*Clinical trials***Is bran efficacious in irritable bowel syndrome? A double blind placebo controlled crossover study**

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SUMMARY Twenty eight patients with classical irritable bowel syndrome completed a double blind placebo controlled crossover trial in which they added to their normal diet a daily supplement of either 12 bran biscuits (1=1.3 g fibre) or 12 placebo biscuits (1=0.23 g fibre). Each biscuit was given for three months in random order with crossover to the alternative biscuit at three months. After the initial three months therapy, there was a significant symptomatic improvement compared with pretreatment in both the bran treated ($p<0.01$) and placebo treated groups ($p<0.01$), but there was no significant difference in symptom scores between these two groups. There was no further improvement in either group after the second three months treatment with the alternative therapy. When crossover data for all 28 subjects were combined, symptoms scores after three months bran therapy and after three months placebo therapy did not differ significantly. Twenty four patients completed three day stool collections in both treatment periods. When the symptomatic response to bran among 15 subjects in whom stool weights rose on bran was compared with that among nine subjects whose stool weights were static or fell on the bran, it was shown that symptomatic improvement was independent of an increase in stool weight. These data suggest that in irritable bowel syndrome, especially that associated with abdominal pain, the beneficial effects of bran are due to a placebo response which is independent of an increase in stool weight.

Standard treatment of irritable bowel syndrome (IBS) includes increasing the oral intake of fibre.¹ In 1977, Manning *et al* reported that the addition of 7 g fibre in the form of wheat bran for six weeks to the diet of patients with IBS resulted in a significant improvement in symptoms.² Subsequent studies in IBS, however, have either failed to show a therapeutic benefit of bran compared with placebo^{3,4} or have suggested that bran is of only limited value.⁵

Interpretation of these clinical trials of dietary fibre is confounded by short duration of study which, as Ritchie and Truelove have shown, can significantly influence the apparent symptomatic response to treatment in IBS.⁶ We, therefore, conducted a double blind placebo controlled crossover study of the efficacy of a three month course of bran supplements in patients with classical IBS.⁷

Methods**SUBJECTS**

Two forms of biscuit, containing 1.3 g dietary fibre and 0.23 g dietary fibre respectively, were used in the study (Fibre data supplied by RHM Foods Limited, Ashford, Kent, UK, and estimated by a modified method of Southgate⁸). Wheat bran was the source of fibre. All subjects were given both biscuits in turn for consecutive periods of three months and in random order. Subjects were asked to gradually increase the supplement to 12 biscuits per day while maintaining a stable background dietary fibre intake for the duration of the study. Thus, at full doses, this provided an increase in fibre intake of 12.8 g per day. Compliance was assessed by monthly dietary questionnaire and by weighing a total three day stool specimen which each subject collected at home in the final week of the third and sixth months and then brought to the clinic. Before starting treatment and at monthly intervals thereafter, subjects were interviewed by one of us (MRL) using a preset symptoms questionnaire. As shown in Table 1, this consisted of (1) a pain score

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Table 1 Details of the symptom scoring system. The aggregate of pain, bowel and general scores gives total symptoms score (TSS). Also shown is the incidence of each symptom on entry into the study in subjects who completed both treatment periods ($n=28$) and subjects who withdrew ($n=16$)

	<i>Point rating</i>	<i>Pretreatment incidence (%)</i>	
		<i>Completion group</i>	<i>Withdrawal group</i>
Pain score			
Infrequent	+1	36%	44%
Frequent	+2	46%	31%
Constant	+3	18%	25%
Severity			
Mild	+1	25%	19%
Moderate	+2	25%	31%
Severe	+3	50%	50%
Bowel score			
Stool frequency			
4–5/day	+1	14%	6%
5/day	+2	25%	31%
Every 4–5 days	+1	0%	0%
Every 6 days	+2	11%	6%
Straining	+1	71%	44%
Incomplete evacuation	+1	89%	81%
Laxative use	+1	25%	19%
General score			
Nausea	+1	46%	50%
Vomiting	+1	46%	50%
Bloating	+1	75%	81%
Severe flatus	+1	32%	25%

which assessed frequency and severity of abdominal pain, (2) a bowel score which assessed frequency of, straining at, and incomplete evacuation of stool and use of laxatives, and (3) a general symptoms score which assessed nausea, vomiting, flatus, and bloating. Each symptom was defined in lay terms. Once supplements had been started, subjects were asked in addition whether abdominal pain, bowel symptoms and general well being were better, the same or worse, and a point score (-2, 0, and +2 respectively) given according to each reply. The sum of all points made the total symptoms score (TSS) in which a rising total symptoms score indicated worsening symptoms, while a falling total symptoms scored indicated an improvement. Subjects and interviewer were unaware of the order of treatment. This study was approved by the ethical committee of Saint Bartholomew's Hospital on 1 February, 1983.

