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Clinical trial: the effects of a fermented milk product containing *Bifidobacterium lactis* DN-173 010 on abdominal distension and gastrointestinal transit in irritable bowel syndrome with constipation

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SUMMARY

Background
A sensation of abdominal swelling (bloating) and actual increase in girth (distension) are troublesome features of irritable bowel syndrome (IBS), which is more common in patients with constipation, especially those with delayed transit.

Aim
To establish whether a fermented dairy product containing *Bifidobacterium lactis* DN-173 010 reduces distension in association with acceleration of gastrointestinal transit and improvement of symptoms in IBS with constipation.

Methods
A single centre, randomized, double-blind, controlled, parallel group study in which patients consumed the test product or control product for 4 weeks. Distension, orocaecal and colonic transit and IBS symptoms were assessed on an intention-to-treat population of 34 patients.

Results
Compared with control product, the test product resulted in a significant reduction in the percentage change in maximal distension [median difference – 39%, 95% CI (−78, −5); $P = 0.02$] and a trend towards reduced mean distension during the day [−1.52 cm (−3.33, 0.39); $P = 0.096$]. An acceleration of orocaecal [−1.2 h (−2.3,0); $P = 0.049$] as well as colonic [−12.2 h (−22.8, −1.6); $P = 0.026$] transit was observed and overall symptom severity [−0.5 (−1.0, −0.05); $P = 0.032$] also improved.

Conclusions
This probiotic resulted in improvements in objectively measured abdominal girth and gastrointestinal transit, as well as reduced symptomatology. These data support the concept that accelerating transit is a useful strategy for treating distension.

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INTRODUCTION

Irritable bowel syndrome (IBS) is a functional bowel disorder characterized by abdominal pain, bloating and disordered defaecation, which may take the form of constipation, diarrhoea or a mixture of the two.[1] IBS affects between 10 and 20% of the population[1–4] and results in significant absenteeism from work[2] as well as considerably reducing quality of life.[5, 6] The condition accounts for nearly half of the referrals to gastroenterology clinics where management remains notoriously difficult, with a strong need for new safe treatment options.[1, 7]

Abdominal bloating is reported by up to 96% of patients with IBS,[8–13] is more common in females[14, 15] and is often ranked as their most bothersome symptom.[10, 16] Typically, it worsens during the course of the day, particularly after meals, is usually at its maximum in the evening and then improves or disappears overnight.[12, 17, 18] Although the terms abdominal bloating and distension are often used synonymously, studies using the recently validated technique of Abdominal Inductance Plethysmography (AIP)[18] have shown that only approximately half of patients reporting the sensation of bloating actually exhibit an increase in girth, which is the characteristic of distension. Furthermore, distension, as opposed to bloating on its own, has been shown to be more common in patients with constipation predominant IBS (IBS-C)[18] and in those with delayed gastrointestinal transit, particularly of the large bowel.[19] This suggests that accelerating transit might have potential in the treatment of distension.

Although the mechanisms responsible for delayed transit in IBS are unclear, there is some evidence to suggest that an in-balance of intestinal microflora might contribute to the problem.[20–24] For instance, patients with IBS-C have been reported to exhibit increased numbers of methane producing bacteria[25, 26] and to excrete methane in direct relationship to the severity of their constipation.[25] Moreover, methane producers appear to have slower gastrointestinal transit with increased segmental and nonpropulsive contractility compared with hydrogen producers.[27] Thus modification of the intestinal microflora might potentially alter motility and there is evidence from both animal and human studies to support this view.[28–34] Probiotics are the centre of considerable interest in relation to the treatment of IBS, although it is important to emphasize that different strains may not necessarily share the same activity.[35, 36] Consequently, if a particular probiotic had the potential to accelerate intestinal transit, it is possible that it might help ameliorate the problem of distension associated with IBS. It is therefore noteworthy that there is some preliminary evidence that the fermented dairy product containing *Bifidobacterium lactis* DN-173 010 together with two classical yogurt starters can accelerate gastrointestinal transit in healthy volunteers, especially in those with slower transit[30–33] and subjectively improve the symptoms of bloating and digestive discomfort in patients with IBS-C.[37]

To date, there has been no study to evaluate the effect of accelerating intestinal transit on abdominal distension or the potential for a probiotic to achieve this goal. It was the purpose of this investigation to assess the effect of the fermented dairy product containing *Bifidobacterium lactis* DN-173 010 on distension as measured objectively by AIP as well as recording bloating, transit and other IBS symptoms.

