Gabexate mesylate in the prevention of post-endoscopic retrograde cholangiopancreatography pancreatitis: a systematic review and meta-analysis update
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CRD summary
The review concluded that no beneficial effects of gabexate mesylate on acute pancreatitis, post-endoscopic retrograde cholangiopancreatography pancreatitis death rate or post-endoscopic retrograde cholangiopancreatography abdominal pain or hyperamylasaemia could be found. The authors’ conclusions should be interpreted with caution since most analyses were based on very small numbers of events or were subject to significant between-study variation.

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

Searching
This was an update of results from three earlier reviews. MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL) and China Biological Medicine Database were searched to July 2007; search terms were reported. Poster presentations were examined, experts in the field were contacted and reference lists of retrieved articles and reviews were checked for further relevant studies.

Study selection
Randomised controlled trials (RCTs) of gabexate mesylate versus placebo (or blank control) in adults (>18 years) due to undergo endoscopic retrograde cholangiopancreatography (ERCP) and/or endoscopic sphincterotomy were eligible for inclusion. Studies that included cointerventions were eligible provided they were given equally to all treatment groups. Trials of patients with active acute pancreatitis, chronic pancreatitis, pancreatic cancer or cancer of the papilla of Vater were excluded. Primary outcomes were PEP, severe PEP and the case-fatality ratio of PEP.

In the included studies doses of gabexate mesylate ranged from 150mg to 1.2g, mostly given either 30 minutes or an hour before endoscopy. Treatments were also given for between two and 12 hours after endoscopy. All studies (except one Chinese study) were conducted in Italy.

Two independent reviewers selected studies for inclusion.

Assessment of study quality
Study quality was evaluated using the Jadad scale of randomisation, blinding and drop-outs and withdrawals. Studies scoring three or more were deemed to be of high quality. Adequacy of allocation concealment was assessed. It appeared that two reviewers independently performed the quality assessment.

Data extraction
Data were extracted in order to calculate odds ratios (OR) or mean differences, with 95% confidence intervals (CI). A value of 0.5 was added to both groups for studies with one group and no events.

Two reviewers independently extracted data. Disagreements were resolved by consensus.

Methods of synthesis
Results were pooled by meta-analysis using a fixed-effect model (heterogeneity not found) or a random effects model (heterogeneity found). Heterogeneity was assessed using X². Sensitivity analyses investigated the effect of treatment duration and study quality. Publication bias was assessed using the Begg test and a funnel plot.

Results of the review
Seven RCTs (n=2,883 participants, range 56 to 776) were included. Five studies scored the maximum of 5 points on the Jadad scale and also had adequate methods of allocation concealment. Two studies scored 2; one scored 2 points for blinding and the other scored a point for mentioning randomisation (method not specified) and one for reporting withdrawals.

There was no evidence that treatment with gabexate mesylate resulted in a reduction of PEP (six RCTs), severe PEP (four RCTs), case-fatality ratio of PEP (three RCTs), post-ERCP hyperamylasaemia (six RCTs) and abdominal pain (five RCTs). There was statistically significant heterogeneity for PEP and abdominal pain analyses.

All sensitivity analyses yielded similar results to the main analyses. There was no evidence of publication bias. Three studies examined adverse events and found no evidence to suggest gabexate mesylate was associated with any adverse events.

**Authors' conclusions**
No beneficial effects of gabexate mesylate on acute pancreatitis, PEP death rate or post-ERCP abdominal pain or hyperamylasaemia were found.

**CRD commentary**
The review addressed a clear question and was supported by appropriate inclusion criteria. A Chinese database was searched, but it was unclear whether the search extended to other languages and some relevant trials may have been missed. Some attempts were made to identify unpublished studies. Suitable methods (such as independent duplicate processes) were used to reduce risks of reviewer error and bias during the review. Basic study details were tabulated, but little information was provided about the participants actually included in the review and this made it difficult to comment on the generalisability of the results. Study quality was assessed and was used in interpreting the results of the review. Suitable methods were used for pooling data and assessing heterogeneity, although the authors decision to pool heterogeneous data was questionable.

The authors' conclusions should be interpreted with caution since most analyses were based on very small numbers of events or were subject to significant heterogeneity.

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

**Practice:** The authors stated that gabexate mesylate could not be recommended for the prophylaxis of PEP.

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

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