

Effect of Prior use of Omeprazole on the Result of Urea Breath Test for the Detection of *Helicobacter pylori* Infection

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ABSTRACT

Background: Use of a proton pump inhibitor may be associated with a false-negative result for *Helicobacter pylori* detection using ¹³C-UBT. In this study the effect of prior use of omeprazole on ¹³C-UBT results was evaluated.

Methods: A total of 36 dyspeptic patients who tested positive for *H. pylori* infection by the rapid urease test were enrolled. Baseline ¹³C-UBT was performed on day 0. All patients received omeprazole 20 mg/day for 14 days. The ¹³C-UBT was performed on day 14, and was repeated one week later (day 21) in those patients who tested negative on day 14.

Results: Thirty-six patients were enrolled, the mean age being 47 ± 13.23 yrs. A total of 8 male (22%) and 28 female (78%) patients completed the study. Five (13.9%) of thirty six patients had negative ¹³C-UBT while receiving omeprazole at day 14 although they did not receive eradication therapy, implying false negative results. These five patients tested positive for ¹³C-UBT after 7 days of discontinuing omeprazole.

Conclusions: Prior treatment with omeprazole 20 mg/day led to a false-negative ¹³C-UBT in 13.9% of case. This effect resolved after 7 days of discontinuation of omeprazole. The result of this study suggested that prior use of omeprazole resulted in a 13.9% false negative rate of ¹³C-UBT, and that omeprazole should be with held at least one week prior to testing to avoid a false negative result.

Key words : Helicobacter pylori, Omeprazole, Urea breath test

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INTRODUCTION

Proton pump inhibitors (PPIs) are among the most commonly prescribed drugs worldwide. They act by blocking the H⁺K⁺ adenosine triphosphatase (ATPase) ion pump, thus inhibiting acid secretion from gastric parietal cells⁽¹⁾. Omeprazole is the first drug of the PPI group and is widely used in Thailand for many disorders. Omeprazole is highly effective in the treatment of peptic ulcers, gastroesophageal reflux disease, symptomatic relief of dyspeptic complaints, and importantly as a part of combination therapy for *H. pylori* eradication.^(2,3)

H. pylori has emerged as an important factor in the pathogenesis of peptic ulcer disease and also of gastric carcinoma.^(4,5) The diagnosis of *H. pylori* infection can be made by various tests, invasive or noninvasive. The invasive tests, such as the rapid urease test, histology and bacterial culture, are accomplished by means of mucosal biopsy during esophagogastroduodenoscopy (EGD). The most commonly employed routine test in practice is the rapid urease test, due to its low cost and a quick result. The urease test has 90-95% sensitivity and 95-100% specificity.⁽⁶⁾ Non-invasive tests, such as urea breath test (UBT), serology test for *H. pylori* antibody, and stool antigen test, do not require mucosal biopsy. In clinical practice UBT is preferred for evaluating successful of H. pylori eradication, with 90-95% sensitivity and 95-100% specificity.⁽⁶⁾

A number of factors can cause false negative results of urease test and UBT, including recent antibiotics ingestion, anti-ulcer drugs (H_2 receptor antagonist, PPIs) and ulcer bleeding.⁽⁷⁾

Clinicians are increasingly confronted with the problem of making a diagnosis of *H. pylori* infection in patients taking PPIs. Such as omeprazole reports have described varying false negative rates, from 5% to 38%, after taking 20 mg omeprazole for 14 days.⁽⁸⁻¹²⁾ The mechanism for false negative results remains unclear. Several hypotheses have evolved to explain the phenomenon. The first hypothesis is related to the effect of the PPIs on intragastric pH, which could make the intragastric environment unattractive for *H. pylori* and thus indirectly reduce the bacterial load. The second hypothesis is related to direct reduction of bacterial load.⁽¹³⁻¹⁷⁾ The latest hypothesis concerns the inhibitory effect of PPIs on the urease activity.⁽¹⁸⁾

Based on previous studies, most authorities cur-

rently recommend cessation of PPIs 7-14 days before UBT.⁽¹⁰⁾ The aim of this study was to prospectively evaluate the false negative rates of taking omeprazole on the detection of *H. pylori*.

