

The Comparison of Biopsy Sites Measured by Rapid Urease Test for Diagnosed of Helicobacter pylori Infection Between a Population with Gastric and Duodenal Ulcers

Shou-Wu Lee, Han-Chung Lien, Chi-Sen Chang, Sheng-Shun Yang, Yen-Chun Peng, Hong-Zen Yeh

Shou-Wu Lee, Han-Chung Lien, Chi-Sen Chang, Sheng-Shun Yang, Yen-Chun Peng, Hong-Zen Yeh, Division of Gastroenterology, Department of Internal Medicine, Taichung Veterans General Hospital, Taichung, Taiwan

Shou-Wu Lee, Chi-Sen Chang, Department of Internal Medicine, Chung Shan Medical University, Taichung, Taiwan

Han-Chung Lien, Sheng-Shun Yang, Yen-Chun Peng, Hong-Zen Yeh, Department of Internal Medicine, Yang-Ming University, Taipei, Taiwan

Correspondence to: Shou-Wu Lee, MD, Division of Gastroenterology, Department of Internal Medicine, Taichung Veterans General Hospital, Taichung, Taiwan. ericest@vghtc.gov.tw

Telephone: +886-4-2359-2525 Fax: +886-4-23741331

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ABSTRACT

AIM: The aim of this study was to compare of biopsy sites for rapid urease test diagnosed of *H. pylori* infection between a population with gastric and duodenal ulcers.

METHODS: Patients received upper gastrointestinal endoscopy due to epigastria and diagnosed as peptic ulcer disease between January and July 2009 were collected. Biopsies were obtained from four sites on the antrum, corpus, fundus and angularis. The specimens all taken for the CLO rapid urease test were observed at 2, 12 and 24 hours.

RESULTS: Among all 109 patients enrolled, the positive rapid urease test was noted in 14 (45.2%) and 52 (66.7%) among those with gastric and duodenal ulcers. Gastric ulcers cases had the same positive rate (85.7%) at different biopsy sites. Duodenal ulcers cases had the significantly low positive rate at fundus (80.8%). The test sensitivity was increased if two biopsies instead of only one. To gastric ulcer patients, two biopsies with one from antrum, were suitable. To duodenal ulcer patients, one biopsy from antrum, or two biopsies with one from antrum, were acceptable to the accurate diagnosis of *H. pylori* infection.

CONCLUSIONS: *H. pylori* was predominantly antral in the patients with duodenal ulcers, and equal distribution over all stomach, though mildly increased corpus colonization density, in those with gastric ulcers. Two biopsies with one from antrum were encouraged to

minimize the false negative rate of rapid urease test.

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Key words: Duodenal ulcer; Gastric ulcer; Helicobacter pylori

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INTRODUCTION

Since the discovery of *H. pylori* by Marshall and Warren in 1983, many researches have demonstrated its associated with peptic ulcer disease, superficial gastritis, gastric carcinoma and B-cell lymphoma^[1-2]. Natural colonization of *H. pylori* is restricted to human stomach, and it is becoming less common over the course of the 20th century due to improved sanitation, smaller family size and the frequent use of antibiotics during childhood^[3]. Up to now, *H. pylori* infection occurring in 40%-50% of the population in developed countries, 80%-90% in developing regions^[4]. Diagnostic methods may be non-endoscopic, including serologic test and breathing test, or endoscopic, including culture, histological stains and rapid urease tests^[5]. The rapid urease test (CLO test), based on the ability of *H. pylori* to secrete the urease enzyme, which catalyzes the conversion of urea to ammonia and bicarbonate, had a sensitivity 75-98% and a specificity of 92-100% according to previous studies^[2]. In general, one or two biopsies from antral sites are performed for urease testing, but still possibility of false negative exists.

The aim of this cross-sectional study was to compare of biopsy sites for rapid urease test diagnosed of *H. pylori* infection between a population with gastric and duodenal ulcers.

