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Reintroducing Foods After Completing Restrictive Low FODMAP Diet

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MOTILITY

This summary reviews Van den Houte K, Colomier E, Routhiaux K, et al. Efficacy and findings of a blinded randomized reintroduction phase for the low FODMAP diet in irritable bowel syndrome. *Gastroenterology* 2024; 167: 333-42.

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STRUCTURED ABSTRACT

Question: Does reintroduction of specific fermentable oligo-, di-, monosaccharides and polyols (FODMAPs) trigger recurrent or worsening irritable bowel syndrome (IBS) symptoms after completing a 6-week restrictive low FODMAP diet?

Design: Single center, 9-week, blinded, randomized crossover trial.

Setting: Leuven University Hospital, Leuven, Belgium.

Patients: Consecutive adults with IBS based on Rome IV criteria to a specialized tertiary care clinic were eligible. Exclusion criteria included concurrent major organic or psychiatric disorders, antibiotic use in previous 12 weeks, history of substance or alcohol abuse in past 2 years, pregnant or lactating women,

and patients who previously tried low FODMAP diets. Drugs known to impact gastrointestinal symptoms were excluded from use during the trial.

Interventions/Exposure: After a 2-week run-in period to confirm active IBS symptoms, enrolled patients completed a 6-week restrictive low FODMAP diet using the Monash FODMAP calculator and under the direction of a dietician (i.e., elimination phase) and completed the IBS Symptom Severity Score (IBS-SSS) at week zero, 2, 4, and 6. Range of IBS-SSS is 0-500 with IBS-SSS of 75-174 = mild IBS; 175-299 = moderate IBS; and, 300-500 = severe IBS. If study patients experienced at least a 50-point reduction in IBS-SSS from baseline during the elimination phase, then they were considered responders and entered the 9-week, blinded randomized crossover trial with reintroduction of FODMAPs in powdered form.

During the blinded randomized crossover trial, patients continued a low FODMAP diet and also completed 7 separate cycles of reintroducing specific FODMAPs in powder form. Each cycle consisted of dissolving a specified powder in water and drinking it during meals 3x daily for 7 days and then completing their IBS-SSS on day 7. This was followed by a 2-day washout period where patients did not consume any study powder before starting the next cycle.

Patients were randomly assigned to dissolve 1 specific FODMAP powder, labeled A-G, during each 7-day reintroduction cycle. The specific FODMAP powders tested over the 9-week trial were daily doses of 20 grams fructans, 60 grams fructose, 12 grams B-Galacto-Oligosaccharides, 60 grams lactose, 15 grams mannitol, 15 grams sorbitol, or 30 grams glucose, which was considered the control powder.

Outcome: A rise of $\geq$ 50 points in IBS-SSS over the mean score in the elimination phase was defined as a specific FODMAP trigger.

Data Analysis: Wilcoxon Signed Rank Tests for within subject contrasts with data presented as mean +/- standard deviation. No allowance for multiple statistical inference was made.

Funding: Methusalem Grant from Leuven University

Results: Between November 2019 and July 2022, 117 IBS patients (mean age 36, 84% female, mean body mass index 24.5) were recruited with 12 dropping out

during baseline evaluation. Distribution based on IBS subtype was 37% IBS with diarrhea (IBS-D), 40% IBS-mixed (IBS-M), 22% IBS with constipation (IBS-C) with average baseline IBS-SSS of 301 +/- 97. The mean IBS-SSS score decreased significantly from baseline compared to 6 weeks of restrictive low FODMAP diet: 301 +/- 97 vs 150 +/- 116 with a responder rate (≥ 50-point reduction in IBS-SSS compared to baseline) of 80%. Although 94 responders entered the FODMAP re-introduction trial, 17 patients were lost to follow-up due to COVID (n = 4) or due to discontinuing intervention (n=13), leaving 77 patients to evaluate at the end of the 9-week trial.

Symptom recurrence, defined as a rise of ≥ 50 points in IBS-SSS, occurred in 85% of study patients. When assessing mean IBS-SSS scores for the entire group from the elimination phase vs FODMAP reintroduction cycles, mannitol (sugar found in multiple fruits and vegetables, including cauliflower, watermelon, kimchi, mushrooms) and fructans (carbohydrate found in wheat, garlic) powder produced significant increases of approximately 71-73 in mean IBS-SSS. However, during blinded reintroduction, an individualized pattern of symptom recurrence occurred with 2.5 +/- 2 different FODMAPs triggering significant increases in IBS-SSS scores. Again, mannitol and fructans were most likely powders to trigger recurrent symptoms among individual patients (54% and 56%, respectively). Rates of symptom recurrence with reintroduction of other FODMAPs were fructose 27%, B-Galacto-Oligosaccharides 35%, lactose 28%, sorbitol 23%, and control/glucose 26%.

