Prokinetics in acute upper GI bleeding: a meta-analysis
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CRD summary
This review investigated the effect of prokinetics on the effectiveness of gastroscopy in patients with acute upper gastrointestinal bleeding. The authors concluded that either erythromycin or metoclopramide effectively decreased the need for repeat endoscopy. Although the review was methodologically sound, the limited evidence and poor-quality included studies mean the authors’ conclusions should be treated with caution.

Authors’ objectives
To assess whether administering prokinetic agents before gastroscopy/endoscopy in patients with acute upper gastrointestinal bleeding reduces repeat gastroscopy.

Searching
Electronic searches of MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL) database and Web of Knowledge were performed for the years 1990 to January 2010. A general description of the search strategy was provided; search terms were not reported. Conference abstracts for the preceding five years were identified from handsearching Digestive Disease Week and United European Gastroenterology and ClinicalTrials.gov. Recursive searches and cross-referencing were performed. Articles identified from the initial searches were handsearched. Searches were limited to studies published in English or French.

Study selection
Randomised controlled trials that assessed prokinetic agents prior to gastroscopy were included if they compared to placebo or to no active control in acute upper gastro-intestinal bleeding. Canadian Registry on Nonvariceal Upper Gastrointestinal Bleeding and Endoscopy definitions of acute upper gastro-intestinal bleeding were used. Trials with broad patient inclusion criteria were eligible for inclusion. The primary outcome was need for a repeat endoscopy to determine the source of bleeding. Secondary outcomes included endoscopic visualisation, the proportion of patients with clots or fresh blood seen at endoscopy, blood transfusions, duration of hospitalisation and surgery. Studies available only in abstract were included if they provided sufficient information.

Patient populations included those admitted to intensive care units because of acute upper gastro-intestinal bleeding and those who presented with overt haematemesis or melena. Interventions evaluated included erythromycin and metoclopramide compared with either placebo or no treatment, with or without gastric lavage prior to administration of the prokinetic. Doses of erythromycin ranged from 3mg/kg intravenously over 30 min to 250mg intravenously over five to 30 minutes. Dose of metoclopramide where reported was 10mg intravenously.

Study eligibility was assessed independently by two reviewers. Discrepancies were resolved after discussion and referral to a third reviewer.

Assessment of study quality
Study quality was graded using the Jadad score of randomisation, allocation concealment, blinding and description of withdrawals alongside a generic quality score that provided methodological quantification of additional content-specific components of the study design (primarily those related to the quality of reporting in the trials).

Study validity was assessed independently by two reviewers. Discrepancies were resolved after discussion and referral to a third reviewer.

Data extraction
The authors did not state how data were extracted for the review, but stated that primary authors were contacted where data were not extractable.

The authors did not state how many reviewers performed data extraction.
Methods of synthesis
The Mantel-Haenszel approach was used to estimate odds ratios (ORs) for dichotomised variables. Inverse variance was used to estimate weighted mean differences (WMDs) of continuous variables, along with their 95% confidence intervals (CIs). Fixed-effect models were used to pool studies; where evidence of heterogeneity was identified, a random-effects model was employed.

The $I^2$ statistic and $X^2$ square test of homogeneity were used to assess between-study heterogeneity.

Homogeneity of patient populations, interventions and outcomes across studies were assessed qualitatively. Meta-regression to investigate sources of heterogeneity was planned if more than 10 studies were identified. Sensitivity analyses that excluded studies one by one was planned and subgroup analyses that restricted studies by type of treatment to those using erythromycin and those that did not perform gastric lavage before the administration of a prokinetic were reported.

Publication bias was assessed using the Begg adjusted rank correlation test and Egger regression asymmetry test.

Results of the review
Five RCTs (316 patients) were included, two of which were published only in abstract format. The mean quality score was 9.8 out of a possible 19 (range 3 to 15 points); scoring on individual quality items was not reported.

Significantly fewer repeat endoscopies were performed when prokinetic agents were administered before gastroscopy (OR 0.55, 95% CI 0.32 to 0.94; five RCTs). The results were reported to be heterogeneous when limited to the three trials published in full ($I^2=58\%$) and a random-effects model was used. The effect became non-significant when the largest and fourth-largest studies were excluded from the analysis. The significant reduction in repeat endoscopy remained when analysis was restricted to the four trials that used erythromycin (OR 0.47, 95% CI 0.26 to 0.84).

Endoscopic visualisation and the proportion of patients with clots or fresh blood seen at endoscopy were not analysed due to their disparate and/or subjective nature. Blood transfusions, duration of hospitalisation and need for surgery were not significantly affected by use of prokinetics. Restricting the analysis to studies that did not use gastric lavage prior to administration of a prokinetic led to a non-significant effect on repeat endoscopy.

No evidence of publication bias was identified.

Authors' conclusions
Despite limited data, intravenous erythromycin or metoclopramide immediately before endoscopy (20 to 120 minutes) in patients with acute upper gastro-intestinal bleeding decreased the need for a repeat endoscopy, but did not improve other clinically relevant measurable outcomes.

CRD commentary
The aim of this review was clearly stated. The inclusion criteria were necessarily broad given the small number of studies available. The literature search included both electronic and manual elements along with an attempt to identify grey literature, which limited the risk of publication bias. Only papers in English and French were included, which left some potential for language bias. The authors reported that two reviewers independently carried out study selection, but did not state how many reviewers performed data extraction. A known tool for validity assessment of RCTs was used and further assessment was made of additional items primarily related to the quality of study reporting.

General study characteristics were provided in table format, but a lack of details of patient characteristics limited any assessment of generalisability. Study quality was not reported in detail and this precluded judgments on individual quality features. The statistical synthesis of included studies was probably appropriate given that limited study heterogeneity was identified, but tests for heterogeneity have low power when applied to small numbers of studies.

Given the limitations in the data, including the small number and poor quality of studies and the small sample sizes, the authors' conclusions should be treated with caution.

Implications of the review for practice and research
Practice: The authors stated that erythromycin (or metoclopramide) may be recommended for selected patients, namely
those with active bleeding who are likely to exhibit blood in the stomach.

**Research:** The authors stated that further trials were needed to add to the robustness of the conclusions and allow better characterisation of further possible clinical impact.

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