MATERIALS AND METHODS

Subjects

Forty-one female subjects aged 20–69 years (mean age 39.6 years) who fulfilled the Rome III criteria for IBS-C[1] and specifically complained of bloating or visible swelling of the abdomen at least twice per week as part of their symptom complex were recruited from the out-patients department of the University Hospital of South Manchester NHS Foundation Trust between January and August 2007. The patients were recruited from consecutive patients approached in out-patients who satisfied the criteria and wished to participate in the study. Tertiary referred patients or those with bowel frequency less than twice per week were excluded from the study in order that patients with intractable severe constipation were not included. All subjects underwent appropriate investigations to exclude organic disease[38] and did not show any functional disorder of the upper gastrointestinal tract that was more prominent than their IBS. All subjects drank below the recommended safe alcohol limit (<14 U/weeks) and did not smoke or take medications that might affect gastrointestinal function for at least 48 h prior to undertaking measurements. In addition, subjects were excluded from the study if they had a history of laxative abuse, had taken antibiotics within 60 days prior to the start of the study, had an allergy or hypersensitivity to milk proteins or consumed any over-the-counter products containing probiotics or

fermented dairy products for at least 11 days before the study. Other than the above restrictions, the patients were encouraged to maintain their usual dietary intake and lifestyle. Patients not using an effective contraceptive method, or who were pregnant or breast feeding were also excluded. The study was approved by the South Manchester Local Research Ethics Committee and all subjects gave written informed consent.

Study design

The study was single centre, randomized, double-blind, controlled, parallel-group in design in which the effect of daily consumption of a fermented milk containing *Bifidobacterium lactis* DN-173 010 (test group) was compared with a nonfermented dairy product (control group) in female patients with IBS-C.

To achieve a 80% power to detect differences in mean abdominal girth (area under the curve), from the beginning to the end of the day referenced to the beginning of day 1, of 2 cm or more, we required (considered as a clinically meaningful effect), 17 subjects in each group (34 in all). This calculation assumed a standard deviation of 2.0 and a simple two-sample *t*-test with the conventional 5% significance level. As previous studies have shown that both IBS symptoms and transit can vary across the menstrual cycle or with menopause status, the randomization was stratified by menstrual cycle/menopausal status.[39–41]

Study products

The test product was a fermented milk (Activia; Danone Research, Palaiseau Cedex, France) containing *Bifidobacterium lactis* DN-173 010 [1.25×10^{10} colony forming units (cfu) per pot] together with two classical yoghurt starters, *Streptococcus thermophilus* and *Lactobacillus bulgaricus* (1.2×10^{9} cfu/pot i.e. bacteria that are used to inoculate the milk to begin the fermentation of lactic acid in the milk). The control product was a milk-based nonfermented dairy product without probiotics and with low content of lactose <4 g/pot as in the test product. Both the test and control products were without flavour and had a similar appearance, texture and taste. Each pot contained either 125 g of test product or control product and were provided by Danone Research (Palaiseau, France).

Protocol

Figure 1 shows a flow diagram of the protocol used for this study. Eleven days before randomization (i.e. day − 11, visit 1) all subjects received a symptom diary and three sets of radio-opaque markers for measurement of colonic transit. Using the symptom diary, the subjects were asked to provide details of the presence and severity of any abdominal pain/discomfort, bloating, flatulence and overall IBS symptom severity at the end of the day using a 1–6 scale (1 = none, 2 = very mild, 3 = mild, 4 = moderate, 5 = quite severe and 6 = very severe), along with the time and consistency of any bowel movement (1 = very hard stool, 2 = hard stool, 3 = somewhat hard stool, 4 = neither loose nor hard stool, 5 = somewhat loose stool, 6 = loose stool, and 7 = watery stool) and the presence of any straining, urgency or feelings of incomplete evacuation at the time of stool passage (1–6 scale as above).

On day-4, subjects were contacted via the telephone and reminded to ingest the first set of radio-opaque markers the following morning on day-3 and subsequent sets on days-2 and -1. In addition, on day-1 fasted subjects attended the Neurogastroenterology

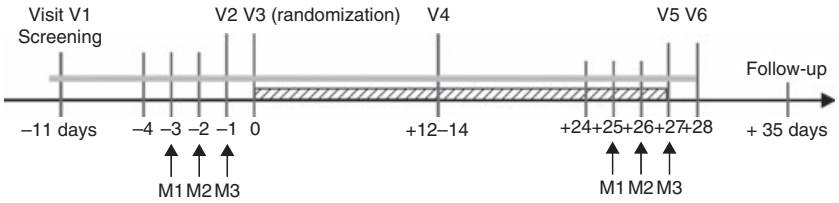

Figure 1. Flow diagram of protocol showing the days of visits to the laboratory (V1 – V6), radiopaque marker ingestion (M1, M2, M3), duration of consumption of test product/control product (hatched area) and duration of restricted diet when patients were advised not to consume any commercial fermented dairy products, yoghurts, probiotic etc (grey line). On days −4 and +24, patients were contacted to remind them to start taking the radiopaque marker. On visits 2 and 5, the Abdominal Inductance Plethysmography (AIP) equipment was fitted, and on visit 3 and 6, AIP equipment was removed, plain abdominal x-ray taken for assessment of colonic transit and small bowel transit measured using breath H_2 technique.

