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BRIEF REPORTS

Effects of Prebiotics vs a Diet Low in FODMAPs in Patients With Functional Gut Disorders

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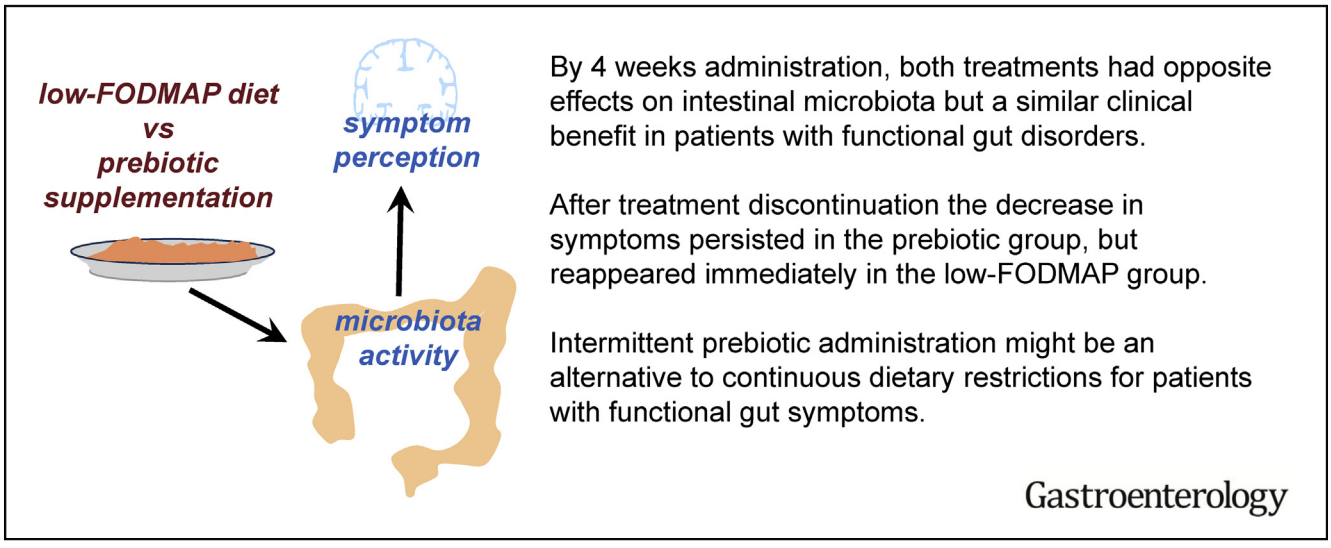

See editorial on page 960.

Prebiotics and diets low in fermentable oligo-, di-, monosaccharides and polyols (low-FODMAP diet) might reduce symptoms in patients with functional gastrointestinal disorders, despite reports that some nonabsorbable, fermentable meal products (prebiotics) provide substrates for colonic bacteria and thereby increase gas production. We performed a randomized, parallel, double-blind study of patients with functional gastrointestinal disorders with flatulence. We compared the effects of a prebiotic supplement (2.8 g/d Bimuno containing 1.37 g beta-galactooligosaccharide) plus a placebo (Mediterranean-type diet (prebiotic group, n = 19) vs a placebo supplement (2.8 g xylose) plus a diet low in FODMAP (low-FODMAP group, n = 21) for 4 weeks; patients were then followed for 2 weeks. The primary outcome was effects on composition of the fecal microbiota, analyzed by 16S sequencing. Secondary outcomes were intestinal gas production and digestive sensations. After 4 weeks, we observed opposite effects on microbiota in each group, particularly in relation to the abundance of *Bifidobacterium* sequences (increase in the prebiotic group and decrease in the low-FODMAP group; $P = .042$), and *Bilophila wadsworthia* (decrease in the prebiotic group and increase in the low-FODMAP group; $P = .050$). After 4 weeks, both groups had statistically significant reductions in all symptom scores, except reductions in flatulence and borborygmi were not significant in the prebiotic group. Although the decrease in symptoms persisted for 2 weeks after patients discontinued prebiotic supplementation, symptoms reappeared immediately after patients discontinued the low-FODMAP diet. Intermittent prebiotic administration might therefore be an alternative to dietary restrictions for patients with functional gut symptoms. ClinicalTrials.gov no.: NCT02210572.

Keywords: Intestinal Gas; Microbiota; Functional Intestinal Disorders.

WHAT YOU NEED TO KNOW

BACKGROUND AND CONTEXT

Non-absorbable residues of the diet are fermented by intestinal microbiota, releasing gas. Thus, diets low in fermentable residues, such as low FODMAP diets, improve gas-related complaints; paradoxically, some products that are selectively fermented by colonic microbiota (prebiotics) produce a similar benefit.

NEW FINDINGS

The decrease in symptoms produced by a low FODMAP diet in patients with functional gut disorders disappeared soon after discontinuation of the diet. In contrast, prebiotic administration enriched the microbiota and the decrease in symptoms persisted for 2 weeks.