PATIENTS AND METHODS

The consecutive patients underwent open-access transoral upper endoscopy due to epigastric pain and diagnosed as peptic ulcer disease in our hospital between January 2009 and July 2009

were collected and analyzed. Written informed consent for upper endoscopy was obtained from all patients before the procedure. The exclusion criteria included patients with previous *H. pylori* eradication or gastric resection, pyloric channel ulcers, combined gastroduodenal ulcers or acute gastritis so undistinguished clearly, gastrointestinal cancers, acid-suppressive therapy with proton-pump inhibitors (PPIs), therapy with antibiotics and medications with non-steroidal anti-inflammatory drugs (NSAIDs) during the past 4 weeks. The definition of peptic ulcers was mucosal break of stomach or duodenum over 3 mm in diameter, or more than 10 gastric or duodenal erosions.

Biopsies were obtained using fixed forceps from four sites on the antrum, corpus, fundus and angularis respectively during the upper endoscopy. The antral biopsy was done toward the greater curvature side but less than 5 mm from the pylorus, and the corpus one was obtained on the middle greater curvature side of the gastric body. The biopsy specimens were taken immediately for the CLO rapid urease test (Delta West Ltd., Perth, Australia), placed in the agar gel containing phenol red and urea. The color change of phenol red, meaning presentation of *H. pylori* urease leading to a rise in pH value, was observed during 24 h duration after biopsies placed. The colonization density of *H. pylori*, assessed by the time of positive rapid urease test observed, was recorded at 2 h, 12 h and 24 h after biopsy samples placed.

This study project was approved by the Institutional Review Board of Taichung Veterans General Hospital. Statistical comparisons were made between the two groups using Fisher's exact test to analyze factors such as gender, positive rate or false negative rate for rapid urease test, and *H. pylori* colonization density. Independent t test was used to compare factors such as age. A *p* value <0.05 was considered statistically significant.

RESULTS

Among all 109 patients with peptic ulcer disease received rapid urease test between January 2009 and July 2009, 31 and 78 cases belonged to those with gastric and duodenal ulcers respectively. The positive rapid urease test was noted in 14 (45.2%) among those with gastric ulcers, and 52 (66.7%) among those with duodenal ulcers. At least, 66 with positive rapid urease test were enrolled in this study, as shown in Table 1. The patients with gastric ulcers (mean age 60 years) were older than those with duodenal ulcers (mean age 53.81 years). Besides, significant female predominant was found in the cases with gastric ulcers (71.4%) compared with those with duodenal ulcers (30.8%).

Table 1 Demographic data and the results of rapid urease test.

Table 1	Gastric ulcers	Duodenal ulcers	<i>P</i> -value	Total
Numbers	14	52		66
Age (mean±SD)	60.00 ± 13.42	53.81 ± 11.87	0.133 ^a	55.12 ± 12.37
Gender			0.576 ^b	
Male	10 (71.4%)	36 (69.2%)		40 (60.6%)
Female	4 (28.6%)	16 (30.8%)		26 (39.4%)
Positive for rapid urease test				
Antrum	12 (85.7%)	50* (96.2%)	0.195 ^b	62 (93.9%)
Angularis	12 (85.7%)	48* (92.3%)	0.599 ^b	60 (90.9%)
Corpus	12 (85.7%)	50* (96.2%)	0.195 ^b	60 (90.9%)
Fundus	12 (85.7%)	42* (80.8%)	1.000 ^b	54 (81.8%)

^a Independent t test; ^b Fisher's exact test. *P* value of *: 0.015; SD: standard deviation.

The results of rapid urease test of our patients with gastric ulcers and duodenal ulcers also summarized in Table 1. In general, the

positive rates of rapid urease test were similar among the biopsy sites of antrum, angularis and corpus, ranging from 90.9% to 93.9%, but relatively lower at the site of fundus (81.8%). Patients with gastric ulcers had the same positive rate (85.7%) at these different biopsy sites. Cases with duodenal ulcers had the lowest positive rate at fundus (80.8%), higher at other biopsy sites, ranging from 92.3% to 96.2%, and these differences were significant (*p* value 0.015).

The *H. pylori* colonization density of our patients meant by the time agar gel color changed was shown in Table 2. The significant difference existed in the cases with duodenal ulcers having more colorization density at the site of antrum (*p* value 0.041) than those with gastric ulcers. To the patients with gastric ulcers, relatively higher colonization density of *H. pylori* occurred at the site of corpus compared with other sites.

