Intravenous pantoprazole as an adjuvant therapy following successful endoscopic treatment for peptic ulcer bleeding


CRD summary
The authors concluded that intravenous pantoprazole administered after endoscopic treatment reduces ulcer re-bleeding, surgical intervention, and length of hospital stay, but not mortality nor blood transfusions. This was a generally well-conducted review and the findings for the overall analyses are likely to be reliable.

Authors' objectives
To evaluate the effectiveness of intravenous pantoprazole as an additional treatment following successful endoscopic haemostasis of peptic ulcer bleeding.

Searching
The Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, and EMBASE were searched up to July 2008; search terms were reported. The Chinese Biomedical Database and Chinese Journals Full-text Database were also searched. The bibliographies of relevant articles were handsearched and companies and experts in the field were contacted.

Study selection
Randomised controlled trials (RCTs) were eligible for inclusion if they compared intravenous pantoprazole with placebo, a histamine type 2 receptor antagonist, or other medication in patients with endoscopically confirmed active bleeding or major stigmata of recent bleeding, after successful endoscopic haemostasis for peptic ulcer bleeding. Patients with other causes of gastrointestinal bleeding were excluded. The primary outcome of interest was the incidence of re-bleeding. Secondary outcomes were the length of hospital stay, mortality, need for surgery, and blood transfusion requirements.

Included RCTs were of pantoprazole 80mg or 40mg intravenous bolus followed by either 40mg over 12 hours or 8mg per hour continuous infusion, for three days compared with ranitidine, somatostatin, or placebo in varying doses, or no treatment. The mean age of patients ranged from 52.4 years to 67.8 years and the mean size of ulcer ranged from 1.0cm to 1.3cm. Follow-up ranged from four to eight weeks and studies were conducted in the USA, China, India, and Greece.

Two reviewers independently selected the studies for the review, with disagreements resolved by consensus.

Assessment of study quality
The methodological quality of the included trials was assessed on randomisation, double-blinding, and withdrawals or dropouts. Each RCT was awarded an overall quality of A, B, or C according to the risk of bias. Details of the assessment were not described in this paper, but were available in another publication. The authors also commented on the comparability of groups at baseline.

Three reviewers independently assessed the quality of the included trials.

Data extraction
Dichotomous data were extracted as relative risks (RRs) and continuous data were extracted as mean differences between groups.

The authors did not state how many reviewers performed the data extraction.
Methods of synthesis
Pooled RRs or weighted mean differences (WMDs) with corresponding 95% confidence intervals (CIs) were calculated using a fixed-effect model. Heterogeneity was assessed using the $\chi^2$ and $I^2$ statistics and visually through inspection of the forest plots. Where there was significant heterogeneity a random-effects meta-analysis was carried out. In one trial with two treatment arms, data were included from both arms in the relevant subgroup analyses, but only data from the continuous intravenous arm were included in the overall analyses. Sensitivity analyses were carried out where trials differed from one another on important criteria. Subgroup analyses were carried out according to the timing of measurement of ulcer re-bleeding, type of control, route of pantoprazole administration, and dosage of pantoprazole.

Results of the review
Five RCTs (n=771) were included in the review. Three were graded A (low risk of bias) on the quality assessment, one was grade B, and one was grade C (high risk of bias). All trials reported adequate randomisation; treatment allocation was concealed in four trials; three trials were double-blinded; and none reported the loss to follow-up.

Re-bleeding: In the overall analysis, pantoprazole was associated with a significantly reduced risk of re-bleeding when compared with controls (five RCTs, n=722; RR 0.31, 95% CI 0.18 to 0.53). There was no evidence of statistically significant heterogeneity and sensitivity analyses excluding the two trials that did not assess bleeding at three days did not significantly alter the results. When the incidence of re-bleeding was measured at three days or at 30 days, pantoprazole significantly reduced the risk compared with controls, but not when the incidence of re-bleeding was measured at four to seven days. Subgroup analyses continued to show a significant effect in favour of pantoprazole for the incidence of re-bleeding irrespective of the control condition, high or low dosage, or bolus or continuous intravenous administration (one to four trials; RRs ranging from 0.21 to 0.37).

Other outcomes: Overall, pantoprazole significantly reduced the need for surgery (three RCTs, n=409; RR 0.28, 95% CI 0.09 to 0.83) and the length of hospital stay (four RCTs, n=618; WMD -1.53, 95% CI -1.91 to -1.16). There was no evidence of significant statistical heterogeneity for these outcomes. Pantoprazole was not associated with a reduced risk of mortality or reduced blood transfusion requirements. Subgroup analyses for these outcomes were also reported, but each was assessed by less than three trials.

Authors’ conclusions
Intravenous pantoprazole administered after endoscopic treatment reduced ulcer re-bleeding, surgical intervention, and length of hospital stay, but not mortality nor blood transfusions compared with placebo, histamine type 2 receptor antagonists, or somatostatin.

CRD commentary
This review addressed a clear question with well-defined inclusion criteria. Several relevant databases were searched and attempts were made to identify unpublished material, thereby minimising the risk of publication bias. It is unclear whether the search was restricted by language and the risk of language bias cannot be ruled out. Validity was assessed using suitable criteria and appropriate steps were taken in study selection and validity assessment to minimise the risk of reviewer error and bias. It is unclear whether similar steps were taken in data extraction and reviewer bias cannot be ruled out. Appropriate methods were used to combine the trials, statistical heterogeneity was assessed, and the sources of heterogeneity were investigated in subgroup analyses. The small number of trials included in some subgroup analyses diminishes the reliability of these findings.

This was a generally well-conducted review and the findings for the overall analyses are likely to be reliable.

Implications of the review for practice and research
Practice: The authors did not state any recommendations for practice.

Research: The authors stated that for ethical reasons future research should compare pantoprazole with other active agents rather than placebo. Further multi-centre high-quality trials were needed in other countries.
Funding
Not stated.

Bibliographic details

PubMedID
19373423

Original Paper URL
http://www.pulsus.com/journals/abstract.jsp?sCurrPg=abstract&jnlKy=2&atlKy=8772&isuKy=850&isArt=t&fromfold=

Indexing Status
Subject indexing assigned by NLM

MeSH
2-Pyridinylmethylsulfanylbenzimidazoles /administration & dosage; Anti-Ulcer Agents /administration & dosage; Blood Transfusion; Chemotherapy, Adjuvant; Drug Administration Schedule; Endoscopy, Digestive System; Humans; Infusions, Intravenous; Length of Stay; Peptic Ulcer Hemorrhage /drug therapy /prevention & control /surgery; Randomized Controlled Trials as Topic; Secondary Prevention; Treatment Outcome

AccessionNumber
12009105808

Date bibliographic record published
02/09/2009

Date abstract record published
24/03/2010

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.