CRD summary
This review concluded that there is no significant benefit from the prophylactic use of gabexate for the prevention of post-endoscopic retrograde cholangiopancreatography pancreatitis. Given the poor reporting of review methods and uncertainty about between-study differences, the reliability of the authors' conclusions is uncertain.

Authors' objectives
To assess the effectiveness and safety of gabexate for the prevention of post-endoscopic retrograde cholangiopancreatography pancreatitis (PEP).

Searching
MEDLINE (from January 1966), EMBASE (from January 1966), the Cochrane Controlled Trials Register (2006) and CBM-disc (from January 1978) were searched to June 2006; the search terms were reported. The reference lists of retrieved articles and reviews were checked for relevant studies.

Study selection
Study designs of evaluations included in the review
Prospective randomised controlled trials (RCTs) were eligible for inclusion. Quasi-randomised trials and non-randomised studies were excluded.

Specific interventions included in the review
Studies evaluating gabexate in comparison with placebo or 'blank' control were eligible for inclusion. Cointerventions, including treatment of complications, were acceptable if administered equally to all intervention groups. Studies with different cointerventions per intervention study arms were excluded. The interventions included in the review were gabexate, 300 mg to 1 g, by intravenous infusion 30 to 90 minutes before endoscopy and continuing for between 2 and 12 hours after (details of regimens were reported).

Participants included in the review
Studies of adults aged over 18 years who were scheduled to undergo endoscopic retrograde cholangiopancreatography (ERCP) and/or endoscopic sphincterotomy were eligible for inclusion. Patients with active acute pancreatitis, chronic pancreatitis, pancreatic cancer, or cancer of the papilla of Vater were excluded.

Outcomes assessed in the review
Studies assessing primary outcomes of PEP, severe PEP and case-fatality ratio of PEP, together with secondary outcomes of post-ERCP hyperamylasaemia and abdominal pain were eligible for inclusion.

How were decisions on the relevance of primary studies made?
It was unclear whether or not two reviewers selected the studies and resolved any disagreements by consensus.

Assessment of study quality
Validity was assessed and scored using the Jadad composite scale, which assesses randomisation, blinding, and drop-outs and withdrawals. The scale ranges from 0 to 5 points, with studies scoring 2 or less considered low quality and studies scoring 3 or more considered high quality. The authors did not state how many reviewers were involved in the validity assessment.

Data extraction
It was unclear whether or not two reviewers extracted the outcomes data and resolved any disagreements by consensus.
Methods of synthesis
How were the studies combined?
The studies were pooled using the general inverse fixed-effect model. Pooled odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. Publication bias was assessed using Begg and Mazumdar's rank correlation test, Egger's linear regression model and a funnel plot.

How were differences between studies investigated?
Heterogeneity of the studies was assessed using the Q statistic. If significant heterogeneity was found (p<0.05), the results were then pooled using a DerSimonian and Laird random-effects model. Sensitivity analysis was also performed by excluding studies with the longest or shortest duration.

Results of the review
Four RCTs (n=1,783) were included.

Three studies were conducted in multicentres in Italy and one was conducted in a single centre in China. Allocation concealment was judged adequate in all studies, and all studies scored the maximum 5 points on the Jadad quality scale.

There was no statistically significant difference between the prophylactic use of gabexate and control in the risk of PEP (random-effects OR 0.67, 95% CI: 0.31, 1.47, p=0.32; including 104 patients with PEP). There was evidence of significant heterogeneity between the studies (p=0.03).

There was no statistically significant difference between the prophylactic use of gabexate and control in the risk of severe PEP (OR 3.78, 95% CI: 0.62, 22.98, p=0.15; 2 studies, including 6 patients with severe PEP), case-fatality ratio of PEP (OR 0.68, 95% CI: 0.19, 2.43, p=0.56; 2 studies, including patients who died) or post-ERCP hyperamylasaemia (OR 0.88, 95% CI: 0.72, 1.07, p=0.20; 4 studies, including 700 patients with hyperamylasaemia). There was no evidence of statistical heterogeneity for any of these analyses.

There was no significant differences between patients treated with gabexate and those given placebo in terms of abdominal pain (OR 0.69, 95% CI: 0.39, 1.21, p=0.19; 3 studies, 183 patient with abdominal pain). There was significant heterogeneity between these studies (p=0.03).

The sensitivity analysis produced similar results. No evidence of publication bias was found.

There was no significant association between adverse events and the use of gabexate. Two studies reported minor adverse events in both the gabexate and placebo groups, none of which required treatment.

Authors’ conclusions
Prophylactic gabexate use was not found to be statistically significantly beneficial for the prevention of PEP. It is therefore not recommended that gabexate be used routinely in the prophylaxis of PEP.

CRD commentary
Inclusion criteria were defined in terms of the interventions, participants, outcomes and study designs. Several relevant sources and were searched, together with reference lists. No specific attempts to minimise publication bias were reported, although the formal assessment of publication bias suggested that this was not present in the review. Review methods were not described clearly for the study selection and data extraction processes and not reported for the validity assessment; it is therefore not possible to assess the potential for reviewer error or bias. Validity was assessed using established criteria and the results tabulated.

The results of the studies were pooled but, since there was evidence of statistical heterogeneity for some outcomes, it might not have been appropriate to combine these in a meta-analysis. In addition, there was only a small number of patients with some events of interest in the included studies; this could undermine the reliability of treatment effects. In summary, lack of complete reporting of review methods and uncertainty about between-study differences mean the
reliability of the authors' conclusions is uncertain.

Implications of the review for practice and research
Practice: The authors stated that the use of gabexate in the prophylaxis of PEP is not recommended for routine use.

Research: The authors stated that further studies are needed to evaluate the safety of gabexate when used in the prophylaxis of post-ERCP pancreatitis.

Bibliographic details

Original Paper URL
http://www.biomedcentral.com/1471-230X/7/6

Indexing Status
Subject indexing assigned by NLM

MeSH
Acute Disease; Cholangiopancreatography, Endoscopic Retrograde /adverse effects; Gabexate /adverse effects /therapeutic use; Linear Models; Odds Ratio; Pancreatitis /etiology /prevention & control; Postoperative Complications /prevention & control; Premedication; Randomized Controlled Trials as Topic; Serine Proteinase Inhibitors /adverse effects /therapeutic use; Statistics, Nonparametric

AccessionNumber
12007000856

Date bibliographic record published
06/12/2007

Date abstract record published
09/08/2008

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.