MATERIAL AND METHOD

Patient

The initial recruitment was made from adult patients with dyspeptic complaints attending outpatient departments of King Chulalongkorn Memorial Hospital, Bangkok, between January 2006 and December 2006. A total of 36 dyspeptic patients who underwent esophagogastroduodenoscopy and tested positive for *H. pylori* infection by the rapid urease test were enrolled. Exclusion criteria included previous gastric surgery, pregnancy or current breast feeding, diagnoses of gastric ulcer, duodenal ulcer or gastric cancer, or history of allergy to omeprazole. The study was approved by the local ethical committee, and all patients gave written informed consent to participate in the study.

Method

Patients underwent ¹³C-UBT on day 0 as a baseline. All patients received omeprazole 20 mg/day for 14 days, and were asked not to take antibiotics and other anti- ulcer drugs. The ¹³C-UBT was performed on day 14 of treatment. Medication compliance was checked by means of pills count. The UBT was repeated one week later (on day 21) in those patients who tested negative on day 14.

The urea breath test was carried out using a previously validated method.⁽¹⁹⁻²¹⁾ Breath tests were performed according to the manufacturer's instruction (Campro Scientific, Netherlands). The ¹³C-UBT consists of a base-line breath sample and a breath sample 30 minutes after the administration of 100 mg of ¹³Clebeled urea tablet with water. The increase in mole fraction of tracer ¹³CO₂ at 30 minutes was compared to baseline. In our laboratory, the cut-off point or threshold for BreathID test has been determined to be 4 delta over baseline (DOB). Therefore, a test result is defined as positive if the final reading of DOB is equal or greater than 4. A test result is defined as negative if the final reading of DOB is less than 4.

Study design

In this descriptive study, data analysis was car-



ried out using SPSS for window version 11 statistical analysis software. Continuous variables such as age, weight, height and DOB level were calculated and reported as means and SD. Categorical variables such as gender and smoking were reported as frequency. Distribution of continuous data variables were tested for normality by using the Kolmogorov-Smirnov test. The DOB distributions before and after 2 weeks of omeprazole exhibited show normal distribution, then the paired t-test was employed. The Fisher exact test was used to compare the rates of false negative results after omeprazole treatment, analyzed by gender, smoking or alcohol. The unpaired t test for independent samples was used to examine the level of DOB at baseline for predicting false negative results. All tests were considered statistically significant at p < 0.05.

RESULTS

Forty patients agreed to take part in this study. Four patients did not complete the protocol due to poor compliance (2 patients) and loss to follow up (2 patients). Thirty-six patients (78%), 8 males (22%) and 28 females with a mean age of 47 ± 13.23 yrs, completed the study (Table 1). The indication for upper endoscopy was dyspepsia. The endoscopic findings were gastritis in thirty-four patients and normal in two patients. All patients tested positive for rapid urease test which was confirmed by urea breath test (UBT) at day 0 baseline (UBT1). The mean base line ${}^{13}CO_2$ (UBT1) was 24 per mil. After 14-days of omeprazole treatment, UBT2 was 20.6 per mil. There was no statistically significant difference the in levels of ${}^{13}CO_2$ value before and after omeprazole (p = 0.315, CI - 3.36 to 10.16). Five (13.9%) of thirty six patients had a negative ¹³C-UBT while receiving omeprazole at day 14, although they did not receive eradication therapy, thus implying false negative results. All five patients had a positive result of ¹³C-UBT after 7 days of stopping omeprazole.

