Prospective study to validate HpOne in the diagnosis of *Helicobacter pylori* infection

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ABSTRACT

Introduction: The HpOne test is a new five-minute rapid urease test developed for the rapid detection of *Helicobacter pylori* infection during gastroscopy. However, evidence in the literature supporting its use clinically is scarce. The most commonly used rapid urease test remains the *Campylobacter*-like organism (CLO) test, which generates accurate readings only after 24 hours. The aim of this study was to evaluate the efficacy of the HpOne test in our local population.

Methods: From August 2007 to May 2008, consecutive patients undergoing gastroscopy for various indications were recruited into this prospective study. Patients who were pregnant, lactating, on proton pump inhibitors, antibiotics, immunosuppressants or had previous gastric surgery were excluded. During gastroscopy, six gastric mucosal biopsies were taken; three from the body and three from the antrum. One body and one antral biopsy were used for each of the HpOne test, CLO test and histology. Results of the HpOne and CLO tests were then compared against the gold standard of histology.

Results: Of the 149 patients recruited, 82 (55 percent) were men and 67 (45 percent) were women. The prevalence of *Helicobacter pylori* infection was 38.9 percent (n is 58). The sensitivity and specificity of the HpOne test were 65.5 percent and 85.7 percent, respectively, while those for the CLO test were 63.8 percent and 84.6 percent, respectively.

Conclusion: The HpOne test is as efficacious as the CLO test, with the added advantage of yielding results faster. It is thus a superior alternative and should be considered for clinical use.

Keywords: CLO test, diagnosis, *Helicobacter pylori*, HpOne, rapid urease test

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INTRODUCTION

Helicobacter pylori (*H. pylori*) is a micro-aerophilic, Gram-negative spirochete that was first isolated by Warren and Marshall almost three decades ago. Since then, it has been shown to be a widespread and infectious bacterium, affecting approximately 50% of the world's population[1] and more than one-third of Singaporeans.[2] Significant clinical outcomes following the infection include[1] chronic gastritis, peptic ulcers, mucosa-associated lymphoid tissue lymphomas and most importantly, gastric adenocarcinoma.

The most recent recommendation by the American College of Gastroenterologists[3] states that if endoscopy is required owing to the patient's presentation, biopsy-based endoscopic tests are the most appropriate tool to diagnose *H. pylori* infection. The most extensively studied and widely used of these tests remains the *Campylobacter*-like organism (CLO) test® (Delta West, Bentley, WA, Australia), an agar gel test. However, evidence has shown that the results of the test are best read only after 24 hours.[4]

The HpOne test® (GI Supply, Camp Hill, PA, USA) may potentially be a superior alternative, as its highest concordance with the gold standard of histology has been reported to be maximal at one hour. However, evidence supporting its use in clinical practice has been scarce, with only a small study[5] being reported in the literature thus far. The authors of this paper thus aimed to validate the efficacy of the HpOne test as compared to the gold standard of histology, to determine its sensitivity and specificity in the detection of *H. pylori* infection, as well as to explore the possibility of its use in our local setting.

METHODS

From August 2007 to May 2008, consecutive patients undergoing gastroscopy for various indications at the Endoscopy Unit of Alexandra Hospital, Singapore were recruited for this study. Patients who had been taking proton pump inhibitors or antibiotics one month prior to the endoscopy session, on chronic immunosuppressant therapy or had previous gastric surgery, as well as pregnant or lactating women, were excluded. Written informed consent was obtained from all participants before enrolment into the study. Approval for the study was obtained from the Domain Specific Review Board (domain D) and funding provided by the NMRC Enabling Grant, thus ensuring that no extra cost was borne by the patients.

Each patient fasted for a minimum of six hours. Thereafter, gastroscopy was performed using an Olympus gastroscope (Olympus Medical Systems Corp, Tokyo, Japan). Six gastric mucosal biopsies were obtained from each patient; three from the antrum and three from the gastric body. Two biopsy specimens (one each from the antrum and gastric body) were each used for the HpOne test, CLO test and histology (Fig. 1). A co-investigator interpreted the results of the HpOne and CLO tests at 30 minutes, 60 minutes and 24 hours after commencement of the tests. The tests were considered positive when either specimen recorded a positive result. An experienced senior pathologist evaluated the biopsy specimens and provided the histological findings.

Statistical analysis was performed using the Statistical Package for the Social Sciences version 15.0 (SPSS Inc, Chicago, IL, USA). Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of the HpOne and CLO tests were calculated using histology as the gold standard for the diagnosis of *H. pylori* infection.

RESULTS

Of the 149 patients enrolled in our study, 82 (55%) were men and 67 (45%) were women. The mean age was 44.7 (range 18–81) years. The main indication for gastroscopy was epigastric pain in 107 (71.8%) patients. The prevalence of *H. pylori* infection was found to be 38.9% (n = 58). The number of positive results for the HpOne and CLO tests at the respective time intervals is presented in Table I. After 60 minutes, all positive HpOne test results were reflected, while only 82.3% of positive CLO test results were seen.

In comparison with the histology results (Table II), the HpOne test had a sensitivity and specificity of 65.5% and 85.7%, respectively, while those for the CLO test were 63.8% and 84.6%, respectively (Table III). Tables IV and V show the positive and negative results of each test. Although both the CLO and HpOne tests were more sensitive when using corpus samples, the highest sensitivity for both tests was obtained when both the findings of the body and antrum were considered together. As the study was not powered or designed to compare sampling from the body to the antrum, no further inference could be made with regard to which biopsy site is better. Our current practice is to obtain biopsies from both sites for each rapid urease test.

