Eradication of helicobacter pylori: an objective assessment of current therapies

Penston J G, McColl K E

Authors' objectives
To provide an objective assessment of the relative merits of different therapies for the eradication of Helicobacter pylori (H. pylori) based on a comprehensive examination of all of the currently available literature.

Searching
MEDLINE was searched from 1990 to 1995 and conference proceedings of the British Society of Gastroenterology, the American Association of Gastroenterology, the United European Gastroenterology Week, the World Congress of Gastroenterology, and the Annual International H. pylori meetings were all searched between 1992 and 1995.

Study selection
Study designs of evaluations included in the review
Full papers or abstracts reporting controlled or uncontrolled studies were included. Studies had to comprise at least 1 month's follow-up of participants after stopping eradication therapy, and had to report eradication rates per treatment arm, in order to be included. Reviews, studies considered to have inadequate data or with treatment regimes unspecified, and duplicate publications, were excluded.

Specific interventions included in the review
Standard triple therapy (bismuth plus a nitroimidazole plus either amoxycillin or tetracycline), with or without additional anti-secretory drugs; dual therapy with an anti-secretory drug (either proton pump inhibitors or H2-receptor antagonists) plus either amoxycillin or clarithromycin; triple therapy with an anti-secretory drug (either proton pump inhibitors or H2-receptor antagonists) plus any two of amoxycillin, clarithromycin or a nitroimidazole.

Participants included in the review
People undergoing treatment for H. pylori infection were included.

Outcomes assessed in the review
Eradication rates (defined as the absence of H. pylori on testing at least 1 month after stopping therapy), frequency of side effects, simplicity of the regime (number of tablets per day and duration of treatment) and cost.

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

Assessment of study quality
The authors do not state that they assessed validity, although studies using an intention-to-treat analysis were analysed separately from the overall results.

Data extraction
Pooled eradication rates were calculated for each treatment group and for individual therapeutic regimes. The method of data extraction is not explained (i.e. whether more than one reviewer extracted data independently).

Methods of synthesis
How were the studies combined?
The eradication rates of treatment arms of the same regimes were pooled to give summary efficacy rates. Results of controlled studies were summarised in a narrative format.
How were differences between studies investigated?
Studies with intention-to-treat data were analysed separately.

Results of the review
A total of 352 studies were included.

Dual therapy.

Omeprazole plus amoxycillin (121 studies with 5725 patients): the overall eradication rate was 61% (95% confidence interval (CI) 59-62%), and 59% (95% CI 58-61%) by intention-to-treat analysis. In general, eradication rates increased as the total daily dose of omeprazole increased. Omeprazole plus clarithromycin (37 studies with 1837 patients): overall eradication rate 70% (95% CI 68-72%) and by intention-to-treat analysis 68% (95% CI 65-70%). Factors associated with lower eradication rates were lower doses of proton pump inhibitor, dual therapy for less than 2 weeks and pre-treatment with omeprazole. Other dual therapies with anti-secretory drugs (31 studies): none of the other regimes reviewed produced eradication rates greater than 68%.

Triple therapy.

Standard triple therapy (143 studies with 7979 patients): the overall eradication rate was 81% (95% CI 81-82%) and 78% (95% CI 77-79) by intention-to-treat analysis. Proton pump inhibitor therapy (79 studies with 5513 patients): there was no difference between the overall eradication rate (87%: 95% CI 86-87%) and that of the intention-to-treat analysis (86%: 95% CI 85-87). H2-receptor antagonist triple therapy (23 studies with 814 patients): overall eradication rate 72% (95% CI 68-75%) and by intention-to-treat analysis 80% (95% CI 77-84%).

Comparative studies.

Dual therapies: there were higher eradication rates with omeprazole plus clarithromycin compared with omeprazole plus amoxycillin. There were inconclusive results for the comparison between omeprazole plus amoxycillin and ranitidine plus amoxycillin.

Dual therapy versus triple therapy.

In general, eradication rates were higher after triple therapy compared with dual therapy. Triple therapy: proton pump inhibitor triple therapy produced higher eradication rates, compared with standard triple therapy. Standard triple therapy without anti-secretory drugs achieved higher rates of eradication, compared with H2-receptor antagonist triple therapy. Higher rates of eradication were found with proton pump inhibitor triple therapy, compared with H2-receptor antagonist triple therapy.

Adverse effects.

Dual therapy: the overall frequency of side-effects during dual therapy with anti-secretory drugs plus a single antibiotic was 18% (3% of patients withdrew due to side effects). Omeprazole plus amoxycillin was associated with a lower frequency of side effects, compared with omeprazole plus clarithromycin, although the proportions of withdrawals due to side effects were similar.

Triple therapy: overall, one-third of patients experienced side-effects, necessitating withdrawal in 3% of patients. Proton pump inhibitor triple therapy was least likely to produce symptoms resulting in withdrawal of treatment.

Comparative studies: dual therapy: side-effects were more frequent with clarithromycin plus a proton pump inhibitor compared with amoxycillin plus a proton pump inhibitor. Side effects were more frequent with triple therapy compared with dual therapy.

Cost information
The relative costs of different regimes are tabulated. For a full discussion of the economic aspects of this study see Database of Abstracts of Reviews of Effects (DARE)
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**Authors' conclusions**
The preferred treatment for the eradication of H. pylori is proton pump inhibitor triple therapy. In particular, low-dose therapy with omeprazole plus clarithromycin plus tinidazole achieves high eradication rates, with a relatively simple regime associated with few side-effects and at modest expense.

**CRD commentary**
The research question and inclusion/exclusion criteria for primary studies are clearly presented. Some details of primary studies are provided in tables, but greater detail would have been useful, particularly relating to characteristics of participants and the methodological quality of studies.

Sources for the literature search are explained, but there is no mention of including languages other than English, nor of trying to locate unpublished data, which may have meant that relevant material was omitted from the review. Authors could have used statistical techniques such as the odds ratio or relative risk to pool data from controlled studies. Although the authors' conclusion appears to reflect the reported evidence, it would be useful to know more about the efficacy of different regimes within various subgroups of people with H. pylori disease.

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- Enzyme Inhibitors /adverse effects /therapeutic use
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**Record Status**
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.