The diagnostic accuracy of different biopsy sites for rapid urease test was summarized in Table 3. If only one biopsy was adapted, the specimen from antrum or corpus owed the most reliable accuracy, meant by the lowest false negative rate (6.1%). On the contrary, the specimen from fundus owned the less reliable result, represented by the highest false negative rate (18.2%). If two biopsies were received, biopsies at antrum and angularis, or antrum and corpus, had no possibility of false negative for rapid urease test. Furthermore, biopsies simultaneously at angularis and corpus, angularis and fundus, or corpus and fundus, owned the significantly higher negative rate (6.1%) among all the patients enrolled in our study.

DISCUSSION

The *H. pylori* is a slow growing, microaerophilic, motile, spiral, Gram negative organism that produces abundant urease. Transmission of *H. pylori* has been described via oro-faecal, oro-oral and water borne^[6]. The features including duodenal ulcers, gastric ulcers, and antral nodularity at the time of upper endoscopy suggest of *H. pylori* infection^[5]. *H. pylori* infection was found in more than 90% and 70% of patients with duodenal and gastric ulcers during the 1980s^[7]. Due to the improvements in hygiene, a recent study reported a lower *H. pylori* infection in 56.4% of patients with duodenal ulcers and less in those with gastric ulcers^[8]. Similarly, our patients had a lower prevalence of *H. pylori* infection with a rate of 45.2% in cases with gastric ulcers, and 66.7% in those with duodenal ulcers. Besides, our results also documented the male predominance in both groups.

Of the various invasive and noninvasive tests that are available for *H. pylori* detection, histological assessment for *H. pylori* provides excellent high sensitive and specific diagnostic accuracy, so it is the accepted as gold standard^[9]. However, rapid urease tests is accepted more common recently because of the advantages of the simplicity, low cost, high specificity, and rapidity of results, although its sensitivity is not consistently high^[5]. The value of sensitivity of rapid urease test is determined by not only the location biopsy obtained, but also the numbers of specimens endoscopists adapted.

Conventionally, the site of gastric biopsy used by most endoscopists is the antrum. However, *H. pylori* can colony the entire gastric epithelium, from the prepyloric antrum to the cardia, and the clinical appearances are dependent on its distribution^[10]. According to previous studies, colonization density of *H. pylori* infection are greatest in the distal antral region with sparing of the body mucosa in patients with duodenal ulcer. In cases with gastric ulcers, *H. pylori* infection affects the body and antral mucosa to a similar degree^[10,11].

One previous study using histological diagnosis showed the significantly higher rate of antral *H. pylori* infection in the patients with duodenal ulcers (97.7%) than those with gastric ulcers (77.5%), but the rates of corpus infection between two groups had no

Table 2 The result of colonization density of *H. pylori* infection.

Table 2	Gastric ulcers				Duodenal ulcers				P-value
	A	B	C	D	A	B	C	D	
<i>H. pylori</i> colonization density									
Antrum	4 (28.6%)	8 (57.1%)	0	2 (14.3%)	32 (61.5%)	14 (26.9%)	4 (7.7%)	2 (3.8%)	0.041
Angularis	6 (42.9%)	6 (42.9%)	0	2 (14.2%)	30 (57.7%)	18 (34.6%)	0	4 (7.7%)	0.555
Corpus	8 (57.1%)	4 (28.6%)	0	2 (14.3%)	16 (57.7%)	30 (30.8%)	4 (7.7%)	2 (3.8%)	0.072
Fundus	4 (28.6%)	8 (57.1%)	0	2 (14.3%)	10 (19.2%)	20 (38.5%)	12 (23.1%)	10 (19.2%)	0.192

All P-value was analyzed with Pearson's Chi-square test.

"A", "B" and "C" mean color change of the rapid urease test noted at 2 hours, 12 hours and 24 hours. "D" means negative for rapid urease test.

Table 3 Diagnosis accuracy of rapid urease test of different biopsy sites.

