



Reduction of dietary poorly absorbed short-chain carbohydrates (FODMAPs) improves abdominal symptoms in patients with inflammatory bowel disease—a pilot study

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Abstract

Objective: Functional gut symptoms are common in patients with inflammatory bowel disease (IBD). Since poorly absorbed, short-chain carbohydrates (FODMAPs) appear to play an important role in the induction of functional gut symptoms, we aimed to determine the effect of their dietary restriction on abdominal symptoms in patients with stable IBD and to examine factors associated with success of and adherence to the diet.

Material and method: 52 consecutive patients with Crohn's disease and 20 with ulcerative colitis who received dietary advice at least 3 months prior at a gastrointestinal dietetic service in Victoria, Australia, underwent a retrospective telephone questionnaire. Information gathered included patient demographics, recall of dietary advice, dietary adherence, and change in gastrointestinal symptoms.

Results: Up to 70% of patients were adherent to the diet. Approximately one in two patients responded (defined as improvement of at least 5 out of 10 in overall symptoms). Overall abdominal symptoms, abdominal pain, bloating, wind and diarrhoea improved in patients with Crohn's disease and ulcerative colitis ($p < 0.02$ for all), but constipation did not. For Crohn's disease, efficacy was associated with dietary adherence ($p = 0.033$) and inefficacy with non-adherence ($p = 0.013$). Sustained response was associated with post-secondary education and working 35 h per week or less ($p < 0.03$).

Conclusions: These data suggest that reduction of FODMAP intake offers an efficacious strategy for patients with IBD who have concurrent functional gut symptoms. A controlled dietary intervention trial is indicated.

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1. Introduction

One of the greatest challenges to gastroenterologists is the management of patients with inflammatory bowel disease (IBD). Since the cause is unknown and medical cure is not currently attainable, the principal aim of therapy is induction of clinical remission. Thus, therapy is generally directed towards reducing gastrointestinal inflammation with subsequent resolution of symptoms. However, patients with IBD often have symptoms related to concurrent functional gut disturbance. These symptoms are less likely to respond to even the most effective anti-inflammatory therapy. Gut symptoms such as bloating, abdominal pain, wind, and diarrhoea are common and have adverse effects on quality of life. In one study, 57% of patients with Crohn's disease, and 33% of patients with ulcerative colitis experienced IBS-like symptoms of at least moderate severity in the preceding week.¹ Recognising functional symptoms in patients with IBD is important not only to avoid inappropriate anti-inflammatory therapy, but also because effective treatment of functional gut symptoms could potentially improve daily functioning and quality of life in many IBD patients.²

Therapy of functional gut disorders has lagged well behind advances in anti-inflammatory therapy. However, there has been a recent resurgence in dietary approaches to functional gut disorders such as irritable bowel syndrome (IBS) and functional bloating. Carbohydrate malabsorption has long been a candidate mechanism by which diet can induce gut symptoms. Lactose malabsorption has been identified as a potential trigger of symptoms due to the rapid fermentability and high osmotic activity of malabsorbed lactose,³ and its prevalence in patients with small intestinal Crohn's disease (70%) is much higher than that of both the general population and of patients with colonic Crohn's disease (15%).⁴ Fructose has also been identified as a possible precipitant of functional symptoms in those who incompletely absorb the sugar, a common occurrence even in the healthy, asymptomatic population.⁵ The prevalence of fructose malabsorption in IBD is unknown, but multiple factors favour its malabsorption. These include the presence of small bacterial overgrowth,⁶ small intestinal mucosal disease and shortened bowel length together with alterations in transit time and exposure to cytokines that might reduce small intestinal absorption of fructose.⁷

Malabsorption of rapidly fermented and osmotically active carbohydrates is not restricted to lactose and fructose. A family of poorly absorbed short-chain carbohydrates is now identified and is collectively termed FODMAPs (*F*ermentable, *O*ligo-, *D*i-, *M*ono-saccharides *A*nd *P*olyols). FODMAPs include (with examples) fructo-oligosaccharides (wheat, onions, legumes), lactose (milk, ice-cream), fructose (apples, honey), galactans (legumes) and sorbitol (stone fruits, artificial sweetener).⁸ In theory, FODMAPs induce gastrointestinal symptoms via rapidity of gas production from their ready fermentation by intestinal bacteria and by increased fluid delivery to the large bowel via their osmotic effect.

