

## Evaluation of the benefit of addition of clidinium C to a *Helicobacter pylori* eradication regimen

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### ABSTRACT

**Aim:** This study aimed to evaluate the success of *H.pylori* eradication therapy in patients with dyspepsia by therapeutics regimes with and without clidinium C.

**Background:** *Helicobacter pylori* infections are reported in all parts of the world. Appropriate antibiotic therapy can treat infection. The ideal treatment regimen has not been specified.

**Patients and methods:** In a randomized, double blind clinical trials study, 250 patients with dyspepsia were enrolled. All patients were treated by Omeprazole, Metronidazole, Amoxicillin and Bismuth (OMAB) for two weeks. One tablet clidinium C before each meal was added to this regimen in the intervention group (A). Urea Breath Test (UBT) was carried out after 8-12 weeks after treatment for evaluation of *H.pylori* eradication.

**Results:** 132 patients in the intervention group (A) and 118 patients in the control group (B) were enrolled to the study. The rate of eradication in group A was significantly higher than group B (62.1% vs. 50%, p=0.04).

**Conclusion:** The results supported the effect of clidinium C for increasing of *helicobacter pylori* eradication, but further studies need to be performed.

**Keywords:** *Helicobacter pylori*, Eradication rate, Quadruple therapy, Clidinium C.

(Please cite as: Chorami M, Zojaji H, Naderi N, Moghimi-Dehkordi B, Mirsattari D, Mohaghegh Shalmani H. Evaluation of the benefit of addition of clidinium C to a *Helicobacter pylori* eradication regimen. Gastroenterol Hepatol Bed Bench 2013;6(3):141-145).

### Introduction

Although there is some evidence on declining the prevalence of *Helicobacter pylori* (*H.pylori*) in developed countries, the infection remains common throughout the world (1).

*H.pylori* is related with common gastrointestinal diseases such as non-ulcer dyspepsia, peptic ulcer and gastric malignancies

(2, 3). *H. pylori* infection persists throughout life. Antibiotic therapy is needed for eradication (4, 5).

Due to the nature of *H.pylori* colonization and resistance, current antibiotic therapy is not ideal. In recent years, different combinations of antibiotics combined with a proton pump inhibitor (PPI) have been standard treatment regimens for *H. Pylori* eradication therapy. In approximately 10-20% of patients, *H. pylori* eradication is not successful and the bacterial infection persists (6). Using standard triple therapy that includes a PPI along with clarithromycin and amoxicillin and/or

Received: 15 January 2013 Accepted: 18 May 2013

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metronidazole (7, 8), treatment rates started from more than 90% and then reduced to 70-80% (9) and in a recent study the eradication rate of triple regimen was about 55% (10).

If *H.pylori* eradication with the triple therapy fails, a quadruple therapy using bismuth, metronidazole, and, tetracycline, together with a PPI is advised (11). Resistance to antibiotics, especially clarithromycin, is an important reason for the loss of eradication therapy (12, 13).

Over the past few years, some studies have investigated the effect of adding a further therapy, such as a supplement of vitamin C, vitamin E, and cobalamin to the therapeutic regimen. Some of these studies have shown that these supplements can improve the efficacy of *H.pylori* eradication regimens, but others have not reported any beneficial effects (14-19).

Duration of penetration is one of the most important factors that can increase the effect of antibiotic efficacy in the treatment of *H.pylori*. A pharmaceutical agent that can increase the duration of antibiotic penetrance may be useful for the successful eradication of infection (20). In this study we investigated the effect of adjunct therapy with clidinium C on the eradication of *H. pylori*. clidinium, in combination with other drugs, has been shown to have an antispasmodic and an anxiolytic effect. It also helps in the treatment of peptic ulcer disease and irritable bowel syndrome (21). We think that reducing gastric acidity and motility due to consumption of clidinium C can increase the efficacy and penetration of amoxicillin to the gastric superficial mucosa and so improve the efficacy of quadruple therapy for eradication of infection.

To our knowledge, no study has been conducted on this issue. Thus, we aimed to investigate the effect of adding one tablet clidinium C to the standard quadruple therapy for the eradication of *H.pylori*.

## Patients and Methods

This study was designed as a double blind randomized clinical trial on 250 consecutive patients who had referred to Taleghani Hospital in Tehran with an indication for endoscopy of dyspeptic or other gastrointestinal symptoms. Patients with angle closure glaucoma, toxic megacolon, ulcerative colitis, intestinal obstruction, pyloric and duodenal stenosis, obstructive uropathy, benign prostatic hyperplasia (BPH) and intestinal atony were excluded from the study. The study protocol was approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences and written informed consent was obtained from all participants before enrolment. A specialist physician who was blinded about the study groups performed endoscopy for all patients and biopsy was obtained. All patients with a positive pathology result were randomly assigned into two groups. Both groups (A and B) were given the quadruple regimen for eradication of *H.pylori*, consisting of omeprazole 20mg b.i.d, metronidazole 500mg b.i.d., amoxicillin 500 mg bid and bismuth 240mg b.i.d. (OMAB) for 2 weeks. In the intervention group, (group A) one clidinium C (Sobhan Darou, Rasht, Iran.) tablet q.i.d for 2 weeks was added to the *H.pylori* eradication regimen. Patient's compliance was evaluated with regular follow-ups.

