

**ELABORATION OF OPTIMAL HELICOBACTER PYLORI
ERADICATION REGIMENS IN DUODENAL ULCER PATIENTS. USE
OF NONPHARMACOLOGIC METHODS**

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INTRODUCTION. Helicobacter pylori is the most successful human pathogen infecting an estimated 50% of the global population. It has been recognized as the major etiologic agent of chronic gastritis and peptic ulcers and a risk factor for gastric cancer and its eradication has a therapeutic or prophylactic effect in many clinical situations [1]. Eradication of Helicobacter pylori prevents peptic ulcer recurrence and may decrease the prevalence of gastric cancer in high-risk populations [2]. The triple treatment including proton pump inhibitors-clarithromycin and amoxicillin or metronidazole proposed at the first Maastricht conference to treat Helicobacter pylori infection has become universal since it was recommended by all the consensus conferences held around the world. However, the most recent data show that this combination has lost some efficacy and often allows the cure of only a maximum of 70% of the patients, which is less than the 80% rate aimed for at the beginning and far below what should be expected for an infectious disease. While no new drug has been developed for this indication, a number of studies have been carried out in recent years using different combinations of known antibiotics [1]. Clarithromycin resistance in Helicobacter pylori infection is one of the main causes of failure of eradication therapies and its prevalence varies geographically. Eradication rates with triple therapy for Helicobacter pylori infection have declined to unacceptable levels. Despite according to the Maastricht IV/ Florence Consensus Report proton pump inhibitors-clarithromycin-containing treatments do not need to be adapted to patient factors except for dosing. [1]. Side effects arising from the use of antibiotics reduce patient compliance. This causes the search for alternative eradication of Helicobacter pylori. In such cases, one of the drugs of choice may be the probiotics. Certain probiotics and prebiotics show promising results as an adjuvant treatment in reducing side effects. [1]. Recent studies have found that probiotics have anti-Helicobacter pylori properties [3]. Lactobacilli could exert an inhibitory effect on Helicobacter pylori both in vitro and in vivo models. Lactoferrin has been used to improve Helicobacter pylori treatment. Use of probiotics carried out in two directions: as an adjuvant treatment to triple eradication therapy [3, 4, 5] and in monotherapy [3, 5]. Probiotics had an in vitro inhibitory effect on Helicobacter pylori [3, 5]. The addition of probiotics to

standard antibiotic treatment improved *Helicobacter pylori* eradication rates [4]. All these treatments are most likely to lead to a decrease of adverse events, especially diarrhoea and indirectly may help to improve the eradication rate. It is also found out that mineral water can be widely used in the treatment of duodenal ulcer in monotherapy as well, as an adjuvant therapy to standard triple eradication regimen based on clarithromycin [4].

PURPOSE: To investigate the effects of proton pump inhibitors, probiotics and mineral water in patients with *Helicobacter pylori*-positive duodenal ulcer and to elaborate the optimal *Helicobacter pylori* eradication regimens in such patients.

MATERIAL AND METHODS. In this study 250 *Helicobacter pylori* -positive patients with duodenal ulcer were randomized into five groups, 50 patients in each. *Helicobacter pylori* infection was confirmed by a histological examination of samples obtained from the antrum and corpus of stomach during endoscopy. Intra-gastric and intraduodenal pH-metry, blood analyses also were performed. The following eradication regimens were recommended: Group I: 10-days twice daily oral administration of proton pump inhibitors in standard dose, amoxicillin 1000 mg, clarithromycin 500 mg, then 20-days twice daily proton pump inhibitors; Group II: the same treatment plus once daily oral administration of probiotics, containing 3,025 billion alive lyophilized *Lactobacillus bulgaricus* DDS-14, *Lactobacillus rhamnosus*, *Lactobacillus acidophilus* DDS-1 and *Bifidobacterium bifidum* (probiotics) during one month; Group III: proton pump inhibitors and probiotics once daily and alkaline hydrocarbonate-chloride sodium mineral water Essentuki-4 200 ml trice daily during one month; Group IV: proton pump inhibitors and probiotics once daily and chloride sodium mineral water Minsk-4 200 ml trice daily during one month; Group V: probiotics and proton pump inhibitors once daily during one month. Therapeutic success was confirmed by a negative histological examination, performed in 4-12 weeks after therapy.

FINDINGS. Before the treatment, 82% of patients had pain syndrome and 70% - dyspeptic complaints. In 50% of patients of group I increased, the frequency of dyspeptic complaints and in 42% of them such complaints appeared for the first time. In Group II, dyspeptic complaints disappeared in 74%, and decreased in 20%. Disappearance of dyspeptic complaints was 78%, 76%, and 74% in III, IV and V groups respectively. Decrease of dyspeptic complaints was 20%, 22%, and 24% in III, IV and V groups respectively. The eradication rate were 70%, 82%, 80%, 78% and 68% in I, II, III, IV and V groups, respectively. Healing of duodenal ulcer was noted in 82%, 84%, 86%, 84% and 78% of cases, in I, II, III, IV and V groups, respectively. Intra-gastric and intraduodenal pH was significantly increased in all groups, especially in III. After treatment in group I significantly increased alanine transaminase, asparagines transaminase, alkaline phosphatase, and triglycerides, which must be noted as drug-related side effects of clarithromycin-based triple therapy. In group II such changes did not happen. In III IV and V groups significantly decreased alanine transaminase, asparagines transaminase, blood bilirubin, alkaline phosphatase, cholesterol and triglycerides.

Thus, several aspects of *Helicobacter pylori* eradication have been analyzed, standard clarithromycin-based triple *Helicobacter pylori* eradication therapy causes or increases the frequency of dyspeptic complaints related with antibiotics, has low efficacy and hepatotoxic effect, regimen containing proton pump inhibitors, mineral water and probiotics was superior to triple therapy based on clarithromycin. The combination of proton pump inhibitors, probiotics and alkaline hydrocarbonate-chloride sodium mineral water is more preferable regimen among above mentioned ones.

CONCLUSIONS. Standard clarithromycin-based triple *Helicobacter pylori* eradication therapy is expensive and causes or increases the frequency of dyspeptic complaints related with antibiotics, has low efficacy and hepatotoxic effect. Probiotics could present a low-cost, large-scale alternative solution to prevent or decrease *Helicobacter pylori* colonization. Mineral water have an inhibitory effect on *Helicobacter pylori*. Adding probiotics to standard triple therapy improves compliance and efficacy of *Helicobacter pylori* eradication, however, the treatment becomes more expensive. The combined use of proton pump inhibitors, probiotics and alkaline hydrocarbonate-chloride sodium mineral water is a highly effective and low-cost alternative therapy in patients with *Helicobacter pylori* - associated duodenal ulcer. This regimen may especially be helpful in patients with a history of gastrointestinal adverse effects with antibiotics, comorbid patients with diseases of the hepatobiliary system and the metabolic syndrome.

Reference

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