

Original Article

Addition of cranberry to proton pump inhibitor-based triple therapy for *Helicobacter pylori* eradication

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Received: May 2016
Accepted: June 2016

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ABSTRACT

Objective: Proton pump inhibitor-based triple therapy with two antibiotics for *Helicobacter pylori* eradication is widely accepted, but this combination fails in a considerable number of cases. Some studies have shown that cranberry inhibits the adhesion of a wide range of microbial pathogens, including *H. pylori*. The aim of this study was to assess the effect of cranberry on *H. pylori* eradication with a standard therapy including lansoprazole, clarithromycin, and amoxicillin (LCA) in patients with peptic ulcer disease (PUD).

Methods: In this study, *H. pylori*-positive patients with PUD were randomized into two groups: Group A: A 14-day LCA triple therapy with 30 mg lansoprazole bid, 1000 mg amoxicillin bid, and 500 mg clarithromycin bid; Group B: A 14-day 500 mg cranberry capsules bid plus LCA triple therapy. A ¹³C-urea breath test was performed for eradication assessment 6 weeks after the completion of the treatment.

Findings: Two hundred patients (53.5% males, between 23 and 77 years, mean age ± standard deviation: 50.29 ± 17.79 years) continued treatment protocols and underwent ¹³C-urea breath testing. *H. pylori* eradication was achieved in 74% in Group A (LCA without cranberry) and 89% in Group B (LCA with cranberry) ($P = 0.042$).

Conclusion: The addition of cranberry to LCA triple therapy for *H. pylori* has a higher rate of eradication than the standard regimen alone (up to 89% and significant).

Keywords: Cranberry; eradication therapy; *Helicobacter pylori*

INTRODUCTION

Helicobacter pylori is a Gram-negative, spiral-shaped microorganism that infects approximately half of the world population.^[1] Gastric infection by *H. pylori* is considered to be the most relevant cause of chronic gastritis, peptic ulcer disease (PUD), mucosa-associated lymphoid tissue lymphoma, and gastric cancer.^[2] Selection of the best drug regimens for eradication of *H. pylori* infection is already challenging. Antibiotic resistance due to frequent and

uncontrolled use and the high prevalence of antibiotic side effects are the most common causes for treatment failure. To increase the eradication rates, as defined in the Maastricht IV report,^[3] several clinical trials have been initiated involving extended treatment duration, the use of new antibiotics, or the addition of probiotics or other drugs to therapy.

There is a growing public interest for cranberry, blueberry, and relatively new gooseberry as a functional food because of the potential health benefits

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How to cite this article: Seyyedmajidi M, Ahmadi A, Hajiebrahimi S, Seyedmajidi S, Rajabikashani M, Firoozabadi M, *et al.* Addition of cranberry to proton pump inhibitor-based triple therapy for *Helicobacter pylori* eradication. *J Res Pharm Pract* 2016;5:248-51.

Access this article online



Website: www.jrpp.net

DOI: 10.4103/2279-042X.192462

linked to phytochemical compounds responsible for secondary plant metabolites (flavonols, flavan-3-ols, proanthocyanidins, and phenolic acid derivatives).^[4] Cranberry (*Vaccinium macrocarpon* Ait.) is a member of the *Ericaceae* (the heath family). This fruit was collected from the wild by American Indians and used for a variety of purposes including as a preservative of fish and meat and medicinally as a poultice for dressing wounds.^[5] Cranberry, in particular,^[6,7] helps prevent urinary tract infections,^[8-10] and has some anticancer properties.^[11,12] Some studies have shown that cranberry juice constituents inhibit the adhesion of a wide range of microbial pathogens, including *H. pylori*, *E. coli*, oral bacteria, and influenza virus.^[13] Cranberry proanthocyanidins can be used as an adjunct to increase intestinal secretory immunoglobulin A (sIgA) levels in mice receiving enteral nutrition.^[14] The aim of this study was to compare the effect of cranberry on *H. pylori* eradication with a triple therapy including lansoprazole, clarithromycin, and amoxicillin (LCA) in patients with PUD.

METHODS

A prospective, open-label, randomized clinical trial study was conducted on 200 consecutive *H. pylori*-infected patients with PUD between

June 2014 and September 2015. All of them were referred to our academic hospital in Gorgan (North of Iran). Exclusion criteria were previous *H. pylori* eradication, consumption of aspirin, nonsteroid anti-inflammatory drugs, proton pump inhibitors, warfarin, bismuth preparations, or antibiotics during the last 8 weeks. Patients with renal and hepatic impairment were not enrolled. Gastroscopy was done using a videoscope (Olympus GIF-XQ260, Japan), and two specimens were obtained from the antrum. *H. pylori* infection was diagnosed by histopathological examination. This research was approved by the Ethical Committee of Golestan University of Medical Sciences. Informed consent was obtained from all patients.

