. The majority of IBS patients report that their symptoms are triggered after food intake [5,6]. Most commonly reported dietary triggers are wheat products, caffeine, dairy products, cabbage, onions, peas, beans and hot spices [7,8]. Several studies have shown that putting patients on a restricted diet or on fasting therapy improved the majority of their symptoms [8-10]. Consequently, changes in food choice have become a well-accepted method to suppress symptoms in IBS patients [11]. Over the last few years, a diet low in FODMAPs has been established as an efficacious management strategy for IBS patients [12]. FODMAPs are poorly absorbed dietary short-chain carbohydrates, including fructose (when present in excess of glucose), lactose, fructo-oligosaccharides, galacto-oligosaccharides, sorbitol and mannitol [13].A recent meta-analysis supported the efficacy of the low FODMAP diet in the treatment of overall GI symptoms in adult patients with IBS to range from 50% to 86%. This analysis included randomised blinded controlled feeding trials from several different countries [14].

FODMAP New and Future Evidence

Physiology

Since 2005, when the first data was published suggesting the low FODMAP diet approach [15], the evidence for the mechanism of action of FODMAPs has focussed mainly on two principals. Firstly, because they are poorly absorbed and due to their osmotic effects in the small intestine, ingestion of FODMAPs leads to an

increased luminal water load [16]. Secondly, rapid fermentation of FODMAPs by the colonic microflora increases the release of gases [17]. Both mechanisms can lead to luminal distention, which can translate into typical IBS symptoms such as bloating and abdominal pain. The exact mechanism of how intestinal distention triggers symptoms is not completely elucidated yet, but most likely, it stimulates mechanoreceptors present in the intestinal wall, leading to reflex responses, and effects on GI motility [18].

Recent work has contributed to our understanding of the different FODMAPs and their inequality in terms of their impact on GI physiology. A magnetic resonance imaging study of healthy controls and IBS patients showed that the response of the small bowel (increased osmotic effects) and large bowel (increased gas volume) to fructose and inulin was similar in both groups [19]. However, IBS patients reported increased GI symptoms compared to the healthy controls, indicating that rather than excessive gas production after FODMAP infusion, an increased hypersensitivity to normal FODMAP-induced gas production and/or osmotic activity, may contribute to the FODMAP-related symptoms in IBS.

Further understanding the different effects of the individual FODMAPs on symptoms is also required, as all FODMAPs are not equal in terms of their impact on GI physiology [20]. Much of the FODMAP mechanistic understanding has focussed on the effects of either fructans or fructose on colonic fermentation and bowel distension. the sugar polyols are a group within the FODMAPs that have received scant attention. Sorbitol and mannitol are known to induce GI symptoms in patients with IBS, independently of their absorptive patterns [21]. However, there is little to no evidence on the other polyols including xylitol and erythritol outside their effects on metabolism, appetite and food intake regulation, and preventive effects in human dental caries [22].

Upper GI

The acute effects of FODMAPs on upper GI motility have only recently been investigated. An intragastric administration of different FODMAPs (fructans, fructose) lead to a rapid onset of GI symptoms (within 30 minutes), specifically cramps, flatulence and pain, in comparison to a glucose-control, in both healthy controls and IBS patients, where the IBS patients showed higher sensitivity [23]. Fructans induced higher postprandial gastric pressures compared to glucose, suggesting that the proximal small bowel can be an important contributor to FODMAP-induced symptom generation. Differences in upper GI motility response may account for this, but needs to be explored further.

The above mentioned acute challenge studies [19,23] have shown that FODMAPs have strong symptom triggering effects, not only in the lower but importantly, also in the upper GI tract, possibly through gastroduodenal and gastro-colonic reflex activities. Duodenal distension has previously been suggested to decrease gastric tone via a vagally mediated enterogastric reflex pathway; this mechanism is nutrient- and region-specific [24]. Further research is needed to unravel the exact neural or potential hormonal mechanisms underlying the increased sensitivity to effects of FODMAPs. In one small study, fructans were shown to increase gastroesophageal reflux [25], additionally less gastric accommodation has been shown to be associated with a higher rate of reflux events [26]. Therefore, it is also likely that FODMAPs may influence gastro-esophageal crosstalk. Further exploration is required to understand how fructans may influence these effects.

