Role of gut microflora and probiotic effects in the irritable bowel syndrome

Article *in* Acta bio-medica: Atenei Parmensis · September 2006

Source: PubMed

11 authors, including:

Lucas Cavallaro
Azienda ULSS numero 1 Belluno
102 PUBLICATIONS **1,831** CITATIONS
SEE PROFILE

Giulia Cavestro
Università Vita-Salute San Raffaele
151 PUBLICATIONS **2,377** CITATIONS
SEE PROFILE

Francesco Di Mario
Iuliu Haţieganu University of Medicine and Pharmacy
802 PUBLICATIONS **13,444** CITATIONS
SEE PROFILE

Original article

Role of gut microflora and probiotic effects in the irritable bowel syndrome

Libera Fanigliulo, Giuseppe Comparato, Giovanni Aragona, Lucas Cavallaro, Veronica Iori, Marta Maino, Giulia Martina Cavestro, Paolo Soliani[2], Mario Sianesi[2], Angelo Franzè[1], Francesco Di Mario

Chair of Gastroenterology, Department of Clinical Sciences, University of Parma; [1] Gastroenterology and Endoscopy Unit, Parma Hospital; [2] Chair of General Surgery, Department of Surgical Sciences, University of Parma, Parma, Italy

Abstract. *Background.* Even though the cause of irritable bowel sindrome (IBS) is not yet known, alterations of the intestinal microflora may be important in its pathogenesis. *Aim.* To evaluate the efficacy of rifaximine alone or in association with the probiotic strain of Bifidobacterium longum W11 in reducing symptoms in patients with IBS. *Methods.* We performed a monocentric, prospective, randomized open trial including 70 patients randomized in to two groups: Group A (41 patients) receiving rifaximin 200 (2 cp bid for ten days in a month) followed by a formulation of the probiotic strain of Bifidobacterium longum W11(one granulated suspension for 6 days on alternate weeks) and Group B (29 patients) receiving only rifaximin 200 (2 cp bid for ten days in a month). The clinical evaluation was performed at admission and after 2-months, taking into account the method of visual analogous. *Results.* At the 2-month follow-up, Group A patients reported a greater improvement of symptoms compared to patients in group B ($p = 0.010$) even if the physician's opinion at T1 did not confirm these results ($p = 0.07$). *Conclusion.* The increased colonisation by Bifidobacterium longum W11, after the cyclic administration of rifaximin, which eradicates the bacterial overgrowth of the small intestine, may reduce symptoms, especially those related to bowel habit and stool frequency in patients with IBS. The abnormalities observed in the colonic flora of IBS suggest, in fact, that a probiotic approach will ultimately be justified. (www.actabiomedica.it)

Key words: Irritable bowel syndrome, intestinal microflora, probiotic strain, poorly absorbable antibiotic, small intestinal bacterial overgrowth, stool frequency.

Introduction

The irritable bowel syndrome (IBS) belongs to the group of functional gastrointestinal disorders, which includes functional dyspepsia and non-cardiac chest pain (1, 2).

IBS is a frequent disease in adulthood affecting from 10 to 20% of the general population (3). Moreover, from 25 to 50% of gastroenterological outpatients suffer from IBS and it is estimated that from 60 to 75% of symptomatic subjects do not seek medical attention (4). The female/male ratio ranges from 1.1 to 2.6% depending on the importance given to individual symptoms (5).

Age and race have no consistent effect on the incidence of symptoms (6); on the other hand, cultural factors including diet and socioeconomic status are thought to be of some importance (7).

Abdominal pain, excessive gas production and variable bowel habit for which no endoscopic, radiological, histological, biochemical or microbiological cause is apparent, are typical symptoms of IBS. The lack of positive tests makes the diagnosis of IBS one of exclusion (8). Modified Rome Criteria provide a way of

standardisation of patients affected by IBS, but do not allow a specific diagnosis. According to Rome 2 (9), which represents a modification of Rome 1 (10), the irritable bowel syndrome is defined as follows: at least 12 weeks (which do not need to be consecutive) in the preceding 12 months of abdominal discomfort or pain relieved by defecation and/or associated change in stool frequency and/or stool altered form or appearance. Non-gastroenterological features such as lethargy, poor sleep, fybromialgia, backache, frequency and urgency of micturition, nocturia, incomplete bladder emptying, an unpleasant taste in the mouth, early satiety, and dyspareunia are symptoms that are more common in patients with IBS than in controls and support the diagnosis (11, 12).