Multiple provocation tests have demonstrated that FODMAPs induce symptoms and increase the production of gases associated with fermentation. Dietary studies have revealed that limiting FODMAPs (as either fructose alone, fructose and sorbitol, or all FODMAPs) results in improvement of symptoms in greater than 50% of patients with IBS or other functional gut disorders.⁹⁻¹² Recent studies have demonstrated that such

effects are unlikely to be purely due to placebo, but related to ingestion of FODMAPs in patients whose intestines adapt poorly to the effects of malabsorbed short-chain carbohydrates.¹³

The present study aimed to address the hypothesis that FODMAPs are clinically significant dietary triggers of functional abdominal symptoms in patients with IBD. To do this, the symptomatic response associated with implementation of a low FODMAP diet in a cohort of patients with IBD whose symptoms were felt likely to be non-inflammatory in origin was examined. The study also aimed to identify factors that relate to the success of the implementation of the diet, including those associated with adherence to the diet and barriers to its use.

2. Materials and methods

2.1. Case ascertainment

The clinical notes of accredited practising dietitians specialising in gastrointestinal disease at Box Hill Hospital public and private practices were screened for patients with IBD using both manual and computer text-searching. Patients with IBD were included in the study if they had received dietary intervention aimed at reducing gastrointestinal symptoms. Referrals were prompted by patients who, in the judgment of the referring clinician, had persistent abdominal symptoms despite apparent control of intestinal inflammatory disease by therapy. They were excluded from the study if they saw a dietitian for advice concerning weight gain and caloric supplementation, or if they also had coeliac disease. These patients were referred from secondary and tertiary Gastroenterology Departments around Victoria, Australia.

Dietary counselling methodology has been previously described in detail.⁹ Briefly, patients were instructed in the low FODMAP diet in a one-on-one session, and were given written information on the diet and food lists to assist. Recipe books were available for purchase. The patients were offered further consultations with the dietitian if desired by the patient. Reasons for repeat consultation for general dietary review, confirmation of understanding of dietary principles, request for strategies and advice regarding purchasing and preparing foods suitable for a low FODMAP diet, or non- or limited-response, requiring further dietary evaluation and advice. In some patients, review was initiated by the dietitian due to uncertainty that the diet was understood. The principles of the dietary education provided have been detailed elsewhere.^{9,14}

2.2. Data collection

A structured telephone interview was performed by one of three of the investigators (RBG, PMI or DN), none of whom were dietitians involved in giving the dietary intervention. Before the interview, the patients were told that they should answer the questions honestly and that the results were confidential. A wide range of data was collected including the following:

- patient characteristics and demographics;
- family and domestic characteristics;
- IBD phenotype and treatment history;
- results of fructose and lactose breath tests (where available);

- recall of dietary advice given;
- adherence to dietary advice, including questioning concerning ingestion of individual FODMAPs and specific questioning concerning FODMAP-containing foods in order to validate the patient's responses concerning overall adherence, *as previously applied*⁹;
- opinions regarding the palatability and ease of following the diet as well as its cost and the availability of specialty foods in shops; and
- change of gastrointestinal symptoms following dietary intervention. These were recorded on a scale from -10 (change to worst symptoms possible) to +10 (change to complete absence of symptoms) in relation to a baseline score of 0 that represented the patient's symptoms at the time of the dietary intervention. Symptoms were scored at least three months following the dietary intervention. A significant change in symptoms was arbitrarily judged as +5 for improvement and -5 for deterioration in keeping with previous research performed by our group.⁷

All subjects gave written informed consent to participate in the study. The protocol was approved by the Eastern Health Research and Ethics Committee.

