Original Article

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Comparison of the Results of Rapid Urease Test (Pronto dry®) at One and Twenty Four Hours in PPIs-Used Patients

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ABSTRACT

Background: Rapid urease test (RUT) is commonly used in diagnosis of *Helicobacter pylori (H. pylori)* infection. Previous studies suggested that if there was low density of *H. pylori* in the stomach, RUT needed longer time to become positive. Therefore, in patients with recent usage of proton pump inhibitors (PPIs) which reduce the density of *H. pylori*, the RUT may require longer reading time as well.

Objective: To compared the RUT (Pronto dry®) results at one and 24 hours in patients who recently used PPIs.

Material and Methods: Four gastric mucosal biopsy specimens, two from the antrum and two from the corpus were obtained from 546 dyspeptic patients taking PPIs. Both antral and corpus specimens were used for RUT (Pronto dry®), Medical instruments Corporation, Solothurn, Switzerland) and histopathologic examinations. The result of RUT was observed at one and 24 hours. The histopathologic examinations were used as the gold standard.

Results: Of 546 dyspeptic patients, 95 patients (17.4%) had positive histopathologic findings for *H. pylori* infection. Whereas 81 (14.8%) and 194 (35.5%) patients had positive RUT at one and 24 hours respectively. There were 113 patients had negative results at one hour and positive results at 24 hours. Among these patients, 16 patients had positive histopathologic findings.

Conclusion: In PPIs- used patients, evaluation of RUT (Pronto dry®) at 24 hours may increase the chance to detect *H. pylori* infection.

Key words : Pronto dry, *Helicobacter pylori,* rapid urease test, histopathology, proton pump inhibitors

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INTRODUCTION

Helicobacter pylori (H. pylori) infection is known as a potential cause of many gastrointestinal diseases such as gastritis, peptic ulcer disease, MALT lymphoma, and adenocarcinoma[1,2]. There are several methods for detecting *H. pylori* infection. Invasive methods required endoscopic biopsy of gastric mucosa (rapid urease test, histopathology, culture and genetic amplification), while non invasive test included urea breath test, serology and stool antigen[3]. Pronto dry is one of the rapid urease test (RUT) widely used in Thailand. This test is easy to perform and convenient to use due to three potential advantages[4]: 1) rapid results in one hour, 2) simple use at room temperature and 3) it can be kept at room temperature for two years. The previous studies had validated this test in dyspeptic patients without taking proton pump inhibitors (PPIs)[4-7]. All positive results were shown within one hour. But, in general practice, most dyspeptic patients had used PPIs before undergoing diagnostic endoscopy. PPIs are known to decrease *H. pylori* density in stomach and to shift their distribution proximally[8]. In vitro study demonstrated that the lower the density of *H. pylori* infection, the longer reaction time of RUT needed[9]. If the patients have previously received PPIs which is known to reduce the density of this organism, it may decrease the sensitivity of the test when the Pronto dry was read at one hour. In contrast, the reading results at longer time may yield more sensitivity for diagnosis of *H. pylori* infection. The aim of the present study was to determine the effect of PPIs on the results of Pronto dry at 1 hour and 24 hours compared with histopathologic examinations in the diagnosis of *H. pylori* infection.

MATERIALS AND METHODS

Patients

Five hundred and forty six consecutive patients with dyspeptic symptoms who underwent upper gastrointestinal endoscopy at Department of Medicine, Prapokklao Hospital from January 2006 to July 2007 were enrolled. All patients had used PPIs. Patients with active upper gastrointestinal bleeding, pregnancy, coagulation disorders and patients who were currently treated with anticoagulants were excluded.

Biopsy specimens

Two gastric mucosal biopsy specimens from antrum and corpus of each patient were obtained and divided into two parts. Both antral and corpus specimens were evaluated by rapid urease test and histopathologic examination for *H. pylori* infection was done.

Rapid urease test (Pronto dry®)

Pronto dry test was performed according to the manufacturer's instructions (Medical Instruments Corporation, Solothurn, Switzerland). Both antral and corpus specimens from each patient were placed into the test dots. After resealing the test the label was pressed over the test dot with the finger to squeeze the tissue fluid out of the specimens. The tissue fluid was absorbed by the filter paper. Results were monitored at room temperature after 1 hour and 24 hours. A positive result was defined as the color change on the test from yellow to pink-magenta.

Histopathologic examination for *H. pylori* infection

Antral and corpus specimens were fixed in 10% buffered formalin, before embedding in paraffin. The sections were stained with hematoxylin and eosin (H & E) and Giemsa solution for detection of *H. pylori.* The presence of spiral organism on the slide was considered positive for *H. pylori*.

Statistical analysis

Data was analyzed using Statistical Package for Social Sciences (SPSS) software, version 13.0 (Chicago, IL). Results were presented as mean ± standard deviation (SD) and percentages as appropriate. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of Pronto dry at 1 hour and 24 hours were calculated by two-by-two standard method. The histopathologic findings were used as the gold standard for diagnosis of *H. pylori* infection.

