Diagnosis of *Campylobacter pylori* Gastritis

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*Campylobacter pylori* is a bacterium that inhabits gastric mucosa. It causes chronic active gastritis and is highly associated with duodenal ulcer. *Campylobacter pylori* has a urease enzyme (not present in man), which allows diagnosis by a $^{14}$C urea breath test. We compared two noninvasive tests, the breath test and serum ELISA, to biopsy and histologic diagnosis. Twenty-two patients who underwent gastroduodenoscopy for evaluation of possible peptic ulcer disease entered the study. The breath test detected the organism in eight of eight patients biopsy-positive for the organism (sensitivity 100%). The breath test was negative in 12 of the 14 patients who were biopsy-negative (specificity 86%). The ELISA was performed in 14 patients. It was positive in 5 of 5 patients biopsy-positive for the organism (sensitivity 100%) and negative in 7 of 9 patients who were biopsy-negative (specificity 78%). We conclude that both the ELISA and the $^{14}$C urea breath test are excellent noninvasive methods to detect *Campylobacter pylori*. However, only the breath test is suitable for following the response to treatment, as it detects the presence of the organism rather than an immune response to it.

KEY WORDS: *Campylobacter pylori*; urease; ELISA; $^{14}$C urea; breath test; chronic active gastritis.

*Campylobacter pylori* is a bacterium found only in association with gastric mucosa. Recently it has been shown to be associated with duodenal ulcer disease and chronic active gastritis (1, 2). Although there is agreement on the strong association between *C. pylori* and duodenal ulcer (>90%), there is controversy regarding its role in pathogenesis. Eradication of the organism, however, can reduce duodenal ulcer recurrence rates (3).

Three methods now exist to identify *C. pylori* infection. Gastroscopy with biopsy and culture has been the gold standard for documenting infection. Culture for *C. pylori* was omitted in this study because of the high correlation between histology and culture results in published studies (2, 4, 5). Serum ELISA tests show the presence of antibodies to the organism and therefore indicate current or prior infection. $^{14}$C urea testing is based on the high urease activity of *C. pylori*, which splits $^{14}$C urea into ammonia and $^{14}$CO$_2$. The $^{14}$CO$_2$ is absorbed and exhaled and can be measured.

This study compares breath testing and serologic testing to biopsy in diagnosis of *C. pylori* infection. The breath test is found to be an excellent noninvasive method to diagnose *C. pylori*. The ELISA is also sensitive and specific but is not useful in assessing treatment because of the persistence of the antibody response after eradication of the infection.

MATERIALS AND METHODS

Patients at the Johns Hopkins Endoscopy Unit who were to undergo esophagogastroduodenoscopy in an evaluation for peptic ulcer disease were offered the $^{14}$C urea breath test. The first 22 patients who gave informed consent for the breath test were entered into the study. Within one week of their endoscopic exam they
underwent breath testing and serologic testing. Fourteen of the patients were inpatients and eight were outpatients. Exclusions from the study were contraindications to biopsy (acute gastrointestinal bleeding, coagulopathy, or thrombocytopenia), small bowel overgrowth syndromes, gastric outlet obstruction, and use of antibiotics within six weeks of the study. To evaluate the effects of antibiotics on the breath test and ELISA, three patients who had received antibiotics within six weeks of testing were also studied. Their results were analyzed separately.

The breath test was performed in a standard fashion as described by Sherr et al for a bile acid breath test (6). After a 6-hr fast, Ensure (30 ml) was administered to slow gastric emptying. \(^{14}\)C-Urea (5 \(\mu\)Ci) was administered by mouth. Expired breath was collected. One millimole of exhaled \(\text{CO}_2\) was quantified by combination with a hyamine stock solution and phenolphthalein indicator. The \(^{14}\)CO\(_2\) was then collected and measured by a scintillation counter. The result was expressed as a percentage of administered dose per millimole of \(\text{CO}_2\) exhaled multiplied by 0.001 and divided by body surface area (referred to as breath test score).

In the majority of patients, a serum ELISA was performed. It was performed within one week of the biopsy and breath test by the Johns Hopkins Department of Microbiology. The test was performed as outlined in the Manual of Clinical Laboratory Immunology (7). \(C.\) pylori antigen was pooled from 10 bacterial isolates (of patients who had previously undergone endoscopy). Goat anti-human IgG conjugated with alkaline phosphatase was used to demonstrate binding of patient antibody to the antigen-coated wells. An ELISA was recorded as positive when its optical density (OD) was greater than the mean OD of the 25 negative controls plus three standard deviations. The negative controls were patients who had gastroscopy and biopsy negative for gastritis and without evidence of \(C.\) pylori by histology and culture.

All patients had two antral biopsies taken. Areas of inflammation were biopsied if present. The biopsies were stained with H&E and Giemsa and were reviewed by Dr. Yardley of the Pathology Department. There was a 0-3 grading scale for \(C.\) pylori, for the chronic component of gastritis, and for the acute (active) component of gastritis. For \(C.\) pylori the findings were typically shaped organisms; for acute gastritis the findings were lymphocytes; for chronic gastritis the findings were intraepithelial polymorphonuclear leukocytes. The grading scale was: 0 = features absent; 1 = minimal (rare findings); 2 = moderate (findings in multiple fields); 3 = marked (findings in most fields).

Any patient with acute gastritis grade greater than 0 was considered to have an abnormal amount of acute gastritis. Any patient with chronic gastritis grade greater than 1 was considered to have an abnormal amount of chronic gastritis.

**RESULTS**

Twenty-two patients entered the study. Eight patients had organisms typical of \(C.\) pylori seen on biopsy and 14 did not. The average breath test score of patients biopsy-positive for \(C.\) pylori was significantly higher than that of the negatives at all time points tested \((P < 0.01\) by Wilcoxon rank sum). In addition the sum of the values from time 0 through 60 min (which approximates the integral of the scores) was significantly higher on average among the patients biopsy-positive \((P < 0.01\) Wilcoxon rank sum). At 10 min, the groups could be divided by a cutoff breath test score of 5.0 with two false positives and no false negatives. The 10-min score \((>5.0)\) was used as the criteria for a positive breath test (Figures 1 and 2).

The sensitivity of the breath test and ELISA were both 100%. The specificity of breath testing was 86% and the specificity of ELISA was 78%. It is notable that the two patients biopsy-negative for \(C.\)