Unit before 10 am (visit 2) and were fitted with the AIP device.[18, 42, 43] Each subject was given a further paper diary in which to record, at 'hourly intervals' the severity of their bloating (0–5 scale) and the time and content of any oral intake (both solids and liquids). The subjects were then allowed to leave the laboratory and were asked to maintain their usual daily activities until they returned for removal of the AIP device 24 h later (day 0). On returning on day 0 again after an overnight fast (visit 3), the AIP device was removed, hourly and daily diaries retrieved and plain abdominal x-ray taken to assess whole and segmental colonic transit.[44] The subjects then ingested a standard meal and orocaecal transit of the head of the meal was assessed using a method similar to that described by Levitt.[45]

The subjects were then randomized to treatment and given either 2 weeks' supply of test product or control product along with a further symptom diary to be completed daily until their following visit between days +12 and 14 (visit 4; see above). All subjects were asked to consume two 125 g pots of product, once at 8 am and again at 8 pm. If the subjects forgot to take the product, they were encouraged to consume it with their next meal. On visit 4, the diary was retrieved and given a further 2 weeks' supply of test product or control product along with new diary and second set of radio-opaque markers. As for pre-treatment, on day 24 (i.e. 4 days before completion of product), the subjects were telephoned and reminded to ingest the first set of radio-opaque markers on day 25 and subsequent sets on days 26 and 27. On day 27 (visit 5), fasted subjects again attended the Unit before 10 am and were fitted with the AIP device and provided with an hourly diary in which to record bloating severity and oral intake (measured on a 0–5 scale). The following day (day 28, visit 6), the subjects had the AIP device removed, hourly and daily diaries retrieved and plain abdominal x-ray taken for whole and segmental colonic transit assessment and orocaecal transit determined (see above). All subjects were followed up by telephone 7 days later (i.e. day +35).

Abdominal inductance plethysmography

The technique we used is described elsewhere,[18, 42, 43] but briefly, it works on the principle that a loop of wire forms an inductor, the inductance of which is dependent on the area enclosed by the loop. For AIP, the wire is sewn into a band of elastic fabric (≈8.5 cm wide) in a zig-zag fashion to allow for expansion (Respitrace inductive sensor; Ambulatory Monitoring Inc., New York, NY, USA) and is worn around the abdomen, similar to a belt. Attached to the wire is a small electronic circuit unit that incorporates an inductor in a resonant circuit whose output frequency varies with the area enclosed by the band, and a small battery-operated microprocessor data logger that records and scores the average frequency of the oscillator circuit for 30 s each minute. The data logger simultaneously records the subject's posture (standing, sitting and lying down) via sealed mercury tilt switches (ASSEMtech Europe Ltd., Essex, UK) taped to the subject's chest and thigh. The cross-sectional area of the abdomen recorded by the equipment is then converted into a circumferential measurement, as described previously.[18, 42, 43]

Mouth to caecum transit time

Mouth to caecum transit time for the head of the meal was determined by a technique previously described by Levitt.[45] After rinsing the mouth with a 1% chlorhexidine mouthwash [Corsodyl P. 534 BNF (45); Glaxo SmithKline, Brentford, UK], base-line end expiratory breath samples were taken every 15 min for 1 h. Subjects then ingested a standard meal consisting of 30 g dry flake potato reconstituted with 150 mL water (107 kcal, Smash original; HL Foods Ltd, Spalding, Lincolnshire, UK) and 120 g baked beans (83 kcal; H J Heinz Co Ltd, Hayes, Middlesex, UK) within 5 min with 50 mL of water, and immediately following consumption rinsed their mouths again with Corsodyl mouthwash. Post-meal end expiratory breath samples were taken every 15 min for a maximum of 10 h. Breath hydrogen concentration was measured using a breath hydrogen monitor (Gastrolyzer 2 Breath H_2 Monitor, Bedfont Scientific Ltd., Rochester, Kent, England) containing an electrochemical sensor which was specific for hydrogen.

Colonic transit time

Subjects ingested three sets of radio-opaque markers (24 of each type) with 100 mL of water at 08:30 hours on three consecutive days. The three types of markers were cut from polyethylene tubing (Portex Limited, Nottingham, UK) to be cylinders of identical mass with external, internal diameter and length of (i) $4.5 \times 3 \times 1.3$ mm; (ii) $3 \times 2 \times 3$ mm and (iii) $2 \times 1 \times 5$ mm, respectively. On the fourth day, after an overnight fast,

the subjects re-attended the hospital and a single abdominal x-ray was taken at 08:30 hours.[44]

Data analysis

AIP assessment of abdominal girth. As previous studies have shown that there is no statistically significant difference between girth measurements taken in the standing and sitting positions,[42] girth whether in the sitting or standing position was averaged over 60 min epochs from the beginning to end of day. The area under the curve (AUC) for these hourly measures was calculated as changes in girth from the first hour of the study standardized for the total number of hours of measurement. In addition, the maximum distension defined as the maximum change in girth from the first hour, over the period from the second hour to bedtime, was derived and the percentage change in maximum distension from pre- to post-treatment was calculated.

