Pooled analysis of anti-Helicobacter pylori treatment regimens

Unger P, Berstad A

Authors' objectives
To assess the effectiveness of treatment regimes used to eradicate Helicobacter pylori (H. pylori).

Searching
MEDLINE was searched from 1985 to 1995; no search strategy was outlined. Other published data from annual meetings were also scrutinised, specifically: Digestive Disease Week (USA) from 1989 to 1995, the European Study Group on H. pylori-related diseases from 1989 to 1995, and United European Gastroenterology Week from 1993 to 1995.

Study selection
Study designs of evaluations included in the review
Studies were included if they met the following criteria: published as a full article or abstract; defined protocol; defined treatment regimen; defined methods of assessment for H. pylori; and, the number of patients in treatment arms, as well as those cured from H. pylori were stated.

Specific interventions included in the review
Seventeen combinations of treatment were assessed in the review: bismuth-nitroimidazole-tetracycline; bismuth-nitroimidazole-amoxicillin; histamine H2 antagonist-bismuth-nitroimidazole-tetracycline; histamine H2 antagonist-bismuth-nitroimidazole-amoxicillin; histamine H2 antagonist-nitroimidazole-amoxicillin; omeprazole-amoxicillin; omeprazole-clarithromycin; lansoprazole-amoxicillin-nitroimidazole; lansoprazole-amoxicillin-clarithromycin; lansoprazole-nitroimidazole-clarithromycin; omeprazole-amoxicillin-nitroimidazole; omeprazole-amoxicillin-clarithromycin; omeprazole-nitroimidazole-clarithromycin; quinolone combinations; rifaximin combinations; augmentin, ecabet sodium, plaunotol combinations; and sucralfate combinations.

Participants included in the review
Patients who were H. pylori positive at entry to study were included.

Outcomes assessed in the review
The outcome was H. pylori eradication (no H. pylori found 4 weeks or more after cessation of therapy).

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 report the criteria used to assess validity, or how the validity assessment was performed.

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

Methods of synthesis
How were the studies combined?
Pooled eradication rates with confidence intervals (CIs) were calculated, with the CIs treated as if the pooled data were one study only and then arbitrarily enlarged by 50% (credibility intervals).
How were differences between studies investigated?
Sensitivity analysis of differences in dose, dosage and duration was performed for some treatment groups, placing doubt on the statistical analysis of the pooled data.

Results of the review
The review included 307 studies (patient numbers unknown). The number of studies included for the different treatment groups were: 50 studies (2,876 patients) of bismuth-nitroimidazole-tetracycline; 30 studies (1,131 patients) bismuth-nitroimidazole-amoxicillin; 4 studies (230 patients) of histamine H2 antagonist-bismuth-nitroimidazole-tetracycline; 3 studies (128 patients) of histamine H2 antagonist-bismuth-nitroimidazole-amoxicillin; 15 studies (607 patients) of histamine H2 antagonist-nitroimidazole-amoxicillin; 132 studies (3,996 patients) of omeprazole-amoxicillin; 43 studies (patient numbers unknown) of omeprazole-clarithromycin; 4 studies (57 patients) of lansoprazole-amoxicillin-nitroimidazole; 1 study (25 patients) of lansoprazole-amoxicillin-macrolide; 5 studies (136 patients) of lansoprazole or pantoprazole-nitroimidazole-macrolide; 22 studies (1,726 patients) of omeprazole-amoxicillin-nitroimidazole; 17 studies (902 patients) of omeprazole-amoxicillin-macrolide; 20 studies (824 patients) of omeprazole-nitroimidazole-macrolide; 3 studies (38 patients) of quinolone combinations; 3 studies (27 patients) of rifaximin combinations; 5 studies (106 patients) of augmentin, ecabet sodium, plaunotol combinations; and 3 studies (152 patients) of sucralfate combinations.

The eradication rates for the different treatment groups were: bismuth-nitroimidazole-tetracycline, 82% (95% CI: 80, 84); bismuth-nitroimidazole-amoxicillin, 75% (95% CI: 71, 79); histamine H2 antagonist-bismuth-nitroimidazole-tetracycline, 68% (95% CI: 59, 77); histamine H2 antagonist-bismuth-nitroimidazole-amoxicillin, 65% (95% CI: 53, 77); histamine H2 antagonist-nitroimidazole-amoxicillin, 65% (95% CI: 59, 71); omeprazole-amoxicillin, 54% (95% CI: 51, 57); omeprazole (twice daily)-amoxicillin, 62% (95% CI: 58, 64); omeprazole-clarithromycin, 66% (95% CI: 62, 70); lansoprazole-amoxicillin-nitroimidazole, 82% (95% CI: 67, 97); lansoprazole-amoxicillin-macrolide, 80% (95% CI: 64, 96); lansoprazole or pantoprazole-nitroimidazole-macrolide, 82% (95% CI: 72, 92); omeprazole-amoxicillin-nitroimidazole, 84% (95% CI: 81, 87); omeprazole-amoxicillin-macrolide, 85% (95% CI: 82, 89); omeprazole-nitroimidazole-macrolide, 87% (95% CI: 83, 90); quinolone dual therapies, 8% (95% CI: 0, 21); quinolone triple therapies, 69% (95% CI: 60, 78); rifaximin combinations, 30% (95% CI: 4, 56); anti-ulcer triples, 57% (95% CI: 43, 70); anti-ulcer quadruples, 50% (95% CI: 25, 75); and sucralfate combinations 61% (95% CI: 49, 73).

Authors' conclusions
The ideal therapy directed towards H. pylori is still lacking. The most effective anti-H. pylori treatment strategies according to this analysis are omeprazole, nitroimidazole and macrolide or omeprazole, nitroimidazole and amoxicillin. Short treatment course and twice daily dosing of both omeprazole and antimicrobials appear to be important. Bismuth-based triple therapies are effective but sensitive to compliance factors, and are slightly inferior to omeprazole-clarithromycin-based triple regimens in the pooled analysis. In addition, it should be noted that the analysis does not evaluate the effect of resistance to antimicrobials on efficacy.

CRD commentary
The objective, interventions, participants, outcomes and study inclusion criteria are adequately discussed in the review. The basic literature search is outlined, though the search strategy is not included. Excluded from the review are the criteria for assessing validity of the primary studies and the procedures for judging relevance, validity and extracting data from the primary studies. The sensitivity analysis assessing the differences between the studies indicates that caution should be taken when interpreting the pooled analysis. In addition, the arbitrary enlargement of the pooled CIs to form 'credibility intervals' should be noted in assessing the strength of the evidence. An error was evident in the tables of data.

Bibliographic details
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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.