Fermentable Carbohydrate Restriction Reduces Luminal Bifidobacteria and Gastrointestinal Symptoms in Patients with Irritable Bowel Syndrome1–4

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Abstract

Preliminary studies indicate that dietary restriction of fermentable short-chain carbohydrates improves symptoms in irritable bowel syndrome (IBS). Prebiotic fructo-oligosaccharides and galacto-oligosaccharides stimulate colonic bifidobacteria. However, the effect of restricting fermentable short-chain carbohydrates on the gastrointestinal (GI) microbiota has never been examined. This randomized controlled trial aimed to investigate the effects of fermentable carbohydrate restriction on luminal microbiota, SCFA, and GI symptoms in patients with IBS. Patients with IBS were randomized to the intervention diet or habitual diet for 4 wk. The incidence and severity of symptoms and stool output were recorded for 7 d at baseline and follow-up. A stool sample was collected and analyzed for bacterial groups using fluorescent in situ hybridization. Of 41 patients randomized, 6 were withdrawn. At follow-up, there was lower intake of total short-chain fermentable carbohydrates in the intervention group compared with controls (P = 0.001). The total luminal bacteria at follow-up did not differ between groups; however, there were lower concentrations (P < 0.001) and proportions (P < 0.001) of bifidobacteria in the intervention group compared with controls when adjusted for baseline. In the intention-to-treat analysis, more patients in the intervention group reported adequate control of symptoms (13/19, 68%) compared with controls (5/22, 23%; P = 0.005). This randomized controlled trial demonstrated a reduction in concentration and proportion of luminal bifidobacteria after 4 wk of fermentable carbohydrate restriction. Although the intervention was effective in managing IBS symptoms, the implications of its effect on the GI microbiota are still to be determined. J. Nutr. doi: 10.3945/jn.112.159285.

Introduction

Irritable bowel syndrome (IBS)9 is a functional gastrointestinal (GI) disorder affecting between 10 and 20% of the population in developed countries. It is characterized by abdominal pain or discomfort with a change in bowel habit, often accompanied by symptoms such as bloating (1). It has a considerable impact on quality of life and on direct and indirect healthcare costs (2). Numerous dietary approaches for the management of IBS have been investigated (3); however, robust and consistent evidence of their efficacy is lacking. Research has recently focused on the restriction of a group of fermentable carbohydrates, including oligosaccharides [e.g., fructo-oligosaccharides (FOS) and galacto-oligosaccharides (GOS)], disaccharides (e.g., lactose), monosaccharides (e.g., fructose), and polyols (e.g., sorbitol) (termed FODMAPs). These carbohydrates exhibit varying absorption, are osmotically active in the GI lumen (4), and their fermentation increases gas production (5). Retrospective studies indicate that restriction of these carbohydrates improves overall IBS symptoms in up to 86% of patients (6,7). Furthermore, a randomized, placebo-controlled, rechallenge trial demonstrated symptom recurrence with fructose and/or fructans, but not with placebo (8), suggesting that these fermentable carbohydrates are responsible for symptoms in some patients with IBS.
Fermentable carbohydrates provide an energy source for the GI microbiota, which exhibit a mutualistic relationship with the host (9) and influence both the innate and adaptive immune systems (10,11). Alterations in the GI microbiota, including lower concentrations of bifidobacteria, occur in IBS (12) and have been associated with immune changes and peripheral hypersensitivity in mice (13) and abdominal pain in humans (14).

Carbohydrate fermentation by the microbiota results in the production of SCFA, the primary metabolite for colonocytes. Furthermore, the prebiotic effect of some fermentable carbohydrates, including fructans (e.g., FOS and GOS) is well established. These stimulate the selective growth of luminal bifidobacteria and Faecalibacterium prausnitzii (15). These bacteria are immunomodulatory in patients with inflammatory bowel disease (16,17) and limit enteropathogenic colonization (18), and F. prausnitzii is a major butyrate producer (19).

Modifying dietary carbohydrate can affect the GI microbiota. Restriction of fruit and vegetables alters the overall bacterial community (20), a gluten-free diet significantly reduces bifidobacteria in healthy individuals (21), restriction of total carbohydrate reduces bifidobacteria (22), and complete removal of fermentable fiber reduces total microbiota (23). Restriction of fermentable short-chain carbohydrates has the potential to be effective in the management of IBS; however, it might elicit alterations in the GI microbiota and fermentation products. Despite the potential for benefit, to our knowledge, no randomized controlled trials examining clinical and microbiological endpoints have been undertaken.

Therefore, this randomized controlled trial (RCT) aimed to investigate the effects of fermentable carbohydrate restriction on the luminal microbiota, SCFA, and GI symptoms in patients with IBS.