Hourly symptom diaries during AIP assessment. The AUC for hourly bloating scores from the start of day to before retiring to bed standardized for the total number of hours of measurement was calculated.

Orocaecal transit. Arrival of the head of the meal in the caecum (i.e. orocaecal transit time) was defined as the first time breath hydrogen rose by 10 ppm above the baseline value and was sustained for three consecutive readings.

Colonic and segmental transit. The numbers and location of markers on the x-ray film were used to calculate both colonic and segmental colonic transit time using the equation, as suggested by Metcalf *et al.*[45]

Daily symptom diaries. The baseline daily symptom diary scores were averaged over the 11 days before product consumption. Symptoms during product consumption were averaged over consecutive 7 day periods.

Statistical analysis

Data were analysed using analyses of covariance and repeated measures analyses of variance (over the four weekly periods), adjusting for baseline values, age and BMI. The latter adjustments were made because previous studies have suggested that both BMI and age can alter transit,[46–48] and age can change the composition of the gastrointestinal flora.[49] For maximal girth, the significance between groups was assessed by comparing percentage change from baseline using the Mann–Whitney *U*-test (unadjusted for age and BMI). Analyses were performed on intention-to-treat basis.

Pearson and Spearman correlations, as appropriate, between changes in abdominal girth and orocaecal and colonic transit were derived. Within-subject Pearson correlations were calculated to assess the relationship between hourly distension and bloating values both before and after intervention.

RESULTS

Forty-one patients were enrolled into the study. Of these, 38 were randomized to treatment and three patients were withdrawn because they did not attend visit 2. Of the patients randomized to treatment, four were withdrawn (one antibiotic usage, three product delivery issues) and two had >10% missing standing/-sitting data for awake abdominal girth measurements, as they had slept during the day. However, the intention to treat population included these latter two subjects and thus there were 17 subjects available for analysis in each group (Figure 2). All patients complied with the protocol and no product was returned to the laboratory.

Baseline data

Table 1 shows the baseline demographic, symptomatic and physiological data. As can be seen, there were no differences in any of these parameters between subjects randomized to receive test and control products.

Test product vs. control product over 4 weeks

Measurement of abdominal distension and bloating. Figure 3 shows the hourly changes in bloating and distension over the awake hours of the 24 h AIP recording both before (a) and after (b) consumption of test and control products. Baseline bloating and distension profiles (a) were similar for test and control products. However, both the bloating and distension profiles appeared to be reduced to some extent by consumption of test product compared with control product (Figure 3). This was associated with evidence

of a trend towards a reduction in mean abdominal distension [AUC; mean overall difference between groups – 1.52 cm (−3.33, 0.39); $P = 0.096$], a significant reduction in the median percentage change in maximal distension [−39% 95% CI (−78, −5); $P = 0.02$] and evidence of a trend towards a reduction in the symptom (AUC) of abdominal bloating [−0.47 (−1.01, 0.07); $P = 0.084$; Figure 4].

Gastrointestinal transit. Both orocaecal [mean difference −1.2 h, 95% CI (−2.3, 0); $P = 0.049$] and colonic [−12.2 h (−22.8, −1.6); $P = 0.026$] transit times were significantly reduced by test product compared with control product (Figure 5). The acceleration in colonic transit was related to significantly decreased right colonic transit time [−8.01 h (−13.94, −2.09); $P = 0.01$] but not left colonic [−5.58 h (−14.46, 3.30); $P = 0.21$] or sigmoid-rectal [1.22 h (−5.38, 7.81); $P = 0.71$] transit times (Figure 5).

Abdominal symptoms and bowel habit. Overall IBS severity [mean overall difference between groups −0.5, 95% CI (−1.0, −0.05); $P = 0.032$] and abdominal pain/discomfort [−0.5 (−1.0, 0); $P = 0.044$] both significantly decreased and bloating [−0.6 (−1.1, 0); $P = 0.059$] and flatulence [−0.6 (1.1, 0); $P = 0.092$] tended to reduce over the 4-week consumption of test product compared with control product (Figure 6). In addition, urgency significantly improved [−0.71 (−1.34, −0.09); $P = 0.026$] whilst the consistency of stool from normal [Bristol Stool Scale = 4; −0.40 (−0.82, 0.01); $P = 0.058$] showed borderline significant improvement and straining during evaluation [−0.64 (−1.34, 0.07); $P = 0.074$] and feelings of incomplete evacuation [−0.69 (−1.50, 0.12); $P = 0.091$] showed a tendency to improve with test product compared with control product. Stool frequency [−0.79 (−1.95, 0.36);

