Clinical Follow-up of 30 Patients Affected by Irritable Bowel Syndrome Treated with **iprob®**

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Irritable bowel syndrome (IBS) is a common disorder affecting millions of people worldwide.
The etiology of irritable bowel syndrome (IBS) is thought to be multifactorial, with several factors (including alterations in gut motility, small-bowel bacterial overgrowth, microscopic inflammation, and visceral hypersensitivity) potentially playing a role. Recent studies have suggested that probiotics may be useful in the treatment of IBS. Probiotics are defined as live microorganisms, which, when administered in adequate amounts, confer a health benefit on the host.
Small-bowel bacterial overgrowth has emerged as a possible cause of IBS.
Several studies have shown that patients with IBS have low-grade inflammation throughout the small bowel and colon. It has been postulated that the release of certain inflammatory mediators, including interleukins and histamine, may affect nearby enteric nerves, causing alteration in gut function and sensory perception.
Probiotics have a beneficial effect on intestinal mucosa via several proposed mechanisms that include suppression of the growth and binding of pathogenic bacteria, improvement of the barrier function of the epithelium, and alteration of the immune activity of the host.
Probiotics secrete short chain fatty acids, an action that results in decreased luminal pH and production of bactericidal proteins.
A product of bacterial fermentation of fiber, has been shown to nourish colonic enterocytes, enhancing mucosal integrity.
The aim of this observational study was to evaluate the effect of the administration of a symbiotic multi-strain mixture for the management of IBS. In this observational study we investigated the efficacy of a formulation composed of four probiotic strains *(L. Acidophilus LA02, L. Delbrueckii subsp. Bulgaricus LDB01, L. Rhamnosus LR04, Streptococcus thermophilus FP04).*

Materials and Methods

A total of 30 adult subjects (19 females, mean age 29.7 years, range 14-56 ys; 11 males, mean age 33.2, range 17-58 ys) affected by IBS according to Rome criteria (Longstreth et al. 2006), attending a single outpatient allergy clinic for a suspected food allergy/intolerance for the period of January 2014 to April 2016 were enrolled in the study. Each subject used 1 sachet per day for a period of two months. Patients were instructed to record improvement, persistence and/or worsening of IBS symptoms such as diarrhea, constipation, bloating, and abdominal pain/discomfort during the study period.
A follow-up evaluation took place at the end of the two-month period, and patients underwent an oral interview during which they were asked if they experienced worsening, no significant improvement, partial improvement or substantial improvement of their IBS symptoms.

An industrial combination of *L. Acidophilus LA02* ≥ 100x106 UFC/sachet, *L. Delbrueckii subsp. Bulgaricus* LDB01≥ 5 x 106 UFC/sachet, *L. Rhamnosus* LR04≥ 1x106 UFC/sachet, *Streptococcus thermophilus* FP04≥ 2x106 UFC/sachet and inulin 0.330 gr/sachet (IPROB, marketed by Anallergo Italia, San Piero a Sieve, Florence, Italy) was used in this study. This content is in agreement with the guidelines of the Italian Ministry of Health on probiotics (Italian Ministry of Health, 2013).
In the group of 30 patients, faecal calprotectin has been measured before and after symbiotic supplementation as a marker of gut inflammation. Statistics were conducted using Excel Microsoft Office.

Diagnostic Criteria* for Irritable Bowel Syndrome

Recurrent abdominal pain or discomfort** for at least 3 days per month in the last 3 months associated with 2 or more of the following:

1. Improvement with defecation
2. Onset associated with a change of frequency of stool
3. Onset associated with a change in form (appearance) of stool

** Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis*
*** Discomfort means an uncomfortable sensation not described as pain. In pathophysiology research and clinical trials, a pain/discomfort frequency of al least 2 days a week during screening evaluation for subject eligibility.*

Table 1 Rome criteria for diagnosis of IBS (Longstreth et al. 2006).

