

A pilot trial of *Saccharomyces boulardii* in ulcerative colitis

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Objectives Probiotics can be useful in the treatment of inflammatory bowel disease. In a previous report, the non-pathogenic yeast *Saccharomyces boulardii* was found to be beneficial in the maintenance treatment of Crohn's disease. The aim of this study was to assess the efficacy of *S. boulardii* in ulcerative colitis patients.

Methods A group of 25 patients with a mild to moderate clinical flare-up of ulcerative colitis received additional treatment with *S. boulardii* 250 mg three times a day for 4 weeks during maintenance treatment with mesalazine. These patients were unsuitable for steroid therapy. Before and after treatment, Rachmilewitz's clinical activity index was calculated. The probiotic treatment was considered a therapeutic success only when the final score was lower than 6.

Results Of the 24 patients who completed the study, 17

attained clinical remission; this was confirmed endoscopically.

Conclusions Our preliminary results suggest that *S. boulardii* can be effective in the treatment of ulcerative colitis. Controlled studies with this probiotic agent are warranted. *Eur J Gastroenterol Hepatol* **15:697-698** © 2003 Lippincott Williams & Wilkins

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Introduction

The role of luminal bacteria in the pathogenesis of inflammatory bowel disease is now recognized, although the mechanisms involved are only partially understood [1-3]. Clinical studies employing antibiotics have yielded promising results in both Crohn's disease [4] and ulcerative colitis [5]. However, the widespread use of antibacterial agents has been hampered by their side effects and the risk of developing bacterial resistance.

Probiotics are living microorganisms that alter the enteric flora and induce beneficial effects on health. The use of probiotics in inflammatory bowel disease represents a more appealing alternative to the use of antibiotics. However, clinical studies with probiotics in inflammatory bowel disease are still limited. A non-pathogenic strain of *Escherichia coli* (Nissle 1917) has been found to be as effective as mesalazine in the long-term treatment of ulcerative colitis [6,7], while a preparation containing a mixture of different probiotics proved to be significantly superior to placebo in both the treatment [3] and prevention [8] of pouchitis.

In one study, clinical relapses of Crohn's disease appeared to be notably less frequent in patients who, in addition to standard mesalazine maintenance, were treated with a preparation of the probiotic agent *Saccharomyces boulardii* [9]. This non-pathogenic yeast is clinically

effective in various types of diarrhoea and is particularly active against *Clostridium difficile* [10-12].

The possible role of *S. boulardii* in the treatment of ulcerative colitis has not been investigated so far. The aim of this present pilot study was to assess the efficacy of *S. boulardii* in patients with a clinical flare-up of ulcerative colitis. These patients had been advised to avoid steroid therapy.

Materials and methods

We studied 25 patients who had suffered a clinical flare-up of ulcerative colitis of mild to moderate degree (Truelove and Witts' criteria) while on maintenance treatment with high-dose mesalazine (1 g three times daily) for at least 3 months. The group consisted of 14 men and 11 women, aged 19-47 years, in whom a previous endoscopic diagnosis (histologically confirmed) of left-sided ulcerative colitis had been made. Endoscopy was not repeated at the time of inclusion in the study, as the relapses were clinically evident.

For ethical reasons, only patients who had a history of poorly tolerated steroid courses during the active phases of the disease were enrolled. The untoward effects of these corticosteroid treatments were: sodium retention (11 cases), decompensated diabetes (eight cases), severe skin rash (three cases), steroid myopathy (one case) and

persistent dyspepsia resistant to proton pump inhibitors (two cases).

For the above reasons, the patients were reluctant to restart treatment with corticosteroids and gave their informed consent to first try a course of the probiotic agent.

S. boulardii was administered for 4 weeks as a 250 mg capsule taken three times daily, while the ongoing mesalazine treatment was continued. No topical treatment with either mesalazine or steroids was allowed during the study period.

Clinical evaluation was performed before and after treatment by means of Rachmilewitz's activity index [13], calculated on the basis of stool frequency, blood in the stools, general condition, fever, abdominal pain, erythrocyte sedimentation rate and haemoglobin values. Only patients with a basal score of 9 or higher were admitted to the study. Patients were instructed to return to the clinic in the event of a further worsening of their symptoms so that they could be shifted to steroid treatment.

The two-tailed Wilcoxon signed rank-sum test was calculated for statistical analysis of the index variations but, for practical purposes, only a final score of 5 or less was considered a therapeutic success. In patients with apparent clinical remission, flexible sigmoidoscopy was performed.

Results

One patient dropped out of the study after 9 days due to worsening of his symptoms and was given prednisone.

The remaining 24 patients completed the 4-week course with *S. boulardii* and reported no side effects induced by the probiotic agent. A significant reduction in the clinical index score was observed at the end of the treatment ($P < 0.05$). However, the most meaningful clinical result was that a successful outcome (a score of 5 or less) was achieved in 17 patients (68% of cases on an intention-to-treat basis). In all instances, sigmoidoscopy confirmed the clinical remission.

Discussion

The rationale for employing probiotics in the treatment of inflammatory bowel disease is mostly based on evidence that intestinal bacteria play a pathogenetic role [1-3]. Clinical data are, however, still scarce. The possible therapeutic mechanisms of probiotics in intestinal inflammatory disorders include: antagonism against enteric pathogens; strengthening of the gut mucosal barrier; inhibition of local secretion of inflammatory mediators; and stabilization of local immunological

activity [13].

S. boulardii has been found to be beneficial in the maintenance treatment of inactive Crohn's disease [9], although its precise mode of action in this setting remains to be determined. The possible efficacy of this probiotic in ulcerative colitis has never been assessed before.

Our preliminary data show that in about two-thirds of patients experiencing a clinical flare-up of ulcerative colitis during maintenance treatment with mesalazine, the addition of the probiotic for 4 weeks resulted in clinical remission, which was endoscopically confirmed. The lack of a control group and the open fashion of this pilot trial make it impossible to draw definite conclusions, but our preliminary results are encouraging and warrant further, controlled trials of *S. boulardii* in inflammatory bowel disease.

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