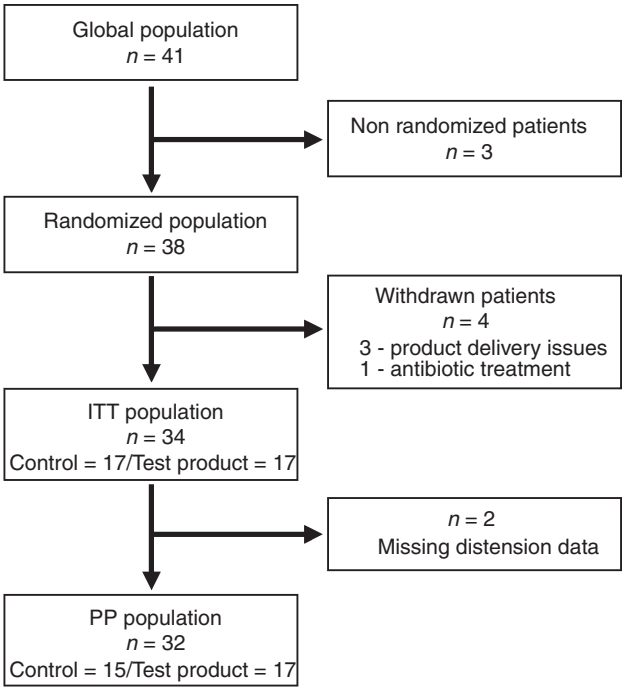

Figure 2. Flow chart describing progress of patients through the study.

Table 1. Baseline demographic, symptomatic and physiological data in subjects receiving test and control products

	DN-173 010 ($n = 17$)	Control ($n = 17$)
Demographic		
Age (years)	42 (24, 69)	37 (20, 59)
BMI	24.6 (19.1, 29.4)	25.0 (20.3, 29.6)
Abdominal symptoms		
Distension – area under the curve (cm)	3.5 (0, 10.3)	3.4 (−4.7, 9.9)
*Distension – max (cm)	5.2 (3.7, 19.0)	6.3 (3.0, 15.8)
Bloating	4.0 (1.8, 5.8)	3.8 (1.4, 5.2)
Flatulence	3.6 (1.8, 6.0)	3.7 (1.6, 4.7)
Abdominal pain	3.4 (1.6, 5.4)	3.6 (2.2, 4.9)
Overall IBS	3.7 (2.4, 5.6)	3.9 (2.1, 5.1)
Bowel habit		
Stool frequency/week	7.9 (2.5, 19.7)	6.3 (1.3, 15.3)
Stool consistency	1.8 (1.0, 2.8)	1.5 (0.5, 2.8)
Straining	3.7 (1.6, 5.0)	3.2 (1.8, 5.0)
Urgency	2.9 (1.0, 4.6)	3.5 (2.0, 4.8)
Feeling of incomplete evacuation	3.2 (2.0, 4.8)	3.8 (2.5, 5.2)
Gastrointestinal transit (h)		
OCTT	6.8 (4.5, 9.0)	6.5 (4.0, 9.0)
CTT	56.1 (24, 72)	51.8 (23, 72)
LCTT	24.7 (4, 55)	23.2 (0, 41)
RCTT	15.6 (0, 44)	15.3 (2, 32)
SRTT	15.2 (0, 34)	13.4 (0, 28)

Date expressed as mean and range, other than *which are expressed as median and range. DN-173 010 = *Bifidobacterium lactis* DN-173 010.
OCTT, orocaecal transit time; CTT, colonic transit time; LCTT, left colonic transit time; RCTT, right colonic transit time; SRTT, sigmoid rectal transit time.

