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Original Article

Comparison between phenol red chromo-endoscopy and a stool rapid immunoassay for the diagnosis of *Helicobacter pylori* in patients with gastritis

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ABSTRACT

Helicobacter pylori infection is a widespread problem all over the world. Non-invasive techniques are demanded for rapid diagnosis and treatment follow up. The aim of this study was to compare the diagnostic value of phenol red chromo-endoscopy and stool (Rapid Strip HpSA) for *H. pylori* detection with reference to histopathology as the gold standard. A total of 80 adult patients with dyspepsia were enrolled on this study. Patients underwent phenol red chromo-endoscopy. Multiple Gastric biopsies were taken and examined for *H. pylori* detection. Stool sample was collected from every patient for Rapid Strip HpSA test. The study included 38 males (47.5%) and 42 females (52.5%) with their ages ranged between 19 and 56 years. According to histopathology, 71 patients (88.8%) were *H. pylori* positive and 9 (11.2%) were negative, most of biopsies showed inflammation with variable degree of activity, which showed significant statistical correlation with the density of *H. pylori* ($P < 0.05$). Phenol red chromo-endoscopy had 90.1% sensitivity, 88.9% specificity, 98.5% positive predictive value (PPV), 53.3% negative predictive value (NPV) and 90% accuracy. Rapid Strip HpSA had a sensitivity 93%, 77.8% Specificity, 97.1% PPV, 58% NPV and 91.3% accuracy. In conclusion; Phenol red chromo endoscopy was more specific and less sensitive than the rapid stool Rapid Strip HpSA® test regarding the detection of *H. pylori* infection with reference to histopathology as a gold standard, yet both showed high diagnostic accuracy; thus they can be used as reliable diagnostic tools for *H. pylori* infection in cases contraindicated for gastric biopsy.

1. Introduction

The prevalence of *Helicobacter pylori* (*H. pylori*) shows large different geographical variations. In various developing countries, more than 80% of the population is *H. pylori* positive, even at young ages [1]. Infections are usually acquired in early childhood in all countries. The higher prevalence among the elderly reflects higher infection rates when they were children rather than infection at late ages [2]. Presence of *H. pylori* is known to be associated with a wide range of gastrointestinal disorders including peptic ulcer, gastric carcinoma, and mucosa-associated tissue lymphoma, thus the diagnosis and eradication of the pathogen is crucial for the management of these diseases [3].

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A variety of highly sensitive and specific tests are available to diagnose *H. pylori* infection; one of them is an invasive method based on endoscopy and gastric biopsies. Histopathology has been considered to be the gold standard test for detection of *H. pylori* infection [4]. Although achieving sensitivity and specificity of >95% in *H. pylori* diagnosis, false negative results are unavoidable due to the uneven distribution of the organism across the gastric mucosa [5]. Furthermore, the detection of *H. pylori* by histopathology relies upon a number of issues including the site, number, and size of gastric biopsies, method of staining, and the level of experience of the examining pathologist [6].

Another method is chromo-endoscopy, which refers to the topical application of stains at the time of endoscopy in an effort to enhance tissue characterization, differentiation, or diagnosis [7], it has been used in the evaluation of various gastrointestinal lesions as Barrett's esophagus, gastric metaplasia and adenocarcinoma. Phenol red is a pH indicator; it detects alkaline pH by a color change from yellow to red, the urease produced by the bacterium catalyzes hydrolysis of urea to NH_3 and CO_2, resulting in an increase in pH. As a result, *H. pylori* can be observed in red stained mucosa after phenol red chromo-endoscopy [8]. The use of phenol red for the diagnosis of *H. pylori* infection was initially described and used by Kohli et al. to assess infection distribution in the gastric mucosa [9].

There are other noninvasive methods for detection of *H. pylori* infection; including serology, urea breath tests (UBTS) and stool antigen test which is based on a rapid immunoassay (Rapid Strip HpSA®) that utilizes a monoclonal *H. pylori* antibody with sensitivity 96.1% (*Meridian Bioscience Europe*). In the last few years, more interest has been paid for the noninvasive techniques [10].