The cause of IBS is not yet known. Some factors that are likely to give rise to symptoms like those of IBS, are, for example, genetic influences, food intake, endocrine imbalances, malabsorption, post-operative changes (7), altered gastrointestinal motility, heightened sensory function of the intestine, or malfermentation of food residues (13, 14) and psychosomatic factors such as a psychological morbidity (15), stress (16) and an abnormal illness behaviour (17).

The intestinal microflora has an important pathogenetic role in IBS: a study by King found that colonic-gas production was greater in patients with IBS than in controls and both symptoms and gas production were reduced by an exclusion diet (18). This might indicate a role of gut bacteria in the IBS symptoms.

An abnormal lactulose breath test in some of the patients with IBS suggested bacterial overgrowth of the small intestine (19). The normalization of the lactulose breath test with antibiotics in these subjects resulted in a consistent improvement of IBS symptoms, and almost 50% of the subjects no longer met the Rome I criteria.

The evidence that the intestinal microflora of patients with IBS differs from that of healthy individuals (18-22) is also supported by the fact that these patients may respond to the manipulation of the flora, as showed by some studies involving probiotics (especially Lactobacillum strain) and IBS . The evidence of a beneficial effect of the use of probiotic bacteria in IBS so far has been inconclusive; some trials have obtained a symptomatic reduction or recovery while others have produced different results (23-25).

In this study, we aimed at evaluating the efficacy of rifaximine (a broad-spectrum, poorly absorbable antibiotic) on its own or in association with the probiotic strain of Bifidobacterium longum W11 in reducing symptoms in patients with IBS.

Materials and methods

This study was a monocentric, prospective open trial. The patients, fulfilling Rome criteria and with normal blood tests, were recruited and included in the study after a gastroenterological clinical evaluation. All patients had a normal colonic examination before beginning the study (colonoscopy or barium enema).

Thereafter, seventy patients with diagnosed IBS were randomized into two groups: Group A and Group B. In Group A 41 patients received rifaximin 400 mg for the first ten days of every month and then a formulation of the probiotic strain of Bifidobacterium longum W11 (one granulated suspension for 6 days at alternate weeks)for the following 6 days.

Group B included 29 patients receiving only rifaximin 400 mg (for the first ten days of the month).

Exclusion criteria were: age under 18 yrs, pregnancy and breast-feeding, previous abdominal surgery or diverticulitis, a concomitant organic intestinal disease or other severe systemic diseases, immunodeficiency, a documented intolerance to rifaximin or to probiotics and a low compliance to the therapy. Patients were also excluded if they had started or ended a treatment with antibiotics, antidiarrhoea agents, laxatives, or spasmolytics during the period of the study.

All criteria were assessed by means of a complete history, physical examination, endoscopy/double contrast X-ray and analysis of biochemical blood samples.

At admission, the patients were classified on the basis of stool frequency: 25 patients had an alternate bowel habit, 18 had a diarrhoic bowel habit and 27 had a constipated one.

A clinical evaluation was performed at admission and after 2 months, taking into account the visual analogous method, which expressed the overall clinical

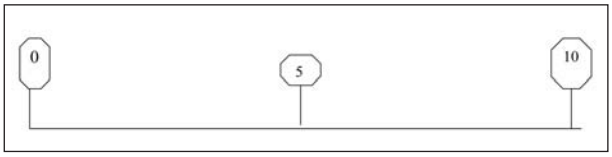

Figure 1. Visual analogous: the method used to evaluate symptomatological score

condition and general well-being of the patient, according to both the gastroenterologist's and the patients' point of view. Visual analogous is a visual score (from 0 to 10) that evaluates the efficacy of the administered therapy on the overall severity of symptoms, especially bowel habit and the overall clinical conditions of the patients during the follow-up (Figure 1).