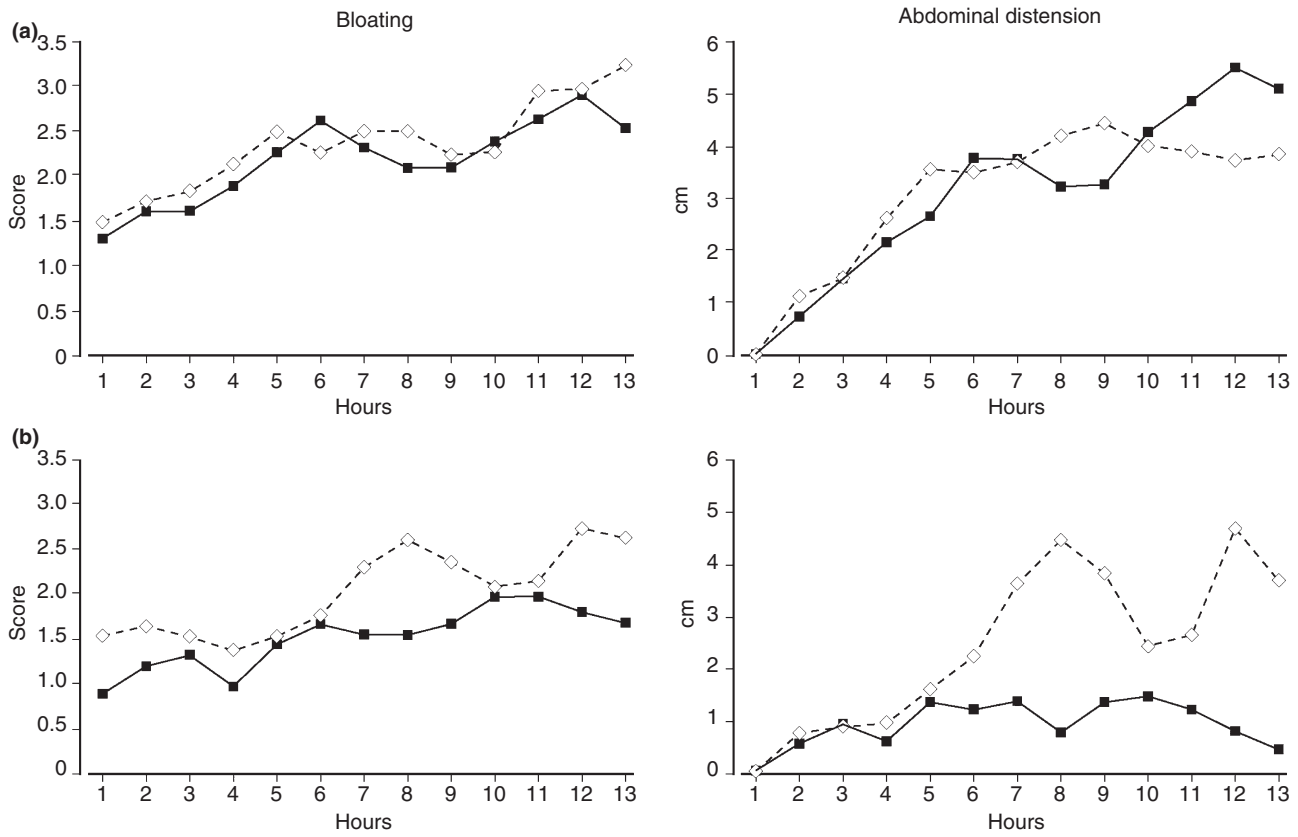

Figure 3. Comparison of the mean hourly bloating scores and abdominal distension measurements over the awake hours of the Abdominal Inductance Plethysmography measurement before (a) and after (b) consumption of test product (■) and control product (◇). Note that after consumption of test product, abdominal distension was no greater at the end compared with the beginning of the day.

$P = 0.17$] was unaltered by consumption of test product (Figure 7).

None of the analyses above was significantly altered if they were performed without adjusting for age and BMI.

Correlations. As in our previous studies,[18] there was a direct positive within-subject correlation between bloating and distension when comparing the hourly data both before ($r = 0.69$; $P < 0.001$) and after ($r = 0.62$; $P < 0.001$) intervention.

Taking the subjects as a whole (those taking test and control products), both the changes in mean abdominal distension (AUC) and percentage change in maximal distension correlated with the changes in orocaecal (AUC, $r = 0.35$, $P = 0.042$; % change in max distension, $\rho = 0.56$, $P = 0.001$) and colonic ($r = 0.40$, $P = 0.02$; $r = 0.38$, $P = 0.025$) transit time.

DISCUSSION

The results of this study show that this fermented milk product reduces abdominal distension in patients with IBS-C as well as accelerating both small and large bowel transit. Furthermore, this probiotic also improved bloating and most of the other cardinal symptoms associated with IBS.

One of the problems of assessing the therapeutic potential of any new therapy for IBS is the lack of objective outcome measures as most of the features of the condition such as abdominal pain and bloating are completely dependent on patient reporting. Even recording bowel function can be unreliable, although the introduction of the Bristol Stool Form Scale[50] has helped to improve the situation. In contrast, an increase in abdominal girth, distension, is amenable to objective measurement and this is the reason why we developed the technique of AIP.[18, 42, 43] The system can record

