

Effect of β -Glucan, Inositol and digestive enzymes in GI symptoms of patients with IBS

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Abstract. – Background: Irritable bowel syndrome (IBS) is a very common functional gastrointestinal (GI). Diagnosis of IBS is based on the fulfilment of the Rome III criteria. Common GI symptoms are lower abdominal pain, bloating and disturbed defecation, such as urgent diarrhoea and/or episodes of chronic constipation. Many agents have been employed in the management of IBS, although only few have been demonstrated to show a relevant efficacy.

Aim: To evaluate the effectiveness of the administration of a mixture of beta-glucan, inositol and digestive enzymes (Biointol[®]) in improving GI symptoms in patients affected by IBS.

Patients and Methods: 50 IBS patients (20 males, 30 females; mean age 51±19) were treated with Biointol[®] (group A) while another group consisting of 40 IBS patients (15 males, 25 females; mean age 50±18) did not receive any therapy (group B).

Results: Biointol[®] administration improved significantly bloating, flatulence and abdominal pain, with a slight increasing of urgency for bowel movements. On the contrary, Biointol[®] did not show any significant effect on the other IBS symptoms.

Conclusions: Currently, only few agents used in the management of IBS have been proven to be effective. Biointol[®] administration has shown to improve some IBS symptoms, such as bloating, flatulence and abdominal pain, all connected to the presence of gas inside the intestinal lumen.

Key Words:

Irritable Bowel syndrome, Rome III Criteria, Beta-glucans, Inositol, Digestive enzymes.

Introduction

Irritable bowel syndrome (IBS) is a common functional gastrointestinal (GI) disorder character-

ized by lower abdominal pain or discomfort, bloating and disturbed defecation, in particular urgent diarrhoea, episodes of chronic constipation or a pattern of alternating between the two¹. IBS is the most common cause of recourse to gastroenterologists and it is estimated as affecting up to 20% of the Western Countries' population, with its symptoms that may be debilitating for some patients. Indeed, patients with IBS consistently report a lower health-related quality of life²⁻⁵ and they have a tendency to visit physicians more frequently than those without IBS¹, thus the annual economic consequences of IBS in the Western Countries are significant⁶. Despite the prevalence and the high impact of this disorder in the population, the etio-pathogenetic mechanisms of IBS are not completely understood. The disorder may appear after a severe bout of gastroenteritis^{7,8}, and/or after the experience of a stressful event, although the link between stress and IBS is not yet completely understood. Other etio-pathogenetic hypothesis include an abnormal GI motor function, visceral hypersensitivity, autonomic dysfunction, mucosal immune activation and psychosocial factors^{1,9,10}. In addition, there is increasing evidence showing the link between alterations in the GI microbiota and IBS. The role of the GI microbiota in the pathogenesis of IBS can be inferred from the following elements: (1) changes in faecal and mucosa-associated microbiota; (2) post-infectious IBS; (3) the relationship between the disease and small intestinal bacterial overgrowth; and (4) an up-regulation of the GI mucosal immune system^{11,12}. Given this evidence, therapeutic use of probiotic bacteria and substances that positively affect the host (by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon) could be beneficial.

IBS is a functional disorder involving a malfunction of the intestinal system and it does not show up in any visible disease process or tissue damage. Its diagnosis is currently based only on signs and symptoms. The diagnostic criteria more widely accepted are the Rome III Criteria¹³. The seriousness of IBS depends on symptoms' frequency and on the impact of such symptoms on patient's daily life and the treatment to be adopted by the physician depends on such evaluation. However, the discovery of an effective therapy for IBS still remains a challenge. Over the years, a wide range of therapies have been proposed and studied. The lack of a single, proven intervention highlights the complex interplay of bio-psychosocial factors and the need for a multidisciplinary, integrated approach.