**Participants and Methods**

We report an RCT conducted in line with CONSORT guidelines. Patients with IBS were assessed for eligibility \((n = 99)\). Those eligible and willing to participate \((n = 41)\) were recruited and randomly allocated to restrict dietary intake of fermentable carbohydrates (FODMAPs) (intervention group) \((n = 19)\) or to continue their habitual diet (control group) \((n = 22)\) for 4 wk (Fig. 1). Symptomatic, stool output, and dietary intake were recorded for 1 wk at baseline and 1 wk at follow-up and a stool sample was collected at baseline and follow-up for analysis of GI microbiota, SCFA, and pH. Patients were recruited from GI outpatient clinics at Guy’s and St Thomas’ NHS Foundation Trust, London. There were no changes to protocol, methods, or outcome measures once the trial commenced. The trial was approved by the Guy’s Research Ethics Committee.

**Participants.** Medical notes of patients aged 18–65 y with a diagnosis of IBS, without a history of other major GI conditions, previous GI resection, or other major organ disorder were reviewed. IBS was defined using Rome III criteria (24). Those with bloating and/or diarrhea were included. Participants were excluded if their major IBS symptom was constipation or if their bloating or diarrhea did not fulfill severity criteria (moderate/severe bloating or type 6 (mushy) or 7 (liquid) stools on at least 2 d during screening). Other exclusion criteria included pregnancy or lactation, use of probiotics, prebiotics, lactulose [also a prebiotic (25)], or bowel preparation in the 4 wk prior to the study, or change to IBS medication in the 4 wk prior to, or during, the study. A total of 53 patients were enrolled in the study.

**Trial protocol.** Informed consent was obtained prior to any study-related procedures. During the 7-d screening period, patients completed a symptom diary based on the GI Symptom Rating Scale (26). Patients recorded IBS symptoms (bloating, abdominal pain, flatulence, borborygms, urgency, diarrhea, constipation, incomplete evacuation, heartburn, nausea, lethargy) at the end of each day using a 4-point scale.

**FIGURE 1** Consort diagram.
(absent, mild, moderate, severe). This scale has been validated in IBS (27) and used in clinical outcome trials (28). A global symptom question regarding satisfaction with symptoms was included on d 7 (“Were your symptoms adequately controlled over the previous week?”). This assessment is the current standard for outcome in treatment trials of IBS (29). Stool frequency and consistency were recorded throughout each day for 7 d using the Bristol Stool Chart. Food and fluid intake was recorded using a 7-d food diary.

After the 7-d baseline screening period, symptom diaries were inspected. Those with sufficient symptom severity to be eligible were recruited. A number of participants failed screening due to mild symptoms (n = 12). Weight, height, and BMI were recorded. A fresh stool sample was collected for molecular microbiology, SCFA, and pH analysis. Patients (n = 41) were randomly allocated to the intervention or control group in a 1:1 ratio and stratified by sex and presence of diarrhea. The random allocation sequence was prepared using a random number generator (Microsoft Excel 2007) and was undertaken by a researcher not involved in patient recruitment (M.C.L.). After recording the baseline measurements, allocation occurred by opening a numbered, sealed envelope. The same researcher undertook all patient screening, enrollment, and assignment of patients to groups (H.M.S.). The intervention group were advised to restrict foods high in fructans (e.g., wheat products, onions), GOS (e.g., legumes), polyols (e.g., pear, sugar-free gums), lactose (e.g., mammalian milk), and excess fructose (e.g., honey). This dietary advice was in line with that used in previous studies (4,5). The control group was advised to continue their habitual diets. All patients were advised to avoid intake of probiotics and prebiotics for the duration of the study. All advice was given by the same experienced dietitian. Baseline visits lasted for at least 45 min for both groups. The same researcher undertook all patient screening, enrollment, and assignment of patients to groups (H.S.) and continued until the required sample size was achieved.

Patients in both the intervention and control groups were contacted weekly via telephone or email. This provided an opportunity to discuss fermentable carbohydrate restriction (intervention group only), avoidance of probiotics and prebiotics, compliance, data recording, medications, and adverse events (both groups). In the final week of the 4-wk study, patients completed another 7-d symptom, stool, and food diary and returned for repeat of all baseline investigations. Dietary compliance of the intervention group was again assessed at wk 4 by examination of the food diaries.

The data on 7-d dietary intake were entered into a computerized database. This was analyzed for nutrient intake using food composition data from standard UK tables (30) and FODMAP intake using published food composition tables (31;32) and the Foodworks software package (Xyris Software).

