The efficacy and safety of adding the probiotic *Saccharomyces boulardii* standard triple therapy for eradication of *H.pylori*: a randomized controlled trial

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**ABSTRACT**

**Aim:** Evaluating the efficacy and safety of adding the probiotic *Saccharomyces boulardii* standard triple therapy for eradication of *Helicobacter pylori*.

**Background:** Several probiotics such as *Saccharomyces boulardii* have been investigated for their clinical efficacy. This probiotic inhibit *H. pylori* urease by lowering the gastric pH, adhesion of *H. pylori* to gastric epithelial cells, stabilize the gastric barrier function and reduce the side effects of antibiotics.

**Patients and methods:** In this randomized controlled trial we evaluated 160 adult patients with biopsy confirmed *H.Pylori* infection referred to gastroenterology ward of Taleghani hospital. The patients were randomized into two treatment regimens: patients in group A (n=80) were given amoxicillin (1000 mg, b.i.d), clarithromycin (500 mg, b.i.d), omeprazole (20 mg, b.i.d) and probiotic of *saccaromyces boulardi* (Yomogi) (250 mg, b.i.d) for 14 days, moreover patients in group B (n=80) were given amoxicillin (1000 mg, b.i.d), clarithromycin (500 mg b.i.d) and omeprazole (20 mg,b.i.d) for 14 days.

**Results:** 160 patients (66 male 41.25%, 94 female 58.75%) with the mean age of 47.1±11.4 years were evaluated. The success rate for *H. pylori* eradication in group A was higher 75(87.5%) than group B 65 (81.2%), but the difference between two groups was not significant (p=0.350). Moreover, in case group side effects as nausea, diarrhea, abdominal discomfort and bloating were significantly lower than control group in first and second weeks.

**Conclusion:** This study showed that *saccaromyces boulardi* decreased the adverse effects associated with *H.pylori* therapy but did not significantly decrease the eradication rate of *H.pylori*.

**Keywords:** *Helicobacter pylori*, Probiotic, *Saccharomyces boulardii*, Anti-*helicobacter pylori* eradication therapy.

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**Introduction**

*Helicobacter pylori* (*H.pylori*) affects approximately 50% of the world’s population and it is a leading cause of peptic ulcers and chronic gastritis. Moreover *H.pylori* was defined as a possible risk factor for gastric adenocarcinoma and mucosa-associated lymphoid tissue lymphoma (1). It was classified as a type 1 carcinogen by the World Health Organization (WHO) in 1994 (2). Treatment with amoxicillin, clarithromycin and a proton pump inhibitor (PPI) is the first-line triple therapy to eradicate *H.pylori*. However, due to high prevalence of treatment failure related to
Efficacy of probiotic in Helicobacter pylori eradication therapy

Antibiotic resistance, frequent and uncontrolled use of antibiotics and severe and frequent antibiotic adverse effects (3,4) the clinicians have considered several alternatives therapies. These methods include: extended treatment duration, the use of new antibiotics, and quadrupl therapy as the first option or recently the addition of probiotics to triple therapy (4-6). Probiotics are live microorganisms that may have a positive effect on gastrointestinal microorganism and recover health conditions (7). These agents have become progressively popular in the world to treat a diverse type of gastrointestinal disease (8-10). In this regard numerous probiotic strains have been investigated for their clinical efficacy, including multiple bacterial strains and fungal strains as *Saccharomyces boulardii* (*S. boulardii*) (11-13). The probiotics inhibit *H. pylori* urease by lowering the gastric pH, adhesion of *H. pylori* to gastric epithelial cells, stabilize the gastric barrier function (14) and reduce the side effects of antibiotics (15,16). However previous studies have provided conflicting information regarding the positive effect of probiotic on *H.pylori* eradication (17).

In our knowledge not enough evidence are available on the beneficial effects of adding probiotics into the eradication regimen of *H. Pylori* in Iran. Therefore this study aimed to evaluate the efficacy and safety of adding the probiotic *Saccharomyces boulardiito* standard triple therapy for eradication of *H.pylori*.

