

Received: 27 May 2013
Revised: 23 Jul 2013
Accepted: 08 Aug 2013

Effect of Proton Pump Inhibitor Based Triple Therapy with Apple Cider Vinegar on Helicobacter Pylori Eradication

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Abstract

Background: The purpose of this study was to evaluate the effect of apple cider vinegar plus PPI-based triple therapy on eradication of Helicobacter Pylori (H.pylori) infection. **Materials and Methods:** 116 patients with H. pylori infection were included in this randomized clinical trial. Patients in control group (n=59) received amoxicillin, clarithromycin, and pantaprazole twice daily. Patients in study group (57 patients) received the same regimen plus 30 mL of apple cider vinegar twice daily. The duration of therapy for study and control were 10 and 14 days respectively. Four weeks after the completion of therapy, Urea breath test was performed to assess the success of H.pylori infection eradication. **Results:** 86% of patients in control group in comparison to 88% in apple cider vinegar group responded to eradication therapy (P=0.41). **Conclusion:** Addition of apple cider vinegar to proton pump inhibitor (PPI)-based triple therapy may decrease the duration of H. pylori treatment but it was not statistically significant. Thus, our results showed no efficacy of apple cider vinegar in H. pylory eradication treatment. [GMJ. 2014;3(2):90-94]

Keywords: Apple Cider Vinager; Helicobacter Pylori; Endoscopy; Proton Pump Inhibitor; Antibacterial Treatment

Introduction

Helicobacter pylori (H. pylori) is a micro-aerophilic Gram-negative, spiral-shaped, motile bacterium that colonizes the gastric mucosa of humans and is estimated to inhabit in at least half of the world's human population [1].

Multiple regimens have been evaluated for H. pylori therapy in randomized controlled trials [2-6]. Despite the number of studies, the op-

timal therapeutic regimen has not yet beendefined.

The regimen most commonly recommended for first line treatment of H. pylori is triple therapy with a proton pump inhibitor, amoxicillin, and clarithromycin for 14 days. However, themulti-drug application is associated with remarkable side effects and sometimes patients do not complete the treatment course. Thus, treatment failure is associated with H. pylori strains that are resistant to the common-

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ly used antibiotics [7]. Crude extracts and isolated compounds from plants used in herbal traditional medicines have been tested for anti-*H. pylori* activity in vitro, in animal models, as well as in clinical studies as possible sources for alternative eradication therapies [8-10]. One study showed the in vitro anti-*H. pylori* activity of some carotenoids of the apple peel extracts [11]. Apple cider vinegar (ACV), which is derived from apple, contains 4% acetic acid, polyphenols, pectin and carotenoids with antibacterial and prebiotic properties [12-14]. As ACV have antimicrobial activity and to our knowledge, there has been no study to assay the anti *H. pylori* activity of ACV; therefore, we conducted a prospective controlled study with the aim of testing whether adding ACV supplement to a ten-day proton pump inhibitor based (PPI-based) triple therapy could have an acceptable influence on *H. pylori* eradication in comparison with the routine two week anti-*H. pylori* regimen.

Materials and Methods

One hundred twenty patients with an indication for endoscopy of dyspeptic symptoms who were admitted to a gastroenterological clinic of Emam Ali university hospital in Ilam from March 2011 to September 2012 were included in this randomized clinical trial study. Patients were matched for sex and randomly divided into two groups. All patients underwent endoscopy and Rapid Urease Test (RUT). RUT positive patients without ulcer were selected for the study. Exclusion criteria were consumption of H₂ antagonists, proton pump inhibitors and antibiotics in four recent weeks. Also, the ones who had gastrointestinal bleeding in recent four weeks were excluded from the study. The study protocol was approved by responsible ethics committee and registered in Iranian registry of clinical trials with code of IRCT2013100614901N1. Furthermore, informed consents were obtained from the participants. Patients were randomised by using a computer-generated list to receive either a standard 14-day triple therapy with 40 mg pantaprazol, 1 g amoxicillin, and 500 mg clarithromycin twice daily in control group or the same drug regimen plus 30 mL of