Extra-intestinal Symptoms

Besides typical GI symptoms, IBS patients often present with extra-intestinal somatic and/or psychological symptoms including fatigue, headaches, anxiety or depressive symptoms [27], demonstrating that dysregulation of the gut-brain axis, a bidirectional communication pathway between the central and enteric nervous systems, is also involved in symptom development [27]. Furthermore, it has been demonstrated that behavioral therapy and centrally acting drugs, such as antidepressants, can improve IBS symptoms [28].

It has been shown that psychological state can affect symptom intensity or onset. For example, stress can alter the motor function of the GI tract and change visceral perception, leading to the onset of exacerbation of symptoms [28,29]. Whether FODMAP intake can trigger psychological symptoms is less investigated and remains controversial. Following an acute fructan infusion, increased levels of tension, sadness and anger in IBS patients were recently found [23]. Additionally, Shepherd *et al*. observed numerically, although not significantly, increased fatigue scores after a 2-week fructan administration compared to glucose and fructose [30]. Another study found no significant differences when investigating the effect of the low and high FODMAP diet on scores of lethargy [31]. Future studies are needed to confirm which extra-intestinal symptoms are influenced by FODMAPs. Additionally, we need to understand whether extra-intestinal symptoms can be a primary response to FODMAPs induced through neural and/or hormonal gut-brain signaling pathways, or whether the effects may be secondary to the development of GI symptoms.

Implementation

There is now high-quality evidence supporting the low FODMAP diet as a first-line therapy in IBS, demonstrating significant improvement in symptoms in 70% of IBS patients [12]. However, the lowFODMAP diet is complex, and requires individualised explanation, follow-up and reintroduction by a skilled and trained dietitian [1]. There are no studies showing the efficacy of the diet when self-taught, however group education may offer a promising alternative and has showed similar improvement in levels of symptom control when compared to one-on-one dietetic counselling [32].Training for health care professionals to increase consistent delivery of advice and allow access to reliable FODMAP compo-

sition data is crucial for optimal dietary advice and accurate food lists. This is an increasing obstacle given the increasing popularity of the FODMAP approach and the consequent rise of inaccurate information available on the Internet. The Monash University Low FODMAP Diet Smartphone Application is an initiative to provide an up to date global food composition database [33].

Alternative Therapies

Recent evidence has highlighted the use of a mixed approach composing of a 'simpler' FODMAP diet plus a focus on altering eating patterns, based on traditional dietary guidelines for IBS from the U.K's National Institute of Health and Care Excellence (NICE) and the British Dietetic Association [34]. Although previous studies have shown the low FODMAP diet to be superior when compared to the NICE diet [35], traditional dietary advice of having regular meals, not eating too much at once and eating slowly should always be included in instruction [34]. Gut-directed hypnotherapy is an example of one alternative management approach, and that has also recently showed similar efficacy to the low FODMAPdiet [36]. Future studies are required to fine-tune such strategies of combining elements from different strategies.

Predictors of Response

Retrospective analyses consistently show that adherence contributes to the low FODMAP diet' efficacy [1]. Implementation of the low-FODMAP diet will be further aided by customising dietary advice for different patient populations and by being able to better predict positive response in IBS. One predictor of response may be gut microbiome composition, recently supported by profiling analyses of an IBS cohort [37] and a small study in children with IBS, where those who responded to the diet had a greater baseline saccharolytic capacity [38]. Other observations have highlighted that genetic polymorphisms altering serotonin synthesis may also predict response to dietary interventions in IBS [39]. Beyond this work, no other prospective predictors of response specific to the low FODMAP diet have been defined.