2.3. Analysis

Statistical analysis was performed using SPSS 14.0 statistical software package (Chicago, IL, USA). The data were analysed descriptively with chi-squared or Fisher's exact testing used to determine the significance of differences between groups as appropriate. The Wilcoxon signed rank test was used to determine whether or not symptoms had changed significantly from baseline. Univariate analysis was used to calculate the relationship between dependent and independent variables leading to odds ratios and 95% confidence intervals (determined using the Poisson approximation). A *p* value less than or equal to 0.05 was considered to be statistically significant.

3. Results

One hundred and fourteen patients with IBD who had received dietary intervention were identified. Ten were excluded because they also had coeliac disease (three), or had received dietary intervention to increase caloric intake (seven). Of the remaining 104 patients, 72 (69%) consented to take part in the study and were interviewed. The characteristics of these patients are shown in Table 1. *The median duration (25th, 75th percentiles) of follow up since the initial dietitian appointment to the time of interview was 17 months (7 months, 26 months).*

There were no significant differences between the Crohn's disease and ulcerative colitis patients with regard to standard demographic characteristics. As one might expect, there were differences with regard to cigarette smoking history and history of bowel resection between the patient groups.

3.1. Effect of the low FODMAP diet on gastrointestinal symptoms

Fig. 1 shows the range and frequency of gastrointestinal symptoms at the time that dietary intervention was

Table 1 Characteristics of the patients with inflammatory bowel disease included in the study

	All patients	Crohn's disease	Ulcerative colitis
Number	72	52	20
Female	39	31	8
Age			
Median (Range)	48 (18–72)	43 (18–72)	51 (22–64)
<i>Education</i>			
Did not complete schooling	11 (15%)	8 (15%)	3 (15%)
Completed secondary school	25 (35%)	18 (35%)	7 (35%)
Post-school qualification	19 (26%)	13 (25%)	6 (30%)
University degree	17 (24%)	13 (25%)	4 (20%)
<i>Employment</i>			
In employment	53 (74%)	40 (77%)	13 (65%)
Working > 35 h/week	31 (43%)	23 (44%)	8 (40%)
Shift work	19 (25%)	15 (29%)	4 (20%)
<i>Number of housemates</i>			
0	11 (15%)	9 (17%)	2 (10%)
1	15 (21%)	11 (21%)	4 (20%)
2	16 (22%)	12 (23%)	4 (20%)
>2	30 (42%)	20 (39%)	10 (50%)
<i>Smoking</i>			
Never	39 (54%)	25 (48%)	14 (70%)
Ex	21 (29%)	16 (31%)	5 (25%)
Current	12 (17%)	11 (21%)	1 (5%)
<i>Age of diagnosis</i>			
A1 (<17 y)	7 (10%)	7 (14%)	0
A2 (17–40 y)	41 (57%)	30 (58%)	11 (55%)
A3 (>40 y)	24 (33%)	15 (18%)	9 (45%)
<i>Location</i>			
		Ileal 12	Proctitis 2
		Colonic 15	Left-sided 9
		Ileocolonic 25	Pancolitis 9
		Upper GI 4	
		Perianal 15	
<i>Behaviour</i>			
B1 (Inflammatory)		27 (52%)	
B2 (Strictureing)		18 (35%)	
B3 (Penetrating)		7 (14%)	
<i>Breath tests</i>			
Performed	56 (78%)	43 (83%)	13 (65%)
+Fructose malabsorption	37 (66%)	27 (63%)	10 (77%)
+Lactose malabsorption	20 (36%)	17 (40%)	3 (13%)
Previous bowel resection	22 (31%)	19 (37%)	3 (15%)

initiated. Abdominal pain, diarrhoea, bloating and wind were most frequent. Figs. 2 and 3 show the change in each gastrointestinal symptom after at least three months of the low FODMAP diet. Overall symptoms, abdominal pain,