**Patients and Methods**

In this randomized controlled trial we evaluated 160 adult patients with biopsy confirmed *H.Pylori* infection referred to gastroenterology ward in Taleghani hospital (a tertiary academic center in Tehran-Iran) during 2011-2012. All adult patients who came to our hospital and were candidate for upper GI endoscopy within 12 months were evaluated in this trial. Patients <15 years old, pregnant women or lactation patients with history of hepatic, cardio-respiratory, renal, neoplastic diseases or coagulopathy, patients receiving antibiotics, PPIs, H2 receptor blockers, bismuth salts, or probiotics within the previous four weeks, patients with previous gastric surgery and sensitivity to any of the drugs used in this study were excluded from this study. The study was approved by the Ethics Committee of Gastroenterology and Liver Diseases Research Center, Shahid Beheshti University of Medical Sciences and it was in agreement with the principles of the Helsinki II Declaration. Moreover the patients were informed about the study protocol and written consent was obtained from all patients. Patients with biopsy confirmed *H.pylori* were included. Then they were randomized into two treatment regimens: patients in Group A (n: 80) were given amoxicillin (1000 mg, b.i.d), clarithromycin (500 mg b.i.d), omeprazole 20 mg bid and *saccharomyces boulardii* probiotic (250 mg, b.i.d) for 14 days, and patients in Group B (n:80) were given amoxicillin (1000 mg, b.i.d), clarithromycin (500 mg b.i.d) and omeprazole (20 mg b.i.d) for 14 days. Patient compliance was evaluated at the end of the treatment by pill count and was considered as good compliance if > 95% of the medication had been taken. Modest compliance > 70%, Poor compliance < 70% and dropped out.

Patients were asked to report any side effects of therapy during the treatment period (end of first, second, third and fourth weeks of treatment) and were given a possible side effect list, such as epigastric pain, diarrhea, taste disturbance, constipation, and stomatitis. Eight weeks after treatment, Urea Breath Test (UBT) was performed in all patients. Successful eradication was defined as a negative 13C-urea breath test result (UBT) eight weeks after discontinuation of the therapy.

**Statistical analysis**

The data were entered in SPSS version 17. Values were reported as mean ± standard deviation. Non-parametric t-test, chi-square test
were used to compare two independent groups. P<0.05 were considered to be significant.

**Results**

In this clinical trial, 160 patients (58.7% female) with mean age 47.1±11.4 years were evaluated. Regarding sex and age the difference between case and control groups was not significant (p>0.05).

The most frequent esophagogastroduodenoscopy (EGD) finding group A and B was antral gastritis (51% and 44% respectively). The difference between two groups was not significant (p>0.05) (figure 1).

The success rate for *H. pylori* eradication was higher in group A 75(87.5%) than in group B 65 (81.2%), but the difference between two groups was not significant (p=0.350) (Table 1).

**Table 1.** Distribution of *H. pylori* eradication and compliance in two groups

| Groups (%) | A (n=80) | B (n=80) | P-value |
|------------|---------|---------|---------|
| Compliance |         |         |         |
| Good       | 52(65)  | 46(58.2)| 0.46    |
| Moderate   | 23(28.8)| 24(30.4)|         |
| Poor       | 5(6.3)  | 9(11.4) |         |
| UBT results|         |         |         |
| Negative   | 70(87.5)| 65(81.2)| 0.27    |
| Positive   | 10(12.5)| 15(18.8)|         |

Group A (n: 80) were given amoxicillin (1000 mg, b.i.d), clarithromycin (500 mg b.i.d), omeprazole 20 mg bid and *saccharomyces boulardii* probiotic (250 mg, b.i.d) for 14 days;
Group B (n:80) were given amoxicillin (1000 mg, b.i.d), clarithromycin (500 mg b.i.d) and omeprazole (20 mg b.i.d) for 14 days.

Regarding drug compliance 52(65.0%) in group A and 46(58.2%) in group B showed good compliance. The difference between case and control groups was not significant (p<0.05) (Table 1).