raw, unfiltered ACV in a glass of water twice daily after meal for 10 days in study group. Red delicious apples were used to produce natural apple cider in laboratory of nutrition department. The duration of the therapy for the study group was ten days (for receiving ACV). The patients were asked to return to assess the compliance with the therapy, and to estimate the incidence of side effects at the end of the treatment. The compliance was defined as the consumption of >90% of the prescribed drugs and ACV by personal interview at the follow-up visit at the end of the therapy. During the four consecutive weeks after discontinuation of the treatment, the patients were free of medication. After this period, urea breath test (UBT) was performed for all the participants. SPSS software 14.0 was used for data analysis. Student t test was used to compare continuous variables in two groups. Categorical data between the groups were compared using the Chi-square test. P-value less than 0.05 was considered as significant.

Results

The mean age of patients was 42.5±3.5 years. One patient in the study group and three patients in control group stopped the treatment due to non-compliance and minor side effects. These side effects in control group were vomiting, loose stool, and headache in the study group. Therefore a total of 59 patients in ACV group and 57 patients in control group completed the study. The duration of therapy in study group was 10 days versus two weeks in control group. Endoscopic results in study group were as 4 patients with ulcer, 20 erythema, 17 erosion and 18 without obvious lesion. These findings in control group were as 4 patients with ulcer, 19 erythema, 18 erosion and 16 without obvious lesion.

The eradication rate of *H. pylori* was 88% in study group and 86% in control group ($P=0.41$) (Table-1). The *H. pylori* eradication rate did not differ between male and female patients (48/55, 87% vs. 53/61, 86%; $p=0.71$). Also eradication rate did not differ between smokers and non-smokers (17/20, 85% vs. 84/96, 87%; $P=0.81$).

Table-1. Characteristics of the Subjects (Mean±SEM)

	Study group (n=59)	Control group (n=57)	P value
Age	43.1±3.4	41.9±3.7	0.9
Sex (%)			
Male	28	27	0.9
Female	31	30	
Smoking	11	9	0.8
Eradication Rate	52.59	49.57	0.4
Days of Therapy	14	10	0.04

Analysis by independent t test

Discussion

In our study we assumed that adding ACV to PPI-based triple therapy might reduce the duration of the antibacterial treatment for the eradication of *H. pylori* infection, though it was not considerable according to statistical analyses. Unfortunately, there are two problems with *H. pylori* treatment; resistance to antibiotics that are commonly used in a number of eradication regimens and compliance with medications. It has been shown that Metronidazole resistance is significantly more common in women and Clarithromycin resistance is significantly associated with the geographic region, older age, and the presence of inactive ulcer disease [15]. The side effects of the medications are reported in up to 50 percent of patients taking the triple therapy regimens [16]. As the duration of anti *H. pylori* therapy is long, the compliance of the patients is weak and they discontinue their treatment. Thus, the treatment failure is associated with the *H. pylori* strains which are resistant to the commonly used antibiotics. Since an initial attempt at eradicating *H. pylori* fails in approximately 20 percent of the patients [17], continuous search for novel therapeutic approaches to cure *H. pylori* is needed. Some new, botanical therapy regimens have been recently proposed [8-11]. Raw, unfiltered ACV is an antibacterial agent and a good source of prebiotics. The anti-bacterial effect of ACV is known

against different pathogens in vitro [12-13]. It has shown that apple has in vitro anti-*H. pylori* activity comparable to metronidazole [11]. ACV is also a good source of prebiotics. In the large intestine and colon, microorganisms degrade pectin and liberate oligofructose and short-chain fatty acids that have prebiotic effects [14]. Prebiotics stimulate the growth and/or the activity of bifidobacteria and lactic acid bacteria in the digestive system. It has been shown that probiotics, which are live nonpathogenic bifidobacteria and lactic acid bacteria that benefit a host through altering gut microflora composition, may reduce the side effects of standard *H. pylori* treatments, especially diarrhea. As a result, they may be useful adjuncts to improve the tolerability and compliance with more traditional antibiotic regimens [18-19]. As some probiotics have antimicrobial effects [20, 21], they have been proposed as treatment for *H. pylori* infection but they should not be considered a substitute for standard antibiotic treatments [22].

ACV also has galacturonic acid which reduces the gastrointestinal tract inflammation in the animal model [23]; thus may reduce the side effects of standard *H. pylori* treatments.