β -glucans (or beta-glucans) are polysaccharides made up of chains of D-glucose molecules, which are present in the cell wall of many bacteria, baker's yeasts (i.e., *Saccharomyces Cerevisiae*) and mushrooms. It has been shown that yeast derived beta-glucans have an immunomodulatory function, so that they have also been considered for cancer therapy¹⁴. Beta-glucans seem to help the immune system by stimulating Th2 cells which, in turn, modulate and mitigate Th1 cells in order to reach a balance between the two lymphoid systems; thanks to this mechanism it is possible to obtain a decrease of the intestinal inflammatory process. Th2 cells stimulate the proliferation of NK and B cells, which promote a defensive action targeted on microorganisms and not on the host tissues. Beta-glucans activate phagocytes through the link to the Toll-like receptors located on the surface of macrophages and dendritic cells. Once activated, the Toll-like receptors can determine the pathogen phagocytosis in order to prevent their proliferation. Moreover, beta-glucans decrease the gut permeability, thus preventing the entrance in blood of dangerous substances. Given this evidence, beta-glucans seem to be particularly effective to enhance immune function and to reduce the susceptibility to infection and even cancer¹⁴.

Inositol (chemical formula $C_6O_6H_{12}$) is a naturally occurring nutrient that is usually classified as a carbocyclic polyol. The most prominent form, which widely occurs in nature, is referred to as myo-inositol (named for its presence in muscle tissue, from which it was first obtained in 1850) and is classified as member of the vitamin B complex (vitamin B8). Myo-inositol (which is one of nine distinct isomers of inositol) is naturally pre-

sent in a variety of foods, including vegetables, fruits, beans, whole grains, nuts, oats, rice, liver, pork and veal, but it is not considered as an essential nutrient and does not have the proper qualities of vitamins since the colonic bacteria are able to convert the phytic acid found in plant fibres¹⁵ into inositol and even the liver can produce it from glucose. Inositol is indispensable for our body because it represents an important component of the cellular membrane, it stimulates and activates mitochondria in order to favour the cellular breathing and it functions as basis for a number of signalling and secondary messenger molecules. Inositol is involved in different biological processes, such as insulin signal transduction, cytoskeleton assembly, nerve guidance, intracellular calcium concentration control¹⁶, cell membrane potential maintenance, break down of fats and reduction of blood cholesterol. In light of this evidence, a big interest is growing up about the possibility of using inositol in different clinical situations. In this respect, researchers produced several studies that suggest the beneficial effect of inositol as a therapeutic agent in the following conditions: (1) bipolar disorder; (2) panic disorder; (3) obsessive-compulsive disorder; (4) Alzheimer's disease; (5) polycystic ovary syndrome; (6) psoriasis; (7) diabetic neuropathy; (8) cancer prevention^{17,18}; and (9) constipation. As regards constipation, it has been demonstrated that inositol has a stimulating effect on the muscular action and on the contraction of the alimentary tract and consequently improves intestinal regularity bloating.

Digestive enzymes are energized protein molecules (proteases and peptidases, lipases, carbohydrases amyloglucosidases, nucleases, lactase, cellulases) that break down polymeric macromolecules into smaller building blocks, in order to facilitate their absorption by the intestinal tract. The importance of digestive enzymes derives from the fact that the human body cannot absorb nutrients in food unless digestive enzymes break them down. Given such action, it has been shown that the administration of oral supplements of digestive enzymes in IBS may be beneficial¹⁹.

Biointol[®] pills are made up of a "fast and slow" double layer allowing their constituents to have a targeted action on the specific GI tract in which they may be useful. The "fast" layer includes beta-glucan and the enzymatic mixture, while the "slow" layer is made up of inositol, which, due to this particular technology, is able to easily reach the duodenum in which it externalizes its main action.

In light of the above mentioned observations, we designed a study aimed at verifying whether the administration of a mix of beta-glucan, inositol and digestive enzymes may improve GI symptoms of patients affected by IBS.

Patients and Methods

IBS patients fulfilling the Rome III criteria for the diagnosis of IBS²⁰ have been considered eligible for the study. Newly diagnosed IBS patients free of therapy were used as control (Group B). Patients have been randomly assigned to treatment or control.

All patients and controls have been investigated for the prevalence and intensity of GI symptoms using the questionnaire below:

- Meteorism (from 0 to 10);
- Flatulence (from 0 to 10);
- Abdominal pain (from 0 to 10);
- Evacuative urgency (from 0 to 10);
- Number of daily evacuation;
- Feeling of incomplete defecation (yes/no);
- Stool transit (from 1/helping with the hands to 7/inability to keep stool inside);
- Stool shape (Bristol stool scale).