Initially, 250 patients were evaluated for inclusion, and finally, 200 patients were studied [Figure 1]. Patients were enrolled into one of the following groups: Group A (control group, $n = 100$): The patients were given a 14-day standard LCA triple therapy for *H. pylori* infection eradication with 30 mg lansoprazole (Lanzo Doctor Abidi Company) bid, 1000 mg amoxicillin bid, and 500 mg clarithromycin bid; Group B (case group, $n = 100$): In this group, the patients were given a 14-day 500 mg cranberry capsules (Liver Company, Canada) bid plus LCA triple therapy. Patients were asked to return at the end of the treatment to assess the compliance with

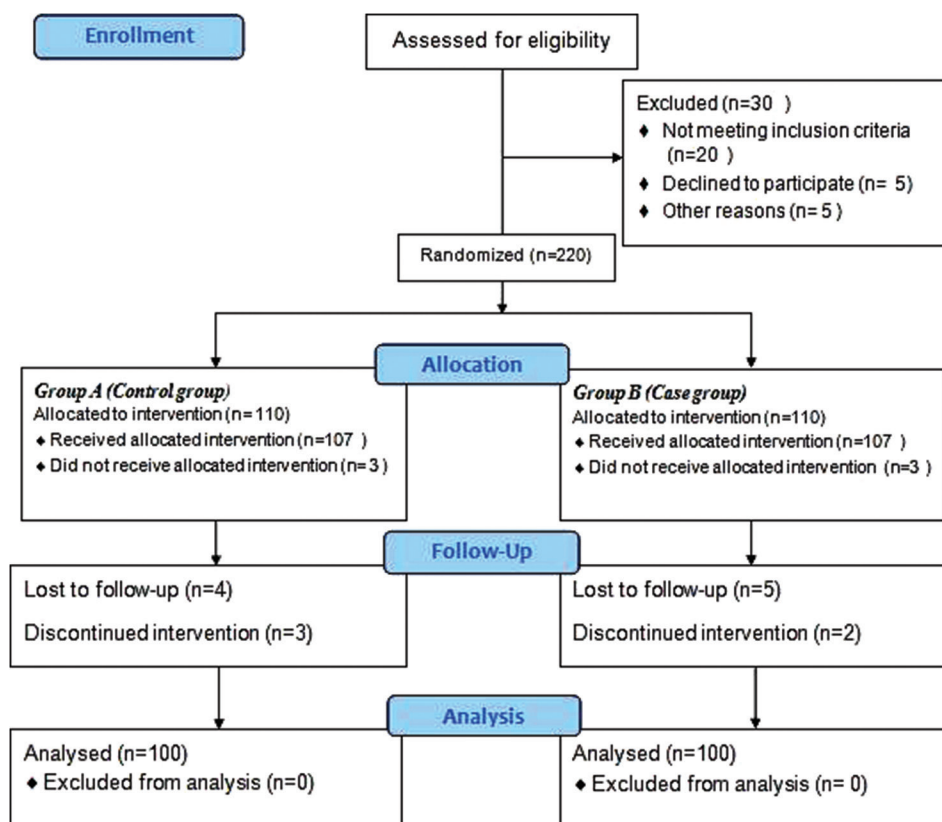


Figure 1: Flow diagram of the study

therapy that was defined as consumption of >80% of the prescribed drugs. A ¹³C-urea breath test was performed for *H. pylori* eradication assessment 6 weeks after the completion of the treatment.

Statistical analysis was performed using Chi-square test, Fisher's exact test, and one-way analysis of variance test. $P \leq 0.05$ was considered statistically significant. All the data were analyzed using SPSS 18 for Windows (SPSS Inc., Chicago, IL, USA) and the values were expressed as the mean \pm standard deviation (SD) for continuous variables and percentages for categorical variables.

RESULTS

Two hundred patients (53.5% males, between 23 and 77 years, mean age \pm SD: 50.29 \pm 17.79 years) continued treatment protocols and underwent ¹³C-urea breath testing. There were no statistically significant differences between the two groups regarding age, gender, and body mass index. *H. pylori* eradication was achieved in 74% patients in Group A (LCA without cranberry) and 89% patients in Group B (LCA with cranberry). The difference was statistically significant ($P = 0.042$) [Table 1]. As shown in this table, there was no significant difference between the study groups in the rate of *H. pylori* eradication on the basis of sex ($P = 0.912$ for standard LCA therapy and $P = 0.785$ for LCA with cranberry).