ACV has significant amount of phenolics [24]. As free radicals play an important role in the pathogenesis of gastroduodenal mucosal inflammation, peptic ulcer disease and probably even gastric cancer, various micronutrients with antioxidant compounds are considered to protect the gastric mucosa by scavenging the free radicals [25].

On the other hand proton pump inhibitor agents which are used in PPI-based triple therapy act by selectively oxidizing thiol targets in the gastric proton pump, but they also appear to be toxic to the gastric mucosa. It has been shown that antioxidant therapy prevents this toxic effect [26]. Thus the presence of significant amount of phenolics in ACV may have preventive effects on the oxidative damage of PPI agents [27].

Conclusions

Addition of raw, unfiltered ACV to *H. pylori* treatment regimen of amoxicillin, clarithromycin and pantaprazole may decrease dura-

tion of *H. pylori* treatment, better compliance in patients and therefore might decrease bacterial resistance to antibiotics. Although our results showed no significant difference in *H. pylori* eradication by adding ACV to the regimen, but the same results was seen in the ACV group by a 10 days trial compared to the control group by a two weeks treatment. Given the small sample size in this trial, larger

studies are needed to confirm these benefits.

Acknowledgments

We convey our gratitude to the Ilam University of Medical Sciences, Ilam, Iran. Funding of this study was provided by the Ilam University of Medical Sciences. There are no conflicts of interest. IRCT ID: IRCT2013100614901N1

References

1. Kusters JG, van Vliet AH, Kuipers EJ. Pathogenesis of *Helicobacter pylori* infection. *Clin Microbiol Rev.* 2006;19(3):449-90.
2. Qasim A, Sebastian S, Thornton O, Dobson M, McLoughlin R, Buckley M, et al. Rifabutin and furazolidone based *Helicobacter pylori* eradication therapies after failure of standard first and second line eradication attempts in dyspepsia patients. *Aliment Pharmacol Ther.* 2005;21(1):91-6.
3. Gatta L, Zullo A, PERNA F, Ricci C, De Francesco V, Tampieri A, et al. A 10 day levofloxacin based triple therapy in patients who have failed two eradication courses. *Aliment Pharmacol Ther.* 2005;22(1):45-9.
4. Gisbert JP, Gonzalez L, Calvet X. Systematic Review and Meta analysis: Proton Pump Inhibitor vs. Ranitidine Bismuth Citrate Plus Two Antibiotics in *Helicobacter pylori* Eradication. *Helicobacter.* 2005;10(3):157-71.
5. Fischbach L, Zanten S, Dickason J. Meta analysis: the efficacy, adverse events, and adherence related to first line anti-*Helicobacter pylori* quadruple therapies. *Aliment Pharmacol Ther.* 2004;20(10):1071-82.
6. Graham D, Hammoud F, El Zimaity H, Kim J, Osato M, El Serag H. Meta analysis: proton pump inhibitor or H2-receptor antagonist for *Helicobacter pylori* eradication. *Aliment Pharmacol Ther s.* 2003;17(10):1229-36.
7. Vakil N. Primary and secondary treatment for *Helicobacter pylori* in the United States. *Rev Gastroenterol Disord.* 2005;5(2):67-72.
8. Wittschier N, Faller G, Hensel A. Aqueous extracts and polysaccharides from Liquorice roots (*Glycyrrhiza glabra* L.) inhibit adhesion of *Helicobacter pylori* to human gastric mucosa. *J Ethnopharmacol.* 2009;125(2):218-23.
9. Ki M-R, Ghim S-Y, Hong I-H, Park J-K, Hong K-S, Ji A-R, et al. In vitro inhibition of *Helicobacter pylori* growth and of adherence of cagA-positive strains to gastric epithelial cells by *Lactobacillus paraplantarum* KNUC25 isolated from kimchi. *J Med Food.* 2010;13(3):629-34.
10. Bekar O, Yilmaz Y, Gulden M. Kefir improves the efficacy and tolerability of triple therapy in eradicating *Helicobacter pylori*. *J Med Food.* 2011;14(4):344-7.
11. Molnár P, Deli J, Tanaka T, Kann Y, Tani S, Gyémánt N, et al. Carotenoids with anti-*Helicobacter pylori* activity from Golden delicious apple. *Phytother Res.* 2010;24(5):644-8.
12. Dornelles-Morgental R, Guerreiro-Tanomaru JM, de Faria-Júnior NB, Hungaro-Duarte MA, Kuga MC, Tanomaru-Filho M. Antibacterial efficacy of endodontic irrigating solutions and their combinations in root canals contaminated with *Enterococcus faecalis*. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2011;112(3):396-400.
13. Lu HJ, Breidt J, Perez-Diaz IM, Osborne JA. Antimicrobial effects of weak acids on the survival of *Escherichia coli* O157: H7 under anaerobic conditions. *J Food Prot.*