Breath hydrogen testing is widely used to help predict whether the specific FODMAP is malabsorbed and whether this is associated with symptoms. However, there are inconsistencies in methodologies and poor reproducibility of results making interpretation difficult and highlight that results do not reflect underlying absorptive capacity [40]. One example is the polyol group. The polyols are regarded as a FODMAP due to their part absorption via passive diffusion across the small intestinal epithelium and being available for rapid fermentation by bacteria. However, studies assessing sorbitol and mannitol malabsorption patterns have revealed inconsistent or discordant results when symptoms of IBS are assessed [21].

Research Settings

The data is lacking for comparisons with a strong control (such as standard medical therapy), and efficacy of the diet in real-life settings (including liberalising FODMAP restriction). In addition, all of the published intervention trials have been conducted in IBS patients in tertiary care settings.

Patient Groups

There is high quality evidence to support the low FODMAP diet in the management of symptoms for adults with IBS [12]. Data from randomised controlled clinical trials show the lowFODMAP is efficacious in all subtypes of IBS [12]. However, the role of FODMAPs in other conditions such as functional dyspepsia or functional esophageal disorders including Gastro-Esophageal Reflux Disease (GERD) remains largely unexplored. Colonic fermentation has been suggested to have potential direct effects on the lower esophageal sphincter motility [25], but the mechanism is not well established. Up to 30% of GERD patients will continue to experience reflux symptoms despite acid-suppressive therapy (PPIs). These patients are termed refractory GERD, where hypersensitivity to non-acid reflux during transient lower esophageal relaxations may be an underlying mechanism [41]. Regardless of there being minimal quality evidence investigating the relationship between meal ingestion and GERD symptoms, dietary and lifestyle measures for GERD are often advised by physicians [42]. Randomised controlled trials across broader populations are needed.

Children

Currently, there is only one controlled trial assessing the low-FODMAP diet to have been conducted in children with IBS [38]. This study showed that the children with IBS had fewer episodes of abdominal pain during the 2-day low FODMAP dietary arm. Although there are other promising paediatric studies assessing a low-fructose diet [43,44], trials of longer duration of the whole FODMAP approach are required.

Long-Term Risks

GI microbiota

GI microbiota: Research has shown that a low FODMAP diet can induce potentially detrimental changes in gut microbiota composition and function [45,46]. A recent Norwegian study showed that just 10 days of fructan supplementation increased the level of the bacteria which had been reduced by 3 weeks of the low-FODMAP diet in patients with IBS [47]. This promising finding highlights the importance of the re-challenge and reintroductions steps to not only liberalise the diet but importantly restore colonic microbiota towards baseline levels, whilst maintaining symptom control. It is not known if some patients will become more sensitive to FODMAP exposure after restriction, where there is potential for an adaptation of the microbiota or enteric nervous system. Further work is needed to examine the clinical significance (including as delivered in a real-life setting in clinical practice) of the bacteria changes on the microbiome in the medium to long term.

Nutritional Adequacy

Nutritional adequacy is an issue for any restrictive diet and the low FODMAP diet should be considered as only one strategy to have shown efficacy in the multi-disciplinary approach sometimes required to manage the heterogeneity of IBS. The low FODMAP diet has been associated with reduced calorie intake [34] however is thought to be nutritionally adequate if appropriate dietary counselling is provided, especially as the approach allows foods from each of the food groups to be consumed. Furthermore, a recent systematic review has highlighted an increased risk for disordered eating practices in patients with GI disorders where there is a need for constant monitoring of their food intake [48]. More evidence is required to enable better screening and identification of such patients.

Conclusions

The principals and efficacy of the low FODMAP diet are well supported and the diet is widely implemented as a key treatment strategy in managing Irritable Bowel Syndrome (IBS) patients. However, there are limitations and the approach must be used with care and in appropriate situations instructed by trained health professionals. There remains gap in our knowledge particularly in regards to long term effects and understanding how to individualize dietary advice, especially in other disorders.