Subsequently, Group A patients started a therapy with Biointol[®], taking one pill at lunch time and one at dinner time, consecutively for 4 weeks. Prevalence and intensity of GI symptoms were daily evaluated by a self-administered questionnaire during the entire treatment period either for Group A or Group B patients.

Statistical Analysis

The primary hypothesis was that the administration of Biointol[®] for 4 weeks would determine a change in the expression of GI symptom described in the Patients and Methods section. Statistical analyses were based on the intention-to-treat principle and involved all patients and controls. Baseline characteristics and demographic data were summarized with the use of descriptive statistics. Comparisons between non-normally distributed data were made with the use of the Mann-Whitney U test. All tests were two-sided, and a *p* value of less than 0.05 was considered to indicate statistical significance. All analyses were performed with the use of SPSS software, version 16.0 (SPSS Inc., Chicago, IL, USA).

Results

Fifty-five IBS patients, were consecutively enrolled in the Group A and forty-seven IBS patients free of therapy in the group B. Five patients of group A and seven of Group B were eventually excluded from the analysis of data because they were not compliant to the therapy or to the daily diary of symptoms. General characteristics of patients and controls enrolled in this study are shown in the Table I.

The main results of this study are reported in the Figures. Figures 1, 2 and 3 shows the effect of Biointol therapy on bloating, flatulence and abdominal pain. In particular, there was a significant improvement of all those symptoms in the group of patients treated with Biointol[®] compared to controls; this effect was significantly visible 3 and 4 weeks after the starting of the therapy.

On the contrary, treatment with Biointol[®] was not associated with any change in the expression of the other GI symptoms assessed by this study, with the exception of urgency for bowel movements, which was significantly increased in the group of patients treated with Biointol[®] during the first week of treatment.

The effect of Biointol[®] was similar in males and females as well as among different IBS subtypes.

Discussion

Many agents have been employed in the management of IBS, although only few have been demonstrated to show a relevant efficacy^{9,12}. Symptomatic therapy continues to be

Table I. Effect of different micronutrient treatments on liver function enzyme activities and total protein in diabetic rats.

Characteristics	Biointol [®]	Controls
N. patients	50	40
Age	51 ± 19	50 ± 18
Gender		
Males	20	15
Females	30	25
IBS subtype		
Diarrhea	10	8
Constipation	12	12
Mixed	28	20

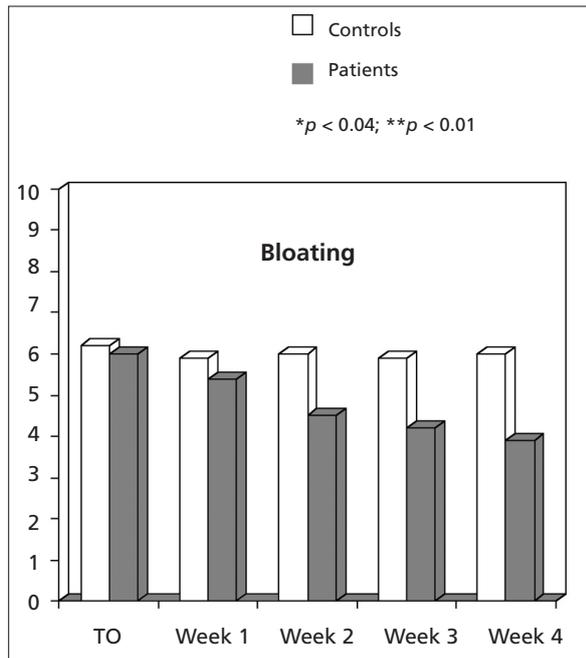


Figure 1. Effect of Biointol® on bloating. A significant decrease of this symptom was observed 3 and 4 weeks after the start of the treatment in IBS patients.