LIMITATIONS

The study is small, did not estimate long-term efficacy and did not determine whether the prebiotic effect is product-specific or generic.

IMPACT

Intermittent treatment with prebiotics might represent an advantage over dietary restrictions for patients with functional gut symptoms.

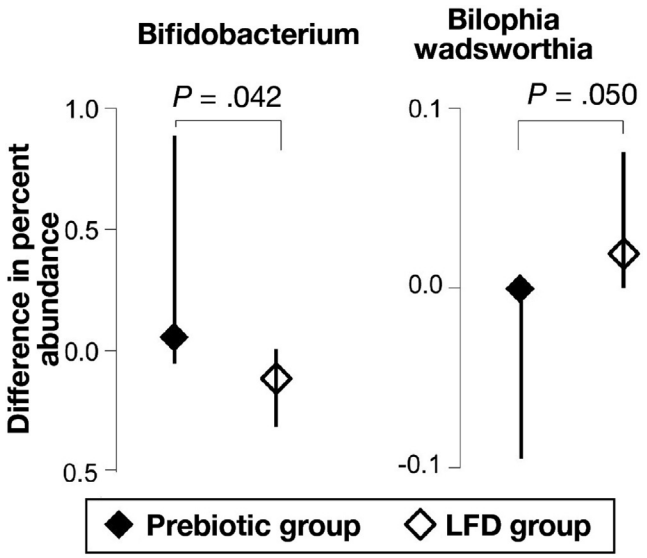

Figure 1. Effect of treatment on relative abundance in *Bifidobacterium* and *Bilophila wadsworthia* measured by 16S ribosomal RNA sequencing. Overall differences were tested by nonparametric Kruskal-Wallis analysis of variance on ranks, and the Mann-Whitney test was used for post hoc comparisons (LFD n = 21; prebiotic group n = 19). Data are median and interquartile range of the difference in abundance of bacterial sequences in fecal samples from pretreatment to treatment (see Supplementary Document 2).

It has been shown that patients complaining of gas-related symptoms significantly improve on various types of diets low in fermentable residues.[1–4] However, other studies have suggested that some nonabsorbable, fermentable meal products (prebiotics) that serve as substrates for colonic bacteria produce a similar effect on gas-related symptoms.[5] To address these apparent inconsistencies, we performed a randomized, 2-center, parallel double-blind study in patients with functional gut disorders who complained of flatulence (Supplementary Document 1). We compared the effect of a prebiotic supplement (2.8 g per day Bimuno containing 1.37 g beta-galactooligosaccharide [B-GOS]; Clasado Biosciences, Jersey, Channel Islands) plus a placebo (Mediterranean-type) diet (prebiotic group) vs a placebo supplement (2.8 g xylose) plus a low FODMAP (fermentable oligo-, di-, mono-saccharides and polyols) diet (LFD group). The primary outcome was the effect of the treatments on gut microbiota composition, specifically the relative abundance of bifidobacteria analyzed by 16S sequencing (Supplementary Documents 1 and 2). Secondary outcomes were intestinal gas production, as an index of microbiota activity, and digestive symptoms (Supplementary Documents 1, 3, 4 and 5). Sample size was calculated based on the effect of the prebiotic B-GOS on fecal bifidobacteria in previous studies.[6]

Forty-four patients (31 with irritable bowel syndrome and 13 with functional abdominal distension) were randomized (21 in the prebiotic and 23 in the LFD group), and 40 of them completed the study (19 and 21 patients, respectively); no demographic or clinical differences between groups were found. Adherence to dietary instructions was good (≥5 on a 1–7 scale).[7] A per intention-to-treat analysis was performed.

Both treatments induced different effects on microbiota, particularly with relation to the abundance of *Bifidobacterium* genus sequences (increased with prebiotic and decreased with LFD; $P = .042$), and *Bilophila wadsworthia* (decreased with prebiotic and increased with LFD; $P = .050$) (Figure 1; Supplementary Document 2).

Before treatment, the patients exhibited mild to moderate symptoms on their habitual diets, recording 15 ± 1 evacuations of gas during the daytime without significant differences between the study groups (Figure 2). By 4 weeks, both treatments reduced the symptom scores on the daily questionnaires (Figure 2); the reductions were statistically significant for all symptoms except for flatulence and borborygmi in the prebiotic group, but no differences in the effect of treatment (treatment values minus pretreatment values) were detected between the study groups ($P = .293$ by multivariate analysis of variance). However, both strategies had different consequences after treatment discontinuation. Although the improvement of symptoms persisted 2 weeks after prebiotic administration, symptoms tended to relapse after discontinuing the LFD (still lower than pretreatment), although the change (from treatment values

Abbreviations used in this paper: **B-GOS, beta-galactooligosaccharide; FODMAP, fermentable oligo-, di-, mono-saccharides and polyols; LFD, low-FODMAP diet.**

Most current article

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