

## Effect of addition of vitamin C to clarithromycin-amoxicillin-omeprazol triple regimen on *Helicobacter pylori* eradication

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### Abstract

**Background :** The use of vitamin C as a supplement with the common regimen for eradication of *Helicobacter pylori* infection is the subject of ongoing controversy. We conducted a prospective controlled study with the aim of testing whether the vitamin C supplement to the therapy includes lower dosage of clarithromycin could have an acceptable influence on *Helicobacter pylori* eradication in comparison with routine anti-*Helicobacter pylori* regimen.

**Materials and methods :** Two hundred and fourteen consecutive patients with the verification of *Helicobacter pylori* infection via positive Rapid Urease Test (RUT) and histology results were included and divided into two therapy groups : 1) a group without vitamin C (n = 100) that were administered 20 mg omeprazol, 1 g amoxicillin, and 500 mg clarithromycin twice daily for 2 weeks and 2) a triple-plus-vitamin C group (n = 114) that was administered 20 mg omeprazol, 1 g amoxicillin, 250 mg clarithromycin plus 250 mg vitamin C twice daily for 2 weeks. Four weeks after the completion of therapy, each patient was scheduled for urea breath test to assess the success of *Helicobacter pylori* eradication.

**Results :** Similar eradication of *Helicobacter pylori* was found between the triple-only group with 500 mg of clarithromycin and the triple with 250 mg of clarithromycin-plus vitamin C group (89% versus 86.8%, P = 0.623).

**Conclusions :** Adding vitamin C might reduce the needed dosage of clarithromycin for eradication of *Helicobacter pylori*. (*Acta gastroenterol. belg.*, 2009, 72, 222-224).

**Key words :** *helicobacter pylori*, vitamin C, clarithromycin, Rapid Urease Test.

### Introduction

Selection of the best treatment regimen with minimized post-treatment complications for eradication of *Helicobacter pylori* infection is quite challenging. The use of vitamin C as a supplement with the common regimen for this aim is the subject of ongoing controversy. Some previous studies stressed the role of vitamin C against infection with *Helicobacter pylori* and its effect on gastric mucosa, probably due the attenuation of oxidative stress and proinflammatory cytokines (1, 2), whereas, according to the results of some others, adding vitamin C to drug therapy could not improve the *Helicobacter pylori* eradication rate and gastric inflammation (3-5). Besides, some studies found that adding vitamin C to therapy not only could not improve the *Helicobacter pylori* eradication rate and gastric inflammation, but adding this vitamin might even reduce the eradication rate of therapy (3).

Moreover, the effect of vitamin C as a component of drug regimen on dosages of other drugs of regimen has not been exactly clear. It seems that the adding vitamin C to anti-*Helicobacter pylori* treatment can reduce the dosage of other drugs such as clarithromycin. However, a few studies could confirm this effect of vitamin C (6).

We conducted this prospective controlled study with the aim of testing whether vitamin C supplement to the therapy including clarithromycin could improve the eradication rate of *Helicobacter pylori*-infected patients, and whether vitamin C supplement allows to lower the dose of clarithromycin.

### Materials and methods

A prospective and double-blinded study was conducted on 229 consecutive patients more than 18 years old with the verification of *Helicobacter pylori* infection via Rapid Urease Test (RUT) and histology results (3). All patients with history of previous treatments of *Helicobacter pylori*, upper gastrointestinal surgery, gastric malignancy, or liver or renal function impairment, were excluded. Also, those who had received a proton pump inhibitor (PPI), bismuth, antibiotics or probiotics within 4 weeks prior to the pretreatment endoscopy were excluded as were pregnant women. Patients who agreed to participate met with the researcher that explained the purpose of the study and obtained informed consent. The study was approved by the Ethical Committee of the Shaheed Beheshti University of Medical Sciences.

Among all enrolled patients, 214 patients completed the research protocol. They were randomly divided into two therapy groups : 1) a group without vitamin C (n = 100) that were administered 20 mg omeprazol, 1 g amoxicillin, and 500 mg clarithromycin twice daily for 2 weeks and 2) a triple-plus-vitamin C group (n = 114) that was administered 20 mg omeprazol, 1 g amoxicillin, 250 mg clarithromycin plus 250 mg vitamin C twice daily for 2 weeks. Four weeks after the completion of

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Submission date : 19/05/2008

Acceptance date : 19/03/2009

Table 1. — Sex and age distribution in the two studied groups

Item	Vitamin C group (n = 114)	Control group (n = 100)	P value
Male gender	43.8	56.0	0.075
Age (year)	47.0 ± 10.5	45.25 ± 8.9	0.193

Data are presented as mean ± SD or percentages.

triple therapy, each patient was scheduled for urea breath test (UBT) to assess the success of *Helicobacter pylori* eradication (7).