The frequency of side effects as nausea, diarrhea, abdominal discomfort and bloating in group A were significantly lower than group B in first and second weeks (p<0.05), where as skin rash, insomnia in case group did not show remarkable difference compared to control group (Table 2).

**Discussion**

Recently, the alternative anti-*H. pylori* treatments have been extended and more studies have been steered to describe components that may effect on *H. pylori* infection. In general, probiotics can strengthen host systems and assist in recovery from certain diseases and in particular *S. boulardii* induces morphologic changes in *H. pylori* cells consistent with cellular damage (18) and in one trial by Gottel et al. was shown *S. boulardii* reduce 12% of *H. pylori* colonization in infected children (19). Furthermore de Bortoli et al. indicated that the addition of probiotics to standard triple therapy (esomeprazole, clarithromycin, amoxicillin) could increase the eradication rate of *H. pylori* infection and reduce the side effects of antibiotic therapy (20).

To evaluate this hypothesis, we designed a comparative clinical trial study to assess any positive effect of *S. boulardii* on *H. pylori* infection and side effects of therapy. The success rate for *H. pylori* eradication was higher in probiotic group (87.5%) than control (81.2%), but the difference between two groups was not significant. However, side effects as nausea, diarrhea, abdominal discomfort and bloating were significantly lower in group A than group B during the first and second weeks. These findings were in accordance with Cremonini et al. study that indicated the efficacy of probiotics for eradication of *H. pylori*.
in 85 asymptomatic carriers. They randomized patients in three probiotic therapy groups (S. boulardii, L.rhamnosus GG or a mixture of L. acidophilus and Bifidobacterium lactis) and placebo for 14 days. After second week, the eradication rates were similar for all groups (81% for S. boulardii, 80% for placebo). But antibiotic-associated diarrhea in all the probiotic groups was significantly lower (5%) than placebo group (30%)(21). Moreover, the other study by Cindoruk et al. in 2007 in turkey evaluated S. boulardii for both eradication of H. pylori and the reduction of side-effects of the standard triple treatment. They studied 124 carriers with dyspepsia who were receiving the triple therapy and randomized to either S. boulardii (1g) or placebo group for two weeks. Then patients were followed up for six weeks regarding side-effects and H. pylori eradication rate. The patients showed no significant difference in H.pylori eradication (71% in S. boulardii; 60% in placebo), however epigastric distress and global dyspepsia symptom scores in S. boulardii group were significantly lower than control group (16).

In addition, Yasar et al. in another survey in turkey in 2010, studied the efficacy of probiotics in H.pylori eradication therapy and specified that the addition of probiotic-containing yogurt to the triple therapy did not significantly increase the H. pylori eradication rates, however, they informed that probiotics decreased the frequency of stomatitis and constipation (22).

Our results and these mentioned studies indicate that S. boulardii did not decrease eradication rate of H. pylori where as it is significantly reduce the side effects of the standard triple therapy. On the other hands, Lesbros-Pantoflickova reported that probiotics reduce the risk of developing disorders associated with high degrees of gastric inflammation (23).

Moreover Wilhelm et al. reported probiotics reduce adverse effects and increase tolerability of H. pylori eradication regimens. They may especially be useful in patients with recurrent H. pylori infection and a history of gastrointestinal adverse effects with antibiotics (24). In addition Kotowska signified that S. boulardii effectively reduces the risk of antibiotic-associated diarrhea in children (25).

The most of reviewed studies signified treatment with probiotics is relatively safe (22,23, 26), however it is not risk free and are potentially pathogenic (27) moreover a study described 3 patients with fungaemia after intake of S. Boulardii (28). In contrast to these findings, we did not detect any remarkable adverse effect related to S. Boulardii in group A of our study.

In conclusion, we showed S. boulardii decreased the adverse effects associated triple therapy but did not significantly decrease the eradication rate of H.pylori. We suggest further trials with higher dose of S. boulardii or other types of probiotics in combination with standard therapy which may provide significant results.
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