Easing Concerns About the Low FODMAP Diet in Patients With Irritable Bowel Syndrome

See "A diet low in FODMAPs reduces symptoms in patients with irritable bowel syndrome and a probiotic restores Bifidobacterium species: a randomized controlled trial," by Staudacher HM, Lomer MCE, Farquharson FM, et al, on page 936.

Dietary management makes sense in patients with irritable bowel syndrome, because food is a major inducer of symptoms, and dietary manipulation empowers patients to influence the outcome of their disorder. It is not surprising, therefore, that the arrival of the low FODMAP diet, which is based on sound scientific evidence,[1] has led to its enthusiastic adoption in clinical practice across the world. However, the diet has been criticized in 4 main areas: (1) the strength of the efficacy data, mainly owing to perceived bias in clinical trial design and the lack of real-world placebo-controlled trials[2,3]; (2) the complexity and difficulty of teaching the diet; (3) safety, especially on the structure of gut microbiota[4]; and (4) longer term efficacy and safety. The article by Staudacher et al[5] in the current edition of *Gastroenterology* addresses three of these issues.

Performance of high-quality, randomized, controlled trials of therapeutic diets is challenging.[6] Theoretically, the standards by which we judge a dietary intervention should be as stringent as those for a pharmacological agent. Critics argue that such standards have not been adequately met for the low FODMAP diet.[2,3] A gold standard approach for evaluating a therapeutic diet is the provision of all food to recipients in a double-blinded way, as was done in the pivotal study for the low FODMAP diet, with unequivocally positive results.[7] Unfortunately, feeding studies do not mimic real-world clinical practice, where diets are taught by health professionals and implemented by patients. Dietitian-led randomized, controlled trials have been conducted where comparator diets have ranged from habitual diet[8] (which lacks the placebo effect of active dietitian-mediated intervention), high FODMAP diet[9–11] (where potential exacerbation symptoms may exaggerate the efficacy of the low FODMAP diet), or currently administered active diets.[12,13] All of these studies were designed to primarily address questions (effects on structure and function of gut microbiota, and on metabolomics profiles, and comparison with currently instituted therapies) other than efficacy over placebo. Furthermore, in the pivotal feeding study, the placebo diet was constructed on the basis of a typical intake of FODMAPs in healthy Australians,[14] which proved to be greater than that retrospectively estimated from the participants' habitual diet. Although the mean difference in oligosaccharide intake of 1.2 g/d was unlikely to induce symptoms, it may have confounding effects on the gut microbiota. In other words, a true dietitian-led placebo diet had not been tested.

Staudacher et al[5] have taken on the enormous challenge of designing and delivering a dietitian-led placebo diet so that such a direct comparison with the low FODMAP diet can be assessed. The approach was clever; carbohydrate manipulation was performed for the placebo diet as it is in the low FODMAPs diet. A measure of the success of its design was that intake of FODMAP and fiber were not affected. Nevertheless, there were unavoidable limitations. As discussed by the authors, collinearity, in which changes in food choice lead to different exposures of other food components that might exert positive or negative effects, might occur.[6] Furthermore, Staudacher et al[5] targeted patients without constipation, which limits generalizability. This has stemmed from the hypothesis that reduced water delivery to, and fermentation in, the proximal colon leads to exacerbation of constipation. However, there is now evidence that this assumption is not correct.[7] Although the primary endpoint of the study from Staudacher et al[5] was not reached, the entirety of the findings was convincing that the low FODMAP diet is more efficacious than the placebo diet in this patient group. These results should calm dissenters regarding the diet's efficacy in real-world practice.

The complexity of and difficulty in delivering the low FODMAP diet is often raised as a limitation to its implementation. Staudacher et al[5] spent only 10 minutes per patient teaching the diet and no explanation of the pathophysiology of FODMAP induction of symptoms was provided to the subjects. Although this approach was less involved than that considered best dietetic practice,[15] which may adversely affect adherence and response rates, it is reassuring that 57% of patients reported adequate relief of symptoms. This suggests the diet is easier to implement than previously thought.

The effect of reducing FODMAPs on the gut microbiota has created considerable safety concerns.[4] Staudacher et al have reported in the current and an earlier study that the relative abundance of fecal *Bifidobacteria* falls in association with reducing FODMAP intake.[10,13] In the pivotal feeding study, strict low FODMAP intake was associated with reduced total abundance of bacteria in feces and, compared with the comparator diet, a microbial profile that might be considered as "unhealthy."[16] What has been largely overlooked, however, is that the profile observed was not different to that found in the feces sampled while the same subjects were consuming their habitual diets. The reason for the differences with those in the "placebo" diet was thus more likely to be the small increase in FODMAP oligosaccharide intake (as outlined), perhaps representing a

manifestation of a prebiotic effect of the control diet rather than a corresponding loss of a prebiotic effect anticipated with FODMAP reduction. Reassuringly, diversity of bacteria did not reduce with FODMAP restriction in any of the studies.[10,11,13,16]

Potential ways of dealing with changes in microbial community structure are first to reintroduce FODMAPs into the diet, as is currently recommended, and a recent report has been reassuring.[17] The second is to supplement with probiotics and indeed Staudacher et al found, using a polymicrobial preparation, that abundance of *Bifidobacteria* was successfully modified,[5] with no convincing impact on symptoms. This strategy provides a means of avoiding theoretically less favorable microbial patterns. Whether such an approach is practical or associated with beneficial health outcomes remains unknown.

The major area of uncertainty left for further study with regard to the low FODMAP diet remains the efficacy and safety of the reintroduction phase. The first report of this phase has been encouragingly positive,[17] but will require innovation and clever study design to fully address. Nevertheless, in the meantime, concerns about the short-term efficacy and safety of instituting a low FODMAP diet in patients with irritable bowel syndrome in normal clinical practice should have been eased.

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Conflicts of interest
The authors have made the following disclosures: Peter R. Gibson reports that his department financially benefits from the sales of a digital application and booklets on the low FODMAP diet. He has published an educational/recipe book on diet.

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