Controlled Trial of Oligofructose in the Management of Irritable Bowel Syndrome

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ABSTRACT A double-blind crossover trial of oligofructose (Raftilose P95) 2 g three times daily against sucrose (1 g) three times daily was performed in patients suffering from irritable bowel syndrome. Each treatment was followed for 4 wk. Patients consumed a standardized diet during the last 14 d of each treatment period, and symptoms were assessed using a previously validated questionnaire. Fecal weight and pH, whole-gut transit time and fasting breath hydrogen concentrations were measured at the start of the study and at the end of each treatment period. Oligofructose produced no significant change in any of these parameters even when patients were divided into those with predominant diarrhea (n = 14) and those with predominant constipation (n = 7). Oligofructose at a dose of 6 g/d had no therapeutic value in patients with irritable bowel syndrome. J. Nutr. 129: 1451S–1453S, 1999.

KEY WORDS: • oligofructose • irritable bowel syndrome • diarrhea • constipation

Irritable bowel syndrome (IBS) is an extremely common gastrointestinal disorder reported to affect as many as 15–20% of the adult population of the Western world at some time in their lives. People with IBS account for ~10% of visits to general practitioners and for at least 50% of those referred to gastroenterologists. Symptoms include abdominal pain, distention, flatulence, and constipation or diarrhea. There may also be extra colonic symptoms such as headache, nausea, tiredness, fluid retention and joint pain. These symptoms may be sufficiently severe to impair the quality of life of the patients concerned, but endoscopic, radiologic and histologic studies of the gut reveal no pathology (Maxwell et al. 1997). Because of the plethora of symptoms with no detectable underlying pathology, many have considered IBS to be a predominantly psychological disorder. Although there can be no doubt that some patients with gut symptoms of this type are suffering from anxiety or depression, it is now known that ~50% of cases of IBS are due to food intolerance. Symptoms can be relieved by the exclusion of specific foods from the diet; wheat, dairy products, caffeine, yeast and citrus fruit are particularly likely to cause problems (Alun Jones et al. 1982). Immunologic studies have revealed no evidence of food allergy. Many cases of IBS follow bouts of gastroenteritis (McKendrick et al. 1994) or courses of antibiotics (Alun Jones et al. 1984), and the gut flora may be abnormal with an increase in the number of facultative anaerobes together with a reduction in Bifidobacteria (Bayliss et al. 1984). Recently, we have shown that patients with IBS have abnormal colonic fermentation with increased hydrogen production that is greatly reduced when the patient is retested after following a diet containing equal amounts of substrates for fermentation such as fiber and non-starch polysaccharides, but excluding those foods that typically provoke symptoms (King et al. 1998). It thus appears that as many as 50% of patients with IBS have abnormal colonic fermentation. Although symptoms may be well controlled by exclusion diets, the management of the condition would be greatly simplified if fermentation could be corrected. We have successfully treated some patients with IBS with probiotic bacteria (Fuller 1991, Hunter et al. 1996). However, probiotics are of limited value because colonization resistance prevents their becoming established permanently in the gastrointestinal tract and patients’ symptoms return shortly after withdrawing treatment.

A recent study in normal human volunteers has demonstrated that supplementation with chicory inulin or oligofructose leads to considerable changes in the composition of the fecal flora with Bifidobacteria increasing greatly in numbers (Gibson et al. 1995). It seemed possible therefore that patients with IBS might benefit from treatment with oligofructose, which might correct imbalances in the fecal flora by encouraging a relative increase in the numbers of indigenous Bifidobacteria. This study was designed to show whether there were indeed symptomatic and objective benefits after treatment with oligofructose in patients with IBS.

PATIENTS AND METHODS

Patients aged 18–65 y of either sex attending Medical Outpatients at Addenbrooke’s Hospital who were found to have a diagnosis of IBS after exclusion of other gastrointestinal disorders were eligible for the study. All had a normal blood count and erythrocyte sedimentation rate and normal serum biochemistry, including urea, glucose, electrolytes, albumin, liver function tests, calcium and phos-
phate. Stool cultures were negative for common pathogens. Sigmoidoscopy was normal in all cases. Barium enema was performed in patients >40 y of age and showed no abnormality other than diverticular disease. Details of inclusion and exclusion criteria are listed in the original protocol. The study was approved by the Local Research Ethics Committee, Addenbrooke’s Hospital, Cambridge.

This was a randomized, controlled, double-blind, crossover study of oligofructose (Raftilose P95) 2 g three times per day or sucrose 1 g three times per day. All patients starting the placebo or active treatment phases followed their normal diets for the first 2 wk. This was followed by 2 wk of consuming a controlled standard UK diet designed to give 45, 40 and 15% of energy from carbohydrate, fat and protein, respectively, in the form of a 3-d rotated menu. Energy requirements for individuals were calculated by Schofield’s equation (Schofield et al. 1985), and total dietary energy was modified accordingly. The diets were also matched for fiber (mean non-starch polysaccharide 12.5 g), starch and resistant starch (mean total starch, 128 g; resistant starch, 3.6 g). This was to avoid fluctuations in fermentation due to dietary variations.

Symptom scores were calculated for 3 d before each treatment period and over the last 14 d of each treatment period. Fecal weights, fecal pH and whole-gut transit time were determined immediately before entry into the study and over the last day of each treatment period.

METHODS

Symptom scores were recorded using a previously validated questionnaire (King and Hunter 1997).

**Fecal weight.** Patients were provided with a weighed container and were instructed to collect all feces passed during the ensuing 72 h. At the end of this time, the container was returned to the department and reweighed.

**Whole-gut transit time.** Radio-opaque markers were swallowed daily for 14 d and the mean whole-gut transit time was derived from an abdominal X-ray taken on the final treatment day using the method of Fotherby and Hunter (1987).

