Diagnosis of Helicobacter pylori infection by stool antigen determination: a systematic review

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Authors' objectives
To review the diagnostic accuracy of the Helicobacter pylori (H. pylori) stool antigen (SA) test for the diagnosis of H. pylori infection, and to assess the different factors that may influence the performance of the test.

Searching
MEDLINE via PubMed was searched up to December 2000. Abstracts from the International Workshop on Gastroduodenal Pathology and Helicobacter pylori, the United European Gastroenterology Week and the American Digestive Disease Week were searched manually (up to 2000). Review articles and the reference lists from identified studies were also checked.

Study selection
Study designs of evaluations included in the review
No inclusion or exclusion criteria were applied to define the design of the studies included in the review. The included studies were diagnostic accuracy studies (diagnostic cohort).

Specific interventions included in the review
Studies of the H. pylori SA test were included in the review.

Reference standard test against which the new test was compared
No inclusion or exclusion criteria were applied to define a reference standard test. The reference standards adopted in the included studies were the urea breath test, rapid urease test, histology, culture or serology. In most cases a combination of tests was used.

Participants included in the review
No inclusion or exclusion criteria were applied to define more specifically the patient population. Studies of both non-treated and treated patients were included in the review. The characteristics of the patient population were not reported.

Outcomes assessed in the review
No inclusion or exclusion criteria relating to the outcome measures were reported. The main outcomes reviewed were the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV). When not directly stated in the research paper, the PPV and NPV were calculated from the sensitivity, specificity and prevalence of H. pylori infection using Bayes's theorem.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.

Methods of synthesis
How were the studies combined?
The studies were combined using the calculated weighted means and respective 95% confidence intervals (CIs) for the sensitivity, specificity, PPV and NPV. Studies of non-treated patients, treated patients tested at least 4 weeks after treatment, and treated patients tested within 4 weeks of treatment were combined separately.

How were differences between studies investigated?
No formal test for heterogeneity was reported. The technical aspects of the test were discussed in the review (selection of cut-off points, effect of anti-secretory drugs, impact of upper gastrointestinal tract bleeding), but their impact on the specified outcome measures were not investigated systematically.

Results of the review
Seventy-four studies were included: 44 were of non-treated patients (n=4,769), 25 were of treated patients tested at least 4 weeks after treatment (n=2,078), and 5 were of treated patients tested within 4 weeks of treatment (n not stated).

Untreated patients (44 studies): the sensitivity was 92.4% (95% CI: 91, 93), the specificity was 91.9% (95% CI: 91, 92), the PPV was 92.1% (95% CI: 91, 93) and the NPV was 90.5% (95% CI: 90, 91).

Treated patients tested at least 4 weeks after treatment (25 studies): the sensitivity was 88.3% (95% CI: 87, 90), the specificity was 92.0% (95% CI: 91, 93), the PPV was 75.1% (95% CI: 73, 77) and the NPV was 94.8% (95% CI: 94, 96). When the results were combined separately for those studies where testing was exactly 4 weeks post-treatment and for those where testing was 4 to 6 weeks post-treatment, the results were not greatly different.

Treated patients tested less than 4 weeks after treatment (5 studies): the sensitivity, specificity, PPV and NPV were not calculated from these studies and only the results of one of the studies was reported. It was unclear why the other studies were not discussed or their findings pooled.

Cost information
The findings of two preliminary studies suggested a high level of cost-effectiveness for the H. pylori SA test. However, further studies are required.

Authors' conclusions
The H. pylori SA test is an accurate noninvasive test for the diagnosis of H. pylori infection in untreated patients. Further studies are required to confirm the generally favourable results seen with this test when testing for eradication post-treatment. The optimal timing of the post-treatment test also warrants further investigation.

CRD commentary
This systematic review addressed an appropriate question, but failed to specify clear inclusion and exclusion criteria. The literature search was primarily based on MEDLINE and, consequently, may have missed studies. The quality of the studies was not assessed or discussed in the review. The conduct of the review, for example what steps were taken to minimise reviewer bias, was not described. All studies of the H. pylori SA test appear to have been eligible for inclusion, but the analysis failed to investigate the effects of obvious clinical and methodological diversity, with the exception of whether patients had been treated or not. Major sources of clinical diversity (heterogeneity) were ignored in the meta-analysis. These included the reference standard, cut-off points, whether the patients had taken antisecretory drugs, and whether the patients were experiencing gastrointestinal bleeding. The method used to pool the studies was inadequate: simple pooling of weighted means without any consideration of clear sources of heterogeneity is of doubtful value. The reliability of the authors' main conclusion is considerably lessened by these omissions, and the secondary conclusions were based on a more general review of the literature rather than on a meta-analysis of the available data.

Implications of the review for practice and research
Practice: The authors stated that the SA test can be considered an accurate noninvasive test for the diagnosis of *H. pylori* infection in untreated patients.

Research: The authors stated that further studies are required to confirm the generally favourable results seen with this test when testing for eradication post-treatment, and that the optimal timing of the post-treatment test warrants further investigation.

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