Disclaimer and Source of Support: The authors have nothing to disclose. Jessica Biesiekierski is a postdoctoral research fellow of the Research Foundation - Flanders (FWO-Vlaanderen).

References

1. Shepherd SJ, Lomer MC, Gibson PR (2013) Short-chain carbohydrates and functional gastrointestinal disorders. Am J Gastroenterol 108: 707-717.

2. Lacy BE,Mearin F, Chang L, Chey WD, Lembo AJ, et al. (2016) Bowel Disorders. Gastroenterology 150: 1393-1407.

3. Lovell RM and Ford AC (2012) Global prevalence of and risk factors for irritable bowel syndrome: a meta-analysis. ClinGastroenterolHepatol 10: 712-721.

4. Posserud I,Strid H, Störsrud S, Törnblom H, Svensson U et al. (2013) Symptom pattern following a meal challenge test in patients with irritable bowel syndrome and healthy controls. United European Gastroenterology Journal 1: 358-367.

5. Simrén M, Månsson A, Langkilde AM, Svedlund J, Abrahamsson H, et al. (2001) Food-related gastrointestinal symptoms in the irritable bowel syndrome. Digestion 63: 108-115.

6. Monsbakken KW, Vandvik PO, Farup PG (2006) Perceived food intolerance in subjects with irritable bowel syndrome-- etiology, prevalence and consequences. Eur J ClinNutr 60: 667-672.

7. El-Salhy (2015) Recent developments in the pathophysiology of irritable bowel syndrome. World J Gastroenterol 21: 7621-7636.

8. Jones VA, McLaughlan P, Shorthouse M, Workman E, Hunter JO (1982) Food intolerance: a major factor in the pathogenesis of irritable bowel syndrome. Lancet 2: 1115-1117.

9. Maagaard L, Ankersen DV, Végh Z, Burisch J, Jensen L, et al. (2016) Follow-up of patients with functional bowel symptoms treated with a low FODMAP diet. World J Gastroenterol 22: 4009-4019.

10. Kanazawa M and Fukudo S (2006) Effects of fasting therapy on irritable bowel syndrome. International Journal of Behavioral Medicine 13: 2014-2020.

11. Gibson PR and Shepherd SJ (2012) Food choice as a key management strategy for functional gastrointestinal symptoms. Am J Gastroenterol 107: 657-666.

12. Halmos EP, Power VA, Shepherd SJ, Gibson PR, Muir JG et al. (2014) A Diet Low in FODMAPs Reduces Symptoms of Irritable Bowel Syndrome. Gastroenterology 146: 67-75.

13. Gibson PR and Shepherd SJ (209) Evidence-based dietary management of functional gastrointestinal symptoms: The FODMAP approach. Journal of Gastroenterology and Hepatology 25: 252-258.

14. Marsh A, Eslick EM, Eslick GD (2015) Does a diet low in FODMAPs reduce symptoms associated with functional gastrointestinal disorders? A comprehensive systematic review and meta-analysis. Eur J Nutr: 1-10.

15. Gibson PR and Shepherd SJ (2005) Personal view: food for thought--western lifestyle and susceptibility to Crohn's disease. The FODMAP hypothesis. Aliment PharmacolTher 21: 1399-1409.

16. Barrett JS, Gearry RB, Muir JG, Irving PM, Rose R et al. (2010) Dietary poorly absorbed, short-chain carbohydrates increase delivery of water and fermentable substrates to the proximal colon. Aliment PharmacolTher 31: 874-882.

17. Ong DK, Mitchell SB, Barrett JS, Shepherd SJ, Irving PM, et al. (2010) Manipulation of dietary short chain carbohydrates alters the pattern of gas production and genesis of symptoms in irritable bowel syndrome. J GastroenterolHepatol 25: 1366-1373.