**Fasting breath hydrogen concentrations.** On the last day of each treatment period, after an overnight fast, samples of end-expired air were collected from patients and analyzed for hydrogen using an electrochemical cell (GMI, Renfrew, Scotland).

RESULTS

Twenty-one subjects completed the trial. Demographic data are given in Table 1. Fourteen patients suffered predominant diarrhea, seven constipation.

**Symptom scores.** There was no difference between the symptom scores in the patients in the 3 d before entering the study compared with the 3 d at the end of the washout before the second treatment period. Thus there appeared to be no hangover effect of either treatment on the second period.

For the group of 21 patients as a whole, there was no significant difference in the total symptom score between the first treatment period and the second. Nor were any changes apparent in any individual symptom. This made a placebo effect of the first treatment unlikely. When symptom scores for those receiving active treatment were compared with those receiving placebo, again no significant difference was discovered, either in the total symptom score (Fig. 1) or for individual symptoms. There was no difference between symptoms when those patients with predominant diarrhea or those with predominant constipation were considered separately.

**Whole-gut transit times (WGTT).** The mean WGTT was 45.77 ± 20.15 h in patients with diarrhea, and 68.11 ± 36.16 h in those with constipation. The corresponding results after oligofructose consumption were 44.22 ± 13.4 and 74.74 ± 29.5; for placebo, they were 48.73 ± 25.98 and 77.82 ± 35.45 h, respectively. There was no significant change.

**Fecal weight.** The mean fecal weight was 665.78 ± 364.05 g in patients with diarrhea and 616.71 ± 529.94 g in those with constipation. With consumption of oligofructose, the corresponding figures were 602 ± 240.4 g and 382.28 ± 364.53 g and with placebo, 545.69 ± 307.89 g and 577.2 ± 516.2 g, respectively. There was no significant difference (Fig. 2).

| TABLE 1 |
| Demographic details of patients in trial |
| Mean age ± SD |
| Group | Male | Female |
| All patients | 43.7 ± 6.9 | 43.9 ± 12.9 |
| n = 4 | n = 17 |
| Diarrhea group | 43.7 ± 6.9 | 48.5 ± 12.6 |
| n = 4 | n = 10 |
| Constipation group | 38.8 ± 12.8 | |
| n = 7 | |
The irritable bowel syndrome is a very variable condition, and symptoms may change considerably from one day to another. Although patients may describe themselves as being predominantly sufferers of diarrhea or constipation, it is apparent from this study that there may be considerable overlap between the groups. Although transit times were longer in the constipated group, fecal weights were only slightly lower compared with those of the 14 patients with diarrhea.

However, in this study, an attempt was made to smooth out symptomatic fluctuations by standardizing the diet and by recording symptoms after treatment over 14 d. Despite these measures, no significant effect of oligofructose could be detected. It may be that the dose of oligofructose was too low. Previous studies in constipation have suggested that 20 g is effective in increasing stool weight and frequency (Kleesen et al. 1997). In this study, there was a decrease in fecal weight in the constipated group receiving oligofructose and transit times were slightly longer. The dose of 6 g was chosen because it was feared that a higher dose might provoke unacceptable diarrhea, pain or flatulence in patients whose IBS was associated with increased stool frequency. In hindsight, it was probably too low. It is of interest that lactulose, a known prebiotic that increases fecal counts of both Lactobacillus and Bifidobacterium, is of great value in the relief of constipation but is not generally considered to have a role in the management of diarrhea (Roberfroid et al. 1998). It may be that oligofructose may prove to have a similar effect.

However, because at least 50% of patients with IBS are known to have food intolerance, which in turn is the effect of abnormal colonic fermentation, it would be premature to discard oligofructose without further investigation, particularly because the counts of Bifidobacterium have been shown to be low in some of these patients (Bayliss et al. 1984). Direct studies of fermentation in these patients with and without fructose-oligosaccharide should be performed using the calorimetry model developed by King et al. (1998) and assessing the value of higher doses. Further clinical studies would be justified if these fermentation studies suggested that oligofructose did indeed improve abnormal colonic fermentation.

**FIGURE 2** Three-day fecal weights in patients at baseline and after treatment with oligofructose (active) and sucrose (placebo).

**Fecal pH.** The mean fecal pH was 6.66 ± 0.88 in subjects with diarrhea and 7.33 ± 1.01 in those with constipation. With consumption of oligofructose, the corresponding figures were 6.4 ± 0.71 and 7.13 ± 1.62; with placebo, they were 6.31 ± 0.7 and 7.43 ± 1.09, respectively. There was no significant difference.

**Fasting breath hydrogen.** The mean fasting breath hydrogen was 8.71 ± 11.61 ppm in those with diarrhea and 21.42 ± 36.84 ppm in those with constipation. Corresponding figures were 4.78 ± 4.85 ppm and 3.42 ± 3.5 ppm with oligofructose and 7.38 ± 13.83 ppm and 18.14 ± 22.34 ppm with placebo, respectively. There was no significant difference.

**DISCUSSION**

Previous studies have shown that oligofructose, as well as native inulin from chicory, has a stool-bulking activity producing an increase in fecal weight of 1–2 g for each gram of inulin or oligofructose ingested, if the initial stool frequency had been low (Gibson et al. 1995). In elderly people, native inulin from chicory had a moderate laxative effect, relieving constipation (Kleesen et al. 1997). However, there was no clear effect on gut transit times. Fructose-oligosaccharide is known to increase counts of Bifidobacteria in healthy volunteers (Gibson et al. 1995); therefore, it may, like lactulose, have therapeutic value in the treatment of constipation (Kleesen et al. 1997).

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