Results were reported as mean ± standard deviation (SD) for quantitative variables and percentages for categorical variables. The groups were compared using the Student's *t*-test for continuous variables and chi-square test (or Fisher's exact test if required) for categorical variables. P values of 0.05 or less were considered statistically significant. All statistical analyses were performed using SPSS version 13 (SPSS Inc., Chicago, IL, USA).

## Results

The mean age of all studied patients was 46.6 ± 13.2 years and female to male ratio was 1.28. There were no statistically significant differences in sex ratio and mean age between the two studied groups (Table 1). Using UBT test, similar eradication rate of *Helicobacter pylori* was found between the triple-only group and the triple-plus-vitamin C group (89% versus 86.8%,  $P = 0.623$ ). No relationships were found between the gender and the results of UBT test in the triple-only group ( $P = 0.918$ ) and vitamin C group ( $P = 0.859$ ).

## Discussion

*Helicobacter pylori* infection is one of the most common bacterial infections in the world. It has been shown that the recurrence of *Helicobacter pylori* infection after eradication is rare in developed countries and more frequent in developing countries so that the calculated annual recurrence rates were 2.67% in developed countries and 13.00% in developing countries (8, 9). Therefore, various treatment protocols of this infection may be accompanied by different responses in different populations.

*Helicobacter pylori* eradication rate with standard triple therapy with amoxicillin, clarithromycin and omeprazole has been reported 80% (10). In recent studies, the impact of antioxidant vitamins such as vitamin C as a supplement therapeutic agent on the treatment of *Helicobacter pylori* infection has been highlighted. These studies showed that the vitamin C concentration in gastric juice is inversely related to the severity of gastritis and the presence of *Helicobacter pylori* infection (11). Moreover, it has been shown that the feeding of this vitamin could reduce gastric inflammation (12). In

vivo and in vitro studies could demonstrate that the protective role of this vitamin can be related to the excessive oxygen derived free radicals (13), inhibition the colonization of *Helicobacter pylori* via its bactericidal activity (14), and the inhibition of the accumulation of lipid peroxides, the resultant product of lipid peroxidation leading to cellular destruction, chromosomal aberration, and finally gastric cancer (15). However, in some other studies, the protective role of vitamin C was not proved. In a study by You *et al.*, it was found that vitamin C intake could not influence *Helicobacter pylori* growth in physiological condition (16). Furthermore, Lee *et al.* using animal models showed that high vitamin C supplement did not reduce *Helicobacter pylori* gastritis and indicated that vitamin C as a supplement could not protect L-gulonon-c-lactone oxidase-deficient mice from *Helicobacter pylori*-induced gastritis and gastric premalignancy (17). We found no difference in *Helicobacter pylori* eradication rate between the group treated with lower dose of clarithromycin and vitamin C and another group treated with routine dose of clarithromycin and without vitamin C. We believe that no detected significance can be related to the compensatory role of vitamin C as a supplement in the regimen including lower dose of clarithromycin. It seems that vitamin C can reduce the need for higher dosage of this antibiotic for *Helicobacter pylori* eradication. Another explanation for the equivalent results between the two groups may be a low rate of clarithromycin resistance in Iran. Furthermore, according to the present results and findings of the previous studies (18, 19) we also believe that some factors such as the concentration of vitamin C in anti-*Helicobacter pylori* regimens, measurement of vitamin consumed, and even the doses of administered drugs in these regimens could influence the response rate of *Helicobacter pylori* infection to the regimens with this vitamin. Sun *et al.* found no effect of antioxidant vitamin supplements on *Helicobacter pylori* colonization (20) that was not consistent with previous studies which showed that oral vitamin C supplements inhibited colonization with *Helicobacter pylori* in animal (14, 21) and human (22) models. One explanation could be that these studies used a higher vitamin C dosage. Therefore, it seems that further studies focused on the effects of some factors such as the measurement of administered vitamin C, the duration of vitamin C consumption, and its serum and gastric juice concentrations are needed to assess the impact of vitamin C as a supplement on *Helicobacter pylori* eradication. Also, we suggest further double blind

randomized studies with or without vitamin C and a low dose clarithromycin with another design (same dose of clarithromycin in the two groups) to address the exact role of low dose of clarithromycin and vitamin C in *Helicobacter pylori* eradication.

## Conclusion

Finally, we conclude that the detectable similar results between the patients who receive anti-*Helicobacter pylori* triple therapy with lower dose of clarithromycin and vitamin C and the patients were administered triple therapy with routine dose of this antibiotic and without vitamin C can be related to the compensatory role of this vitamin as a supplement. However, the effects of the dosage and duration of vitamin C administration should be considered in anti-*Helicobacter pylori* drug regimens.

## Acknowledgements

The authors would like to thank the Farzan Institute for Research and Technology for its technical assistance.

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