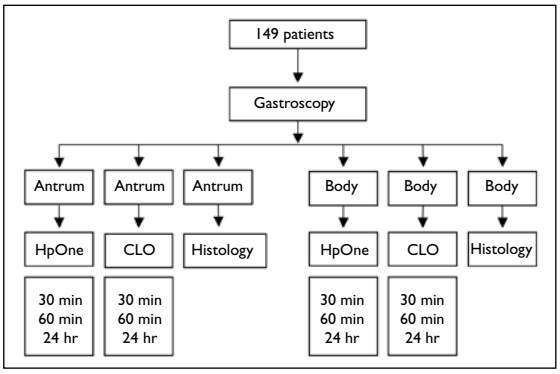

Fig. 1 Flowchart shows the study design and biopsy protocol.

Table I. Results of positive HpOne and CLO tests at various time intervals.

Time interval	No. of positive tests (%)	
	HpOne	CLO
30 min	27 (52.9)	25 (49.0)
60 min	51 (100)	42 (82.3)
24 hr	51 (100)	51 (100)

Table II. The results of CLO and HpOne tests compared with histology.

	Positive histology (n = 58)	Negative histology (n = 91)
CLO Test		
Positive	37	14
Negative	21	77
HpOne Test		
Positive	38	13
Negative	20	78

Table III. The results of CLO and HpOne tests compared with histology.

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
HpOne	65.5	85.7	74.5	79.6
CLO test	63.8	84.6	72.5	78.6

PPV: positive predictive value; NPV: negative predictive value

Table IV. HpOne test results in comparison with histology.

	Antral		Body		Both/either antral or body	Both antral and body
	HpOne positive	HpOne negative	HpOne positive	HpOne negative	HpOne positive	HpOne negative
Histology positive (n = 58)	35	23	38	20	38	20
Histology negative (n = 91)	13	78	12	79	13	78

Table V. CLO test results in comparison with histology.

	Antral		Body		Both/either antral or body	Both antral and body
	CLO positive	CLO negative	CLO positive	CLO negative	CLO positive	CLO negative
Histology positive (n = 58)	34	24	37	21	37	21
Histology negative (n = 91)	11	80	14	77	14	77

DISCUSSION

H. pylori infection is a widespread infection, and its prevalence rates are influenced by age, race, geographic distribution and the socioeconomic status of the patient.[6,7] The prevalence rates in developing countries may be as high as 70%, in contrast to approximately 40% in developed countries.[8] In the current study, the local prevalence rate of *H. pylori* infection, at 38.9%, is not significantly different, and closely mirrors that reported by Fock[2] more than a decade ago. Despite reports of falling prevalence rates, particularly in developed countries, there remains considerable morbidity and mortality associated with *H. pylori* infection for clinicians to maintain a vested interest in its diagnosis and subsequent management.

Endoscopic biopsy and rapid urease testing is the most simple and rapid method for identifying *H. pylori* infection during endoscopy.[9] Although the CLO test has been shown to be efficacious in the diagnosis of *H. pylori*,[9] it requires refrigeration for storage and warming to room temperature before use, and most importantly, has a recommended incubation period of 24 hours.[10] Another test that has been used in Singapore is the HpFast test (GI Supply, Camp Hill, PA, USA), which must be read after a period of 24 hours. These requirements present clear obstacles to efficient patient management, as the patient would need to present for a second consultation on a separate day to review the test results, thereby delaying the initiation of treatment.

In this study, the authors used a defined gold standard of histology and compared the HpOne test with the CLO test, the latter usually used as the benchmark when validating newer rapid urease tests. It was found that all positive results from the HpOne test kit could be read within 60 minutes, with 52.9% of the positive results reflected within 30 minutes. The sensitivity and specificity of the test were not significantly different from those of the CLO test. Similarly, a study conducted by Tseng et al[5] reported that the sensitivity, specificity, PPV and NPV of the HpOne test were not significantly different from those of the CLO test.

No true gold standard, however, exists for the diagnosis of *H. pylori*, and biopsy-based testing is usually used as a reference point.[10] The most commonly used methods are bacterial culture, histological identification and rapid urease testing. As such, there is a fairly wide range in the sensitivity and specificity values of *H. pylori* diagnostic tests reported in the literature, depending on what was used as the 'gold standard' in the study design. The CLO test has a sensitivity and specificity of 56.6%–97.4% and 93.5%–100%, respectively.[5,10-12] The sensitivity and specificity of our CLO test is well within the abovementioned reported ranges.

Up till 2009, four out of five of the teaching hospitals in Singapore were still using rapid urease tests that had to be read at 24 hours (either CLO or HpFast tests). Using such tests creates problems in the workflow with regard to patient reviews after gastroscopy, and may result in an unnecessary delay in the treatment of *H. pylori*. There is also the possibility that some positive results may be missed if the test is read too early or if it is not read at the 24-hour mark. As a validated and faster test kit that has been shown to be comparable to the widely used CLO test, the HpOne test presents itself as a viable alternative.

A test that could be read sooner would address the systemic problems in the workflow in terms of reading the rapid urease test. Furthermore, it is less expensive than the CLO test. The fact that positive results can be interpreted within the hour would overcome the logistical issues discussed above. The patient can potentially have a doctor review the results of the test on the same day as his gastroscopy appointment, leading to reduced patient expenses, time saved by both parties and more efficient patient management on the whole. Of note is the fact that despite both the HpOne and HpFast test kits being available from the same company in Singapore, some hospitals continue to use the latter. Thus, it is important that the results of this study be presented, as HpOne is a rapid urease test that is not only highly accurate but capable of yielding faster reading.

In conclusion, our study shows that the HpOne test is as efficacious as the CLO test in the diagnosis of *H. pylori* infection from gastroscopy biopsy specimens. The authors believe that HpOne is a reliable, affordable and highly attractive rapid urease test that clinicians can use for the rapid diagnosis of *H. pylori* infection.

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