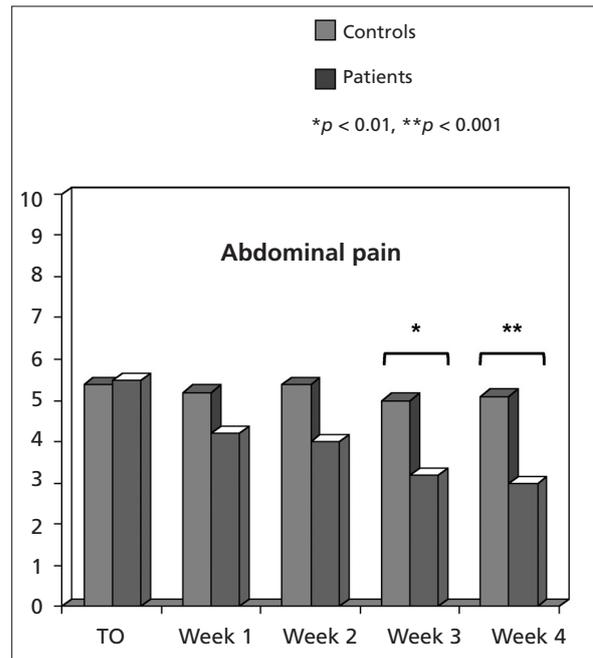


Figure 3. Effect of Biointol® on abdominal pain. A significant decrease of this symptom was observed 3 and 4 weeks after the start of the treatment in IBS patients.

very important in the therapy of IBS, even though the evidence for anti-spasmodics, anti-diarrheal agents, and laxatives or stool softeners in IBS patients is quite poor. Currently, oth-

er approaches have been proposed in the management of IBS, ranging from antibiotic and/or probiotic administration, to dietary modification and hypnotherapy^{9,12}.

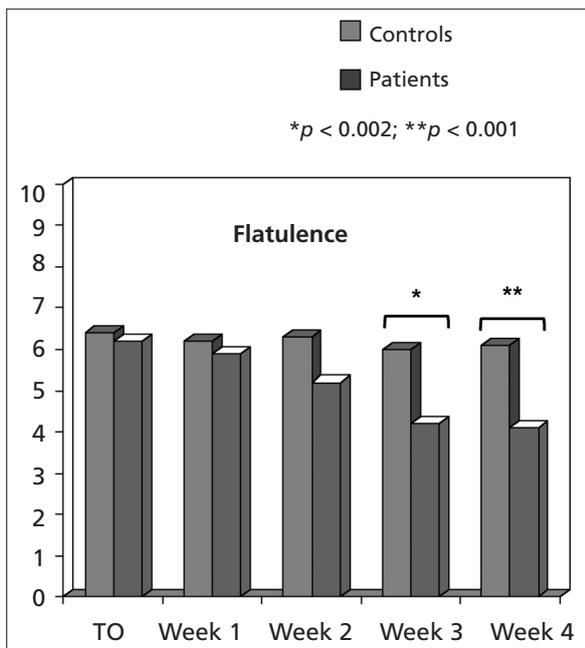


Figure 2. Biointol® determined a significant decrease in the intensity of flatulence, 3 and 4 weeks after the start of the treatment in IBS patients.

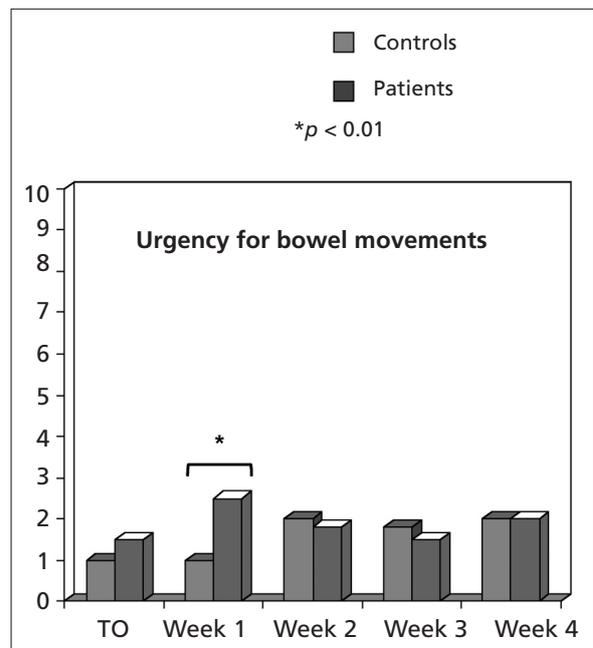


Figure 4. Effect of Biointol® on urgency for bowel movements. A significant change was observed only in the first week of treatment.