COMMENTARY

Why Is This Important?

Current ACG guidelines[1] recommend a limited trial of a low FODMAP diet in patients with IBS to improve global symptoms. This is because foods high in FODMAPs lead to increased water retention in the colon and increased colonic fermentation by bacteria in the gut, producing increases in short-chain fatty acid production and gaseous colonic distention. Thus, a low FODMAP diet may be particularly helpful for IBS-D patients with predominant bloating symptoms, although it may be helpful for bloating symptoms in all types of IBS patients. Unfortunately, the ACG guideline recommendation on low FODMAP diets is a "Conditional Recommendation, Very Low-Quality Evidence," since there is very limited randomized controlled trial (RCT) data from small studies with inadequate blinding of patients. Furthermore, when recommending a low FODMAP diet, it's important to educate patients that this diet is fairly restrictive and should

only be followed for 4-6 weeks before FODMAP foods are reintroduced in small quantities in order to see which foods trigger symptoms. Randomized trial data on this reintroduction phase has been virtually non-existent prior to the current study by Van den Houte et al.

By using FODMAP powders to facilitate blinding, utilizing a randomized crossover trial design, and by individually testing multiple categories of FODMAPs in the reintroduction cycle, the authors have performed a rigorous study to assess this topic. They should be commended for this great effort, which confirms that IBS patients demonstrate an individualized pattern of FODMAPs triggering recurrent symptoms and identifies specific categories of FODMAPs that are most likely to trigger symptoms.

Key Study Findings

Mannitol, which is a sugar found in multiple fruits and vegetables and may be a food additive in ultra-processed foods, and fructans, a carbohydrate found in wheat, produced significant increases of approximately 71-73 in mean IBS-SSS and were most likely to trigger IBS symptoms among individual patients.

Nevertheless, an individualized pattern of symptom recurrence occurred with 2.5 +/- 2 different FODMAPs triggering significant increases in IBS-SSS scores. This indicates the importance of gradually reintroducing multiple different FODMAP foods to determine the multiple triggers to IBS symptoms after patients complete a restrictive low FODMAP diet.

Caution

This is a small (n = 77) study of patients with severe IBS seen at a single institution in Belgium. Therefore, similar studies in larger groups of patients in more diverse settings are needed before generalizing these results.

My Practice

In my practice, diet modification is a cornerstone of IBS management. Initially, I advise patients to complete a 4-week lactose-free diet, especially if they have IBS-D with predominant bloating symptoms. I also ask them to try and identify specific food triggers while recommending that they greatly reduce their intake of ultra-processed foods and to use a soluble fiber supplement (e.g., 1 tablespoon of psyllium in 8 ounces of water daily). Having said that, many of my IBS patients have already tried and failed these basic diet modifications.

Consistent with ACG guidelines[1], I recommend a trial of a low FODMAP diet for motivated IBS patients, especially if bloating is a predominant symptom, while also emphasizing that a restrictive low FODMAP diet should only be followed for 4-6 weeks. However, I do not simply provide a hand-out with a list of high and low FODMAP foods. Instead, I refer these patients to a dietician to

develop a meal plan for the initial restrictive low FODMAP diet phase, followed by additional dietary counseling to reintroduce small amounts of FODMAPS in order to identify specific food triggers, eventually followed by a final phase of dietary counseling where the patient establishes a long-term diet plan that does not deprive the patient of important nutrients. For patients that are comfortable using phone apps, I prefer the Monash University FODMAP app to facilitate diet planning, although multiple apps are available.

For Future Research

While the authors are to be commended for performing a blinded, crossover trial of reintroducing FODMAPs, RCTs of patients with moderate IBS in more diverse settings are needed. Qualitative research to identify optimal approaches to implementing restrictive low FODMAP diets and the FODMAP reintroduction phase would also be helpful.

Conflict of Interest

Dr. Schoenfeld reports no potential conflicts of interest for this summary.

REFERENCE

1. Lacy B, Pimentel M, Brenner D, et al. ACG Clinical Guideline: Management of irritable bowel syndrome. *Am J Gastroenterol* 2021; 116: 17-44.