Pharmacologic treatment can prevent pancreatic injury after ERCP: a meta-analysis

Authors' objectives
To examine the use of therapeutic agents in prevention of pancreatic injury after endoscopic retrograde cholangiopancreatography.

Searching
Published full reports and abstracts were sought in MEDLINE, from 1978 to 1998, under the following headings: 'somatostatin'; 'octreotide'; 'gabexate mesilate'; 'ERCP'; 'amylase'; and 'acute pancreatitis'. Reference lists of pertinent reviews and identified articles were examined. No language restrictions were applied.

Study selection
Study designs of evaluations included in the review
Placebo controlled clinical trials published as complete papers or abstracts were eligible. Randomised trials (RCTs) were included.

Specific interventions included in the review
The prophylactic use of the following agents was compared with either placebo or no treatment: somatostatin (SS); octreotide (OCT); and gabexate (FOY). SS was given either as a bolus injection (4 micrograms/kg or 50 micrograms) or as a continuous infusion (250 or 300 micrograms/hr for between 3 and 26 hours). FOY was given in doses ranging from 100 to 1000 mg for between 2 and 12 hours. OCT was given either before or before and after (up to three doses) ERCP in doses ranging from 0.01 to 0.2 mg.

Participants included in the review
Patients undergoing endoscopic retrograde cholangiopancreatography were included.

Outcomes assessed in the review
The following three indicators of pancreatic injury were assessed: occurrence of acute pancreatitis; frequency of serum amylase elevation; and presence of pancreatic pain.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the reviewers performed the selection.

Assessment of study quality
Validity was assessed according to randomisation but no other criteria were considered. The authors do not state how the papers were assessed for validity, or how many of the reviewers performed the validity assessment.

Data extraction
Tables reported in the review included the following information: author; year of publication; study design; control and active treatment details; number of patients per intervention group; and percentage of patients reporting specified outcomes. Studies were independently evaluated by two of the authors considering the three outcomes with discrepancies resolved by discussion.

Methods of synthesis
How were the studies combined?
Pooled odds ratios (OR) and 95% confidence intervals were calculated for each drug and each outcome using the fixed-
effect model described by Peto (see Other Publications of Related Interest no.1) with a random-effects model used whenever heterogeneity was significant. Publication bias was assessed by estimating the minimum number of negative studies it would take to reverse a significant effect and the number needed to treat (NNT) to prevent one adverse effect was calculated. Meta-analytical results were taken as providing evidence of treatment efficacy if pooled OR were significantly reduced, if one or more studies showed significant benefit, and if there was no clinical or statistical heterogeneity across the trials.

How were differences between studies investigated?
Statistical heterogeneity was assessed using the chi-squared test. Pooled estimates were re-calculated for RCTs only and for studies reported in full papers only.

Results of the review
A total of 22 controlled trials were included (2179 patients), of which 19 were RCTs.

Results reported below are for all available studies.

Somatostatin (SS): incidence of acute pancreatitis, hyperamylasemia and pain were significantly reduced with SS.

Acute pancreatitis (10 studies, including 8 RCTs): OR = 0.38 (95% CI: 0.22, 0.65). Publication bias = 15. NNT = 13.

Hyperamylasemia (10 studies, including 7 RCTs): OR = 0.65 (95% CI: 0.48, 0.90). Publication bias = 6. NNT = 9.

Pain (6 studies, including 5 RCTs): OR = 0.24 (95% CI: 0.14, 0.42). Publication bias = 20. NNT = 6.

No evidence of statistical heterogeneity was found.

No change in significance of results was found by considering only RCTs or only full publications.

Octreotide (OCT): the incidence of hyperamylasemia was significantly reduced with OCT though no effect was found on either acute pancreatitis or pain.

Acute pancreatitis (8 studies, including 7 RCTs): OR = 1.43 (95% CI: 0.82, 2.49).

Hyperamylasemia (7 studies, including 6 RCTs): OR = 0.51 (95% CI: 0.31, 0.83).

Pain (3 studies, including 3 RCTs): OR = 0.63 (95% CI: 0.28, 1.43). There was evidence of statistical heterogeneity.

No change in significance of results was found by considering only RCTs or only full publications.

Gabexate mesilate (FOY): incidence of acute pancreatitis, hyperamylasemia and pain were significantly reduced with FOY when considering all studies combined. After limiting studies to RCTs no effect was noted for FOY compared to control and acute pancreatitis and pain were only reported in one RCT. No change in significance of results was found by considering only full publications for any of the outcomes.

Acute pancreatitis (4 studies, including 1 RCT): OR = 0.27 (95% CI: 0.13, 0.57). Publication bias = 5. NNT = 27.

Hyperamylasemia (6 studies, including 2 RCTs): OR = 0.66 (95% CI: 0.48, 0.89). Publication bias = 5. NNT = 11. Two RCTs with OR = 0.82 (95% CI: 0.55, 1.22).

Pain (3 studies, including 1 RCT): OR = 0.33 (95% CI: 0.18, 0.58). Publication bias = 5. NNT = 10. No evidence of statistical heterogeneity was found.

Authors' conclusions
The pancreatic injury after ERCP can be prevented with the administration of either somatostatin or gabexate mesilate, but the former is more cost effective. Additional studies comparing the efficacy of short-term infusion of somatostatin
versus gabexate mesilate in patients at high risk for post-ERCP complications seem warranted.

**CRD commentary**

The aims were stated and inclusion criteria defined in terms of study design, intervention, participants and outcomes. Only one relevant database was searched thus limiting potentially eligible studies and no attempt was made to locate unpublished studies, though the likelihood of publication bias was assessed. Methods used to select primary studies were not described. Primary studies were restricted to controlled clinical trials but no formal validity assessment was undertaken. Most relevant details of the included studies were tabulated but no details were given of patient characteristics or criteria used to define outcomes in the individual studies. Adverse reactions were not considered. Statistical heterogeneity was assessed and the influence of study design (randomised or not) and publication type (full report or abstract) on the results examined. The authors appear to base their judgment of the most cost effective treatment on the lower NNT results for one preparation without taking cost of drugs into account. Results for one of the recommended drugs were based on evidence from one RCT for two outcomes and two RCTs for one outcome.

In view of the above limitations (restricted search, lack of validity assessment and results based on small numbers of RCTs), the conclusion should be interpreted with caution.

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

**Practice:** The authors report that more information is needed before recommending the use of somatostatin or gabexate mesilate in every patient undergoing ERCP.

**Research:** The authors report that additional studies comparing the efficacy of short-term infusion of somatostatin versus gabexate mesilate patients at high risk for post-ERCP complications seem warranted.

**Bibliographic details**


**PubMedID**

10625786

**Other publications of related interest**


**Indexing Status**

Subject indexing assigned by NLM

**MeSH**

Acute Disease; Amylases /secretion; Cholangiopancreatography, Endoscopic Retrograde /adverse effects; Gabexate /therapeutic use; Hormones /therapeutic use; Humans; Octreotide /therapeutic use; Pain /prevention & control; Pancreas /injuries; Pancreatitis /etiology /prevention & control; Serine Proteinase Inhibitors /therapeutic use; Somatostatin /therapeutic use; Treatment Outcome

**AccessionNumber**

12000000327

**Date bibliographic record published**

31/07/2001
Date abstract record published
31/07/2001

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.