Is antimicrobial susceptibility testing necessary before first-line treatment for Helicobacter pylori infection? Meta-analysis of randomized controlled trials

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CRD summary
This well-conducted review concluded that culture-guided triple therapy was more effective than standard triple therapy for the first-line treatment of Helicobacter pylori infection. Evidence appeared to support the authors’ conclusions, but the limited quality of the included studies and potentially limited applicability (to only two countries) may weaken the strength of this evidence.

Authors’ objectives
To compare the efficacy and cost of culture-guided triple therapy with standard triple therapy for the first-line treatment of Helicobacter pylori infection.

Searching
PubMed, EMBASE, the Cochrane Library, Science Citation Index Expanded and Chinese Biomedical Literature Database were searched in December 2008 for studies in any language. Search terms were reported. Reference lists of selected studies were screened.

Study selection
Randomised controlled trials (RCTs) and quasi-RCTs were eligible for inclusion if they compared culture-guided triple therapy/susceptibility test group with standard therapy for the first-line treatment of Helicobacter pylori (H pylori) infection. Standard triple therapy was described as including a proton-pump inhibitor or ranitidine bismuth citrate plus two antibiotics given for seven to 14 days. Culture-guided triple therapy was described as triple therapy where the antibiotics were selected on the basis of susceptibility testing. Eligible trials had to confirm infection based on urea breath testing and confirm H. pylori eradication at least four weeks after treatment completion. The primary review outcome was the H. pylori eradication rate.

Triple therapy regimens in the primary trials included omeprazole or less commonly bismuth citrate and various combinations of the antibiotics amoxicillin, clarithromycin, metronidazole, and/or tinidazole. Trials included both male and female patients; their mean age ranged from 32 to 58 years. Patients in the susceptibility test group were resistant to different combinations of antibiotics (previously given as quadruple therapy that included the above-mentioned drugs plus furazolidone and levofloxacain). Most trials were conducted in Italy; one trial was set in China.

Two reviewers independently conducted searches and resolved disagreements by consensus.

Assessment of study quality
Two reviewers independently assessed trial quality using methods advised by the Cochrane Handbook. Differences were resolved by consensus. Criteria included randomisation, allocation concealment, blinding, reporting of withdrawals/losses to follow-up, and the number of drop-outs.

Data extraction
Two reviewers extracted or calculated numbers of patients with successful eradication of H. pylori on an intention-to-treat and a per-protocol basis. Data were used to calculate risk ratios (RRs) and 95% confidence intervals (CIs).

Methods of synthesis
Pooled risk ratios and 95% confidence intervals were calculated using a fixed-effect model. Heterogeneity was assessed using I².

Results of the review
Five RCTs were included in the review (n=701 patients). One trial reported adequate randomisation. All trials described
withdrawals/losses to follow-up. None of the trials reported clear allocation concealment or blinding. The number of drop-outs ranged from two to 10. The duration of follow-up ranged from four to 12 weeks.

Compared with standard triple therapy, culture-guided triple therapy was associated with a significant increase in *Helicobacter pylori* eradication rates in the intention-to-treat analysis (RR 0.84, 95% CI 0.77 to 0.90) and the per-protocol analysis (RR 0.83, 95% CI 0.78 to 0.89).

No significant heterogeneity was found for either analysis.

**Cost information**

One study reported that the culture-guided triple therapy regimen was associated with overall cost savings of $5 (US dollars) per patient compared with standard therapy.

**Authors' conclusions**

Culture-guided triple therapy was more effective than standard triple therapy for the first-line treatment of *Helicobacter pylori* infection. Antimicrobial susceptibility testing is necessary before first-line treatment of *H. pylori*.

**CRD commentary**

The review question was clearly stated and inclusion criteria were appropriately defined. Several relevant sources were searched and no language restrictions were applied, but no attempts were made to minimise publication bias. Methods were used to minimise reviewer errors and bias during the review process.

Trial quality was assessed and the results were reported; included trials appeared to be of limited quality. Appropriate methods were used for the meta-analyses and heterogeneity was assessed. Some weaknesses of the review were discussed including the potentially limited generalisability resulting from trials set in only two countries. Few patient details were reported and evidence was based on small number of trials.

The review was generally well-conducted. Evidence appeared to support the authors’ conclusions, but the limited quality of the included trials (which was acknowledged by the authors) and potentially limited generalisability may weaken the strength of this evidence.

**Implications of the review for practice and research**

**Practice:** The authors acknowledged that review findings may not apply to countries other than those in which the included trials were based (Italy and China). The authors stated that clinicians should note that antimicrobial susceptibility testing should be taken into account when selecting treatment for *H. pylori* infections, especially in areas with high rates of resistance to antibiotics.

**Research:** The authors stated that further well-designed, double-blind RCTs are required to evaluate culture-guided therapy in different geographical regions.

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