ORIGINAL ARTICLE

Abincol® (*Lactobacillus plantarum* LP01, *Lactobacillus lactis subspecies cremoris* LLC02, *Lactobacillus delbrueckii* LDD01), an oral nutraceutical, pragmatic use in patients with chronic intestinal disorders

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Summary. Chronic intestinal disorders (CID), including inflammatory bowel disease (IBD), such as ulcerative colitis and Crohn's disease, irritable bowel syndrome (IBS), and diverticular disease (DD), are diseases that relapse episodes. There is evidence that patients with CID have intestinal dysbiosis, so probiotics may counterbalance the impaired microbiota. Therefore, the current survey evaluated the efficacy and safety of Abincol®, an oral nutraceutical containing a probiotic mixture with *Lactobacillus plantarum* LP01 (1 billion of living cells), *Lactobacillus lactis subspecies cremoris* LLC02 (800 millions of living cells), and *Lactobacillus delbrueckii* LDD01 (200 millions of living cells), in 3,460 outpatients (1,660 males and 1,800 females, mean age 55 years) with chronic intestinal disorders. Patients took 1 stick/daily for 8 weeks. Abincol® significantly diminished the presence and the severity of intestinal symptoms and improved stool form. In conclusion, the current survey suggests that Abincol® may be considered an effective and safe therapeutic option in the management of patients with chronic intestinal disorders. (www.actabiomedica.it)

Key words: inflammatory bowel disease, irritable bowel syndrome, diverticular disease, probiotic, survey

Introduction

Chronic intestinal disorders (CID), including inflammatory bowel disease (IBD), such as ulcerative colitis and Crohn's disease, irritable bowel syndrome (IBS), and diverticular disease (DD), are diseases that relapse episodes; CID have still unknown etiology (1). It has been widely accepted that IBD is the conse-

quence of overly activated response of mucosal immune system to the environmental, dietary, or infectious antigens in a genetically susceptible host (2). Studies on the animal models have indicated that aggressive cell-mediated immune reaction caused by commensal enteric bacteria plays a vital role in the development and maintenance of IBD. Evidence from patients also showed innate immune system would be activated and aberrant immune response would be initiated through secreting inflammatory mediators caused by endogenous bacterial flora, which would result in IBD (3).

A chronic, low-grade, subclinical inflammation has been also implicated in the disease process and is thought to perpetuate the symptoms of IBS (4). A recent meta-analysis of 13 studies has reported a high prevalence of IBS symptoms in patients with IBD (up to 40%), even in those with quiescent disease and under remission (5). Thus, an overlap exists between IBS and IBD as both share common pathogenic mechanisms.

Several studies have showed clearly the role of a low-grade inflammation both in the occurrence of symptoms in people having diverticulosis, both in symptom persistence following acute diverticulitis (6).

Therefore, increasing attention has been payed to the potential role of probiotics in the treatment of CID as they could solve inflammation through improving an intestinal microbial balance (7). In particular, there is evidence that patients with CID have intestinal dysbiosis, so probiotics may counterbalance the impaired microbiota (8).

Initially, Mecnikov suggested in 1907 that microbial ingestion improved host health, as the consumption of lactic-acid-producing bacteria (LAB) strains found in yogurt might enhance longevity (9). LAB is a heterogeneous group of microorganisms that are often present in the gut, introduced through the ingestion of fermented foods. Some of these strains have probiotic effects. In particular, strains belonging to *Bifidobacterium*, *Enterococcus*, and *Lactobacillus* are the most widely used probiotic bacteria (10). In current use, the term probiotic refers to living microorganisms that confer a health benefit to the host when administered in adequate amounts; when ingested, probiotics produce microbial transformation in the intestinal microbiota and exert several health-promoting properties, including maintenance of the gut barrier function and modu-

lation of the host immune system (11). Probiotics are therefore commonly used as therapeutic option in the management of CID based on the assumption that dysbiosis is present in CID patients (12-15).

Abincol® is an oral nutraceutical containing a probiotic mixture with *Lactobacillus plantarum* LP01 (1 billion of living cells), *Lactobacillus lactis subspecies cremoris* LLC02 (800 millions of living cells), and *Lactobacillus delbrueckii* LDD01 (200 millions of living cells) and it has been recently placed on the market.

On the basis of this background, an Italian survey explored the pragmatic approach of a group of gastroenterologists in the management of CID in clinical practice. Therefore, the aim of the current survey was to evaluate the efficacy and safety of Abincol® in outpatients with chronic intestinal disorders.

Materials and Methods

The current survey was conducted in 83 Italian Gastroenterology centers, distributed in the whole Italy, so assuring a wide and complete national coverage, during the fall-winter 2018-2019. Gastroenterologists were asked to recruit all consecutive outpatients visited because of chronic inflammatory disorders, including IBD, IBS, and uncomplicated diverticulitis.

Patients were consecutively enrolled during the specialist visit. The inclusion criteria were: to have chronic intestinal symptoms, both genders, and adulthood. Exclusion criteria were to have comorbidities and concomitant medications able to interfere the evaluated outcomes.