DISCUSSION

In vitro studies have shown that cranberry juice inhibits the adhesion of microbial pathogens, including *H. pylori*, uropathogenic *E. coli*, oral bacteria, and influenza virus.^[13] Cranberry proanthocyanidins can be used as an adjunct to increase intestinal sIgA levels in mice receiving enteral nutrition.^[14] A clinical

investigation found that consuming a cranberry for 10 weeks resulted in a 5-fold increase in proliferation of T cells, a 30% increase in NK cell proliferation, and a 20% reduction in interleukin 17 secretion, as well as a significant reduction in cold and flu symptoms compared to placebo.^[15] Nantz *et al.* reported that consumption of the cranberry modified the *ex vivo* proliferation of $\gamma\delta$ -T cells. As these cells are located in the epithelium and serve as the first line of defense, improving their function may be related to reducing the number of symptoms associated with infection.^[16]

Some studies showed that cranberry inhibited the adhesion of two-thirds of tested clinical isolates of *H. pylori* including bacteria expressing sialic acid-specific adhesion, and researchers hypothesized that cranberry juice might have the ability to eradicate *H. pylori in vivo*.^[17,18] However, cranberry juice in a mice model of *H. pylori* infection caused a significant clearance of the *H. pylori* mass; however, it had no effect on eradicating the pathogen from the gastric lumen.^[19] In one study, cranberry juice alone accounted for a 15% of the *H. pylori* eradication, compared to 5% for placebo. Although this effect was significant, the rate of eradication was still considerably lower than that of conventional therapy.^[20]

Here, we reported that adding cranberry capsules to the standard regimen for treating *H. pylori* has a higher rate of eradication than the standard regimen alone (up to 89% and significant). Assessment of cranberry extract and probiotics^[21] showed that the combination of the cranberry with a probiotic is the most effective treatment in *H. pylori* in children. Zhang *et al.* used cranberry juice for treatment of *H. pylori* in adults for 90 days and reported that regular consumption of cranberry juice could suppress *H. pylori* infection in endemically afflicted populations.^[20] In another study, adding cranberry juice to the standard treatment improves the rate of *H. pylori* eradication in females;^[13] however, in our study, there was no significant difference between two groups in the rate of *H. pylori* eradication on the basis of sex.

This study indicated a potential beneficial effect of cranberry in increasing the rate of *H. Pylori* eradication; however, the results shown here are only preliminary, and further studies are necessary. Two-week cranberry consumption is an inexpensive and available supplement; however, cranberry is a native North America plant, and in Iran, the only form available is capsules. In most of the studies, juice and dried fruit of cranberry were used and maybe the capsule forms are not as effective as the other forms. Further assessment for defining the best form of cranberry for different clinical situations is necessary.

Table 1: *Helicobacter pylori* eradication rates of study subjects in two groups

<i>H. pylori</i> eradication regimens	<i>H. pylori</i> eradication rate (%)
Group A (only LCA) (n=100)	74 (74)
Male (n=54)	40 (74.1)
Female (n=46)	34 (73.9)
P*	0.912
Group B (cranberry + LCA) (n=100)	89 (89)
Male (n=52)	46 (88.4)
Female (n=48)	43 (89.6)
P*	0.785
P**	0.042

*P value for comparison between males and females in each group,

**P value for comparison between Group A and Group B. Data presented as number (%) of patients. LCA=Lansoprazole, amoxicillin, and clarithromycin, *H. pylori*=*Helicobacter pylori*

AUTHORS' CONTRIBUTION

Mohammadreza Seyyedmajidi: Reviewing of literature, Study design, Data collection, analysis and manuscript preparation Reviewing of literature and manuscript editing. Anahita Ahmadi: Reviewing of literature, Data collection, Shahin Hajiebrahimi: Reviewing of literature, Data collection, Seyedal Seyyedmajidi: Reviewing of literature, Data collection, Majid Rajabikashani: Reviewing of literature, Data collection, Mona Firoozabadi: Reviewing of literature, Data collection, Jamshid Vafaeimanesh: Reviewing of literature, Study design, and manuscript editing.

Acknowledgments

This study was supported by the Golestan Research Center of Gastroenterology and Hepatology. We wish to thank all the researchers who took part in this research project and Doctor Abidi Company members for drugs provision.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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