**Fluorescent in situ hybridization.** A whole, fresh stool sample was collected in a sterile bag and placed on ice prior to being homogenized in a stomacher for 2 min. Processing occurred within 1 h to minimize postvoiding changes in concentration of microbiota.

Stool samples were analyzed for luminal microbiota using fluorescence in situ hybridization (FISH) using a widely adopted protocol (33). The bacteria were fixed, suspended, and stored at −20°C until analysis. The bacteria were serially diluted and mounted onto 3-amino-propyltriethoxysilane treated slides dried at 46°C and the cells were serially dehydrated in 60, 80, and 96% (v/v) ethanol. Total cells counts were quantified using the nucleic acid stain, 4′,6-diamidino-2-phenylindole, dihydrochloride (34). Individual bacterial groups were quantified using Cy3-labeled oligonucleotide probes (Microsynth) targeting specific regions of the bacterial 16S rRNA and which have been used extensively in FISH protocols (33) (Supplemental Table 1). These probes were chosen, because they target bacterial groups that constitute numerically large numbers of the microbiota, some of which are altered in IBS (e.g., bifidobacteria) (12). Removal of dietary prebiotics may also specifically affect microbiota, some of which are altered in IBS (e.g., bifidobacteria) (12). Removal of dietary prebiotics may also specifically affect them (bifidobacteria, F. prausnitzii) (36).

Probes were diluted to 4.5 ng/µL in sterile hybridization buffer [0.9 mol/L NaCl; 0.02 mol/L Tris HCl; 0.01% (wt/v) SDS]. Then, 10 µL of probe solution was added to each well and the slides incubated overnight at 46°C in a saturated humidity chamber. Slides were washed in hybridization buffer at 48–50°C and mounted in PBS-glycerol (50:50).

The hybridized bacteria were manually quantified using an Axiosplan-2 imaging microscope (Zeiss) equipped with an HBO-100 florescent lamp (Osram) by a microscopist who was unaware of the sample allocation. For each probe, 15 randomly selected fields were quantified in duplicate wells. Counts were converted to concentrations, which were log-transformed and also presented as proportions of each bacterial group (compared with 4′,6-diamidino-2-phenylindole, dihydrochloride counts) to standardize for water content.

**SCFA and pH.** Homogenized stool samples were frozen at −80°C within 1 h of voiding to prevent SCFA production or loss. SCFA were extracted from defrosted feces as previously described (23). Extracted SCFA (0.2 µL) were separated on a Hewlett Packard 6890 series GLC system (Agilent Technologies) equipped with a BP21 25-m capillary column with internal diameter of 0.22 mm and film thickness of 0.25 µm (SGE).

Fecal pH was measured on fresh stool, which was diluted 1:4 (vol:vol) in pH buffer (1 × 10−3 mol/L Na2HPO4, KH2PO4, 0.1 g HgCl2), homogenized, and incubated at room temperature for 1 h. The pH was then measured using a pH meter and a pH electrode specifically designed for slurries (VWR).

**Statistical analysis.** The primary endpoint was the effect of fermentable carbohydrate restriction on luminal microbiota. Predefined secondary endpoints were the effect on symptoms, stool output, fecal SCFA and pH, and nutrient intake.

Sample size was calculated to detect a difference of 0.4 log10 in the concentration of luminal bifidobacteria between intervention and control groups. Using a SD for the concentration of bifidobacteria in patients with IBS of 0.32 (37), an α of 0.05 and a power of 0.90, 14 patients were required to compete the study in each group. A target of 20 patients/group was chosen to allow for attrition or insufficient stool sample for measurement of the primary endpoint.

Statistical analyses were performed using SPSS v.18. Data are presented as mean ± SD or n (%) for demographic data. Continuous data at baseline were compared using independent samples t tests. Categorical data were compared using chi-square tests. Continuous data at the 4-wk endpoint were compared between groups using ANCOVA with baseline measures as a covariate and the data presented as estimated marginal means and 95% CI. Data were tested for equality of variances using Levene’s test and residual plots were examined. Where necessary, data were transformed to achieve a satisfactory residual plot. The correlation between baseline concentrations of and change in bifidobacteria were assessed using a Pearson correlation coefficient. Differences were considered significant when P < 0.05.

**Results**

**Participants.** Of the 99 patients assessed for eligibility, 41 patients were randomized to intervention (n = 19) or control (n = 22). All 41 patients were included in the intention-to-treat (ITT) population (predefined endpoints of improvement in symptom scores, response to global symptom question) and 35 were included in the per-protocol analysis (follow-up symptom scores, microbiota, SCFA, pH, nutrient analysis). Of the 6 who were not analyzed, 4 withdrew during the study (2 commenced antibiotics, 1 lost to follow-up, 1 poor symptom control) and 2 were withdrawn from analysis due to protocol violations (one control patient adopted the intervention diet, one did not return a follow-up stool/symptom diary) (Fig. 1). There were no differences in age, sex, weight, BMI, smoking, vegetarianism, or IBS medication in the ITT or per protocol populations (Table 1). There was no change to IBS medication in either group throughout the study.