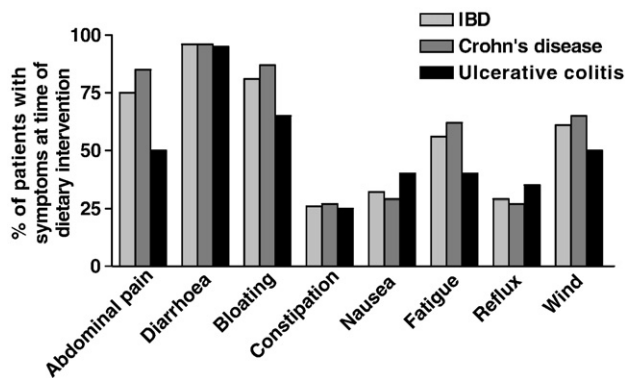


Figure 1 The frequency of gastrointestinal symptoms when dietary intervention was initiated.

diarrhoea, bloating and wind were the symptoms most likely to respond to dietary intervention in both Crohn's disease and ulcerative colitis. On average, constipation became worse (but not significantly) following initiation of the FODMAP diet in patients with ulcerative colitis.

An arbitrary improvement of 5 or more was used as a measure of unequivocal improvement for each symptom. This allowed patients to be divided into "responders" and "non-responders" on the basis of each symptom. The number of responders for each symptom is outlined in Table 2. More than half of patients with abdominal pain, diarrhoea and bloating improved with reduction of dietary FODMAPs.

3.2. Nature of and adherence to dietary advice

Fifty-eight (81%), three (4%) and 11 (15%) of the patients received their dietary advice in a one-on-one session with the dietitian, a group session or both, respectively. Thirty-two (44%) patients saw the dietitian once, 28 (39%) twice, and twelve (17%) three or more times. On specific questioning, patients recalled that specific advice was given concerning

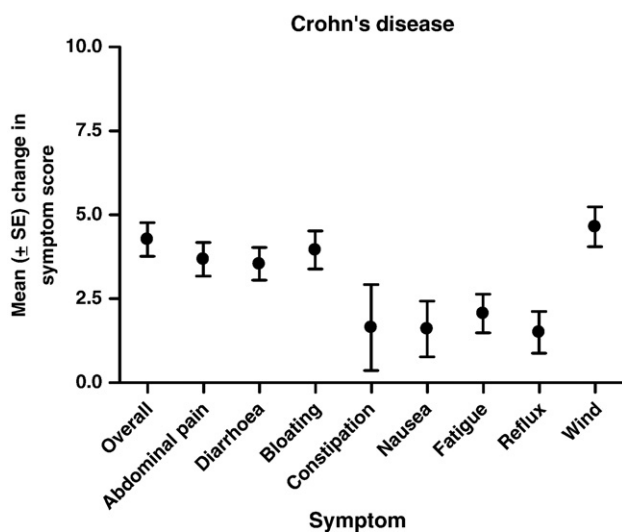


Figure 2 Change in gastrointestinal symptoms in patients with Crohn's disease following three to six months of FODMAP diet. Overall symptoms, abdominal pain, diarrhoea, bloating and wind all significantly improved ($p < 0.001$ for all; Wilcoxon ranked sign test).