18. De Giorgio R, Volta U, Gibson PR (2016) Sensitivity to wheat, gluten and FODMAPs in IBS: facts or fiction? See comment in PubMed Commons below Gut 65: 169-178.

19. Major G, Pritchard S, Murray K, Alappadan JP, Hoad CL et al. (2017) Colon Hypersensitivity to Distension, Rather Than Excessive Gas Production, Produces Carbohydrate-related Symptoms in Individuals with Irritable Bowel Syndrome. Gastroenterology 152: 124-133.

20. Murray K,Wilkinson-Smith V, Hoad C, Costigan C, Cox E, et al. (2014) Differential effects of FODMAPs (fermentable oligo-, di-, mono-saccharides and polyols) on small and large intestinal contents in healthy subjects shown by MRI. Am J Gastroenterol 109: 110-119.

21. Yao CK, Tan HL, van Langenberg DR, Barrett JS, Rose R et al. (2013) Dietary sorbitol and mannitol: food content and distinct absorption patterns between healthy individuals and patients with irritable bowel syndrome. J Hum Nutr Diet 27: 263-275.

22. Steinert RE, Frey F,Topfer A, Drewe J, Beglinger C, et al. (2011) Effects of carbohydrate sugars and artificial sweeteners on appetite and the secretion of gastrointestinal satiety peptides. Br J Nutr 105: 1320-1328.

23. Masuyet al. (2016) Effect of FODMAPS on gastric accommodation, upper GI motility and symptom generation in health and in IBS PP277. NeurogastroenterolMotil 28: S182-S183.

24. De Ponti F, Azpiroz F, Malagelada JR (1987) Reflex gastric relaxation in response to distention of the duodenum. American Journal of Physiology-Gastrointestinal and Liver Physiology 252: G595-G601.

25. Piche T, des Varannes B, Sacher-Huvelin S, Holst JJ, Cuber JC, et al. (2003) Colonic fermentation influences lower esophageal sphincter function in gastroesophageal reflux disease. Gastroenterology 124: 894-902.

26. Pauwels P, Altan E, Tack J (2014) The gastric accommodation response to meal intake determines the occurrence of transient lower esophageal sphincter relaxations and reflux events in patients with gastro-esophageal reflux disease. NeurogastroenterolMotil 26: 581-588.

27. Van Oudenhove L, Levy RL, Crowell MD, Drossman DA, Halpert AD et al. (2016) Biopsychosocial Aspects of Functional Gastrointestinal Disorders: How Central and Environmental Processes Contribute to the Development and Expression of Functional Gastrointestinal Disorders. Gastroenterology 150: 1355-1367.

28. Alaradi O and Barkin JS (2002) Irritable bowel syndrome: update on pathogenesis and management. Med PrincPract 11: 2-17.

29. Barbara G, De Giorgio R, Stanghellini V, Cremon C, Salvioli B, et al. (2004) New pathophysiological mechanisms in irritable bowel syndrome. Aliment PharmacolTher 20 Suppl 2: 1-9.

30. Shepherd SJ, Parker FC, Muir JG, Gibson PR (2008) Dietary Triggers of Abdominal Symptoms in Patients with Irritable Bowel Syndrome: Randomized Placebo-Controlled Evidence. ClinGastroenterolHepatol 6: 765-771.

31. Ong DK, Mitchell SB, Barrett JS, Shepherd SJ, Irving PM, et al. (2010) Manipulation of dietary short chain carbohydrates alters the pattern of gas production and genesis of symptoms in irritable bowel syndrome. J GastroenterolHepatol 25: 1366-1373.

32. Whigham L, Joyce T, G Harper, PM Irving, Staudacher HM et al. (2015) Clinical effectiveness and economic costs of group versus one-to-one education for short-chain fermentable carbohydrate restriction (low FODMAP diet) in the management of irritable bowel syndrome. J Hum Nutr Dietetics 28: 687-696.

33. Monash University, Central Clinical School's Department of Gastroenterology. The Monash University Low FODMAP Diet Smartphone Application 2012, Melbourne, Australia.

