Sind Protonenpumpeninhibitoren den H2-Rezeptorantagonisten im Rahmen der H.-pylori-Eradikationstherapie überlegen: Metaanalyse vorliegender Parallelgruppenvergleiche

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Authors' objectives
The authors aimed to assess the available parallel-group eradication studies with proton-pump inhibitors (PPIs) and H2-receptor antagonists, and to compare Helicobacter pylori (H. pylori) eradication rates for both classes of acid lowering drugs.

Searching
A search of MEDLINE was combined with handsearches of the American Journal of Gastroenterology, Digestion, Digestive Diseases and Sciences, Gut, Gastroenterology and Zeitschrift fuer Gastroenterologie for the years 1984 to 1995. In addition, the abstracts of the annual conferences of the American Gastroenterological Society and the British Society of Gastroenterology, and specific H. pylori conferences were screened.

Study selection
Study designs of evaluations included in the review
Studies that compared the effectiveness of PPIs and H2-receptor antagonists directly were eligible for the review. To be eligible, the difference in the number of patients in the treatment arms could not exceed 20%. The number of patients, the eradication rates, and the type and duration of treatment had to be stated for the study to be included in the review.

All of the included studies randomised the patients to the treatment groups.

Specific interventions included in the review
Studies that compared PPIs with H2-receptor antagonists were eligible for the review. The PPI used in the included studies was omeprazole (20 to 40 mg/day). The H2-receptor antagonist used was, in most cases, ranitidine (150 mg twice daily to 300 mg twice daily), and in one case, nizatidine (300 mg twice daily). The included studies administered additional antibiotics (one or a combination of two) between 7 and 15 days.

Participants included in the review
Patients treated for H. pylori eradication participated in the individual studies.

Outcomes assessed in the review
The percentage of eradication success using a urease-rapid-test was assessed. To be eligible for the review, the studies had to assess the outcome 4 weeks after the end of the treatment, at the earliest.

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. Data were extracted on the sample sizes, design features of the study, the type and dose of acid suppressors, the types and duration of treatment for all antibiotics, and the eradication rates.
Methods of synthesis
How were the studies combined?
The studies with H2-receptor antagonists were compared with PPIs using non-parametric tests. In addition, the influence of both variables on eradication success was analysed in a logistic regression. The mean eradication rates and corresponding confidence intervals (CIs) were calculated.

How were differences between studies investigated?
The durations of therapy (less than 10 days versus more than 10 days) and antibiotic administration (one versus two antibiotics) were compared using non-parametric tests. Both variables were also analysed in a logistic regression predicting eradication success. The mean eradication rates and corresponding CIs for these distinctions were also compared.

Results of the review
The review was based on seven randomised controlled trials (RCTs), providing data for eight comparisons with data from 538 patients.

Eradication rates.

H. pylori eradication was successful for 77.5% of the patients (95% CI: 74.0, 81.0; 8 parallel-group trials).

H2-receptor antagonist versus PPI.
The H. pylori eradication rate was 78.6% (95% CI: 73.6, 83.5) for PPI-treated patients and 76.5% (95% CI: 71.4, 81.5) for those treated with H2-receptor antagonists; the difference was not statistically significant. The differences in eradication rate between the two acid lowering drugs ranged from 1 to 20% in the individual studies, with varying advantages for both drug classes. The authors reported that the logistic regression showed no difference in the eradication rates with H2-receptor antagonists and PPIs (P>0.4), even when adjusting for the duration of therapy and the number of antibiotics.

One versus two antibiotics.
The average eradication rate was 70.4% (95% CI: 65.3, 75.6) for treatment protocols with one antibiotic (4 studies) and 86.5% (95% CI: 82.1, 90.8) for protocols with two antibiotics (4 studies); the difference was significant (P<0.001). The eradication rates varied widely in the studies with only one antibiotic; in the studies with two antibiotics, all the eradication rates were above 80%. The logistic regression showed a significant influence of the number of antibiotics on the eradication rate (P<0.0005). Within the two study groups, the difference in eradication rates due to the type of acid lowering drug was not significant.

Duration of therapy.
In the one study with a treatment duration of less than 10 days, the eradication rates were 92% (95% CI: 80.8, 97.8) for the PPIs and 86% (95% CI: 73.2, 94.2) for the H2-receptor antagonists; the difference was not significant. In the long-term therapy studies (7 comparisons), the average eradication rate was 75.5% for PPIs and 74.3% for H2-receptor antagonists (95% CI reported as 69.7, 81.2 for both means); the difference was not statistically significant.

Authors’ conclusions
The H. pylori eradication rates for treatments containing an acid lowering drug in combination with one or two antibiotics are not different for PPIs or H2-receptor antagonists.

CRD commentary
This was a review with an elaborate search strategy and carefully selected studies. The authors conducted many handsearches, successfully identifying conference papers as well as usual publications, restricting possible publication
bias. The authors gave no details on the process, i.e. how objectivity was maintained while selecting the studies for the review.

The review was based on sound evidence with all the included studies being RCTs. The authors did not explain why they did not apply classic meta-analyses models to compare the effectiveness of the two acid lowering drugs. It was unclear whether there were attempts to weight the studies according to the study size, or quality aspects, when pooling the results in the chosen analysis.

There were a few incongruities in the numbers reported (i.e. the eradication rates reported in the abstract and the result section differed slightly; identical CIs for slightly different means), which did not help in evaluating the evidence. The variance in the study results might have been explored even further: the authors investigated the effect of the number of given antibiotics thoroughly, but not the type of H2-receptor antagonists, i.e. the highest rate and the greatest difference in eradication rates occurred in a trial where nizatidine, rather than ranitidine, was administered. The dose of acid lowering drug was not statistically analysed, although it was considered in the discussion.

No other information than the significance level of two variables in the regression analysis was presented for the supposedly multivariate analysis; this makes it difficult to evaluate the results.

Overall, the conclusion should, strictly speaking, be that there was no evidence of a difference in the efficacy of the two acid lowering drugs. The conclusion was plausible judging from the individual study results, but an additional more traditional meta-analysis would have given the evaluation of the evidence more strength.

**Implications of the review for practice and research**
Practice: The authors stated that the choice between H2-receptor antagonists and PPIs in combination with antibiotics for H. pylori eradication therapy is without clinical relevance.

Research: The authors did not state any implications for further research.

**Bibliographic details**

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**Other publications of related interest**

**Indexing Status**
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**MeSH**
Anti-Ulcer Agents /adverse effects /therapeutic use; Enzyme Inhibitors /adverse effects /therapeutic use; Gastric Acidity Determination; Helicobacter Infections /drug therapy; Helicobacter pylori /drug effects; Histamine H2 Antagonists /adverse effects /therapeutic use; Humans; Omeprazole /adverse effects /therapeutic use; Proton Pump Inhibitors; Randomized Controlled Trials as Topic; Ranitidine /adverse effects /therapeutic use

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Record Status
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