Second-look endoscopy with thermal coagulation or injections for peptic ulcer bleeding: a meta-analysis

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CRD summary
This review concluded that second-look endoscopy with thermal coagulation, but not injection therapy, reduced recurrent peptic ulcer bleeding, but not surgical intervention or overall mortality. Routine second-look endoscopy with treatment could not be recommended. Given the limitations with reporting in the review, a small number of studies and potential for bias, the authors' conclusions should be interpreted with some caution.

Authors' objectives
To compare the effectiveness of second-look endoscopic treatment with thermal coagulation or injections versus single endoscopy for management of peptic ulcer bleeding.

Searching
MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), DARE and IPA were searched up to 2008 for articles published in English. Search terms were reported. In Digestive Disease Week, United European Gastroenterology Week, Asia-Pacific Digestive Week, and American College of Gastroenterology international conferences were searched manually over the previous 10 years. Reference lists of retrieved articles and other clinical reviews were searched manually.

Study selection
Prospective randomised controlled trials (RCTs) that compared second-look endoscopy with repeated injections or thermo-coagulations versus single endoscopy for the treatment of patients with non-variceal upper gastrointestinal bleeding (as defined in the review) were eligible for inclusion. The primary outcome of interest was recurrent bleeding after the first endoscopic therapy. Secondary outcomes included unit of blood transfusion, requirement of surgical intervention and all-cause mortality within 30 days of the first endoscopy.

Included trials were of patients with gastric or duodenal ulcers or ulcers at other sites. Re-bleeding was defined by clinical symptoms and/or endoscopic confirmation. Mean age of participants ranged from 62.0 to 68.1 years. The proportion of males ranged from 60% to 100%. Some included trials used adjuvant ranitidine; others used a proton pump inhibitor (intravenous omeprazole) with or without antibiotic treatment. Trials of second-look endoscopy with thermal coagulation added thermal coagulation to injection therapy in patients identified with high-risk ulcer.

Two reviewers independently screened articles for inclusion. Discrepancies were resolved through referral to a third reviewer.

Assessment of study quality
Study quality was assessed using the criteria: prospective randomisation; allocation concealment; patient exclusion criteria; clear definitions of recurrent bleeding; and predefined salvage procedures when bleeding was not controlled.

The authors did not state how many reviewers performed the quality assessment.

Data extraction
Two reviewers independently extracted outcome data to calculate relative risk (RR) and 95% confidence intervals (CIs). The authors appeared to extract the units of blood transfusion to calculate mean differences. Discrepancies were resolved through referral to a third reviewer.

Methods of synthesis
Relative risks and 95% CIs were pooled using a fixed-effect model; a random effects model was used where statistical
heterogeneity was present. The authors did not explicitly state how mean differences were pooled. Statistical heterogeneity was assessed using the \(X^2\) test and \(I^2\) statistic. Trials that used thermal coagulation were analysed separately from those that used injections alone. Subgroup analyses were undertaken for trials that used injection with epinephrine or fibrin glue. Sensitivity analyses were performed for trials on adjuvant therapy with proton pump inhibitor and trials published in full.

**Results of the review**

Five RCTs (n=979 calculated, range 40 to 536 participants) were included in the meta-analysis. There was some discrepancy between the figures reported in the text and tables and we have reported the figures from the tables. Three RCTs scored 5 on the quality score and two scored 4.

Second-look endoscopy with injections (three RCTs) did not significantly reduce re-bleeding compared to single endoscopy (RR 0.85, 95% CI 0.63 to 1.14). There were no significant differences in blood transfusion (mean difference -0.15, 95% CI -1.42 to 1.13), requirement of surgical intervention (RR 0.69, 95% CI 0.37 to 1.28) and all-cause mortality (RR 0.83, 95% CI 0.44 to 1.60). The authors stated that there was significant statistical heterogeneity among trials that assessed unit of blood transfusion, but the statistical value reported suggested otherwise (p>0.1). Sensitivity analyses did not significantly alter the results. Subgroup analyses showed that neither epinephrine nor fibrin glue injection significantly reduced re-bleeding.

Second-look endoscopy with thermal coagulation (two RCTs) showed a statistically significant reduction in re-bleeding compared with single endoscopy (RR 0.29, 95% CI 0.11 to 0.73), but not in all cause mortality (RR 0.75, 95% CI 0.17 to 3.30). One RCT reported no statistically significant difference in blood transfusion and the requirement of surgical intervention.

**Authors’ conclusions**

Second-look endoscopy with thermal coagulation, but not injection therapy, reduced recurrent peptic ulcer bleeding. There was no proven benefit in reducing surgical intervention and overall mortality. Routine second-look endoscopy with treatment could not be recommended.

**CRD commentary**

The review question and supporting inclusion criteria were clearly defined. A comprehensive literature search was undertaken to identify abstracts and fully published papers. The search was restricted to articles in English, so language bias may have been introduced. Abstracts were excluded from the meta-analysis, which meant that potentially relevant trials may have been excluded. The validity assessment was somewhat limited and it was unclear whether this was conducted in duplicate, so reviewer error and bias could not be ruled out. The synthesis was a little unclear and some of the results reported in the text and tables did not appear to support one another or were a little difficult to follow. The authors acknowledged that there were some clinical differences between trials in terms of definitions. There were only small numbers of studies and participants included in the comparisons. It appeared from the forest plots presented that the results for each comparison were weighted towards one RCT and as confidence intervals were wide, this may have impacted on the robustness of the findings. Although this review appeared generally well-conducted in parts, given limitations with the reporting in the review, a limited number of studies and the potential for bias, the authors’ conclusions should be interpreted with some caution.

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

**Practice:** The authors did not state any implications for practice.

**Research:** The authors stated that future studies should focus on identification of patients who were most likely to benefit from routine second endoscopy. Future studies should address the effects of proton pump inhibitor as an adjuvant therapy to endoscopic treatment of patients who received second-look endoscopy in combination with proton pump inhibitor compared with a control group of second-look endoscopy without proton pump inhibitor.

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