RESULTS

546 patients were recruited. Of these patients, 259 (47.4%) were male and 287 (52.6%) were female. The mean age was 57.7 ± 18 years with a range of 15 to 93 years. The endoscopic findings were shown in Table 1. The most common findings were gastritis, peptic ulcer and normal study.

Rapid urease test (Pronto dry®) and histopathologic results

Pronto dry was positive in 14.8% (81/546) and

Table 1. Baseline characteristics, endoscopic findings, results of rapid urease test and histopathology.

Factors	Patients (%)
Gender	
Male	259 (47.4)
Female	287 (52.6)
Age (year) mean ± SD	57.7 ± 18
Endoscopic findings	
Gastritis	287 (52.6)
Peptic ulcer	122 (22.3)
Gastric erosions	21 (3.8)
Esophagitis	20 (3.7)
Adenocarcinoma of stomach	12 (2.2)
Esophageal varices	37 (6.7)
Normal	54 (9.9)
Urease test	
1 hour	
positive	81 (14.8)
negative	465 (85.2)
24 hours	
positive	194 (35.5)
negative	352 (64.5)
Histopathology	
positive	95 (17.4)
negative	451 (82.6)

35.5% (194/546) when observed at 1 hour and 24 hours, respectively. Although the histopathology was positive in 17.4% (95/546) (Table 1). Among 95 patients who had positive histopathology for *H. pylori*, 55 patients had positive RUT at one hour and 71 patients had positive RUT at 24 hours. There were 113 patients had negative results at 1 hour and positive results at 24 hours. Among these patients, 16 patients had positive histopathologic findings (Table 2).

The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of Pronto dry at 1 hour were 57.9%, 94.2%, 67.9%, 91.4% and 87.9%, respectively. At 24 hours, they were 74.7%, 72.7%, 36.6%, 93.2% and 73.8%, respectively (Table 3).

Discussion and Conclusion

In general practice, PPIs are commonly used in dyspeptic patients. Most of the patients usually administer PPIs for a period of time before endoscopy. Previous report showed that the sensitivity of several diagnostic tests for *H. pylori* was reduced by recent usage of PPIs[10].

In Thailand, the prevalence of *H. pylori* infection varies from 40-60%[6]. In the present study, the prevalence of *H. pylori* infection was very low due to all of

Table 2. The results of rapid urease test at one and 24 hours compared with histopathologic examinations.

Diagnostic test	Pronto dry at 1 hour		Pronto dry at 24 hours	
	Positive (n)	Negative (n)	Positive (n)	Negative (n)
Histopathologic examination				
Positive (n)	55	40	71	24
Negative (n)	26	425	123	328

Table 3. The sensitivity, specificity, PPV, NPV and accuracy of rapid urease test at one and 24 hours compared with histopathologic examination.

Test	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Urease test at 1 hour	57.9	94.2	67.9	91.4	87.9
Urease test at 24 hour	74.7	72.3	36.6	93.2	73.1

PPV = positive predictive value
NPV = negative predictive value

our patients had used PPIs before endoscopy. Many studies reported that PPIs reduce the density of *H. pylori* in the stomach and shift their distribution proximally[8]. This effect may reduce the sensitivity of many diagnostic tests for *H. pylori* infection such as RUT, histopathology, culture, urea breath test, polymerase chain reaction and stool antigen test[10,11]. The author found that the sensitivity of Pronto dry test at one hour in diagnosis of *H. pylori* infection was lower than the sensitivity at 24 hours, but yielded more specificity. 113 patients had negative results at 1 hour and positive results at 24 hours. Among these patients, 16 patients had positive histopathologic findings. This suggested that, reading the results at 24 hours may increase not only the sensitivity but also the false positive results. Previous studies demonstrated that RUT needed longer reaction time in detection of *H. pylori* when there was a low density of this organism[9,12]. Since PPIs can reduce the *H. pylori* load in the stomach, RUT in PPIs-used patient may need longer time to detect this organism. In the present study, the author found that 97 patients had negative Pronto dry test at 1 hour and negative histopathologic examination for *H. pylori* infection, but Pronto dry test at 24 hours were contrary positive. These Pronto dry results at 24 hour might be the false positive results because patients who were taking PPIs might develop achlorhydria with subsequent superficial colonization by other urease-producing organisms (eg. *Proteus mirabilis* or *Klebseilla*) that produced urease enzyme and this subsequently provided false positive RUT results[13,14]. On the other hand, these results might be the false negative results because the present study used histopathologic examination as the gold standard. This test had high sensitivity, specificity and accuracy when performing in patient who were not taking PPIs, but the sensitivity decreased in PPIs- used patients[10]. Therefore, in patients who are taking PPIs, histopathologic examination may not be sensitive enough to determine whether the results of Pronto dry at 24 hours are true positive or false positive.

In conclusion, the present study demonstrated that RUT (Pronto dry®) at 24 hours yielded higher sensitivity but lower specificity comparing with RUT at one hour for diagnosis of *H. pylori* infection in patients who recently used PPIs. However, this observation was inconclusive because histopathologic examination might not the proper gold standard in patients who had used PPIs. Further studies are needed to determine the proper diagnostic methods for *H. pylori* infection in PPIs-used patients.

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