- 2011;74(6):893-8.
14. Podbeltsev D, Nikitiuk D, Pozdniakov A. Influence of prebiotics on morphologic structure of the mucouse membrane of intestinum crassum of rats. *Vopr Pitan.* 2006;75(2):26-9.
 15. Osato MS, Reddy R, Reddy SG, Penland RL, Malaty HM, Graham DY. Pattern of primary resistance of *Helicobacter pylori* to metronidazole or clarithromycin in the United States. *Arch Intern Med.* 2001;161(9):1217-20.
 16. de Boer WA, Tytgat GN. The best therapy for *Helicobacter pylori* infection: should efficacy or side-effect profile determine our choice? *Scand J Gastroenterol.* 1995;30(5):401-7.
 17. Vakil N. *Helicobacter pylori*: factors affecting eradication and recurrence. *Am J Gastroenterol.* 2005;100(11):2393-4.
 18. Cindoruk M, Erkan G, Karakan T, Dursun A, Unal S. Efficacy and Safety of *Saccharomyces boulardii* in the 14-day Triple Anti-*Helicobacter pylori* Therapy: A Prospective Randomized Placebo-Controlled Double-Blind Study. *Helicobacter.* 2007;12(4):309-16.
 19. Song MJ, Park DI, Park JH, Kim HJ, Cho YK, Sohn CI, et al. The Effect of Probiotics and Mucoprotective Agents on PPI-Based Triple Therapy for Eradication of *Helicobacter pylori*. *Helicobacter.* 2010;15(3):206-13.
 20. Lesbros-Pantoflickova D, Corthesy-Theulaz I, Blum AL. *Helicobacter pylori* and probiotics. *J Nutr.* 2007;137(3 Suppl 2):812S-8S.
 21. Kaur IP, Kuhad A, Garg A, Chopra K. Probiotics: delineation of prophylactic and therapeutic benefits. *J Med Food.* 2009;12(2):219-35.
 22. Franceschi F, Cazzato A, Nista EC, Scarpellini E, Roccarina D, Gigante G, et al. Role of probiotics in patients with *Helicobacter pylori* infection. *Helicobacter.* 2007;12 Suppl 2:59-63.
 23. Wakuda T, Azuma K, Saimoto H, Ifuku S, Morimoto M, Arifuku I, et al. Protective effects of galacturonic acid-rich vinegar brewed from Japanese pear in a dextran sodium sulfate-induced acute colitis model. *J Funct Foods.* 2012.
 24. Budak NH, Kumbul Doguc D, Savas CM, Seydim AC, Kok Tas T, Ciris MI, et al. Effects of apple cider vinegars produced with different techniques on blood lipids in high-cholesterol-fed rats. *J Agric Food Chem.* 2011;59(12):6638-44.
 25. Correa P, Fontham ET, Bravo JC, Bravo LE, Ruiz B, Zarama G, et al. Chemoprevention of gastric dysplasia: randomized trial of antioxidant supplements and anti-*Helicobacter pylori* therapy. *J Natl Cancer Inst.* 2000;92(23):1881-8.
 26. Kohler JE, Blass AL, Liu J, Tai K, Soybel DI. Antioxidant pre-treatment prevents omeprazole-induced toxicity in an in vitro model of infectious gastritis. *Free Radic Biol Med.* 2010;49(5):786-91.
 27. Budak HN, Guzel-Seydim ZB. Antioxidant activity and phenolic content of wine vinegars produced by two different techniques. *J Sci Food Agric.* 2010;90(12):2021-6.