The 44 subjects were chosen from patients newly referred to the outpatient clinics of St. Bartholomew's Hospital. Patients were chosen irrespective of whether they had previously taken bran or other bulking agents. No patients refused to enter the study. All had classical IBS, that is they described, in the absence of underlying organic disease, three

or more of the following six indicative symptoms defined by Manning *et al*, namely abdominal distension, pain relief with defaecation, more frequent stools with onset of pain, looser stools with the onset of pain, passage of mucus and the sensation of incomplete evacuation.⁷ Organic disease was excluded by physical examination, haematology (haemoglobin, mean cell volume, erythrocyte sedimentation rate, serum B₁₂ and red cell folate, 12 channel autoanalyser screen) and sigmoidoscopy in all, and stool culture, faecal fat estimation, barium meal, barium enema, jejunal biopsy, and colonoscopy where clinically indicated. All subjects gave informed consent in writing.

The distribution of symptoms in all patients on entry to the study is shown in Table 1. Twenty eight subjects completed both treatment periods. There were 29 women and nine men with a median age of 32 years (range 22-78 years) and a median duration of symptoms of 60 months (range 2-360 months). The 16 subjects who withdrew did not significantly differ from those completing the study in age, sex, duration, severity of symptoms, or order of treatment. The predominant reason for withdrawal was social inconvenience, either in eating the biscuits or attending the clinic. Of the 28 subjects who completed the study, 14 subjects (Group A) were allocated to receive bran for the initial three months and placebo for the second three months and 14 subjects (Group B) received the supplements in reverse order. These two groups were similar in age, sex and duration of symptoms, and total symptoms score (TSS) before therapy (Table 2).

STATISTICAL ANALYSIS

The Mann Whitney U test was used to compare those completing and those failing to complete the study. When assessing data within the group completing the study, the Mann Whitney U test and the Wilcoxon's

Table 2 Details of patients entering the study

44 patients randomised			
28 completed		16 withdrew	
Group A		Group B

14 (10 Females)		14 (9 Females)	
Median age 37y (22-61)		32y (22-78)	
Median duration of symptoms 60/12 (12-158)		48/12 (2-360)

Fig. 1 Total symptoms score before and on completion of initial three months therapy in Group A (receiving bran), and Group B (receiving placebo).

rank sum test for matched pairs were used where appropriate and $p < 0.05$ considered as significant. In calculating the change in symptoms scores – that is, pain score, bowel score and total symptoms score on bran compared with that on placebo in Figure 3, the following was used:

$$\Delta \text{score} = (\text{score after 3/12 bran} - \text{score before bran}) - (\text{score after 3/12 placebo} - \text{score before placebo})$$

Results

After three months' supplementation with bran in Group A, there were significant reductions, that is improvement, when compared with pretreatment scores in pain score ($p < 0.01$), bowel score ($p < 0.01$), general score ($p < 0.05$) while TSS fell from a pretreatment median of 8 (range 4,13) to a post-bran median of 1 (range -5,10) ($p < 0.01$). In group B after three months supplementation with placebo, when compared with pretreatment scores, there were significant reductions in pain score ($p < 0.05$) and bowel score ($p < 0.01$) while TSS declined from a pretreatment median of 9 (range 5,11) to a median of 5 (range -6,12) ($p < 0.01$) (see Figure 1). When the individual symptom scores and TSS after the initial three months therapy with bran (Group A) or placebo (Group B) were compared, no significant differences were found.

In Group A three months treatment with placebo was accompanied by a moderate rise, that is deterioration, in bowel score from a median of 0 (range -2,3) at three months, to a median of 3 (range -1,6) at 6 months ($p < 0.05$). Pain score, general score and TSS did not differ significantly at three and six months. In Group B, there were no significant differences in pain, bowel, general scores or total symptoms score at three and six months, corresponding to conversion from bran to placebo therapy (see Figure 2).

Before combining crossover data from the two groups, we considered whether either bran or placebo biscuits had a carry over effect on subsequent responses to the alternative treatment in the second study period.⁹ The total symptoms score after three months bran did not significantly differ in Groups A and B, subjects in Group B having received three months prior treatment with placebo. The total symptoms score after taking placebo biscuits for three months did not differ in Groups A and B, subjects in Group A having received three months prior treatment with bran. These observations suggest that there was no carry over influence into the second study period after use of either bran or placebo in the initial study period. Consequently crossover data were combined. The changes in individual symptoms scores and total symptoms score for all 28 subjects before and after bran were compared

Fig. 2 Total symptoms score before and on completion of second three months therapy in Group A (receiving placebo) and Group B (receiving bran).

with the changes in these scores before and after three months placebo and no significant differences were demonstrated.

