Platelet count response to H. pylori treatment in patients with immune thrombocytopenic purpura with and without H. pylori infection: a systematic review

CRD summary
This review concluded that eradication therapy in immune thrombocytopenia purpura should be reserved for H. pylori positive patients. The authors have drawn relatively cautious conclusions based on a small number of poor-quality non-randomised studies and these conclusions should be considered tentative.

Authors’ objectives
To determine the effect of Helicobacter pylori (H. pylori) eradication therapy on platelet count response in patients with immune thrombocytopenia purpura.

Searching
Published trials were identified through a search of MEDLINE, EMBASE and Cochrane Central Register of Controlled Trials (CENTRAL). Search dates were not reported. Abstracts from the American Society of Hematology were searched (2003 to 2007). Experts were contacted for additional references and handsearching was undertaken. Search terms were reported. No language restrictions were applied. Two reviewers independently searched the databases.

Study selection
Studies that described platelet count response following H. Pylori eradication in patients with immune thrombocytopenia purpura (ITP) were eligible for inclusion. Studies were required to report platelet counts for both infected and non-infected patients. Eradication therapy had to include at least one antibiotic and a proton pump inhibitor. Studies that reported only H. pylori-positive patients and case reports of fewer than five patients were excluded. Outcomes included platelet count response, bleeding and quality of life.

H. pylori was diagnosed using the urea breath test in all but one study. Treatment consisted of amoxicillin (200 to 400mg bid) and clarithromycin (200 to 400mg bid) and a proton pump inhibitor for seven days in all but one study. Platelet count values varied between studies (range ≤50x10⁹/L to ≤120x10⁹/L). Most patients (68%) were female. Average age was 51.6 ± 17.1 years. Eight of the 11 studies were conducted in Japan.

Two reviewers independently selected studies for inclusion. Disagreements were resolved by consensus.

Assessment of study quality
Methodological quality was assessed by two independent reviewers who derived four key study design features from two scales, MOOSE statement and a methodological index tool for non-randomised studies. Items included: prospective data collection; consecutive patients unselected for H. pylori infection status; duration of follow-up reported; and loss to follow-up reported. Disagreements were resolved by consensus.

Data extraction
Two independent reviewers used data on the number of events in each group (overall, partial and complete response) following eradication therapy to derive odds ratios (OR) and 95% confidence intervals (CI). Disagreements were resolved by consensus. Two definitions of overall response were used: definitions from the included studies; and a standard definition of a platelet count rise to at least 30x10⁹/L within six months. Authors of included trials were contacted for any unpublished data.

Methods of synthesis
Pooled odds ratios and corresponding 95% CIs were calculated using a fixed-effect meta-analysis for overall response outcomes. A descriptive sensitivity analysis was conducted to test the influence of studies that enrolled consecutive patients whose infection status was not known until after the effect of treatment had been assessed. Publication bias was assessed using funnel plots.
Results of the review

Eleven studies were included in the review (n=282 of which 205 were H. pylori-positive and 77 were H. pylori-negative). Overall study quality was average. All except one included study was prospective. Four studies enrolled consecutive patients. Four studies reported follow-up duration. Only one study reported loss to follow-up. Mean duration of follow-up was 34.5 ± 23.9 months. Eight of the 11 studies were conducted in Japan.

A platelet count response following eradication therapy was significantly more likely in patients with H. pylori infection compared to non-infected patients (OR 14.51, 95% CI 4.17 to 83.01). Use of the variable definitions of platelet count defined by individual studies did not change results (OR 24.0, 95% CI 7.1 to 125.1).

Two of the studies that enrolled consecutive patients reported a positive effect of treatment in infected compared to uninfected patients; one study showed no significant difference.

Funnel plots suggested that publication bias may have been present.

**Authors’ conclusions**

H. pylori eradication therapy was of little benefit for H. pylori-negative patients. These findings strengthened the causal association between H. pylori infection and immune thrombocytopenia in some patients. Randomised trials were needed to determine the applicability of H. pylori eradication therapy across diverse geographical regions.

**CRD commentary**

This review addressed a clear question supported by appropriate inclusion criteria. Relevant databases were searched without language restrictions, attempts were made to identify unpublished data and publication bias was considered in the report. Suitable methods were used throughout the review process to minimise risks of reviewer error and bias. Results were pooled using meta-analysis, although it appeared that heterogeneity was not assessed. A planned descriptive sensitivity analysis was undertaken, but it was unclear whether this influenced results. In terms of methodology, this review was carried out robustly. The authors have drawn relatively cautious conclusions based on a small number of poor-quality non-randomised studies. The conclusions should be considered tentative.

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

**Practice**: The authors stated that although empiric H. pylori eradication therapy in ITP was appealing because of its simplicity and low toxicity, treatment should be reserved for H. pylori-positive patients only.

**Research**: The authors stated that randomised trials in unselected patients from diverse geographical regions were needed to confirm the findings of this review and determine the durability of the platelet count response.

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