All patients signed an informed consent. All the procedures were conducted in a real-world setting.

The treatment course lasted 8 weeks. The oral nutraceutical Abincol® (Aurora Biofarma, Milan, Italy) was taken following the specific indications, such as one stick/daily. Patients were visited at baseline (T0), after 4 weeks (T1), and after 8 weeks (T2).

Clinical examination was performed in all patients at T0, T1, and T2. The following parameters were investigated: abdominal pain, abdominal bloating, flatulence, borborygmi, eructation, malaise, weakness, headache. These symptoms were assessed as present/absent and were scored using a four-point scale

(0=absent, 1=mild, 2=moderate, 3=severe), but for abdominal pain the scale was 5-point (4=very severe).

A physical examination of stool was performed using the Bristol stool form scale (16).

Safety was measured by reporting the occurrence of adverse events.

All clinical data were inserted in an internet-platform that guaranteed the patients' anonymity and the findings' recording accuracy.

The paired T-test was used. Statistical significance was set at p <0.05. Data are expressed as medians and 1th and 3rd quartiles. The analysis was performed using STATA, College Station, Texas, USA.

Results

Globally 3,460 outpatients (1,660 males and 1,800 females, mean age 55 years) were visited and completed the treatment course.

The frequency of symptoms (abdominal pain, abdominal bloating, flatulence, borborygmi, eructation, malaise, weakness, headache) at baseline (T0), and at T1 and T2 is reported in Table 1 and 2. In particular, abdominal pain and abdominal bloating were the most common symptoms at baseline. The frequency of both significantly diminished after the treatment course.

Consistently, the severity of the most relevant symptoms did significantly diminish after the treatment (Figure 1). In particular, abdominal pain and bloating significantly diminished at T1 and T2 (p<0.001 respectively for both symptoms).

In addition, stool form significantly improved as a normal form (type 3 and 4) was detectable in 29.1% at baseline, in 47.8% at T1, and in 49.5% at T2 (p<0.001 as linear trend).

The treatment was well tolerated by all patients and no clinically relevant adverse event was reported.

Table 1. Frequency of patients for each symptom at baseline (T0). M=males; F=females, Mean age in years

N= 3,460

	n	%	M/F	Mean age
Abdominal pain	3084	89.2%	1468/1616	55
Abdominal bloating	2808	81.2%	1318/1490	55
Flatulence	2639	76.3%	1249/1390	55
Borborygmi	2265	65.5%	1029/1236	55
Eructation	1945	56.2%	925/1020	55
Malaise	1312	37.9%	601/711	56
Weakness	877	25.4%	407/470	56
Headache	371	10.7%	168/203	56

Table 2. Comparison of proportion of patients with symptoms at baseline (T0), and at T1 and T2