Four patients had adverse events, 2 in the intervention group (bronchitis, laryngitis) and 2 in the control group (exacerbation of asthma, pharyngitis), none of which were considered related to the trial or intervention.

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Fecal microbiota, SCFA, and pH. Total bacteria, Bacteroides-Prevotella, E. rectale-C. coccoides, F. prausnitzii, and Lactobacillus-enterococcus did not differ at baseline or follow-up. There were lower concentrations ($P < 0.001$) and proportions ($P < 0.001$) of bifidobacteria in the intervention group at follow-up compared with the control group when adjusting for baseline (Table 2). In the intervention group, the change in concentrations of bifidobacteria was negatively correlated with baseline concentrations (Pearson $r = -0.54$, $P = 0.033$) (Fig. 2).

There was no difference in total or individual fecal SCFA between groups at baseline or follow-up adjusting for baseline values (Supplemental Table 2). Furthermore, fecal pH did not differ between the intervention [marginal mean = 6.5 (95% CI = 6.2, 6.7)] and control [6.5 (95% CI = 6.3, 6.8)] groups at baseline when adjusted for baseline values or at follow-up when adjusted for baseline values (not shown). Differences between sexes for fecal microbiota, SCFA, and pH could not be determined due to small numbers of males.

**Symptom response and stool output.** At baseline, in response to the global symptom question, there were no significant differences in those reporting adequate symptom control between the intervention (7/19, 37%) and control groups (9/22, 58%; $P = 0.79$). However, at follow-up, more patients in the intervention group reported adequate symptom control compared with the control group when analyzing ITT (13/19, 68% vs. 5/22, 23%; $P = 0.005$) and per protocol (13/16, 81% vs. 5/19, 26%; $P = 0.002$).

Symptom response was also measured by comparing the incidence and severity of symptoms at follow-up (with adjustments for baseline values). Incidence was the number of days in 7 d that the symptom was experienced and the severity score was calculated as the mean of 7 d of symptoms using the scale 0 (absent), 1 (mild), 2 (moderate), and 3 (severe). The number of patients who experienced a reduction in mean daily symptom score (a combination of incidence and severity) between baseline and follow-up was calculated. In the ITT population, more patients in the intervention group experienced a reduction in scores for bloating ($P = 0.007$), borborygmi ($P = 0.04$), urgency ($P = 0.047$), and overall symptoms ($P = 0.006$) compared with the control group (Fig. 3).

**TABLE 2** GI microbiota in IBS patients after 4 wk of habitual diet intake or fermentable carbohydrate restriction

<table>
<thead>
<tr>
<th>Control$^2$</th>
<th>Intervention$^3$</th>
<th>$P$</th>
<th>Control$^2$</th>
<th>Intervention$^3$</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total bacteria</td>
<td>9.7 (9.5–9.8) 9.7 (9.6–9.9)</td>
<td>0.52</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Bacteroides-Prevotella</td>
<td>8.7 (8.6–8.9) 8.8 (8.6–8.9)</td>
<td>0.52</td>
<td>17.4 (9.2–25.7) 15.2 (6.2–24.3)</td>
<td>0.72</td>
<td></td>
</tr>
<tr>
<td>E. rectale-C. coccoides</td>
<td>8.8 (8.6–8.9) 8.7 (8.6–8.9)</td>
<td>0.58</td>
<td>15.7 (10.9–20.5) 11.8 (6.8–17.0)</td>
<td>0.27</td>
<td></td>
</tr>
<tr>
<td>F. prausnitzii</td>
<td>8.6 (8.6–9.0) 8.8 (8.5–9.0)</td>
<td>&lt;0.001</td>
<td>17.9 (13.3–22.6) 13.1 (8.0–18.2)</td>
<td>0.16</td>
<td></td>
</tr>
<tr>
<td>Bifidobacteria</td>
<td>7.4 (7.1–7.7) 7.4 (7.1–7.7)</td>
<td>0.98</td>
<td>1.0 (0.7–1.4) 0.6 (0.2–1.1)</td>
<td>0.17</td>
<td></td>
</tr>
</tbody>
</table>

1 Values are estimated marginal means (95% CI) analyzed on the per-protocol population, control $n = 19$, intervention $n = 16$.