Table 3	Disease	Gastric ulcers	False negative result		
			Duodenal ulcers	P-value	Total
Single one biopsy site					
Antrum	2 (14.3%)	2 (3.8%)	0.195	4 (6.1%)	
Angularis	2 (14.3%)	4 (7.7%)	0.599	6 (9.1%)	
Corpus	2 (14.3%)	2 (3.8%)	0.195	4 (6.1%)	
Fundus	2 (14.3%)	10 (19.2%)	1.000	12 (18.2%)	
Two biopsy sites					
Antrum + angularis	0	0	1.000	0	
Antrum + corpus	0	0	1.000	0	
Antrum + fundus	0	2 (3.8%)	0.865	2 (3.0%)	
Angularis + corpus	2 (14.3%)	2 (3.8%)	0.195	4 (6.1%)	
Angularis + fundus	2 (14.3%)	2 (3.8%)	0.195	4 (6.1%)	
Corpus + fundus	2 (14.3%)	2 (3.8%)	0.195	4 (6.1%)	

All P-value was analyzed with Fisher's exact test.

difference (68.2% in gastric ulcer patients, 72.5% in duodenal ulcer patients)^[12]. Another study concluded high-grade antral *H. pylori* infection associated with duodenal ulcers, and high-grade *H. pylori* in antral and corpus increased gastric ulcer risk^[13]. The third study provided that the antrum and angularis are the best place for the histological diagnosis of *H. pylori*, and the corpus specimen had the worst accuracy^[14].

Our patients had the similar *H. pylori* distribution: the distal part of stomach, including antrum and angularis, had the highest positive rate of rapid urease test (93.9%), and the proximal portion, fundus, had the lowest (81.8%). This trend was extremely significant in the patients with duodenal ulcers, but loss in those with gastric ulcers.

Although the colonization of the gastric antrum and corpus by *H. pylori* was equally common between those with gastric and duodenal ulcer disease, the density of colonization had difference in these patients. To the specimen obtained from antrum, the patients with duodenal ulcers had significantly more colonization density of *H. pylori* than those with gastric ulcers. On the contrary, the cases with gastric ulcers owned more colonization density than those with duodenal ulcers at the site of corpus. The reason might be a reflection of the chronicity of *H. pylori* infection. Patients with gastric ulcers had older mean age, and tended to own presence of chronic gastritis with mucosa atrophy or intestinal metaplasia, so resisted to the colonization by *H. pylori*. Besides, those with duodenal ulcers had antral *H. pylori* infection, following by increased acid secretion, and in turn protected the oxyntic mucosa of corpus from further colonization of *H. pylori*^[12].

Consider the relationship between the numbers of biopsies obtained and the accuracy of diagnosis, a lower sensitivity of 75% was noted when using only one antral biopsy^[15], and it can be increased to 93% with obtaining four antral specimens^[16]. Similarly in our patients, the sensitivity was increased dramatically if two biopsies instead of only one biopsy obtained. To the patients with gastric ulcers, single one biopsy was not encouraged due to the high false negative result (14.3%). Two biopsies, preferably one from

antrum, were suitable in these patients. Besides, one biopsy from antrum, or two biopsies, preferably one from antrum, were acceptable to the accurate diagnosis of *H. pylori* infection in the cases with duodenal ulcers.

There are some limitations in our study. Firstly, our study adapted only rapid urease test for the diagnosis of *H. pylori* infection. There were probable some false negative results existed in those undetected by this examination. Second, we did not consider the false positive results of rapid urease test in our study. It could be caused by overgrowth of urease-producing commensal organisms, such as *Proteus saprophyticus*, especially in the patients with achlorhydria^[2]. Thirdly, the severity of gastritis, measured by histopathologic scores according to the update Sydney system^[17], was not evaluated in our study. Further combined histological examination for *H. pylori* and severity of gastritis should be investigated and compared.

CONCLUSION

This study demonstrated the different distribution of *H. pylori* in the patients with peptic ulcer disease. *H. pylori* was predominantly antral in the patients with duodenal ulcers, and equal distribution over all stomach, though mildly increased corpus colonization density, in those with gastric ulcers. Two biopsies obtained were encouraged, and preferably one from the site of antrum, to minimize the false negative rate of rapid urease test.

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