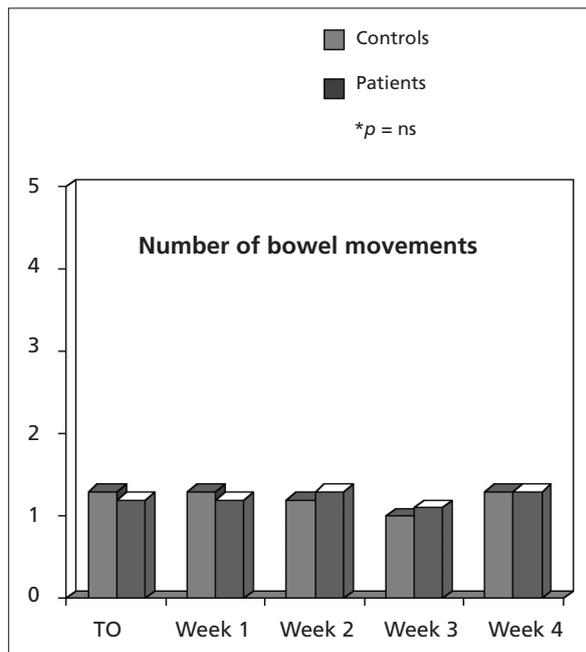


Figure 5. Biointol[®] did not show any effect on the number of bowel movements during the entire time of treatment.

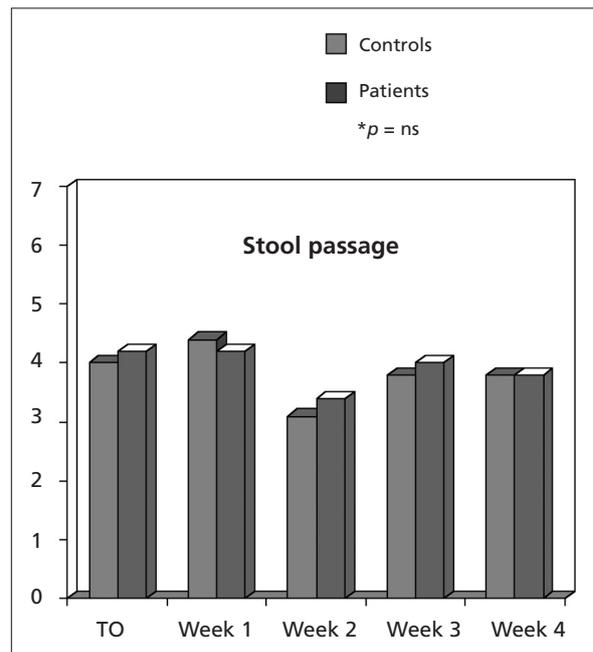


Figure 7. Biointol[®] administration did not show any effect on stool passage.

In the present study we administered Biointol[®], a mix of beta-glucan, inositol and digestive enzymes in patients affected by IBS for 4 weeks, in order to verify whether it may affect GI symptoms. Results from this study clearly showed that this drug is able to improve some of the IBS-re-

lated GI symptoms, such as bloating, flatulence and abdominal pain in comparison to the control group. Interestingly, all the improved symptoms are determined by the presence of gas inside the intestinal lumen. The administration of substances that modify the bacterial pabulum, change also their metabolism and growth and, therefore, are able to modulate the gas production and improve gas-related symptoms. In our treatment the digestive enzymes contained in the mix may have played a major role in reducing the quantity of unadsorbed nutrient that reach the colon. Beta-glucans known to decrease the gut permeability¹⁴, which has been found to be altered in IBS patients²² may also have contributed to the perception of relief of treated patients. Finally, the stimulating effect on the muscular contraction of the alimentary tract by inositol^{15,16} although did not increase the number of evacuation may have helped the expulsion of gas, reducing bloating.