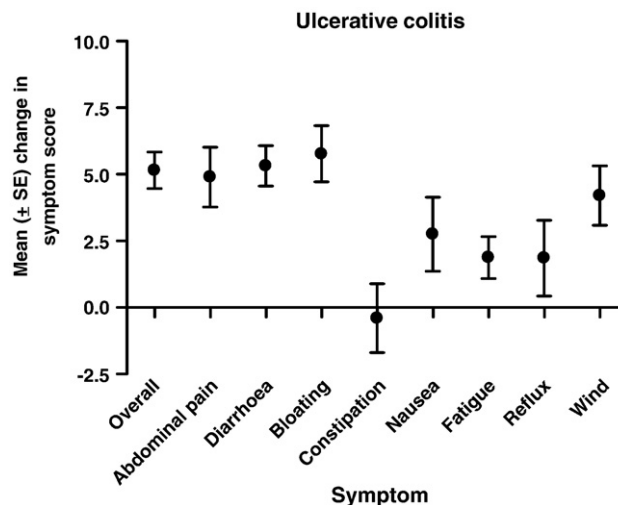


Figure 3 Change in gastrointestinal symptoms in patients with ulcerative colitis following three to six months of FODMAP diet. Statistically significant improvements were found for overall symptoms ($P < 0.001$), abdominal pain ($P = 0.016$), diarrhoea ($P < 0.001$), bloating ($P = 0.004$), and wind ($P = 0.008$).

reduction or elimination of the following food components: fructose in 70/72 (97%), fructans in 68/72 (94%), lactose in 50/72 (69%), sorbitol in 43/72 (60%) and raffinose in 30/72 (42%). Their current adherence to the dietary advice that had previously been given is shown in Table 3.

3.3. Opinions regarding the diet

Patients were asked to score on a scale of 0–10 (0=easy, 10=impossible) how easy it had been to implement the diet. The median response was 3 (SD 2.9, range 0–10, interquartile range 0.25–5). Using the same scale, patients were also asked how easy it had been to buy appropriate food (median response 3 (SD 2.9, range 0–10, interquartile range 0–5) and their opinion of the overall taste of the diet (0=completely palatable, 10=intolerable) with a median response of 2 (SD 2.2, range 0–10, interquartile range 1–4). Fifty-seven of 72 (79%) stated that the labelling of food was sufficient to follow the diet, 44/72 (61%) stated that the foods were available at their normal shops, while 26/72 (36%) also used specialty shops to buy appropriate food.

Table 2 The proportion of patients who responded to a reduction of FODMAPs in their diet

Symptom	All patients	Crohn's disease	Ulcerative colitis
Overall symptoms	40/72 (56%)	29/52 (56%)	11/20 (55%)
Abdominal pain	28/54 (52%)	22/44 (50%)	6/10 (60%)
Diarrhoea	34/69 (49%)	23/50 (46%)	11/19 (58%)
Bloating	30/58 (52%)	22/45 (49%)	8/13 (62%)
Constipation	4/20 (20%)	4/15 (27%)	0/5 (0%)
Nausea	5/24 (21%)	2/16 (13%)	3/8 (38%)
Fatigue	9/41 (22%)	7/33 (21%)	2/8 (25%)
Reflux	2/21 (10%)	1/7 (12%)	1/14 (7%)
Wind	23/44 (52%)	19/34 (56%)	4/10 (40%)

Table 3 Adherence to FODMAP dietary advice at time of recruitment into the present study

	Complete exclusion/minimal consumption of food group	Moderate consumption/non-adherent with exclusion of food group
Fructose	49 (69%)	22 (31%)
Fructans	50 (70%)	21 (30%)
Lactose	40 (63%)	23 (37%)
Sorbitol	37 (59%)	26 (41%)
Raffinose	32 (54%)	27 (46%)

The cost of the diet was thought to be more for 46/72 (64%), less for two (3%) and the same for 24 (33%). The median estimated increase in the cost of food while on this diet was 10% (SD 19, range -10–110%, interquartile range 10–25%). Thirty-four of 72 (47%) patients found the diet bland. Fifty-one of 71 patients identified family members and flatmates as factors that reduced adherence to the diet, although only 24/72 (33%) identified dining at restaurants in the same way. FODMAP-specific cookbooks and food manufacturer's guides were used by 43 (60%) and 40 (56%) patients, respectively.