34. Böhn L, Störsrud S, Liljebo T, Collin L, Lindfors P, et al. (2015) Diet low in FODMAPs reduces symptoms of irritable bowel syndrome as well as traditional dietary advice: a randomized controlled trial. Gastroenterology 149: 1399-1407.

35. Staudacher HM, Whelan K, Irving PM, Lomer MCE (2011) Comparison of symptom response following advice for a diet low in fermentable carbohydrates (FODMAPs) versus standard dietary advice in patients with irritable bowel syndrome. J Hum Nutr Diet 24: 487-495.

36. Peters SL, Yao CK, Philpott H, Yelland GW, Muir JG, et al. (2016) Randomised clinical trial: the efficacy of gut-directed hypnotherapy is similar to that of the low FODMAP diet for the treatment of irritable bowel syndrome. Aliment Pharm Ther 44: 447-459.

37. Bennet, et al. (2016) Multivariate modelling of gut microbial profiles predicts responsiveness to a diet low in FODMAPS. United European Gastroenterology Journal 4(S1): OP003.

38. Chumpitazi BP, Cope JL, Hollister EB, Tsai CM, McMeans AR, et al. (2015) Randomised Clinical Trial: Gut Microbiome Biomarkers are Associated with Clinical Response to a Low FODMAP Diet in Children with Irritable Bowel Syndrome. Aliment Pharm Ther 42: 418-427.

39. Merchant JL, Photenhauer A, Eswaran SL, Jackson K, Chey WD et al. (2016) Tu1807 A US, Randomized, Controlled Trial Comparing the Low FODMAP Diet vs NICE Guidelines in Adults IBS-D Adults: Predictive Value of a Tryptophan Hydroxlase 1 (TPH1) Promoter Variant. Gastroenterology 150: S953.

40. Yao CK, Tuck CJ, Barrett JS, Canale KEK, Philpott HL, et al. (2016) Poor reproducibility of breath hydrogen testing: Implications for its application in functional bowel disorders. United European Gastroenterology Journal. doi/abs/10.1177/2050640616657978.

41. Scarpellini E, Ang D, Pauwels A, De Santis A, et al. (2016) Management of refractory typical GERD symptoms. Nat Rev GastroenterolHepatol 13: 281-294.

42. Meining A and Classen M (2000) The role of diet and lifestyle measures in the pathogenesis and treatment of gastroesophageal reflux disease. See comment in PubMed Commons below Am J Gastroenterol 95: 2692-2697.

43. Escobar Jr MA,Lustig D, Pflugeisen B, Amoroso P, Sherif D, et al. (2014) Fructose intolerance/malabsorption and recurrent abdominal pain in children. Journal of Pediatric Gastroenterology and Nutrition 58: 498-501.

44. Wintermeyer, et al. (2012) Fructose malabsorption in children with recurrent abdominal pain: positive effects of dietary treatment. KlinischePädiatrie 224: 17-21.

45. Halmos EP, Christophersen CT, Bird AR, Shepherd SJ, Gibson PR, et al. (2015) Diets that differ in their FODMAP content alter the colonic luminal microenvironment. Gut 64: 93-100.

46. Staudacher HM, Lomer MCE, Anderson JL, Barrett JS , Muir JG et al. (2012) Fermentable Carbohydrate Restriction Reduces Luminal Bifidobacteria and Gastrointestinal Symptoms in Patients with Irritable Bowel Syndrome. J Nutr 142: 1510-1518.

47. Hustoft TN, Hausken T, Ystad SO, Valeur J, Brokstad K, et al. (2016) Effects of varying dietary content of fermentable short-chain carbohydrates on symptoms, fecal microenvironment, and cytokine profiles in patients with irritable bowel syndrome. NeurogastroenterolMotil.

48. Satherley R, Howard R, Higgs S (2015) Disordered eating practices in gastrointestinal disorders. Appetite 84: 240-250.