Patients who developed complications or side effects, recorded by means of a structured clinical interview during each clinical evaluation or whenever necessary, were withdrawn from the study. Patients who voluntarily stopped the treatment or who did not attend the follow-ups were considered drop outs. Non compliance was defined as an interruption of drug intake for more than 4 weeks, or if less than 80% of the appropriate dose was taken. All patients included in the study had given informed oral consent before entering the study.

Statistical methods

Demographic and clinical characteristics were shown as mean ± standard deviation and range.

We used the Wilcoxon test to compare a single group at baseline and after two months and the Monn Whitney U test for the comparison of the two groups at baseline and after two months.

Results

Group A was composed as follows: 58.5% were male patients with a mean age of 53 ± 14 years.

Gropu B was composed as follows: 44.8% were male patients with a mean age of 53 ± 13 years. No statistically significant demographic difference was observed between the 2 groups (Table 1).

Table 1. Demographic and clinical characteristics of the patients at baseline (all differences are non significant)

	Group A	Group B
Patients	41	29
Males	24 (58.54%)	13 (44.82%)
Females	17 (41.46%)	16 (55.18%)
Age (mean ± S.D.)	53 ± 14	53 ± 13
Range	(25-76)	(29-81)

At baseline, no significant difference was shown between the visual analogous of the two Groups both from the physician' s point of view (p = ns) and from the patient' s point of view (p = ns) .

At the 2 month follow-up, patients reported an improvement in the visual analogous both in Group A (p = 0.000) and in Group B (p = 0.002) (Figure 2; Table 2).

The remission of symptoms was also confirmed by a physician both in Group A (p = 0.000) and in Group B (p= 0.000) (Figure 3; Table 2).

However, after 2 months, there was a statistically significant difference between Group A and B in the decrease in the visual analogous according to the pa-

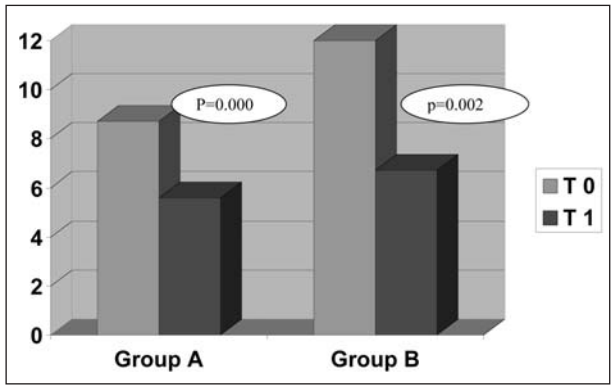

Figure 2. Evolution of patients' visual analogous in the two groups

Table 2. Evolution of visual analogous at the 2 month follow-up in the two groups

	Patient visive analogous			Gastroenterologist visive analogue		
	T 0	T 1	P	T 0	T 1	p
Score Group A	8.7	5.6	0.002	6.5	4.32	0.000
Score Group B	8.5	6.7	0.000	6.1	5.1	0.000