3.4. Characteristics of patients responding to the FODMAP diet

The characteristics of those who did and those who did not respond to overall or individual symptoms were compared for the Crohn's disease group, but not the ulcerative colitis group due to low numbers (only 20 patients). Univariate analysis revealed that several factors were associated significantly with responding to dietary intervention (score of ≥ 5 for each symptom) and these are outlined in Table 4. There were also associations with sustained response to the diet and no significant improvement for any symptom (Table 4).

4. Discussion

In this cohort of patients with IBD, dietary intervention focussing on reduction of FODMAPs was associated with a durable improvement in symptoms in the majority of patients. The most common symptoms described by these patients were abdominal pain, diarrhoea, bloating and wind. These were also the symptoms that were most likely to respond to dietary intervention, suggesting that a reduction in dietary FODMAPs is an effective therapeutic option in such patients.

The design of the study did not permit a detailed analysis of disease activity over the period of study. Patients were considered by the referring physicians to have predominantly functional symptoms and had stable symptoms when assessed by the dietitians. These are frequent presenting complaints in patients with IBD, and occur two to three times more commonly than in the general population.^{1,2} Since the patients' assessment of the impact of dietary change over a period of several months was addressed, no formal evaluation of how this related to changes in medication was undertaken. In conditions characterised by waxing and waning of symptoms (and disease activity), it might be anticipated that some of the improvement in symptoms might have related to improved inflammatory activity, but, at the same time, some patients would have had worsening symptoms due to increased inflammatory activity.

A retrospective study of this nature inherently has limitations. Cause and effect are difficult to prove with regard to this diet and alleviation of gastrointestinal symptoms. But there is a significant association nonetheless. Referral bias may have affected the results in that those referred for dietary advice may have been more likely to respond than those not referred. However, the high incidence of functional symptoms in IBD patients means that such patients are still likely to represent a significant proportion of symptomatic IBD patients without inflammation. Recall bias and the lack of blinding of the investigator may also be problematic in such studies. However, there are

Table 4 Factors significantly associated with response or not (see Materials and methods for definition of response) in overall or specific symptoms on univariate analysis in all patients with Crohn's disease

Change in symptom(s)	Associated factors	Odds ratio [95% CI]	P value
Reduction of symptoms overall	▪ Ongoing adherence to reduced fructose	4.4 [1.2–15.5]	0.033
	▪ Ongoing adherence to reduced fructans	4.4 [1.2–15.5]	0.033
	▪ Using the cookbooks	4.4 [1.2–15.5]	0.033
Reduction of abdominal pain	▪ Fructose malabsorption on breath H ₂ test	5.14 [1.2–22]	0.038
	▪ Adherence to reduction of fructose ingestion	1.44 [1.44–28]	0.022
Reduction in wind	▪ Lactose malabsorption on breath H ₂ test	7.5 [1.2–47]	0.047
	▪ Dietary advice to reduce raffinose ingestion	19.3 [2.1–179]	0.003
Sustained response to diet	▪ Worked ≤ 35 h per week	1.4 [1.0–1.9]	0.042
	▪ Post-secondary school qualification	2.3 [1.6–3.3]	0.002
	▪ Those stating foods required not available from patient's usual shops	1.6 [1.1–2.0]	0.022
No improvement in any symptom	▪ Non-adherent to fructose restriction	5.7 [1.6–21]	0.013
	▪ Non-adherent to fructan restriction	5.7 [1.6–21]	0.013
	▪ Did not have a cookbook	3.6 [1.0–10]	0.045

Results are expressed as odds ratios and 95% confidence intervals (CI).

several reasons to suspect that the dietary changes were specifically responsible for reduction in symptoms, rather than improvement being a reflection of a non-specific placebo response or the desire of patients to give the 'correct' answers to the questions. First, the hypothetical model by which FODMAPs induce symptoms describes luminal distension due to rapid gas production and increased delivery of fluid to the large bowel due to an increased osmotic load.¹⁵ The pattern of symptom improvement described by patients in this study fits well with this model. Notably, constipation did not improve, but numerically (not statistically significantly) worsened in patients with ulcerative colitis, an observation consistent with the concept that removing dietary substrates responsible for increasing fluid delivery to the bowel may be associated with worsening of constipation. Furthermore, FODMAP reduction in patients who have IBS without IBD has been shown to reduce the same spectrum of functional symptoms.⁹

Second, adherence to the diet was paramount to its success, as we have previously described in a cohort of patients with IBS.⁹ In the present study, the majority of patients were able to adhere to the diet for greater than 3 months and sustained response in patients with Crohn's disease was found to be associated with adherence to restriction of fructose and fructans. Conversely, non-responders did not adhere to the diet, which is hardly surprising.

