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ORIGINAL ARTICLE

Performance of a one-step fecal sample-based test for diagnosis of *Helicobacter pylori* infection in primary care and mass screening settings

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Background/Purpose: An alternative screening test is needed to efficiently eradicate *Helicobacter pylori* from a population with prevalent upper gastrointestinal lesions. We evaluated the performance of a new one-step fecal test for *H. pylori* for diagnosis of *H. pylori* infection in Taiwan.

Methods: We developed a fecal test to detect *H. pylori* based on the immunochronomatographic assay and a mixture of monoclonal antibodies. We first recruited symptomatic patients from the primary care setting to evaluate fecal test performance using a reference standard consisting of ^{13}C urea breath test, rapid urease test, and histology. We also compared the performance of the fecal test with that of others. Next, we recruited asymptomatic participants from the mass screening setting to evaluate population attendance for the fecal test and compared its performance with that of ^{13}C urea breath test.

Results: In the primary care setting, 117 patients were recruited; *H. pylori* infection was confirmed in 58 (49.6%). Fecal test sensitivity, specificity, positive and negative predictive

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values, and accuracy were 88.0% [95% confidence interval (CI): 79.6—96.4%], 100%, 100%, 89.4% (95% CI, 82.0—96.8%), and 94% (95% CI, 89.7—98.3%), respectively. Fecal test specificity and positive predictive value were significantly higher than those of the serological test, whereas the sensitivity and negative predictive value were lower than those of the ^{13}C urea breath test ($p < 0.05$). In the mass screening setting, 2720 of 3520 invited individuals participated (77.3%; 95% CI, 76—78.7%); 649 (23.9%) showed positive results. Concordance rate and kappa statistic between the fecal test and ^{13}C urea breath test were 91.7% (563/614; 95% CI, 89.9—94.1%) and 0.78 (95% CI, 0.73—0.84), respectively.

Conclusion: Given the acceptable sensitivity, excellent specificity, and high participation rate to screening, the one-step *H. pylori* stool antigen test is feasible for wide application in the community.

Introduction

Chronic insidious infection by *Helicobacter pylori* can lead to gastritis, peptic ulcer disease, and gastric cancer, and research attention has increased in noninvasive methods that are able to identify carriers at the presymptomatic stage.[1,2] Past efforts based on the serological test or the ^{13}C urea breath test have been limited by the fact that participants are needed to attend the local screening units,[3] professionals are required to perform the test, and, specifically for the former, serological test results may remain positive many years after the elimination of *H. pylori*. Therefore, an alternative screening test is needed to efficiently eradicate *H. pylori* from a community population with prevalent upper gastrointestinal lesions.[4] The ideal screening test should be able to reach asymptomatic patients who do not attend the screening unit, allow sampling of biospecimens to be done at home, and provide easy interpretation of results without the need of technical expertise.

Lessons from colon cancer screening have demonstrated that a fecal sample-based test can possibly meet the above requirements[5]; however, the benefit of such a test for cancer prevention depends on test performance.[6] A fecal sample-based test is also available for the diagnosis of *H. pylori* infection through the detection of *H. pylori* antigens in feces using specific antibodies. However, the performance of *H. pylori* fecal tests varies across studies.[7—9] This heterogeneity is mainly related to the difference in biochemical designs of the tests—that is, an enzyme immunoassay or an immunochromatographic assay—and to the antibody selection, such as monoclonal or polyclonal antibodies. The biochemical design of the immunochromatographic assay satisfies the needs of first-line healthcare workers in the public health centers and primary care clinics who do not have laboratory facilities but must efficiently identify *H. pylori* carriers in the community and initiate treatment. As for antibody selection, the use of monoclonal antibody technology is reported to produce more specific results. However, in the Taiwanese population, which may be considered a typical presentation of Asian populations, the prevalence rate of *H. pylori* infection is high and bacterial strains are heterogeneous, so a false positive result is not uncommon (9—18%) when the fecal test is based on a single monoclonal antibody; as such, a positive fecal test result has an error rate of 10—15% and does not completely guarantee positive *H. pylori* infection.[10—12] Such a shortcoming may become a serious concern when a mass screening program is being administered in the community and may lead to unnecessary workups and treatment subsequently.[13] Therefore, it is worthwhile to develop a new fecal test with specific antibodies tailored to the local *H. pylori* strains.[14]

The purpose of this study was to develop and evaluate the performance of a new one-step fecal test for diagnosis of *H. pylori* infection in Taiwan. We had two priorities in this study: the first was to develop the new one-step fecal test based on the immunochromatographic assay using a mixture of monoclonal antibodies and to evaluate its performance in a primary care setting. Theoretically, the specificity of such a test can be maintained based on the monoclonal characteristics while the coverage of different *H. pylori* strains would be increased by mixing multiple monoclonal antibodies. The second priority was to evaluate whether such a rapid and convenient test could attract asymptomatic individuals to attend mass screening for *H. pylori* infection, while reserving the ^{13}C urea breath test or other invasive tests as second-stage confirmatory tests.

Materials and methods

Participants and study design

This prospective study was conducted to evaluate the performance of the fecal *H. pylori* test in the primary care setting as well as in the mass screening setting. In the first part of the study, we recruited consecutive symptomatic patients referred from the primary care setting and validated the performance of a new one-step *H. pylori* stool antigen test using a reference standard consisting of two invasive tests (rapid urease test and histology) and one noninvasive test (^{13}C urea breath test). In addition to the performance comparison between the fecal test and the above three tests, we further evaluated the value of the fecal test on the diagnosis of active infection, rather than a previous one, by comparing its performance with that of a serological test known to be limited in differentiation.[15]

In the second part of study, we invited asymptomatic individuals who underwent health screening to receive the