Twenty four subjects completed stool collections in both treatment periods. The mean 24 hour stool weight on bran, 148 ± 20 g ($\pm$ SEM) and placebo 123 ± 14 g were not significantly different. Stool weight was significantly correlated to total dietary fibre intake including biscuit ingestion as estimated by dietary questionnaire ($p < 0.05$). In 15 subjects the stool weights during the bran treatment exceeded those in the placebo treatment (median increase 63 g/24 h, range 7–208 g), while in nine subjects stool weights on bran were less than or equal to those on placebo (median decrease 20 g/24 h, range 0–82). There was, however, no correlation between symptomatic response to bran and change in stool weight. Of the 15 subjects whose stool weights rose during bran supplements, eight showed an increase – that is, worsening, in total symptoms score compared with the placebo period. Of the nine subjects with static or reduced stool weights on bran six showed a reduction, that is – improvement, in total symptoms score during the bran period compared with the placebo period (see Figure 3).

Discussion

The present study helps clarify whether or not bran is efficacious in irritable bowel syndrome. Eleven of 14 patients (79%) initially treated with bran showed a symptomatic improvement after three months. Ten of 14 (71%) initially treated with placebo, however, also showed improvement at three months. In both groups, there were significant improvements in both abdominal pain and symptoms related to disturbed bowel habit. Therefore, this study confirms that there is an apparent symptomatic response to bran in the short term, but suggests that much if not all of this may be a placebo effect. The study of Manning *et al.*,² which showed a beneficial effect of bran, did not have an appropriately treated placebo group. When such an appropriate placebo group was used by Soltoft *et al.*, they reported symptomatic improvement in bran treated and placebo treated patients comparable with the present study.³ Cann *et al.* found recently that 18 of 38 patients with IBS improved after four weeks bran and they attributed this 'apparent efficacy' to placebo effect.⁵ Similarly Longstreth and coworkers found a marked response to the placebo when studying the efficacy in IBS of the bulking agent psyllium.¹⁰

Sixteen (36%) of patients randomised in this study withdrew before completing both treatment periods. This high drop out rate is similar to the frequency of refusal or withdrawal in a comparable study of bran

Fig. 3 Total symptoms score in 15 subjects whose stool weights rose during bran supplements and 9 subjects whose stool weights were static or reduced during bran supplements.

in diverticular disease.¹¹ In the present study, there were no distinguishing features among those who withdrew when compared with those who completed the study.

We used a symptom score system to assess response to treatment. This system was in part based on six defining symptoms, but in addition included other symptoms such as nausea, vomiting and wind which, while not discriminators of IBS, are common features of it.^{7,12} Furthermore, as Ritchie and Truelove suggested that a patient's subjective appreciation of improvement or deterioration should be assessed, patients were asked whether their pain, bowel or general symptoms had changed for better or worse⁶ and from these data, a total symptoms score was reckoned. Using this system, no clear benefit for bran over placebo could be demonstrated.

The definition of IBS used in the present study was based on the criteria of Manning *et al.*² These criteria are weighted in favour of painful IBS. As shown in Table 1, all subjects recruited to the study gave a history of abdominal pain. Only a minority gave a history of infrequent bowel movements or use of laxatives. Thus the observation that bran and placebo biscuits are similarly efficacious may not apply to IBS patients in whom pain is not the principal complaint. Cann *et al.* have reported that bran was significantly better than placebo in relieving symptoms of constipation.⁵ In the present study, no conclusions can be

drawn on the value of bran in treating constipation as because of the selection criteria, few patients with constipation were recruited.

In the present study of fibre, a dose was chosen which is in excess of that reported to be efficacious,² and which is commonly used in clinical practice. One difficulty of long term administration of dietary fibre supplements is achieving compliance both in taking the trial agent and in maintaining for the duration of the study a stable background intake of dietary fibre. In this study, the increase in stool weights during the bran period compared with the placebo period did not achieve significance. It is of interest that Cann *et al* failed to show an increase in daily stool weights during a short course of bran supplements given to IBS patients without constipation but did find a significant increase in daily stool weights among constipated IBS patients given the same supplements.⁵ Thus the absence of a significant increase in stool weights on bran in the present study may reflect the relative absence of constipated patients in the study. In the present study none-the-less, total dietary fibre intake including biscuits did correlate significantly with stool weight. This suggests that subjects either did not eat the bran biscuits or they manipulated the fibre content of their background diet and so ameliorated the bulking effect of bran. As this might have influenced the outcome of the study, we compared the symptomatic responses to bran of those subjects showing an increase in stool weight during the period of bran supplementation with the responses of those in whom stool weights fell or were static during the bran period. This analysis showed that the benefit of treatment with either bran or placebo was independent of an effect on stool weight. This is further evidence that the therapeutic benefit of bran is due to its placebo effect.

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