# Vitamin C does not improve the efficacy of *Helicobacter pylori* eradication in smokers

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## ABSTRACT

**Purpose**: To evaluate the hypothesis that vitamin C improves the efficacy of *Helicobacter pylori* eradication in smokers when combined with pantoprazole, amoxicillin, and clarithromycin.
**Materials and methods**: The study completed 90 subjects of 98 enrolled, 58 smokers 32 non-smokers. *Helicobacter pylori* status was determined by two methods, CLO test, and histology. Vitamin C (500 mg) was administered three times daily. The patients were considered as cured of *H. pylori* if the CLO test result and histology were negative 4 weeks after completion of eradication therapy.
**Results**: Smokers had lower effectiveness of eradication therapy than non-smokers and the administration of vitamin C had not affected the outcome of eradication therapy.
**Conclusions**: Vitamin C (500 mg tid) does not improve the eradication therapy when pantoprazole, amoxicillin, and clarithromycin were used.
**Keywords**: *Helicobacter pylori*, treatment, vitamin C

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## INTRODUCTION

The discovery of bacterium *Helicobacter pylori* and document its relationship with the occurrence of peptic ulcers caused that antimicrobial therapy has become a treatment of choice for ulcer disease. At the moment in use are several sets of drugs; a classical one includes the most potent inhibitor of gastric acid secretion and at least two antibacterial agents. There have been ongoing attempts to introduce new drugs for *H. pylori* eradication, because the effectiveness of old ones from year to year systematically decreases [1-5].

Bacterial drug-resistance is not the only factor determining the efficacy of the eradication therapy. This is also influenced by a number of additional factors including smoking habit. The effect of smoking on the outcome of *H. pylori* eradication is particularly apparent when omeprazole, amoxicillin, and clarithromycin are used; the efficacy of antimicrobial treatment with these drugs was significantly lower in smokers than non-smokers [6,7].

It was proposed that the difference may be at least in part due to concentration of vitamin C in gastric juice; it is lower in smokers than non-smokers [8,9].

Interestingly vitamin C was found to increase the antibacterial effect of amoxicillin [10] and also to inhibit urease activity of *H. pylori* [11]. Additionally, vitamin C release into the gastric juice was significantly lower in patients with *H. pylori* stomach infection, and *H. pylori* eradication restores the concentration of vitamin C in gastric juice to a normal level [12].

Since the proton pump inhibitors significantly reduce the release of vitamin C into the gastric juice [13], by including the vitamin C in the therapy for treating *H. pylori* infection one can expect its profitable effect. Another argument for the use of vitamin C is the finding that 30% of *H. pylori* infected subjects might be eradicated by administration of vitamin C at a daily dose of 5 g, used alone for 4 weeks [12].

The aim of the study was to evaluate whether the administration of vitamin C with pantoprazole, amoxicillin, and clarithromycin increases the efficiency of *H. pylori* eradication in the stomach in the smokers group.

## MATERIALS AND METHODS

The study was conducted in 98 patients of both sexes, aged 20-72 years, diagnosed with peptic ulcer disease and gastritis; among them were smokers and non-smokers (Table 1).

**Table 1.** The characteristics of patients who completed the study

| | PAC+vitC (n= 46) | PAC (n =44) |
|---|---|---|
| Age – years (mean, range) | 46.2 (20-71) | 47.9 (22-70) |
| Gender (M/F) | 32/14 | 30/14 |
| Smokers | 27/46 | 31/44 |
| Diagnosis | | |
| Gastritis | 17 | 10 |
| Gastric ulcer | 25 | 28 |
| Duodenal ulcer | 4 | 6 |

Information on smoking was derived from the questionnaire, which was filled out by each patient before the study begun. We included patients as smokers if they smoked 5 or more cigarettes daily. Patients with diseases requiring permanent use of medication, pregnant or nursing women were not eligible for the study. For inclusion in the study was to document infection of the stomach with *H. pylori* by two methods *Campylobacter* like organism test (CLO test) and histological examination of endoscopic mucosal specimens, good general condition of the candidates, and lack of their allergic reactions to the drugs planned for eradication therapy. Gastroscopic examinations were performed by an experienced endoscopist. During the gastroscopy the mucosal specimens were taken from the prepyloric and corpus regions, one from each location to the CLO test, two for histological examination. The CLO test was prepared in the Department of Physiology Medical University of Białystok basing on the method of Marshall et al. [14]. The sensitivity and specificity of the test as compared to the histological examination, the antigen stool test, and culture were 78.1% and 80.2%, 84.0% and 88.0% and 81.0% and 88.0%, respectively [15]. The CLO test was accepted as positive, if within 24 hours its color changed from orange to pink. The mucosal

specimens for microscopic evaluation were placed in buffered formalin, and subjected to standard workup and staining with hematoxylin-eosin and Giemsa reagent. The patients eligible for treatment had at baseline positive results of both tests for *H. pylori*. Control gastroscopy with mucosal biopsies was performed 4 weeks after completion of eradication therapy. The patient was considered as cured of *H. pylori* infection, if the result of CLO test and histology was negative (Table 2).