The availability of various tests for detection of gastric *H. pylori* infection with variable efficiency raises the question of which of these methods is more efficient? Thus the current study was done to compare between the diagnostic value of phenol red chromo-endoscopy in *H. pylori* detection and the rapid immunoassay in stool specimens (Rapid Strip HpSA®) with reference to histopathology as the gold standard.

2. Patients and methods

This study was done at the Gastrointestinal Endoscopy Unit; Ain Shams University Hospital in the period between Jan and Jun 2014. The hospital ethical committee approved the study protocol. Informed consent was obtained from each patient enrolled on the study.

80 patients were included in this study. All patients were >18 years old and suffered of dyspepsia, they were referred for upper gastrointestinal endoscopy. Any patient received *H. pylori* eradication therapy up to 6 months before the endoscopic procedure, or those with gastric surgery were excluded.

Upper gastrointestinal endoscopy was carried out for all patients using Olympus XQ-30 endoscope (Olympus Co., Tokyo, Japan) with forward vision. Gastric juice was aspirated to improve visibility during endoscopy. Chromo-endoscopic staining, using a spray type catheter (PW-5L-1; Olympus Co., Tokyo, Japan) was done. 20 ml of phenol red at 0.1% concentration were instilled over the mucosa of the gastric cavity in a homogeneous way in all patients. After a minute the reaction of the mucosa to the application of the dye was visualized. Red staining of the mucosa either diffuse or focal indicated a positive reaction while yellow staining meant negative.

Multiple biopsy samples of both the antrum, corpus, lesser and greater curvatures of gastric mucosa were taken, using standard biopsy forceps. The samples were fixed in 10% formalin and routinely processed. After staining with hematoxylin and eosin, the slides were examined by experienced pathologist who was unaware of the red phenol stain results. Adequacy of the biopsies was evaluated; 77 cases were adequate, in the remaining three cases the biopsy procedure was repeated. The histopathological examination was done to detect the presence and extent of activity (neutrophilic infiltrate), chronic inflammation (lymphocytes and plasma cells infiltrate), surface epithelial atrophy, the intestinal metaplasia and the density of *H. pylori* organism infection. The changes were scored semi-quantitatively as (0 for absent, 1+ for mild, 2+ for moderate or 3+ for severe) according to Sydney' system [11]. Geimsa stain was used in suspicious cases.

H. pylori stool antigen test (HpSA®) was done for every patient; a fresh stool sample was collected from each case and delivered to an expert technician who was unaware of the phenol red stain results; a small portion was emulsified with diluents in a test tube by using an applicator stick. A diluted patient stool sample is dispensed into the sample port of the test device (containing *H. pylori* monoclonal antibody) and the appearance of a pink-red line in the reading window next to the letter T after 5 minutes of incubation at room temperature (20°–26° C) indicated a positive result. The test was considered negative when only one blue colored band (control band) appeared across the white central area of the reaction strip (Meridian Bioscience; Inc.).

3. Statistical analysis

Data was collected and statistically analyzed using SPSS v.18.0 (IBM Corp., Armonk, NY, USA). Quantitative and semi-quantitative variables were described as mean ± SD, while qualitative variables were described as frequency and percentage. Also sensitivity, specificity, positive and negative predictive values (PPV) (NPV), accuracy, positive and negative likelihood ratios, and diagnostic odds ratio were calculated. Concordance correlation coefficient (kappa coefficient) and Kappa index for agreement test were done to estimate the correlation between the two diagnostic methods (phenol red chromo-endoscopy and stool antigen test) with reference to histopathology as the gold standard. Chi-Square test was used to assess the statistical difference between the semi-quantitative histopathological variables and density of *H. pylori* infection. *P* value <0.05 was used to indicate statistical significance.