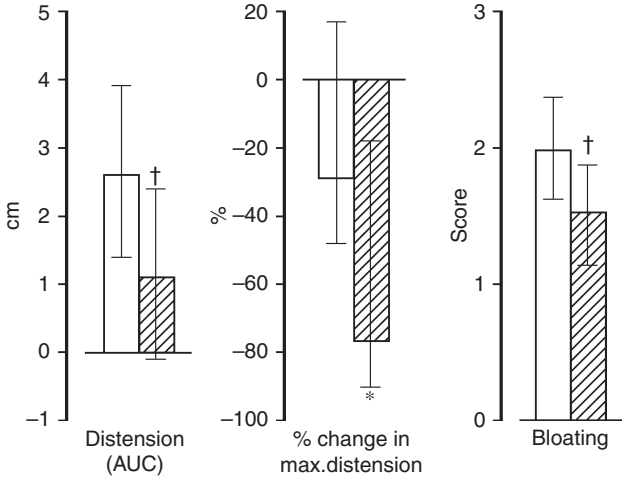

Figure 4. Comparison of abdominal distension [area under the curve (AUC)], percentage change in maximal distension [(maximal distension post treatment minus maximal distension at baseline)/maximal distension at baseline × 100], and bloating scores (AUC) during the Abdominal Inductance Plethysmography assessment between patients consuming test product (hatched) vs. control (open) product. For the AUC for abdominal distension and bloating, the data represent the marginal means and 95% CI. For percentage change in maximal distension, the data represent the median and 95% CI. *$P < 0.05$, †$P < 0.10$ compared with control.

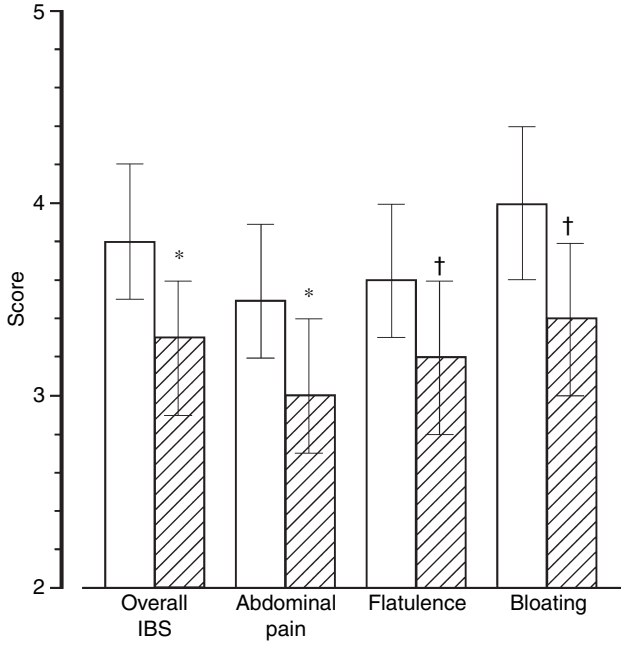

Figure 6. Comparison of symptom scores for overall IBS, abdominal pain, flatulence and bloating between patients consuming test product (hatched) vs. control (open) product. Data represent the marginal means and 95% CI over the 4 week period. *$P < 0.05$, †$P < 0.10$ compared with control.

abdominal girth as well as whether the patient is lying, sitting or standing for up to 24 h in an ambulatory fashion and is accurate down to 1 mm. Thus, if a particular therapeutic approach has the potential to relieve distension, AIP is ideally suited to address this question.

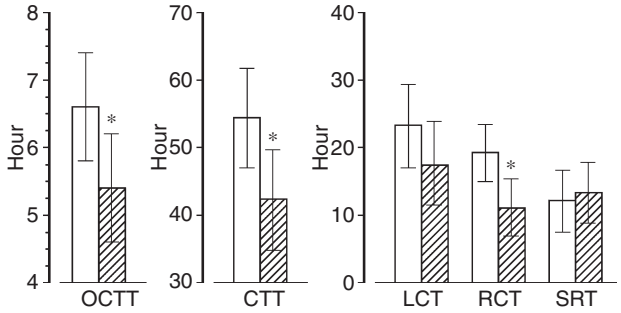

Figure 5. Comparison of orocaecal (OCTT), colonic (CTT), left colonic (LCT), right colonic (RCT) and sigmoid-rectal (SRTT) times between patients consuming test product (hatched) vs. control (open) product. Data represent the marginal means and 95% CI. *$P < 0.05$ compared with control.