The measurement of outcome was based on urea breath test (UBT) and all patients underwent UBT 8 to 12 weeks (regarding to gastric of duodenal involvement) after the end of *H.pylori* treatment. The negative results of UBT test were considered as successful treatment.

For statistical analysis, Chi-square test was used to compare the eradication rates between group A and B.  $P < 0.05$  was considered statistically significant.

**Table 1.** Endoscopic findings in patients under study

Endoscopic findings	Treatments groups		Total
	A	B	
Gastroduodenitis	88(66.7%)	71(60.2%)	159(63.6%)
Gastric ulcer	5(3.8%)	4(3.4%)	9(3.6%)
Duodenal ulcer	1(0.8%)	5(4.2%)	6(2.4%)
Gastroduodenal ulcer	3(2.3%)	2(1.7%)	5(2.0%)
Gastroduodenitis and gastric ulcer	15(11.4%)	13(11.0%)	28(11.2%)
Gastroduodenitis and duodenal ulcer	7(5.3%)	15(12.7%)	22(8.8%)
Unknown	13(9.8%)	8(6.8%)	21(8.4%)
Total	132(100%)	118(100%)	250(100%)

## Results

266 patients including 135 patients [54 male (40%) and 81 female (60%)] in group A (OMAB plus clidinium C), and 131 patients [56 male (43%) and 75 female (57%)] in group B (OMAB) underwent endoscopy. The 2 groups were similar with respect to age ( $48.72 \pm 56.30$  years vs  $40.11 \pm 14.13$  years;  $p=0.091$ ). Three patients in group A did not complete the treatment, and were therefore, excluded from further analysis. Thirteen patients in group B were excluded from the study for reasons, such as gastrointestinal bleeding (two patients), or failure to complete course of treatment (eleven patients). A total of 132 patients in group A and 118 patients in group B were entered to the data analysis.

Table 1 shows the endoscopic findings of the patients at the beginning of the study. Gastroduodenitis was the most observed endoscopic finding in both groups. No significant differences were seen between group A and B regarding to endoscopic findings ( $p=0.218$ ).

As shown in table 2, group A has shown higher eradication rates compared to group B (62.1% vs. 50%,  $p=0.04$ ) and adding clidinium C could increase the efficacy of the quadruple regimen for eradication of *H.pylori*.

**Table 2.** Eradication rates (UBT negative test) in patients under study on the basis of type of treatments

	Treatment		P-value	
	A		B	
UBT results	N	%	n	%
Positive	37	28	51	43.2
Negative	82	62.1	59	50
Borderline	13	9.8	8	6.8

## Discussion

Since 1980, which *H.pylori* has been explored, several eradication regimens have been proposed for the treatment of this infection. All treatment regimens were based on antibiotic components and in recent years, many reports have been published on the antibiotic resistance from all parts of the world (22-28). Widespread use of antibiotics, acquired resistance, poor compliance, and insufficient antibiotic penetration into the site of infection are the most important factors causing this problem. Thus, some researchers have tended to propose new regimens to improve the eradication rates. Addition of probiotics, vitamins, cobalamin and so other components are some of these efforts. In this double blind clinical trial study, we assessed the influence of adding clidinium C to the quadruple regimen for eradication of *H.pylori* infection. Our results shows that group A (OMAB plus clidinium C) have had a significant higher response rate to

treatment in comparison to group B (62.1% vs.50%). Clidinium C with reducing the acidity and motility of the stomach could increase the duration of antibiotic penetrance and therefore, lead to better responses. Lozniewski et al. (20) suggests that that the penetration of amoxicillin into the superficial gastric mucosa may be substantially increased in the case of *H. pylori* infection.

Other investigators have studied the efficacy of addition of vitamins, such as C and E to the triple or quadruple therapy for treatment of *H.pylori* infection. Chuang et al. (29) and Li et al.(19) reported that adding vitamin C and E to triple therapy could not improve the *H. pylori* eradication rates. Kaboli et al. (18) obtained the same results on vitamin C supplement.

But, Zojaji et al. (17) have found that addition of vitamin C to *H.pylori* treatment regimen of amoxicillin, metronidazole and bismuth can significantly increases *H.pylori* eradication rate.

Although many efforts have been spent to improving the efficacy of *H.pylori* eradication regimens, there is a substantial need for novel therapeutic strategies. Our study is one of these efforts that have shown addition of clidinium C to the standard quadruple therapy may increase the chance of *H.pylori* eradication. However, we recommend further studies to confirm our results.

## Acknowledgements

This study was founded by the Gastroenterology and Liver Diseases Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran. This study resulted from Dr. Maryam Chorami thesis.

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