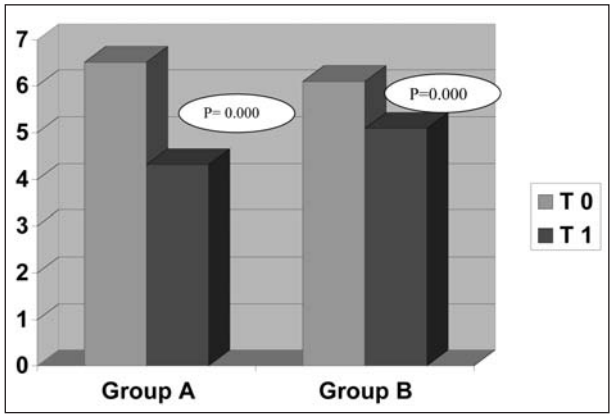

Figure 3. Evolution of gastroenterologist' visual analogous in two groups

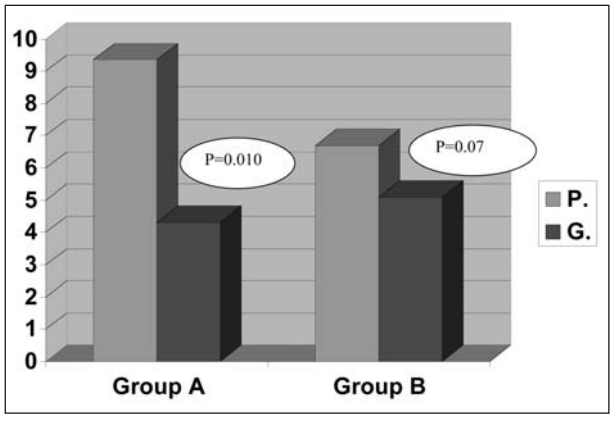

Figure 4. Evaluation at the 2 month follow-up of symptoms score in the 2 groups according to the patients and physicians opinion

tient's opinion (p = 0.010): in fact, at T1 patients in Group A thought their symptoms had improved more than patients in Group B. The physician's opinion at T1 did not confirm these results (p = 0.07). (Figure 4).

Discussion

The results of this study indicate that the administration of Bifidobacterium longum W11 in association with rifaximin decreases symptoms in patients with IBS.

Probiotics are living micro-organisms that, if ingested in a certain quantity, exert health benefits that go beyond basic inherent nutrition (26). According to this definition, probiotics do not necessarily colonise the human intestine. The crucial point regards showing a distinct health benefit that is achieved by the consumption of specific strains. The effect of a bacterium is strain specific and cannot be associated to other strains of the same species.

The range of specific symptoms associated with IBS may indicate a variety of etiological influences and some of them may advocate a multicomponent therapy (27).

We performed this study to test the hypothesis that an increased intestinal colonisation of Bifidobacterium longum W11, after the cyclic administration of rifaximin (a broad-spectrum, poorly absorbable antibiotic), which eradicates the bacterial overgrowth of the small intestine, may reduce symptoms, especially those related to bowel habit and stool frequency.

At the 2-month follow-up, a continuous improvement in the visual analogous in both patients who received rifaximin and bifidobacterium and in patients who received only antibiotic therapy (without the probiotic formulation) was demonstrated, but symptoms benefited most from the combined therapy.

Currently, no organism can be recommended to patients as being likely to help their symptoms. However, the abnormalities observed in the colonic flora of IBS suggest that a probiotic approach will ultimately be justified. In the future, probiotics may be used in the prevention of intestinal microflora damage following antibiotic administration or gastroenteritis, which in turn may prevent the onset of symptoms associated with IBS (28).

References

1. Quigley EMM. Current concepts of the irritable bowel syndrome. *Scand J Gastroenterol* 2003; 38 Suppl 237: 1-8.
2. Jones J, Boorman J, Cann P, et al. British Society of Gastroenterology guidelines for the management of the irritable bowel syndrome. *Gut* 2000; 47 Suppl 2: 1-19.
3. Everhart JE, Renault PF. Irritable bowel syndrome in office-based practice in the United States. *Gastroenterology* 1991; 100: 998-1005.
4. Farthing MJG. Irritable bowel, irritable body, or irritable brain? *Br Med Journal* 1995; 310: 171-5.
5. Heaton KW, Radvan J, Cripps H, Mountford RA, Braddon

