

ORIGINAL ARTICLE

Saccharomyces boulardii and infection due to *Giardia lamblia*

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Abstract

Therapy with metronidazole is the recommended option in giardiasis. However, some clinical trial reports suggest the appearance of drug resistance to explain therapeutic failure. Several investigations have been carried out on the effect of probiotic microorganisms for preventing or treating gastrointestinal diseases, but little is known about their efficacy against protozoal infections. The principal objective of our study was to evaluate the efficacy of *Saccharomyces boulardii* against *Giardia lamblia* infections. A double-blind, placebo-controlled study was carried out on adult patients with giardiasis. Group 1 (30 patients) included metronidazole 750 mg 3 times daily along with *S. boulardii* capsules (250 mg b.i.d. orally) for 10 d while group 2 (35 patients) was treated with metronidazole 750 mg 3 times daily and with empty capsules as placebo for 10 d. Patients were re-examined at 2 and 4 weeks after treatment, and stool examinations were performed. At week 2, *G. lamblia* cysts were detected in 6 cases (17.1%) of group 2 and none in group 1. At the end of the fourth week, presence of the cysts continued in the same 6 cases in group 2 (control group). These findings indicated that *S. boulardii* may be effective in treating giardiasis when combined with metronidazole therapy.

Introduction

Giardiasis is an important public health problem with long lasting diarrhoea. The infection is characterized by symptoms varying from asymptomatic infection to diarrhoea, weight loss, abdominal pain and weakness. Patients with giardiasis should be treated even when asymptomatic [1].

Saccharomyces boulardii is a non-pathogenic yeast originally isolated from the surface of lichee nuts. It has been widely used in Europe to treat diarrhoea. It is popularly called 'yeast against yeast' in France. Clinical trials have demonstrated the effectiveness for *S. boulardii* in the treatment or prevention of *C. difficile* diarrhoea, antibiotic associated diarrhoea and traveller's diarrhoea [2,3]. Rapid healing of the jejunal mucosa due to the protective effects of *S. boulardii* has been reported in some experimental studies [4,5]. It is very well-known that secretory IgA is the key immunological component of intestinal barrier function and experimental data suggest that

stimulation of sIgA secretion is a key beneficial effect of this yeast [6].

Many investigations have been carried out on the effect of probiotic microorganisms for preventing or treating gastrointestinal diseases, but little is known about their efficacy against protozoal infections. Recently, *S. boulardii* has been used to prevent or treat infectious diarrhoea of many aetiologies. It deconjugates bile acids, decreases cholesterol absorption in the bowel and inhibits the adhesion of pathogens to intestinal epithelium [4,7]. In this study, we aimed to assess the potential effects of *S. boulardii* in the management of giardiasis.

Materials and methods

A double-blind placebo-controlled study was carried out on adult patients with giardiasis. The study protocol was approved by the Institutional Review Board (Ethics Committee) of Gulhane Military Medical Academy, Ankara, Turkey. 65 patients

Table I. Characteristics of the patients with *G. lamblia* in the present study.

	Female	Male	Age (Mean)	Symptomatic	Asymptomatic
Group 1 (metronidazole+probiotic)	11	19	31.2	17	13
Group 2 (metronidazole+placebo)	9	26	28.7	15	20

Table II. Clinical manifestations in patients symptomatic at time of recruitment.

	Group 1 (%)	Group 2 (%)
Diarrhoea	17 (100%)	15 (100%)
Abdominal pain	17 (100%)	15 (100%)
Flatulence	12 (70.6%)	10 (66.6%)

with presence of *G. lamblia* trophozoites/cysts in their stool specimens were enrolled, and randomly assigned into 2 groups. The stool samples were examined by direct microscopy initially, and when the parasite was seen, permanent staining was performed as a confirmatory method.

In group 1, 30 patients (11 F, 19 M) were treated with metronidazole (Flagyl® tb., Aventis-Pharma, France) 750 mg 3 times daily and oral lyophilized capsule of *S. boulardii* (Reflor®, Biocodex, Montrouge, France) 250 mg twice daily for 10 d. In this group, 17 patients were symptomatic and the other 13 patients were asymptomatic. 35 patients (9 F, 26 M) in group 2 were treated with metronidazole 750 mg 3 times daily and with empty capsules carrying the same characteristics with *S. boulardii* formulation, but without any active ingredient for 10 d. In this second group, 15 patients were symptomatic and the other 20 were asymptomatic. None of the patients had any underlying pathology or recent use of antimicrobial drugs. The patients were controlled at the end of second and fourth weeks with stool examinations.

