Is there an increased risk of GERD after Helicobacter pylori eradication? A meta-analysis

Yaghoobi M, Farrokhyar F, Yuan Y, Hunt RH

CRD summary
The authors concluded that there was no association between Helicobacter pylori eradication and the development of new cases of gastro-oesophageal reflux disease in dyspeptic patients; however, in cohort studies there appeared to be a two-fold higher risk of erosive gastro-oesophageal reflux disease in patients with peptic ulcer disease. The review was generally well conducted and the authors’ conclusions appear appropriate.

Authors' objectives
To investigate whether Helicobacter pylori eradication is associated with the development of gastro-oesophageal reflux disease in patients with no history of gastro-oesophageal reflux disease.

Searching
Medical databases (not specified) were searched from 1983 to February 2007 for articles in any language. Search terms were reported. Congress abstracts and sources of unpublished data were also searched.

Study selection
Randomised controlled trials (RCTs) and cohort studies of patients with Helicobacter pylori (H. pylori) infection and no evidence of gastro-oesophageal reflux disease, with a follow-up of up to 24 months, were eligible for inclusion. RCTs had to compare H. pylori eradication therapy with placebo, and had to test all patients for H. pylori eradication by histology, culture or urea breath test between one and three months after therapy before categorising patients into H. pylori positive or negative, and then patients had to be followed-up for the development of new gastro-oesophageal reflux disease cases. Cohort studies had to be treated with H. pylori eradication therapy before being categorised into H. pylori positive or negative, and then followed-up to detect new gastro-oesophageal reflux disease cases. Gastro-oesophageal reflux disease was defined as more than one incidence of heartburn per week as described by the patient or found by endoscopic erosion in the distal oesophagus. Studies had to provide symptomatic or endoscopic assessment before and after H. pylori eradication. H. pylori-resistant populations and paediatric populations were excluded. Studies were also excluded if they did not provide heartburn or endoscopic outcomes.

The included studies where of patients with peptic ulcer disease or functional dyspepsia. The mean age of patients ranged from 40 to 55 years and the majority were male (where reported). The rate of alcohol use varied from 19 to 54% and the rate of smoking varied from 9 to 66% (where reported).

The authors did not state how many authors undertook the selection process, but did state that Kappa scores were calculated to determine reviewer agreement, indicating that at least two authors were involved in study selection.

Assessment of study quality
RCT quality was assessed using the Jadad 5-point scale. Cohort studies were assessed using the Newcastle-Ottawa scale, which gave a score out of 9.

Two authors performed quality assessment and a third reviewer was consulted if required.

Data extraction
Two authors independently extracted the data to calculate odds ratios (OR), and 95% confidence intervals (CIs). A third author was consulted if necessary.

Methods of synthesis
The pooled odds ratios, together with 95% confidence intervals, were calculated using a fixed-effects meta-analysis, or a random-effects meta-analysis if statistical heterogeneity was detected. Statistical heterogeneity was assessed using the I^2 statistic.
Subgroup analysis of RCTs versus cohort studies, and erosive gastro-oesophageal reflux disease versus symptomatic gastro-oesophageal reflux disease were undertaken.

Sensitivity analysis was undertaken for RCTs and cohorts studies separately, based on study quality (high versus low) and length of follow-up (under 12 months versus 12 months or longer).

**Results of the review**

Twelve studies were included in the review (n=4,058 patients): seven RCTs and five cohort studies. The length of follow-up ranged from six to 24 months. The quality of RCTs varied from 2 to 5 out of 5 points; the quality of cohort studies ranged from 4 to 7 out of 9 points.

There were no statistically significant differences between persistent *Helicobacter pylori* (*H. pylori*) group compared with the *H. pylori*-eradicated group in terms of the frequency of post-eradication gastro-oesophageal reflux disease in the RCTs (six RCTs and five cohort studies on erosive gastro-oesophageal reflux disease; n=4,058 patients; $I^2=27$).

Subgroup analyses found no statistically significant differences between persistent *Helicobacter pylori* groups in RCTs using erosive gastro-oesophageal reflux disease as the outcome (six RCTs; n=2,085 patients; $I^2=31\%$), RCTs using symptomatic gastro-oesophageal reflux disease as the outcome (five RCTs; n=760 patients; $I^2=31\%$), or the five cohort studies (n=1,895 patients; $I^2=35\%$).

In patients with peptic ulcer disease, there was no difference between the frequency of post-eradication gastro-oesophageal reflux disease in the *H. pylori*-eradicated group compared with the persistent *H. pylori* group in the RCTs (five RCTs; $I^2=16\%$). In the four cohort studies, there was a statistically greater rate of post-eradication gastro-oesophageal reflux disease in the *H. pylori*-eradicated group compared with the persistent *H. pylori* group with peptic ulcer disease (OR 2.04, 95% CI 1.08 to 3.85; $I^2=6\%$).

**Sensitivity analysis:** There was no difference between the frequency of post-eradication gastro-oesophageal reflux disease in the *H. pylori*-eradicated group compared with the persistent *H. pylori* group in either the RCTs or cohort studies grouped by quality (high versus low) or length of follow-up (under 12 months versus 12 months or longer). There was evidence of statistical heterogeneity in the sensitivity analysis of high versus low quality cohort studies ($I^2=73\%$).

**Authors’ conclusions**

There was no association between *Helicobacter pylori* eradication and the development of new cases of gastro-oesophageal reflux disease in the population of dyspeptic patients. However, in cohort studies there appeared to be a two-fold higher risk of erosive gastro-oesophageal reflux disease in patients with peptic ulcer disease.

**CRD commentary**

Inclusion criteria for the review were clearly defined, but the authors did not state which databases were searched. There was no restriction by language, which should have minimised language bias, and the authors stated that sources of unpublished studies were sought, although publication bias was not formally assessed. Two authors performed study selection, data extraction and quality assessment, minimising the potential for error and bias in the analysis.

Quality assessment indicated the variable quality of the included studies, which the authors acknowledged. Few details were provided on patient characteristics, but the authors acknowledged this limitation and the potential for clinical differences. Studies were combined using meta-analysis and subgroup and sensitivity analyses were undertaken, which was appropriate.

Overall, the review was generally well conducted and the authors’ conclusions appear appropriate.

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

**Practice:** The authors stated that they did not recommend waiving *H. pylori*-eradication therapy in patients with peptic ulcer disease for the sake of preventing gastro-oesophageal reflux disease.
Research: The authors stated that studies with longer follow-up (over two years) might help determine the development of gastro-oesophageal reflux disease in the long term. They also suggested that analysis of individual patient data might help in detecting which patients are at higher risk of developing gastro-oesophageal reflux disease after H. pylori eradication.

Funding
None.

Bibliographic details

PubMedID
20087334

DOI
10.1038/ajg.2009.734

Original Paper URL
http://www.nature.com/ajg/journal/v105/n5/abs/ajg2009734a.html

Indexing Status
Subject indexing assigned by NLM

MeSH
Anti-Bacterial Agents /therapeutic use; Drug Therapy, Combination; Esophagitis, Peptic /epidemiology /etiology /physiopathology; Esophagoscopy; Female; Follow-Up Studies; Gastroesophageal Reflux /epidemiology /etiology /physiopathology; Helicobacter Infections /complications /diagnosis /drug therapy; Helicobacter pylori /drug effects /isolation & purification; Humans; Incidence; Male; Randomized Controlled Trials as Topic; Risk Assessment; Severity of Illness Index

AccessionNumber
12010004218

Date bibliographic record published
14/07/2010

Date abstract record published
08/09/2010

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.