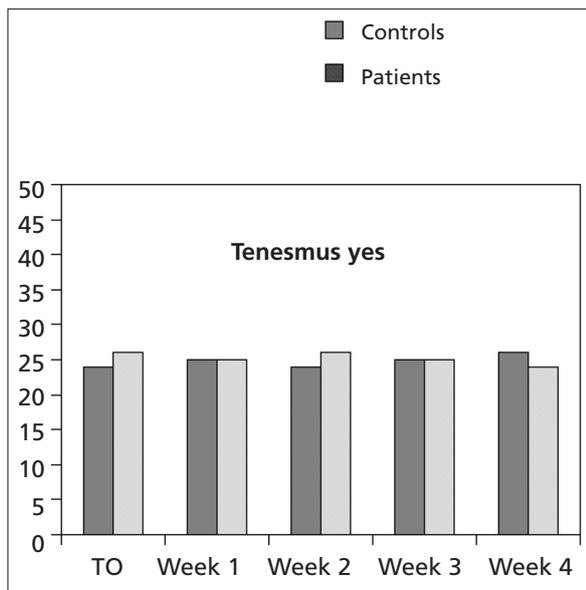


Figure 6. Tenesmus was not affected by the administration of Biointol[®].

In this study we did not observe any significant difference in the change of GI symptoms between males and females during the treatment with Biointol[®]. Similarly, the effect of Biointol[®] was equally distributed among patients with different subtype of IBS. Whether this effect is real or is just related to the small number of enrolled patients is still unclear.

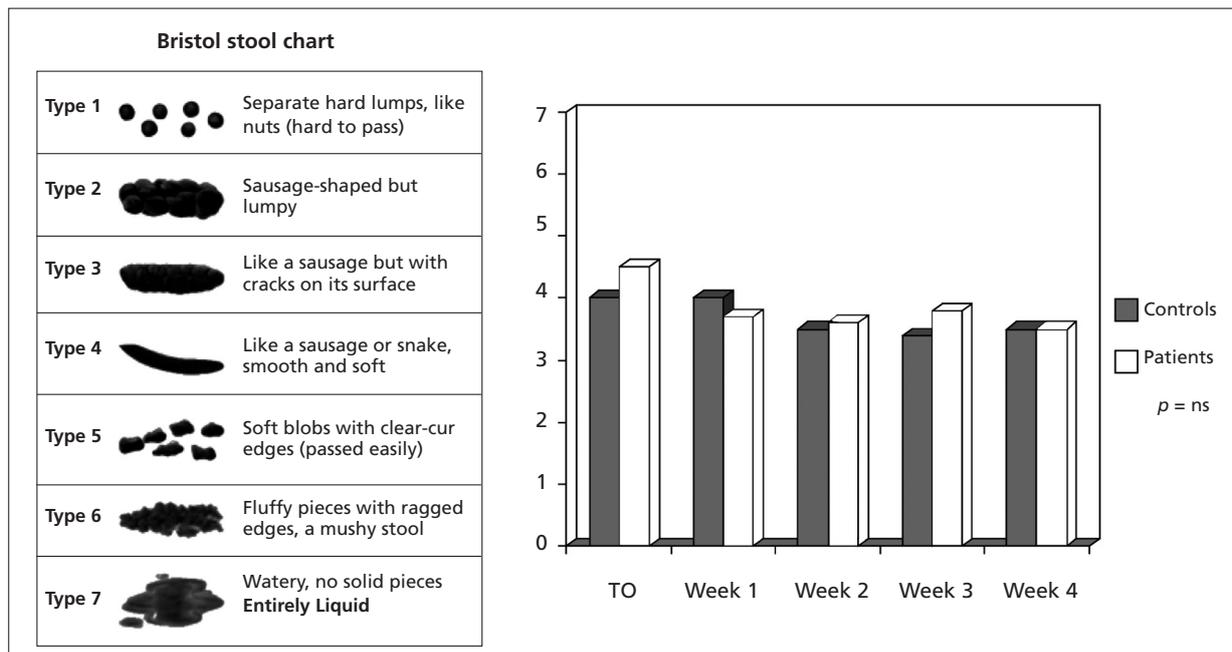


Figure 8. Biointol® did not determined any change in the characteristics of stools based on the Bristol stool chart.

The main limit of this study, in fact, is that it has been conducted on a quite small number of patients assuming this therapy for only 4 weeks. Nevertheless, the result obtained by this study may be useful to calculate the sample power to design a larger and longer trial. In fact, considering the promising results obtained, we believe that further studies are now needed in order to confirm our findings.

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