Results are expressed as median (range) and proportions. Statistical analysis was performed by the Mann-Whitney *U*-test and Fisher's exact test. Statistical significance was accepted as $p < 0.05$. SPSS 10.0 (Chi., Ill., USA) package program was used for statistical analysis.

Table III. The results of the treatment in Group 1 and Group 2.

	Resolution of clinical symptoms by end of week 2	Median complete resolution time of the clinical findings	Clearance of microscopical findings after 2nd week	Clearance of microscopical findings after 4th week
Group 1 Symptomatic: 17, Asymptomatic: 13	17 (100%)	24 h	30 (100%)	30 (100%)
Group 2 Symptomatic: 15, Asymptomatic: 20	15 (100%)	30 h	29 (82.8%)	29 (82.8%)
<i>p</i> -value			0.027	0.54

Results

Tables I, II and III show the characteristics of the patients, manifestations, and results of treatment. In all of the symptomatic cases for both groups, the clinical manifestations were cleared at the end of the second week following the initiation of therapy. While the median clearance of the symptoms in group 1 was 24 h (min = 12, max = 36), the median time for group 2 was recorded as 30 h (min = 12, max = 36). No statistical difference was observed between the groups ($p = 0.54$).

At the end of the second week, *G. lamblia* cysts were detected in 6 cases (17.1%) of group 2, but no *G. lamblia* cysts were detected in group 1. The proportion of patients with clearance of microscopical findings after 2 weeks was 100% (group 1) and 82.8% (group 2) ($p = 0.027$). Three of these 6 cases with cyst carriage in group 2 were symptomatic, while the remaining 3 were asymptomatic at the beginning of the medications and the cyst presence continued also in all of the 6 cases at the end of the fourth week.

Discussion

There is only a limited range of drugs available for treatment of giardiasis. These drugs comprise the nitroimidazoles, quinacrine and furazolidone. Metronidazole is the drug of choice, but alternatives such as albendazole are available [8,9]. Some clinical reports suggest the appearance of drug resistance to explain therapeutic failures [9]. Given the fact that the disease is a long lasting infection, the resistance multiplies the burden.

A number of investigations have been carried out on the effects of probiotic microorganisms that use various principles in preventing or treating infectious

or non-infectious diseases. Guillot et al. evaluated the effects of *S. boulardii* in children 6–36 months old. The probiotic was found to be effective in the management of chronic diarrhoea due to *G. lamblia* [10].

The first line of protection against dysbiosis and intestinal toxicity is strict control of intestinal permeability, the ability of the gut to allow some substances to pass through its walls while denying access to others. The pathogenic mechanisms by which the *G. lamblia* trophozoites impair absorption have not been clarified. Damage to the intestinal mucosa, due to either bacterial proliferation associated with the presence of the parasite, or deconjugation of bile salts by the bacteria; the parasites have been considered in this connection [1,11].

In the present study, we aimed to evaluate the effectiveness of *S. boulardii* for the clearance of *G. lamblia* cysts and trophozoite forms in patients suffering giardiasis. The prolonged excretion of the parasite was significantly lower in *S. boulardii* group, i.e. the probiotic seemed to enhance clearance of the infecting pathogen. On the other hand, the symptoms were entirely eliminated in both groups. Although the median time period for the resolution of symptoms was shorter in the *S. boulardii* group than in group 2, this did not achieve statistical significance.

S. boulardii has been shown to decrease the number and severity of lesions caused by another protozoan parasite, *Entamoeba histolytica* [12]. This probiotic can inhibit the attachment of *E. histolytica* trophozoites to erythrocytes in vitro [13]. Probably, the ability to adhere to gastrointestinal mucosa is an important prerequisite for *G. lamblia* to induce sustainable infection [1,11]. *S. boulardii* might interfere with this adhesion. Although the mechanisms of action in the clearance of *G. lamblia* from the gut have not been clarified, the effects listed below may well be involved:

1. Trophical effects on the small intestine [14]
2. Increasing intestinal disaccharides levels [15]
3. Enhancing and stimulating of the gut immune system [6]
4. Alteration of enzymatic activation in gut [14]
5. Capability of assembling host defences against potential pathogens [5]

According to our results, *S. boulardii* is effective in decreasing microscopic findings of giardiasis over a period of 2 weeks. Since *G. lamblia* infections are often asymptomatic, cyst carriers are hazardous owing to spread of parasite to the environment.

The effects of *S. boulardii* may contribute to the prevention of the dissemination of the disease in the community.

Based on the present results, we suggest that *S. boulardii* may serve as an effective adjunct in the treatment of giardiasis.

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