Third, factors that might be anticipated to assist patients in adhering to the diet were positively associated with sustained improvement of symptoms. These included the use of resources such as FODMAP-specific cookbooks and a fructose malabsorption product guide, which enable greater variety in the diet and provide low FODMAP food lists and recipes. These factors make the diet easier to follow and foods consumed are more likely to conform to the diet. Achievement of a higher education level and being employed for no greater than 35 h per week may be associated with a greater understanding of the diet and more time to seek out the foods required. Sourcing specialty stores and having enough money to seek out specialty products were also associated with improved compliance and sustained symptom benefit. These associations might also reflect greater understanding but, alternatively, could be markers for higher motivation to follow the diet.

Most patients were instructed only once or twice in the dietary principles. It is remarkable that knowledge of the diet was so good many months later in the majority of patients. This might just be a result of good teaching methods, but is more likely a reflection of the fact that the diet has efficacy and that the patient takes responsibility in its delivery. The greater apparent adherence and efficacy in the better educated, in those with more time, and in those who purchased cookbooks and food composition guides specifically directed towards this dietary approach support this view. Furthermore, patients can adhere in the longer term to the diet with sustained benefits. The acute symptomatic effects of breaking the diet provide an excellent reminder of the benefits and reinforce adherence. The taste of the diet was unlikely to encourage adherence since many patients described the diet as bland.

Are there any potential disadvantages to following a low FODMAP diet? Inulin and fructo-oligosaccharides are FODMAPs. They are of particular interest because of their

potential prebiotic activity, as is also exhibited by malabsorbed fructose.¹⁶ Reducing such substrates for the colonic microbiota might potentially lead to expansion of potentially pro-inflammatory bacteria, counteracting the positive effects of reduction in rapidly fermentable substrates and increased osmotic load. Indeed, a pilot study has suggested that fructo-oligosaccharides may be an effective treatment for Crohn's disease, although there was no control over dietary fructan intake,¹⁷ and fructan supplementation reduced faecal calprotectin in active ulcerative colitis.¹⁸ On the other hand, recent animal studies have shown that fructo-oligosaccharide supplementation worsens colitis in Salmonella-infected rats and in a rat model of IBD.^{19,20} There is as yet, no concrete evidence to suggest that a FODMAP-modified diet has either beneficial or detrimental effects on the underlying activity of IBD, but the possibility of the latter must be borne in mind before unrestricted enthusiasm about this dietary approach is displayed. However, the improvement seen in functional symptoms and the likely impact on quality of life suggests a reduction in FODMAPs is worth considering.

In conclusion, this study of patients' impression of the low FODMAP approach indicates that such dietary change might play a significant role in the control of abdominal symptoms in patients with IBD. The diet has a remarkable uptake by patients, and not only in the short term, with durable apparent benefits. It does rely upon a considerable input of time and energy of the patients themselves, and in that way favours those with higher education and more time to spend in the purchase of food. Nevertheless, the low FODMAP diet may be the first effective dietary therapy for patients with IBD with coexistent functional gut symptoms. A controlled dietary intervention trial is warranted in this patient group in order to truly test these observations and to define whether such a dietary approach deserves wide application.

Competing interests

FODMAP is a registered trademark of Sue Shepherd and Peter Gibson.

Sue Shepherd has authored a food manufacturer's guide and two cookbooks concerning a FODMAP-reduced diet.

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