**Table 2.** The results of CLO test and histology after performed therapy

| | PAC+vitC (n=46) | PAC (n=44) |
|---|---|---|
| CLO(-)/Hist(-) | 32 | 33 |
| CLO(+)/Hist(-) | 1 | 1 |
| CLO(-)/Hist(+) | 3 | 1 |
| CLO(+)/Hist(+) | 10 | 9 |

To complete antibacterial treatment one of the following regimens was used: 1 / pantoprazole (Controloc) 40 mg bid, amoxicillin (Ospamox) 1000 mg bid, clarithromycin (Klacid) 500 mg bid (PAC), 2 / pantoprazole (Controloc) 40 mg bid, amoxicillin (Ospamox) 1000 mg bid, clarithromycin (Klacid) 500 mg bid, vitamin C 500 mg tid (effervescent tablets)(PAC + vit C).

The treatment lasted seven days; three drugs were taken half an hour before a meal, vitamin C after a meal. The evaluation of microscopic preparations for the presence of *H. pylori* infection in the stomach has conducted by two pathologists.

For statistical analysis $\chi^2$ test was used. STATISTICA 7.1. was used for statistical analysis. Differences were considered significant if $p<0.05$.

## RESULTS

Of the 98 patients enrolled, the study completed 90 of them; the study has not been completed by 3 patients taking vitamin C and 5 patients from the control group. The efficacy of eradication therapy in patients receiving vitamin C compared to patients treated traditionally did not differ significantly (69.6% vs 75.0%) (PP analysis) (Table 3). The separate analysis which was performed for smokers and non-smokers revealed that vitamin C did not affect significantly the effectiveness of eradication therapy (Table 3). Due to the convergence of results for the group receiving and not receiving vitamin C a common analysis for these two groups was performed. It revealed that smokers had lower effectiveness of eradication therapy than non-smokers (63.8% vs. 87.5%, $p<0.02$) (Table 3).

**Table 3**. The smoking habit and effectiveness of eraditacion therapy

| | Smokers | Non-smokers | Total |
|---|---|---|---|
| PAC+ Vit.C | 16/27 (59.3%) | 16/19 (84.2%) | 32/46 (69.6%) |
| PAC | 21/31 (67.7%) | 12/13 (92.3%) | 33/44 (75.0%) |
| Total | 37/58 (63.8%) | 28/32 (87.5%)* | |

*P<0.02 vs smokers

## DISCUSSION

In the past, attempts were made to assess the effect of vitamin C on the efficacy of *H. pylori* eradication; increase the effectiveness of treatment was only observed when omeprazole, amoxicillin, and clarithromycin were used [16]. No such effect was observed when lanzoprazole, amoxicillin, and metronidazole were tested [17]. As the previous studies using various eradication regimens have shown better result of *H. pylori* eradication therapy in non-smokers than smokers [6,7], in the present study the effect of vitamin C supplementation was analyzed separately and jointly in these two groups. We did not confirm the hypothesis indicating the vitamin C beneficial effect on *H. pylori* eradication in the smokers group when pantoprazole, amoxicillin and clarithromycin is used.

*In vitro*, vitamin C inhibited the growth of *H. pylori* only under microaerophilic conditions [18]. As the concentration of vitamin C used in the aforementioned experiment was very high, it is uncertain whether many times lower concentrations of vitamin C in gastric juice obtained after oral supplementation exert a similar effect. In addition, supplementation of vitamin C in a dose of 500 mg bid *per os* increases the concentration of vitamin C in the gastric juice, particularly in those without inflammatory changes in the gastric mucosa [19]; in

patients infected with *H. pylori*, inflammatory changes are observed in all cases [20].

Chuang et al. [16] found a positive effect of vitamin C on the efficacy of *H. pylori* antibacterial therapy when omeprazole, amoxicillin, and clarithromycin 250 mg bid were used; this set of drugs is not currently recommended because of its low efficiency. More popular at the moment is the eradication regimen consisting of omeprazole, amoxicillin, and clarithromycin 500 mg bid. However, Chuang et al. did not test this regimen with vitamin C supplementation [16]. In our study we used higher doses of clarithromycin (500 mg bid) and vitamin C (500 mg tid) than Chuang et al. did, but we did not repeat his results. According to Chuang observation, the positive effect of vitamin C in *H. pylori* eradication was more evident for bacteria sensitive to clarithromycin [16]. Current results of much lower effectiveness of eradication therapy than in the study of Chuang et al. and also than in our previous studies may be a consequence of the increase of *H. pylori* resistance to clarithromycin [21,22].

## CONCLUSIONS

We did not find a beneficial effect of vitamin C (500 mg tid) administration to increase *H. pylori* eradication from the stomach in the smokers group, when pantoprazole, amoxicillin, and clarithromycin were used.

### Conflicts of interest

None declared.

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