2 Participants who continued habitual diet.

3 Participants who received fermentable carbohydrate restriction advice.

4 Log transformation required, geometric mean reported. GI, gastrointestinal; IBS, irritable bowel syndrome; ITT, intention-to-treat.
At baseline, the incidence of symptoms did not differ between groups, except for nausea, which was less frequent in the intervention group. However, at follow-up, there was a lower incidence of bloating, abdominal pain, and overall symptoms in the intervention group compared with the control group (Table 3).

Likewise, the severity of symptoms was similar between groups at baseline, except for nausea, which was less severe in the intervention group. However, at follow-up, there were lower mean daily severity scores for bloating, flatulence, tiredness, and overall symptoms in the intervention group compared with the control group. Diarrhea severity scores were similar in groups at follow-up (Table 3).

Stool frequency and consistency was similar at baseline, but at follow-up, after adjusting for baseline, the intervention group reported lower stool frequency than the control group and a greater proportion of stools with normal consistency (type 3 or 4) in the intervention group (Table 4).

Diet. Consumption of total fermentable carbohydrates, FOS, GOS, polyols, and fructose was lower in the intervention group compared with the control group after adjusting for baseline values (Table 5). At follow-up, intakes of carbohydrates, starch, total sugars, and calcium were lower in the intervention group than in the control group despite no differences at baseline. Weight was lower in the intervention group [marginal mean = 71.7 kg (95% CI = 71.2, 72.2)] compared with the control group [72.4 kg (72.0, 72.9)] at follow-up after adjustment for baseline values (P = 0.036).
paradox, specifically, that a dietary intervention that improves
(42). Our results lead to the emergence of an interesting
potential therapeutic benefit of bifidobacteria probiotics in IBS
(41). Finally, a number of studies have indicated the
wean low bifidobacteria and abdominal pain in healthy
teria (40). Furthermore, studies have found an association bet-
(39) and a specific role in IBS is emerging. Patients with IBS may
bifidobacteria was, until now, unclear.

**Discussion**

This is the first RCT, to our knowledge, to investigate the
microbiological sequelae of dietary restriction of this novel
dietary approach that restricts short-chain fermentable carbo-
hydrates in patients with IBS (38). This restriction resulted in a
large and significant reduction in fecal bifidobacteria, an effect
that is most likely due to the reduced availability of fructans
(including FOS) and GOS for bacterial fermentation in the GI
tract. The effects of prebiotic supplementation and augmenta-
tion of luminal bifidobacteria have been extensively investigated
(39); however, the consequences of prebiotic restriction on
bifidobacteria was, until now, unclear.

The potential benefits of bifidobacteria are well established
(39) and a specific role in IBS is emerging. Patients with IBS may
have lower concentrations of luminal and mucosal bifidobac-
teria (40). Furthermore, studies have found an association be-
 tween low bifidobacteria and abdominal pain in healthy
indivduals (14) and the number of days of pain in patients with
IBS (41). Finally, a number of studies have indicated the
potential therapeutic benefit of bifidobacteria probiotics in IBS
(42). Our results lead to the emergence of an interesting
paradox, specifically, that a dietary intervention that improves
IBS symptoms also results in a reduction in bifidobacteria.
Whether a bifidobacteria probiotic in addition to fermentable
carbohydrate restriction enhances the symptom response in this
patient group is yet to be determined.

It is unknown whether the changes that occurred in the
microbiota are acute (occurring very rapidly) or chronic (taking
4 wk). More frequent fecal sampling would have helped track the
timing of these alterations, although it would have added to the
burden on participants. It is also not known whether the reduction
in bifidobacteria persists once fermentable carbohydrates are re-
introduced to tolerance, which is advised after a 4–6 wk restriction
(38), and hence whether this change is long term. It is clear
that microbiota are resilient to permanent changes in the absence
of environmental stressors. For example, in most healthy humans,
the microbiota return to their relatively stable state after the
cessation of antibiotics (43,44) and diet-driven changes in the
microbiota rapidly reverse (45).

The capacity for the microbiota to respond to dietary change
differs markedly between individuals (45). For example, healthy
people with lower fecal bifidobacteria have a greater increase in
this genus following prebiotic supplementation (46). For the first
time, to our knowledge, we demonstrated that the reverse is true
when prebiotic carbohydrates are restricted in that IBS patients

**TABLE 3** Incidence and severity of symptoms in IBS patients after 4 wk of habitual diet intake or fermentable carbohydrate restriction

