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Title **Systematic Reviews of the Clinical Effectiveness and Cost Effectiveness of Proton Pump Inhibitors in Acute Upper Gastrointestinal Bleeding**

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Aim

1) To evaluate clinical and cost effectiveness of proton pump inhibitors (PPIs) in preventing and treating acute upper gastrointestinal (GI) hemorrhage. 2) To evaluate clinical and cost effectiveness of PPI therapy vs H_2-receptor antagonist (H_2RA), *Helicobacter pylori (H. pylori)* eradication, or no therapy for preventing first and /or subsequent bleeds in patients who continue to use nonsteroidal anti-inflammatory drugs (NSAIDs). 3) To evaluate clinical effectiveness of PPI therapy vs H_2RA, *H. pylori* eradication, or no therapy for preventing subsequent bleeds in patients with previous peptic ulcer (PU) bleeding.

Conclusions and results

1a) PPI treatment initiated after endoscopic diagnosis of PU bleeding significantly reduced re-bleeding (Odds ratio, OR 0.49; 95% confidence interval, CI 0.37 to 0.65) and surgery (OR 0.61; 95% CI 0.48 to 0.78) compared with placebo or H_2RA. No evidence of an overall effect of PPI treatment on all-cause mortality (OR 101; 95% CI 0.74 to 1.40). PPIs significantly reduced mortality among studies conducted in Asia (OR 0.35; 95% CI 0.16 to 0.74) or among patients with high-risk endoscopic findings (OR 0.53; 95% CI 0.31 to 0.91). 1b) PPI treatment initiated prior to endoscopy in upper GI bleeding significantly reduced the proportion of patients with stigmata of recent hemorrhage (SRH) at index endoscopy compared with placebo or H_2RA (OR 0.67; 95% CI 0.54 to 0.84). No evidence that PPI treatment affected mortality, re-bleeding, or need for surgery. 1c) Oral PPI before and after endoscopy, with endoscopic hemostatic therapy (EHT) for those with major SRH, is likely to be the most cost-effective strategy.

Recommendations

See Executive Summary link at www.hta.ac.uk/project/1385.asp.

Methods

See Executive Summary link at www.hta.ac.uk/project/1385.asp.

Further research/reviews required

Regarding PPIs in the acute hospital management of patients with upper GI bleeding: i) The issue of PPI administration prior to endoscopic diagnosis needs to be explored further in large randomized controlled trials that randomize patients with acute upper GI bleeding to PPI therapy before endoscopy. ii) A large, multicenter trial is needed in Europe and North America that would randomize patients to high-dose intravenous PPI or control treatment after any appropriate endoscopic intervention and address mortality as the primary endpoint. Unfortunately, such a trial faces major obstacles. iii) Randomized trials directly comparing different doses of PPIs and/or oral and intravenous administration of PPIs in patients with PU bleeding are also needed. iv) Evidence is very limited on head-to-head clinical outcome comparisons between different PPIs in PU bleeding, so such trials may be relevant.

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