The mean baseline ${}^{13}\text{CO}_2$ value (UBT1) of patients who developed false negative results by 14days of omeprazole was 17.6 ± 14.4 per mil, compared with 25 ± 14.8 per mil for those who remained positive. Although there was a trend toward a lower baseline ${}^{13}\text{CO}_2$ in those whose tests became negative after 14-days omeprazole, this was not statistically significant (p = 0.3) (Figure 1). No effects of sex, alcohol and smoking on the values of ${}^{13}\text{CO}_2$ (level of UBT2)

Table 1	Demographic	characteristic	of patients
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Number of patients	36	
Male	8	
Female	28	
Age (years)	47 ± 13.23	
Weight (kg)	59.8 ± 11.04	
Height (cm)	160.39 ± 7.4	
Male weight (kg)	68.57 ± 8.53	
Female weight (kg)	57.31 ± 10.48	
Male height (cm)	169.31 ± 5.13	
Female height (cm)	157.83 ± 5.81	
Alcohol intake		
Yes	3	
No	33	
Smoker		
Yes	2	
No	34	



Figure 1 ${}^{13}CO_2$ value (UBT1) of patients in the two groups



Figure 2 ¹³CO₂ value before and after 2 weeks after administration of omeprazole

were shown in those who were taking omeprazole. No serious side effects from omeprazole were observed only two patients had mild diarrhea with spontaneous resolution after stopping the drug.

DISCUSSION

Our study shows that omeprazole at standard dose is able to negatively affect the result of the urea breath test for the diagnosis of *H. pylori* infection. The rate of false-negative tests after 14 days of omeprazole therapy was 13.9%. Variability of false negative rates between reports range from 5-38% for 20 mg omeprazole after 14 days.⁽⁸⁻¹²⁾ The study by Levine A, et al. found that false negative rates by PPIs depended on the type of medications, 4.1% in omeprazole, 2.2% in pantoprazole, 16.6% in lansoprazole and 13.6% in esomeprazole.⁽²²⁾ This may be explained by differences in antibacterial activity of medications, lansoprazole being the most potent while pantoprazole the least active compound in vitro.^(23,24) False negative results occurred as early as 1 week after omeprazole, but the total number of subjects with false negative tests increased with longer durations of omeprazole usage.⁽⁹⁾ The drug dosage and duration chosen in our study were based on the widely used empirical treatment for dyspepsia. The time points selected were chosen according to the kinetics of acid suppression by PPIs,⁽²⁵⁾ as well as the minimum duration of treatment known to be effective for acid suppression which was 2 weeks.⁽²⁶⁾

The occurrence of false-negative urea breath tests in patients taking PPI has been attributed to a pHdependent mechanism by Chey, *et al.*, who found a statistically higher acid inhibition in patients with falsenegative tests compared to those who maintained positive results.⁽²⁶⁾ An additional mechanism for explaining these false negative results of UBT can be the well known antiurease activity of omeprazole and other PPIs.^(27,28) In our study, there was no statistically significant difference in the levels of ¹³CO₂ value before and after omeprazole, in spite of the false negative rate of 13.9%. Our findings cast doubt on this hypothesis, suggesting that factors other than anti-urease activity and anti-*H. pylori* activity may play a part.

All patients in our study who had false negative UBT returned to a positive test one week after stopping omeprazole. As the negative effects appeared to resolve within 7 days of PPI cessation, the withdrawal of this drug can thus be practically limited to 1 week to exclude any negative interference on the accuracy of UBT. Patients undergoing upper endoscopy for evaluation of dyspepsia should not take omeprazole 1 week before the procedure to avoid false negative urease test results. The time taken for the false negative urease test after omeprazole ingestion to revert to positivity may vary depending on the duration of prior omeprazole treatment. The possibility is that the longer the latter, the longer time may be required before employing the urease *H. pylori* test.

The value of ${}^{13}\text{CO}_2$ 14 days after taking omeprazole declined in some cases and increased in others (Figure 2). The reasons for this inconsistency may be differences in drug pharmacokinetics, baseline acidity in the stomach, or *H. pylori* bacterial load. Further studies are needed to elucidate these questions.

In conclusion, the present study shown that prior treatment with omeprazole 20 mg/day led to a 13.9% false-negative ¹³C-UBT. This effect resolved within 7 days of omeprazole discontinuation. The result of this study suggests that omeprazole should be stopped at least one week prior to employing an endoscopic urease test for *H. pylori* in order to avoid a false negative test result.

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