Results

Of the 30 subjects evaluated, all took the symbiotic formulation once daily for 60 days, as the schedule prescribed, without reporting any adverse effect. Subjective evaluation of IBS symptoms after two months of IPROB supplementation in our study population is showed in Figure 1.
Twenty-three patients reported an improvement of IBS symptoms, with 7 of them reporting a substantial improvement. One patient discontinued the treatment after a 2 weeks because of worsening of symptoms, but no serious adverse effects were reported.
All patients underwent faecal calprotectin dosage. This marker of gut inflammation was significantly decreased (148.5 vs 84.9, $p < 0,01$) after two months of IPROB supplementation in respect to the baseline (Figure 2).

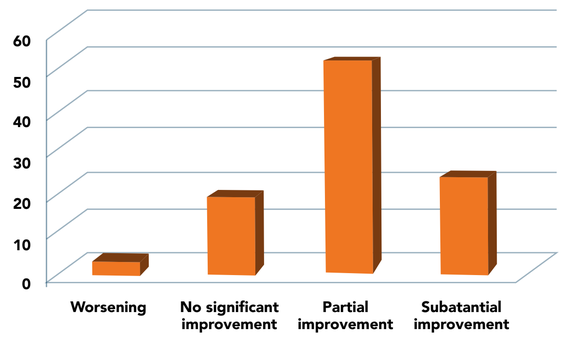

Fig. 1 Subjective evaluation of IBS symptoms after 60 days of IPROB treatment.

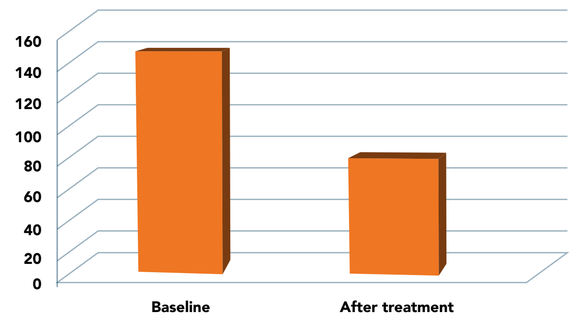

Fig. 2 Faecal calprotectin dosage (mg) at baseline and after 60 days of IPROB treatment

Discussion

Bacterial fermentation has been associated with many IBS symptoms such as flatulence, abdominal distension, and bloating. Moreover, qualitative changes in the microbiota have been described in IBS. Some probiotics have considerable metabolic activity, including: capability of fermentation of nondigested carbohydrates and their conversion into short-chain fatty acids, modulation of the inflammatory response to some enteropathogens, vitamin synthesis and deconjugation of bile salts.
It has been demonstrated that some probiotics are capable of producing and secreting neurotransmitters and neuromodulators that modify some gastrointestinal functions, such as motility or visceral sensation. Finally, they can also modulate inflammation and enhance mucosal barrier function.
In this observational study, a sixty-day dietary supplementation of IPROB multi-strain symbiotic, composed of *L. Acidophilus LA02, L. Delbrueckii subsp. Bulgaricus LDB01, L. Rhamnosus LR04, Streptococcus thermophilus FP04,* has been associated with an improvement of symptoms, with respect to the baseline, in 22 of the 30 adult IBS patients (Figure 1). Of these, 7 reported a substantial improvement, while 16 reported a partial improvement. Six patients reported no improvement, while only one patient discontinued therapy after 2 weeks because of a worsening of IBS symptoms (mainly abdominal distension and bloating). No serious adverse effects were reported in remaining subjects.
Faecal calprotectin dosage was performed to assess gut inflammation in 30 patients. In these subjects, faecal calprotectin was significantly decreased after two months of IPROB supplementation with respect to the baseline (Figure 2).
Our data, obtained from an observational study of 30 adult patients, confirms that IPROB is well tolerated and supports the hypothesis that this symbiotic improves IBS symptoms. An increase of dosage or duration of the supplementation could be taken into account, at least for those patients who reported a partial improvement of symptoms with the standard dosage. As far as we known, possible explanation for the group of 23 patients who did not report any significant improvement of symptoms rely on the fact that IBS is multifactorial syndrome and that changes in the microbiota are just one of the involved pathogenic mechanisms.
The main limitations for this study include observational design without a control group and the lack of a standardized tool and/or scoring system for subjective evaluation of symptoms.
Further studies and randomized trials with larger patient populations are needed to confirm this positive effect.

Conflict of Interests

Renato Rossi received consultancy fees from Anallergo Italia S.p.A.

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