Endoscopic clipping versus injection and thermo-coagulation in the treatment of non-variceal upper gastrointestinal bleeding: a meta-analysis

CRD summary
This review found that endoscopic haemoclips are superior to injection therapy but comparable to thermocoagulation in patients with gastrointestinal bleeding. The review was generally well conducted and the authors’ conclusions appear justified.

Authors’ objectives
To compare the efficacy of haemoclips versus injection or thermocoagulation in patients with non-variceal upper gastrointestinal bleeding.

Searching
Trials published in English were identified through a search of MEDLINE (1950 to January 2007), EMBASE (1980 to January 2007) and the Cochrane Controlled Trials Register (Issue 1, 2007); the search terms were reported. Abstracts published in major international conferences over the previous 10 years were searched manually and the bibliographies of retrieved articles were checked.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion in the review.

Specific interventions included in the review
Studies that assigned patients to haemoclips or alternative therapies (thermocoagulation or injection) were eligible for inclusion. Studies were included if they applied endoscopic therapy only to active bleeding ulcers or ulcers with adherent blood clots or protruberant vessels. Studies were required to administer concomitant therapy equally in both intervention and control groups.

Participants included in the review
Studies in patients with a diagnosis of acute bleeding from peptic ulcers or Dieulafoy lesions made endoscopically were eligible for inclusion. Patients diagnosed with bleeding from a Mallory Weiss tear were excluded. Male and female participants were included and the median age was 61.7 years.

Outcomes assessed in the review
Studies that reported at least one of the outcome measures were eligible for inclusion. The primary outcome measure was definitive haemostasis, defined as successful control of bleeding after the first endoscopic therapy until the end of follow-up. The secondary outcomes included initial haemostasis, recurrent bleeding, requirement for surgical intervention and all-cause mortality. Studies were required to present data for patients with bleeding peptic ulcers separately. Failure of clips was also reported in some included studies.

How were decisions on the relevance of primary studies made?
Two reviewers independently assessed each trial for inclusion and a third reviewer resolved any disagreements.

Assessment of study quality
Trials were assessed for randomisation, allocation concealment, exclusion criteria for ineligible patients, clear definitions of outcomes, and predefined salvage procedures when endoscopic treatment failed to control bleeding. These criteria were used to assign a score of between 1 and 5. The authors did not state how the validity assessment was performed.

Data extraction
Two reviewers independently extracted the data into a standard data extraction form and a third reviewer resolved any disagreements. Data on the numbers of events in each group were used to calculate the relative risk (RR) and 95% confidence intervals (CIs) for each study.

**Methods of synthesis**

How were the studies combined?
The studies were pooled by meta-analysis, using the Mantel-Haenszel fixed-effect model where there was no evidence of heterogeneity and a random-effects model where statistically significant heterogeneity was observed. Publication bias was not assessed.

How were differences between studies investigated?
Statistical heterogeneity was assessed using the chi-squared test (p<0.1) and the I-squared test (high values show increasing heterogeneity). Subgroup analyses were conducted for the different comparisons included. One-way sensitivity analyses were conducted on study duration, adjuvant proton-pump inhibitors and study quality.

**Results of the review**

Fifteen RCTs (n=1,156) were included in the review. Two studies were included in abstract form and were preliminary results from RCTs; the other 13 studies were completed RCTs.

Of the 15 included trials, four were graded below 3 out of 5 for quality.

**Haemoclips versus injections (8 RCTs).**
There were no significant differences between groups in initial haemostasis (RR 1.01, 95% CI: 0.96, 1.06) or all-cause mortality (RR 1.45, 95% CI: 0.44, 4.74). Haemoclips showed a significant reduction in re-bleeding (RR 0.49, 95% CI: 0.30, 0.79) and the need for surgery (RR 0.37, 95% CI: 0.15, 0.9), and a marginally higher probability in achieving definitive haemostasis (RR 1.14, 95% CI: 1.00, 1.30). Statistical heterogeneity was observed for the outcome of definitive haemostasis (I-squared 6.6%; p=0.07).

**Haemoclips plus injections versus injections (7 RCTs).**
There were no significant differences between groups in initial haemostasis (RR 1.00, 95% CI: 0.95, 1.05) or all-cause mortality (RR 1.23, 95% CI: 0.45, 3.37). Haemoclips showed significantly higher success in definitive haemostasis (RR 1.13, 95% CI: 1.03, 1.23) compared with injection alone and also showed a significant reduction in re-bleeding (RR 0.47, 95% CI: 0.28, 0.76) and the need for surgery (RR 0.23, 95% CI: 0.08, 0.70). There was no evidence of statistical heterogeneity for any outcome (p<0.1).

**Haemoclips versus thermocoagulation with or without injection (4 RCTs).**
There were no significant differences for any outcome: initial haemostasis (RR 0.94, 95% CI: 0.84, 1.07), definitive haemostasis (RR 1.00, 95% CI: 0.77, 1.31), re-bleeding (RR 0.65, 95% CI: 0.21, 2.02), need for surgery (RR 0.84, 95% CI: 0.32, 2.24) or all-cause mortality (RR 0.96, 95% CI: 0.34, 2.76). Statistical heterogeneity was observed for initial and definitive haemostasis (I-squared 75.5% and p=0.006; I-squared 84.0% and p<0.01) and re-bleeding (I-squared 53.3%; p=0.09).

Sensitivity analyses showed the results for initial and definitive haemostasis, re-bleeding and the need for surgery to be consistent for study duration, the use of proton-pump inhibitors and study quality.

Some data on clip failure were also reported.

**Authors’ conclusions**
Endoscopic clipping is superior to endoscopic injection and comparable to thermocoagulation in securing haemostasis of bleeding peptic ulcers and Dieulafoy lesions.

**CRD commentary**
The review addressed a clear question in terms of the participants, interventions, outcomes and study design, although there were slight discrepancies in the numbers of participants reported. A thorough search for relevant trials was
undertaken, but the restriction to English language publications may indicate that not all relevant data were included. The potential influence of publication bias was not considered in the report. The authors attempted to minimise bias and errors during parts of the review process by carrying out the study selection and data extraction in duplicate. An appropriate validity assessment was undertaken. The decision to use meta-analysis with subgroup and sensitivity analyses appears appropriate, although the presence of statistically significant heterogeneity for a minority of the outcomes could have been further investigated. The authors’ conclusions were based on the meta-analysis and seem likely to be reliable given the evidence presented.

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

**Practice:** The authors stated that the choice of therapy remains at the discretion of the endoscopist, based upon the nature and position of the ulcer, experience of the endoscopist and the patients' previous endoscopic therapy.

**Research:** The authors did not state any implications for research.

**Funding**

Not stated.

**Bibliographic details**


**PubMedID**

17566018

**DOI**

10.1136/gut.2007.123976

**Indexing Status**

Subject indexing assigned by NLM

**MeSH**

Electrocoagulation; Hemostasis, Endoscopic /methods; Humans; Peptic Ulcer Hemorrhage /surgery /therapy; Randomized Controlled Trials as Topic; Recurrence; Treatment Outcome

**AccessionNumber**

12007003635

**Date bibliographic record published**

07/02/2008

**Date abstract record published**

01/09/2008

**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.