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Control Incidence, d/wk</th>
<th>Intervention Incidence, d/wk</th>
<th>P</th>
<th>Control Severity score</th>
<th>Intervention Severity score</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bloating</td>
<td>5.7 (4.9–6.4)</td>
<td>3.8 (3.0–4.6)</td>
<td>0.002</td>
<td>1.4 (1.2–1.6)</td>
<td>0.9 (0.6–1.1)</td>
<td>0.002</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>4.8 (4.1–5.5)</td>
<td>3.6 (2.8–4.4)</td>
<td>0.02</td>
<td>1.1 (0.9–1.4)</td>
<td>0.8 (0.5–1.1)</td>
<td>0.07</td>
</tr>
<tr>
<td>Flatulence</td>
<td>5.6 (4.6–6.5)</td>
<td>4.3 (3.3–5.3)</td>
<td>0.07</td>
<td>1.2 (1.0–1.5)</td>
<td>0.8 (0.5–1.1)</td>
<td>0.018</td>
</tr>
<tr>
<td>Borborygmi</td>
<td>2.8 (1.9–3.7)</td>
<td>2.0 (1.0–3.0)</td>
<td>0.22</td>
<td>0.7 (0.4–0.9)</td>
<td>0.4 (0.2–0.6)</td>
<td>0.11</td>
</tr>
<tr>
<td>Urgency</td>
<td>3.7 (2.7–4.7)</td>
<td>2.6 (1.5–3.7)</td>
<td>0.15</td>
<td>0.8 (0.6–1.1)</td>
<td>0.6 (0.3–0.8)</td>
<td>0.13</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>2.2 (1.3–3.1)</td>
<td>1.4 (0.4–2.4)</td>
<td>0.24</td>
<td>0.4 (0.2–0.6)</td>
<td>0.3 (0.1–0.5)</td>
<td>0.34</td>
</tr>
<tr>
<td>Constipation</td>
<td>1.0 (0.5–1.5)</td>
<td>0.8 (0.3–1.3)</td>
<td>0.56</td>
<td>0.2 (0.1–0.2)</td>
<td>0.1 (0.1–0.2)</td>
<td>0.69</td>
</tr>
<tr>
<td>Incomplete evacuation</td>
<td>3.1 (2.1–4.1)</td>
<td>2.1 (1.0–3.2)</td>
<td>0.16</td>
<td>0.7 (0.4–0.9)</td>
<td>0.4 (0.2–0.7)</td>
<td>0.16</td>
</tr>
<tr>
<td>Heartburn</td>
<td>0.5 (0.0–1.1)</td>
<td>0.7 (0.0–1.3)</td>
<td>0.70</td>
<td>0.1 (0.0–0.2)</td>
<td>0.1 (0.0–0.2)</td>
<td>0.98</td>
</tr>
<tr>
<td>Nausea</td>
<td>1.8 (0.9–2.7)</td>
<td>1.5 (0.5–2.5)</td>
<td>0.67</td>
<td>0.4 (0.2–0.6)</td>
<td>0.3 (0.1–0.5)</td>
<td>0.64</td>
</tr>
<tr>
<td>Tiredness</td>
<td>2.0 (1.1–3.9)</td>
<td>1.3 (0.6–2.6)</td>
<td>0.36</td>
<td>0.9 (0.7–1.1)</td>
<td>0.5 (0.3–0.7)</td>
<td>0.015</td>
</tr>
<tr>
<td>Overall</td>
<td>1.6 (1.3–1.9)</td>
<td>0.9 (0.8–1.1)</td>
<td>0.001</td>
<td>1.7 (1.4–1.9)</td>
<td>1.1 (0.8–1.3)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

1 Participants who continued habitual diet. IBS, irritable bowel syndrome.
2 Participants who received fermentable carbohydrate restriction advice.
3 The estimated marginal mean (95% CI) for number of days >1 wk that patients experienced a symptom, comparing the control group, n = 19, with the intervention group, n = 16. Data are from the per-protocol population.
4 Proportion of stools rated as type 3 or 4 on BSC.
5 Log transformation required, geometric mean reported.

**TABLE 4** Stool frequency, consistency, and percentage of stools with normal consistency in IBS patients after 4 wk of habitual diet intake or fermentable carbohydrate restriction

<table>
<thead>
<tr>
<th>Stool output</th>
<th>Control</th>
<th>Intervention</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stool frequency, n/wk</td>
<td>13.5 (11.9–15.1)</td>
<td>10.2 (8.5–11.9)</td>
<td>0.008</td>
</tr>
<tr>
<td>Stool consistency, BSC score</td>
<td>4.7 (4.2–5.1)</td>
<td>4.5 (4.0–5.0)</td>
<td>0.56</td>
</tr>
<tr>
<td>Percentage of stools with normal consistency, %</td>
<td>6.65 (5.6–14.9)</td>
<td>23.65 (11.9–38.1)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

