Systematic review: rabeprazole-based therapies in Helicobacter pylori eradication

CRD summary
This review assessed rabeprazole-based treatments for Helicobacter pylori (H. pylori) eradication. This well-conducted review found no statistically significant difference in rates of H. pylori eradication between rabeprazole and other proton-pump inhibitors when combined with antibiotics. However, the authors’ conclusions of equivalence of efficacy are inappropriate.

Authors’ objectives
To assess the effects of rabeprazole-based treatments in Helicobacter pylori (H. pylori) eradication, and to compare rabeprazole plus antibiotics with other proton-pump inhibitors (PPIs) plus antibiotics.

Searching
The Cochrane Controlled Trials Register (Issue 3, 2002), MEDLINE (1966 to September 2002), EMBASE (1988 to September 2002) and CINAHL (1982 to September 2002) were searched; the search terms were reported. In addition, abstracts from the International Workshop on Gastroduodenal Pathology and Helicobacter pylori, American Digestive Disease Week and United European Gastroenterology Week were handsearched (1995 to 2002). Abstracts were included. The reference lists in identified studies were also screened. Studies published in any language were eligible.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion in the meta-analysis. No criteria were specified for studies of rabeprazole to be excluded from the meta-analysis.

Specific interventions included in the review
Studies of rabeprazole plus antibiotics were eligible for inclusion, as were studies that compared rabeprazole plus antibiotics with other PPIs plus antibiotics. The included studies used rabeprazole (10 to 80 mg/day) plus one antibiotic (levofloxacin, clarithromycin or amoxicillin) and rabeprazole plus two antibiotics, most commonly amoxicillin plus clarithromycin (other triple-therapy regimens used clarithromycin plus metronidazole, clarithromycin plus tinidazole, amoxicillin plus metronidazole, amoxicillin plus levofloxacin, levofloxacin plus tinidazole, levofloxacin plus clarithromycin). Regimens containing rabeprazole were compared with regimens containing omeprazole or lansoprazole. The studies used antibiotics for 3 to 14 days.

Participants included in the review
The inclusion criteria were not explicitly stated in terms of the participants. The patients in the included studies had H. pylori and peptic ulcer disease or non-ulcer disease.

Outcomes assessed in the review
Only studies clearly stating the number of treated patients and the number of patients with successful H. pylori eradication were eligible for inclusion.

How were decisions on the relevance of primary studies made?
Two reviewers independently conducted the searches and selected studies. Any disagreements were resolved by consensus.

Assessment of study quality
Studies were assessed and scored using the 5-point Jadad scale which considers randomisation, blinding and withdrawals. Two reviewers independently assessed validity and resolved any disagreements through discussion.
Data extraction
Two reviewers independently extracted the data and resolved any disagreements through discussion. The data extracted included treatment regimens, sample size, duration of antibiotic treatment and eradication rates. Some results were extracted on an intention-to-treat basis, while other studies presented only per protocol results. Authors of abstracts or studies with incomplete or missing information were contacted for complete data. For studies reported in multiple publications, only the most recent data were extracted. For each study, the percentage of patients with eradication of H. pylori was extracted for each treatment arm.

Methods of synthesis
How were the studies combined?
Weighted mean H. pylori eradication rates and 95% confidence intervals (CIs) were calculated for regimens containing rabeprazole. Studies that clearly reported the number of treated patients and the number of patients with successful H. pylori treatment, and used the same type and dose of antibiotics in both treatment arms, were combined in a meta-analysis. Pooled odds ratios (ORs) and 95% CIs for rabeprazole compared with other PPIs were calculated using fixed-effect and random-effects models.

How were differences between studies investigated?
For all studies, a subgroup analysis was used to calculate the effects of rabeprazole according to the number of antibiotics co-prescribed (one or two), the type of antibiotic, the dose of rabeprazole (low dose, 10 mg twice daily, b.d.; high dose, 40 mg/day) and the duration of treatment.

For the meta-analysis, statistical heterogeneity was assessed using the chi-squared statistic and results from fixed-effect and random-effects models were reported. A subgroup analysis was used to calculate the effects of rabeprazole according to the number of antibiotics co-prescribed, the type of PPI (omeprazole or lansoprazole) and the dose of rabeprazole. It was not possible for the authors to explore the influence of quality scores on the results as they had intended, as only one RCT scored 3 or more on the Jadad scale.

Results of the review
Overall, 7 studies used rabeprazole plus one antibiotic (451 patients) and 37 studies used rabeprazole plus two antibiotics. Twelve RCTs (2,226 patients) were used in the meta-analysis.

All studies.
Eradication rate with rabeprazole plus one antibiotic: the weighted mean eradication rate with rabeprazole plus amoxicillin for 14 days was 73% (95% CI: 69, 77).

Eradication rate with rabeprazole plus two antibiotics: the weighted mean eradication rate with rabeprazole plus amoxicillin plus clarithromycin was 44% (95% CI: 38, 49) for 3 days, 72% (95% CI: 64, 80) for 5 days, 78% (95% CI: 76, 79) for 7 days, and 75% (95% CI: 69, 80) for 10 days. The weighted mean eradication rate with low-dose rabeprazole (20 mg/day) plus amoxicillin plus clarithromycin for 7 days was 81% (95% CI: 78, 83) and for high-dose rabeprazole (40 mg/day) plus amoxicillin plus clarithromycin was 75% (95% CI: 73, 77).

Meta-analysis of rabeprazole versus other PPIs.
There was no statistically significant difference in H. pylori eradication rates between regimens containing rabeprazole and regimens containing other PPIs; the OR (fixed-effect model) was OR 1.16 (95% CI: 0.94, 1.43). No statistically significant heterogeneity was detected (P=0.5).

Low-dose rabeprazole (7 RCTs): the meta-analysis showed no statistically significant difference between regimens containing low-dose rabeprazole (10 mg b.d.) compared with standard doses of PPIs (20 mg b.d. omeprazole or 30 mg b.d. lansoprazole); the OR (random-effects model) was 1.21 (95% CI: 0.75, 1.95). Slight statistically significant heterogeneity was detected (P=0.087).
The results from other subgroup analyses were reported in the paper.

**Authors’ conclusions**
When combined with antibiotics, rabeprazole has similar H. pylori eradication rates to omeprazole and lansoprazole. Low-dose rabeprazole (10 mg b.d.) plus two antibiotics may adequately eradicate H. pylori.

**CRD commentary**
The review question was clear in terms of the study design, intervention and outcomes. Several relevant sources were searched and the search terms were stated. Attempts were made to limit language and publication bias. Two reviewers independently selected the studies, assessed validity and extracted the data, and this reduced the potential for bias and errors. Validity was assessed using specified, established criteria and scores were reported for studies included in the meta-analysis. Some information on the included studies was presented in tabular format, but there was no description of the methods used to assess H. pylori eradication and no comment on the validity of the methods used to measure this. The data were appropriately combined in a meta-analysis and statistical heterogeneity was assessed. This was a well-conducted review. However, the authors’ conclusions are inappropriate. The review provided evidence of no statistically significant difference between rabeprazole and other PPI agonists in terms of H. pylori eradication, rather than equivalence of efficacy of the two treatments.

**Implications of the review for practice and research**
Practice: The authors did not state any implications for practice.

Research: The authors stated that there is a need to evaluate the cost-effectiveness of using low doses of rabeprazole plus two antibiotics for eradicating H. pylori. They also stated the role of the CYP2C19 genotype on H. pylori eradication rates needs evaluation.

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