FE, Hughes AO. Defecation frequency and timing, and stool form in the general population: A prospective study. *Gut* 1992; 33: 818-24.
6. Taub E, Cuevas JL, Cook IIE, et al. Irritable bowel syndrome defined by factor analysis. Gender and race comparisons. *Dig Dis Sci* 1995; 40: 2647-55.
7. Zuckerman MJ, Guerra LJ, Drossman DA, et al. Healthcare seeking behaviors related to bowel complaints: Hispanic versus non-Hispanic whites. *Dig Dis Sci* 1996; 41: 77-82.
8. Maxwell PR, Mendall MA, Kumar D. Irritable bowel syndrome. *Lancet* 1997; 350: 1691-5.
9. Thompson WG, Longstreth GF, Drossman DA, Heaton KW, Irvine EJ, Muller-Lissner SA. Functional bowel disorders and functional abdominal pain. *Gut* 1999; 45 Suppl II: 43-7.
10. Thompson WG, Dotevall G, Drossman DA, Heaton KW, Kruis W. Irritable bowel syndrome: guidelines for the diagnosis. *Gastroenterol Int* 1989; 2: 92-5.
11. Whorwell PJ, Mc Callum M, Creed FH, et al. Non-colonic features of irritable bowel syndrome. *Gut* 1986; 27: 37-40.
12. Triadafilopoulos G, Simms RW, Goldenberg DL. Bowel disfunction in fybromialgia syndrome. *Dig Dis Sci* 1991; 36: 59-64.
13. Hunter JO, Alun Jones V. Studies on the pathogenesis of irritable bowel syndrome produced by food intolerance. In Read NW, ed: Irritable Bowel Syndrome. London: Grune & Stratton Ltd., 185-90.
14. Camilleri M. Management of the irritable bowel syndrome. *Gastroenterology* 2001; 120: 652-68.
15. Ford MJ, Miller PC, Eastwood J, et al. Life events, psychiatric illness and the irritable bowel syndrome. *Gut* 1987; 28: 160-5.
16. Cann PA, Read NW, Cammack J, et al. Psychological stress and the passage of a standard meal through the stomach and the small intestine in man. *Gut* 1983; 24: 236-40.
17. Smith RC, Greenbaum DS, Vancouver JB, et al. Psychosocial factors are associated with health care seeking rather than diagnosis in irritable bowel syndrome. *Gut* 1987; 28: 160-5.
18. Balsari A, Ceccarelli A, Dubini F. The fecal microbial population in the irritable bowel syndrome. *Microbiology* 1982; 5: 185-94.
19. Nobaek S, Johansson M-L, Molin G, Ahrnè S, Jeppsson B. Alteration of the intestinal microflora is associated with reduction in abdominal bloating and pain in patients with irritable bowel syndrome. *Am J Gastroenterol* 2000; 95: 1231-8.
20. Wyatt GM, Bayliss CE, Lakey AF, et al. The fecal flora of two patients with food-related irritable bowel syndrome during challenge with symptom-provoking foods. *J Med Microbiol* 1998; 26: 295-9.
21. Cummings JH, Macfarlane GT. The control and consequences of bacterial fermentation in the colon. *J Appl Bacteriol* 1991; 70: 433-59.
22. Sen S, Mullan M, Parker TJ, Woolner J, Tarry SA, Hunter JO. Effects of Lactobacillus plantarum 299v on symptoms and colonic fermentation in irritable bowel syndrome (IBS). *Dig Dis Sci* 2002; 47 (11): 2615-20.
23. Pimentel M, Chow EJ, Lin HC. Eradication of small bowel overgrowth reduces symptoms of irritable bowel syndrome. *Am J Gastroenterol* 2000; 95: 3503-6.
24. O'Sullivan MA, O'Morain CA. Bacterial supplementation in the irritable bowel syndrome. A randomized double-blind placebo-controlled crossover study. *Dig Liver Dis* 2000; 32: 294-301.
25. King TS, Elia M, Hunter JO. Abnormal colonic fermentation in irritable bowel syndrome. *Lancet* 1998; 352: 1187-9.
26. Guarner F, Schaafsma GJ. Probiotics. *Int J Food Microbiol* 1998; 39: 237-8.
27. Drossman DA, Thompson WG. Irritable bowel syndrome: A graduated, multicomponent treatment approach. *Ann Intern Med* 1992; 116: 1009-16.
28. Madden JAJ, Hunter JO. A review of the role of the gut microflora in irritable bowel syndrome and the effects of probiotics. *Br J Nutr* 2002; 88: S67-S72.

Accepted: 31th July 2006
Correspondence: Prof. Francesco Di Mario,
Department of Clinical Sciences,
University of Parma,
Via Gramsci, 14
43100 Parma
Tel: + 390521702772;
Fax + 390521291582
E-mail: francesco.dimario@unipr.it, www.actabiomedica.it