1 Values are estimated marginal means (95% CI) analyzed on the per-protocol population, control, n = 19, intervention, n = 16. BSC, Bristol Stool Chart; IBS, irritable bowel syndrome.
2 Participants who continued habitual diet.
3 Participants who received fermentable carbohydrate restriction advice.
4 Proportion of stools rated as type 3 or 4 on BSC.
5 Square root transformed, squared estimated marginal mean reported.
TABLE 5  Daily nutrient and fermentable carbohydrate intakes by IBS patients after 4 wk of habitual diet intake or fermentable carbohydrate restriction

<table>
<thead>
<tr>
<th>Nutrients</th>
<th>Control²</th>
<th>Intervention³</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy, kcal</td>
<td>1850 (1700–1900)</td>
<td>1810 (1650–1700)</td>
<td>0.74</td>
</tr>
<tr>
<td>Protein, g</td>
<td>71 (64–78)</td>
<td>73 (65–81)</td>
<td>0.74</td>
</tr>
<tr>
<td>Fat, g</td>
<td>70 (61–79)</td>
<td>75 (65–85)</td>
<td>0.45</td>
</tr>
<tr>
<td>Carbohydrate, g</td>
<td>234 (218–250)</td>
<td>203 (186–221)</td>
<td>0.012</td>
</tr>
<tr>
<td>Starch, g</td>
<td>130 (118–142)</td>
<td>111 (98–124)</td>
<td>0.038</td>
</tr>
<tr>
<td>Total sugars, g</td>
<td>97 (88–106)</td>
<td>78 (68–88)</td>
<td>0.008</td>
</tr>
<tr>
<td>Nonstarch polysaccharide, g</td>
<td>15 (13–16)</td>
<td>14 (12–15)</td>
<td></td>
</tr>
<tr>
<td>Calcium, mg</td>
<td>730 (663–796)</td>
<td>603 (530–675)</td>
<td>0.016</td>
</tr>
<tr>
<td>Iron, mg</td>
<td>10.4 (9.4–11.5)</td>
<td>9.0 (7.9–10.2)</td>
<td>0.09</td>
</tr>
<tr>
<td>Total fermentable carbohydrates⁴</td>
<td>29.6 (24.5–35.7)</td>
<td>17.7 (14.4–21.7)</td>
<td>0.001</td>
</tr>
<tr>
<td>FOS, g</td>
<td>3.6 (2.9–4.2)</td>
<td>1.7 (1.0–2.4)</td>
<td>0.001</td>
</tr>
<tr>
<td>GOS, g</td>
<td>2.0 (1.4–2.5)</td>
<td>1.0 (0.5–1.6)</td>
<td>0.023</td>
</tr>
<tr>
<td>Polyols, g</td>
<td>0.6 (0.4–0.8)</td>
<td>0.2 (0.1–0.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sorbitol, g</td>
<td>0.4 (0.2–0.5)</td>
<td>0.1 (0.0–0.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mannitol, g</td>
<td>0.3 (0.1–0.4)</td>
<td>0.0 (0–0.3)</td>
<td>0.24</td>
</tr>
<tr>
<td>Lactose, g</td>
<td>7.0 (4.9–9.1)</td>
<td>5.0 (2.8–7.3)</td>
<td>0.20</td>
</tr>
<tr>
<td>Fructose, g</td>
<td>16.6 (13.4–20.6)</td>
<td>9.8 (7.8–12.4)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

1 Values are estimated marginal means (95% CI) analyzed on the per-protocol population, control n = 19, intervention n = 16. FOS, fructo-oligosaccharide; GOS, galacto-oligosaccharide; IBS, irritable bowel syndrome.
² Participants who continued habitual diet.
³ Participants who received fermentable carbohydrate restriction advice.
⁴ Fermentable carbohydrates do not sum to total fermentable carbohydrate value due to transformation of data.
⁵ Log-transformed, geometric mean reported.
⁶ Square root-transformed, squared estimated marginal means reported.

with higher fecal bifidobacteria at baseline had a greater reduction. It is likely that the effect of microbial changes on colonic health will be individually variable and long-term studies are required to confirm the implications of these findings on disease risk. Should this reduction persist, supplementation with probiotic bifidobacteria may be one approach to augment bifidobacteria. Furthermore, the luminal microbiota may be distinct from that in the mucosa (47) and whether change occurred at the mucosal level remains unknown.

Culture-based approaches detect ~20% of the number of phylotypes that some culture-independent techniques can detect (48). FISH provides accurate information on the concentration of selected bacterial groups (9). However, only a select number of probes were used and changes in other numerically less dominant microbiota cannot be excluded.

