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Probiotics can prevent drug-induced gastrointestinal symptoms

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Probiotics such as *Bacillus clausii* reduce the occurrence of gastrointestinal side effects of commonly used medications such as antibiotics and proton pump inhibitors in placebo-controlled randomized trials. Their use can make *Helicobacter pylori* eradication schemes more tolerable.

Antibiotics may disturb the physiological microbiome in the gut and can lead to diarrhea. Probiotics can prevent antibiotic-induced diarrhea as summarized by a review from the Cochrane Collaboration [1] and confirmed in recent large-scale studies [2]. However, antibiotics are not the only drug class to cause intestinal dysfunction. As highlighted in a recent systematic review [3], various other drug classes including proton pump inhibitors are associated with a decrease of diversity of the gut microbiome. For instance, proton pump inhibitors are linked to a decrease in Clostridiales and an increase in Actinomycetales, Micrococcaceae and Streptococcaceae, all are changes previously implicated in dysbiosis and increased susceptibility to Clostridioides difficile infection.

Against this background, two placebo-controlled, randomized, double-blind studies have evaluated the effects of the probiotic *Bacillus clausii* strains O/C, N/R, SIN and T against digestive side effects of *Helicobacter pylori* eradication treatment. The first of the two studies randomized 120 patients undergoing triple therapy with rabeprazole 20 mg twice daily, clarithromycin 500 mg twice daily and amoxicillin 1 g twice daily for 7 days to either receive placebo or *B. clausii* suspension thrice daily (total daily dose of 6 billion colony-forming units [CFU]) for 14 days starting on the first day of treatment [4]. Gastrointestinal side effects were recorded for 4 weeks from the start of therapy based on a validated questionnaire. A second study of similar design randomized 130 patients using similar inclusion criteria to receive placebo or *B. clausii* as capsule [5]. The main protocol difference was that the sample size in the second study was based on a power calculation and that it had a defined primary endpoint, i.e., occurrence of diarrhea in the first week.

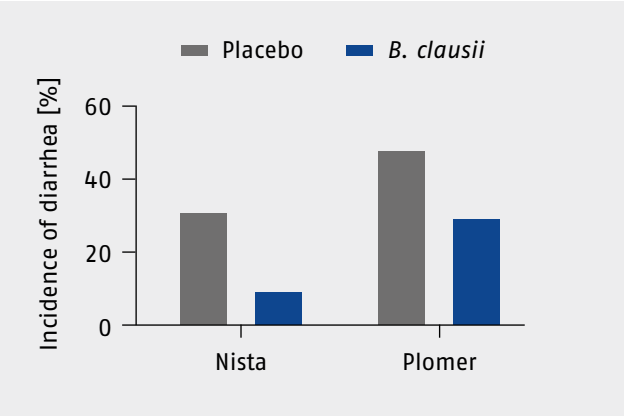

Fig. 1. Incidence of diarrhea in patients undergoing triple therapy for *Helicobacter pylori* eradication in the studies by Nista et al. [4] and Plomer et al. [5]. Corresponding relative risk was 0.301 [95% confidence interval 0.12; 0.76] and 0.61 [0.39; 0.97].

B. clausii reduced the incidence of diarrhea to a clinically meaningful and statistically significant extent in the first week of treatment irrespective of differences in the incidence of diarrhea between the two studies (**Fig. 1**). Despite a lower incidence of diarrhea in the second week, the risk reduction by *B. clausii* was similar. Moreover, when diarrhea occurred in the *B. clausii* group, it was of shorter duration than in the placebo group. Regarding other outcome parameters, the Nista study found a reduction of epigastric pain in both weeks, whereas the Plomer trial made this observation only in the second week. Of note, *H. pylori* eradication rates were similar in the presence of placebo or *B. clausii*. We conclude that treatment with *B. clausii* compared to placebo reduces the incidence of the most common gastrointestinal side-effects related to *H. pylori* eradication triple treatment in symptom-free, *H. pylori*-positive subjects.

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