| Symptoms	T0	T1				T2			
	n	n	%	Diff %	p	n	%	Diff %	p
Abdominal pain	3084	1748	56.7%	-43.3%	<0.001	961	31.2%	-68.8%	<0.001
Abdominal bloating	2808	1568	55.8%	-44.2%	<0.001	897	31.9%	-68.1%	<0.001
Flatulence	2639	1351	51.2%	-48.8%	<0.001	745	28.2%	-71.8%	<0.001
Borborygmi	2265	1089	48.1%	-51.9%	<0.001	539	23.8%	-76.2%	<0.001
Eructation	1945	868	44.6%	-55.4%	<0.001	488	25.1%	-74.9%	<0.001
Malaise	1312	410	31.2%	-68.8%	<0.001	111	8.5%	-91.5%	<0.001
Weakness	877	228	26.0%	-74.0%	<0.001	66	7.5%	-92.5%	<0.001
Headache	371	84	22.6%	-77.4%	<0.001	45	12.1%	-87.9%	<0.001
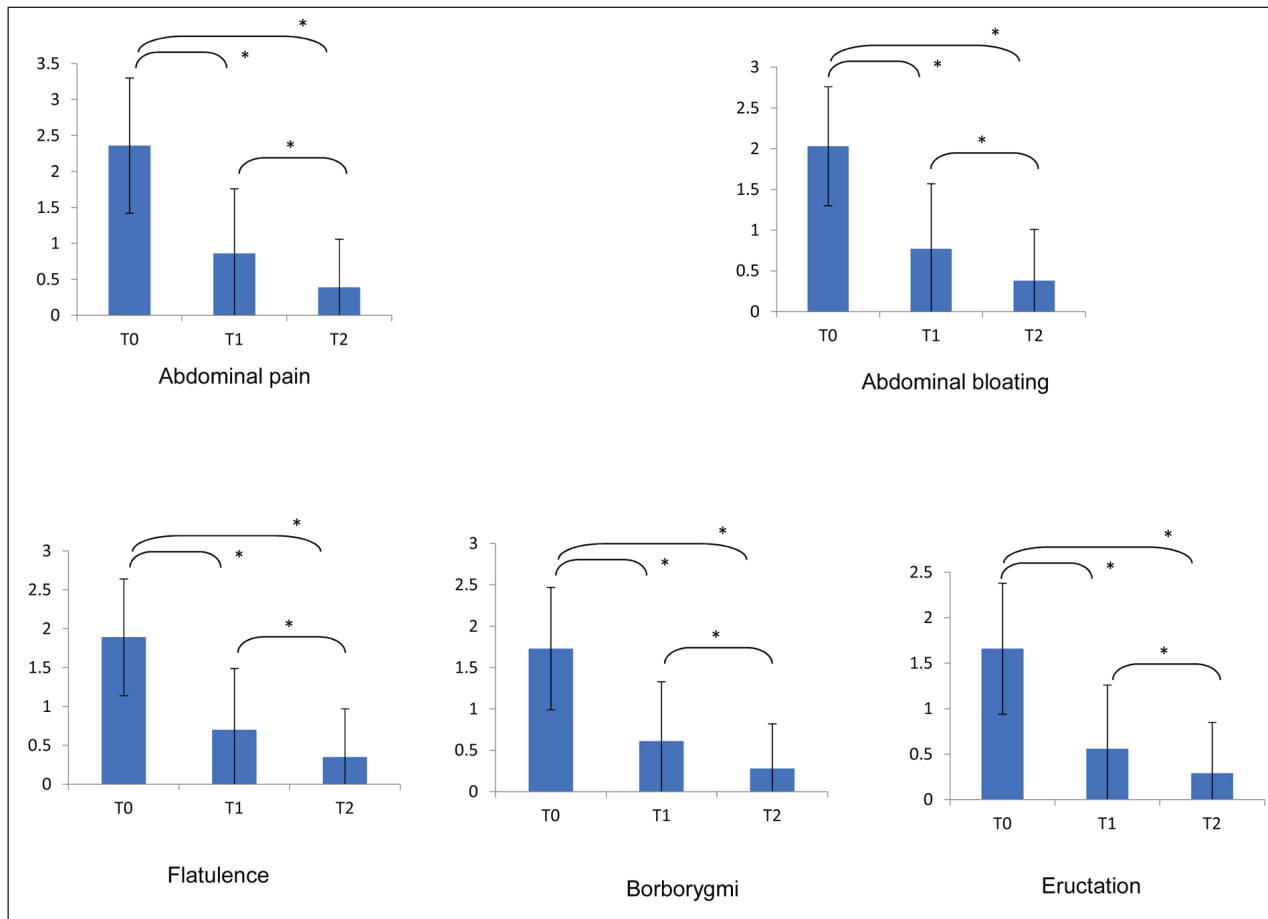
Figure 1. Symptoms severity at baseline (T0), at T1 and T2. Symptoms' score scale was 0-3 for all symptoms but abdominal pain (0-4). Comparisons were made by paired Wilcoxon test. *= p<0.001

Discussion

There is no standard therapy for IBD and the most common treatment option is to establish systemic or topical immunoregulation with different medications, including mesalazine, sulfasalazine, anti-TNFα agents, and thiopurines which could also reduce the associated risk of cancer in bowel (2). Unfortunately, serious adverse effects may occur after long time treatment; thus, an alternative therapy may be required in many patients. It has been reported that almost 40% of adults and children who suffered with IBD have been treated with alternative therapies, including probiotics (17). A recent meta-analysis concluded that, according to its pathogenesis, the use of some types of probiotics could prevent the induction of inflammatory reactions in patients with IBD (1).

Current evidence from systematic reviews and meta-analyses supports the use of probiotics also for symptomatic relief of IBS, however, no recommendation on the specific species/strains or combinations has been defined at present (14).

The goals of treatment in diverticular disease are symptom relief, inflammation control, and prevention of disease progression or recurrence (18). The basis for preventing disease progression remains a high-fiber diet and physical exercise, although the evidence level is poor. Other current strategies include modulation of gut microbiota dysbiosis with rifaximin or probiotics, or using mesalazine for low-grade inflammation in uncomplicated symptomatic diverticulosis. (18).

Therefore, probiotics could be considered a fruitful therapeutic option in the management of CID.

The current survey demonstrated that Abincol®

was able to significantly and progressively reduce the most common digestive complaints occurring in patients suffering from chronic intestinal disorders. In particular, Abincol® did diminish impressively abdominal pain and bloating that are bothersome symptoms and significantly affect the quality of life. The improvement of stool form in many patients could be considered the indirect proof of the mechanism of action of Abincol® as it modified the intestinal microbiota inducing a physiological digestive function.

In addition, Abincol® was safe and well tolerated.

All these issues suggest that this probiotic mixture may be a useful option in the management of patients with chronic intestinal disorders, including IBD, IBS and DD.

Of course, the present survey cannot be considered a formal investigative study. Consequently, further studies should be conducted by a rigorous methodology, such as designed according to randomized-controlled criteria.

On the other hand, the strength of this survey is the huge number of enrolled patients and the real-world setting. The reported outcomes could therefore mirror the facts observable in clinical practice.

In conclusion, the current survey suggests that Abincol® may be considered an effective and safe therapeutic option in the management of patients with chronic intestinal disorders.

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