Change in the microbial population might be expected to affect total or proportions of fecal SCFA (22). However, the total bacteria did not differ between groups or in total or individual SCFA at follow-up. Fecal SCFA better reflect colonic absorption rather than production as a result of being influenced by colonic transit time (49), which of course may be altered by dietary change. Measuring SCFA in the ascending colon would be a better marker of the rapid fermentation of short-chain fermentable carbohydrates that occurs there; however, accessing this is unfeasible. Finally, total carbohydrate intake at follow-up was still high even in the intervention group and this may have contributed to colonic fermentation and maintenance of SCFA.

Four weeks of dietary restriction of fermentable short-chain carbohydrates resulted in lower incidence and severity of bloating and overall symptoms in patients compared with controls. Importantly, the responses to the global symptom question highlighted the effectiveness of the intervention (68–81% reported adequate symptom control). The sample was representative of those with IBS seen in routine gastroenterology practice (Table 1) and therefore these results are likely to be reproducible in a wider population of IBS patients whose symptoms include diarrhea or bloating. These results are also in line with previous non-RCT trials of this dietary approach and its effect on symptom response (6–8). “Symptom improvement” in IBS trials is difficult to define, because significant differences in mean scores may not necessarily equate to patient symptom experience. Conversely, a clinical improvement may not be represented by a significant reduction in score. We therefore presented a range of symptom data, including the gold standard dichotomous global score as well as severity and incidence data to capture a fuller picture of patient symptomology.

There was no difference in stool consistency or the incidence or severity of self-reported diarrhea between groups at follow-up despite evidence that restriction of fermentable carbohydrates decrease water delivery to the proximal colon (4). This might reflect aspects of the study design and outcome measurement. There was a lower stool frequency and greater proportion of stools with normal consistency (type 3 or 4) in the intervention group using objective measures and reduced urgency compared with controls, indicating a role for this diet in normalizing stool output. An alternative explanation might be that any advantage of fermentable carbohydrate restriction in reducing ileal water absorption might be compensated for by decreased colonic water absorption due to reduced SCFA production in the ascending colon (50).

We acknowledge that there are limitations of this study design. Although the control group received similar contact time at study visits and weekly communication, they did not receive any advice for their symptoms. Symptomatic response in the intervention group could therefore at least partly be due to the placebo response. This limitation could be overcome by blinding the dietary treatment, which can be achieved through providing all food and drink to participants; however, this is not only prohibitively expensive but also does not reflect the real-world clinical situation. Instead, alternative dietary advice could have been implemented in the control group. However, because the primary outcome of this study was the effect of the intervention on the GI microbiota, the control group were advised to continue with a stable habitual dietary intake in order to provide a suitable microbiosa control. The placebo effect is unlikely to affect the GI microbiota, although this might have occurred for symptom response data. Lastly, the effect of this dietary treatment was not investigated in constipation-predominant IBS and therefore the clinical effectiveness of fermentable carbohydrate restriction can only be applied to those without constipation as a predominant symptom.

Dietary intake analysis revealed the intervention group complied with the dietary advice provided, because total short-chain fermentable carbohydrate intake was lower at follow-up compared with controls (P = 0.001). Lactose and fructose intake was reduced in the intervention group, as per the advice provided. The utility of hydrogen or methane breath testing in this population was previously described (38). The impact of fermentable carbohydrate restriction on breath gas profile would have been informative in the current study but was not measured in order to minimize participant burden.

Although baseline nutrient intakes did not differ, there were lower intakes of total carbohydrate, starch, and total sugars in the fermentable short-chain carbohydrate-restricted group at follow-up compared with the control group. This is partly expected, because patients were advised to make considerable
changes to their dietary carbohydrate sources. Calcium intake was lower in the intervention group, which may be due to a real reduction in intake (e.g., reduction in dairy intake), to measurement error (poor availability of nutrient composition data for novel lactose-free products), or a combination of the two. It is unlikely that the differences in calcium intake had any impact on the GI microbiota. The reduction in total carbohydrate intake might be argued to be responsible for the reduction in bifidobacteria in the intervention group. Certainly, reduced carbohydrate intake has been associated with reduced bifidobacteria concentrations (22,35); however, the carbohydrate intake in these studies was very low (20–24 g/d), ~10% of that found in the current study. Furthermore, there were no significant changes in the intake of total carbohydrate within groups during the study and changes that did occur were likely specifically due to the restriction of short-chain fermentable carbohydrates.

Restriction of fermentable short-chain carbohydrates is an effective management strategy for IBS, resulting in reductions in overall symptoms and bloating. However, this dietary therapy results in significant reductions in luminal bifidobacteria after 4 wk. Whether this effect persists over time or has any detrimental effects on long-term colonic health is yet to be determined.

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Literature Cited