It is well known that a majority of patients with IBS suffer from abdominal bloating and that it is an especially intrusive symptom.[8–16] Moreover, more women report bloating than men.[12] In 50% of cases, bloating is accompanied by distension, which exacerbates the problem even further with sufferers reporting that they have to loosen clothing or even change into a different size of clothes over the course of the day.[18] In patients with IBS-C, the prevalence of distension is even higher approaching 70% and in extreme cases, the patients girth can increase by as much as 12 cm,[18] typically being at its maximum late in the day or in the evening. The exact cause of distension remains unknown, but a whole range of putative mechanisms have been postulated.[51] However, the observations that it is more common in IBS-C[18] or in those patients with delayed transit,[19] raises the possibility that accelerating this might help relieve this troublesome problem especially as those IBS-C patients with delayed transit have greater distension than those who do not have delayed transit.[19] In contrast, there are data to suggest that bloating in the absence of distension may be more of a sensory problem[52] and therefore may not be so amenable

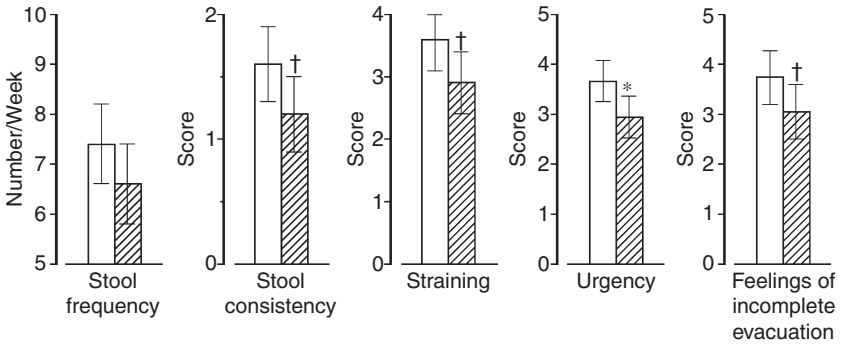

Figure 7. Comparison of stool frequency and symptom scores for stool consistency (absolute difference from normal i.e. Bristol Stool Scale score 4), straining, urgency and feelings of incomplete evacuation between patients consuming test product (hatched) vs. control (open) product. Data represent the marginal means and 95% CI over the 4 week period. *$P < 0.05$, †$P < 0.10$ compared with control.

to this treatment strategy, especially as it is more frequently encountered in the diarrhoea form of IBS.

As a result of increasing evidence suggesting a possible role for inflammation[7, 53] or microbial imbalance[20–24] in the pathophysiology of IBS, there has been recent interest in the use of probiotics in this condition.[35, 36] The results of therapeutic trials to date have been rather variable,[7, 35] which could be explained by the heterogeneity of the IBS subtype included, the variability in study design and high diversity of probiotic strains tested. It is now well established that different organisms vary considerably in their properties and hence it is inappropriate to combine the results of different trials. For instance, some organisms may exhibit greater anti-inflammatory activity,[54] whereas others may have more of an effect on motility[28] or visceral sensation.[55] Consequently, it is necessary to select an organism or a mixture of probiotics that exhibits the properties most suitable for the particular expected health benefit or physiological effect. In this context, the previous preliminary observations that the fermented milk product containing *Bifidobacterium lactis* DN-173 010 appears to accelerate colonic transit[30–33] as well as to improve IBS symptoms[37] makes it a potential candidate for ameliorating distension in IBS, and hence our decision to confine the study to IBS patients with constipation.

In this study, the potential for the fermented milk product containing *Bifidobacterium lactis* DN-173 010 to hasten colonic transit significantly was confirmed as well as the new observation of a significant acceleration of small bowel transit. It may generally be supposed that the improvement in colonic transit may be the main reason why distension was improved, but it is possible that a change in small bowel transit could also be contributory. This is based on the clinical observation that patients with functional constipation who have had a previous colectomy for their problem can still exhibit visible distension of the abdomen, although this has never been confirmed by any form of objective measurement. The distension endpoint in this study was after 4 weeks of product consumption and it is not known whether an equally good result could have been achieved within a shorter period of time. Similarly, it is possible that an even better result might have been achieved if treatment had gone even longer. These are important practical questions as, with the possible exception of antidepressants, most of the medications currently used in IBS can be expected to take effect within a relatively short period of time and therefore patients tend to 'give up' on their treatments comparatively quickly if they are not seen to be working. Unfortunately, it might be anticipated that, given the possible mode of action of probiotics, the onset of benefit may not be instantaneous and there is support for this from the literature.[56]

During the course of treatment, it is noteworthy that a range of IBS symptoms also improved (Figures 6 and 7) despite the numbers of patients in this study being much smaller than would usually be required to produce a meaningful result in a clinical trial recording only symptoms. Obviously, in a study such as this involving a number of physiological measurements, only a limited number of patients can be assessed, although the results indicate that changes in transit and abdominal girth are accompanied by symptom improvement. This further supports the results of a much larger symptom based trial suggesting that this

particular probiotic is beneficial in patients with IBS.[37] Interestingly, a similar degree of change in symptomatology was seen in this compared with the current study, and notably was associated with a significant improvement in the quality of life of these patients.[37]

This is the first study to demonstrate that a probiotic preparation can reduce objectively measured distension in female patients with IBS-C. It also supports the concept that accelerating gastrointestinal transit might be a good target for future therapeutic approaches aimed at improving distension in IBS.

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