Meta-analysis: octreotide prevents post-ERCP pancreatitis, but only at sufficient doses

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CRD summary
This review concluded that octreotide was effective in preventing post-ERCP pancreatitis and hyperamylasaemia, but only at doses of 0.5mg or more. The optimal route and timing of administration were unclear. These conclusions appeared to be supported by the data presented, but the poor quality of many of the included studies suggests that the findings may not necessarily be reliable.

Authors' objectives
To assess the effects of different doses of octreotide for the treatment of post-endoscopic retrograde cholangiopancreatography pancreatitis (ERCP).

Searching
MEDLINE, EMBASE, The Cochrane Library, Science Citation Index and meeting abstracts were searched for studies in any language up to March 2008. Search terms were reported. Reference lists of retrieved articles were searched for additional studies.

Study selection
Randomised placebo-controlled trials that assessed prophylactic administration of octreotide in patients with diagnostic or therapeutic ERCP over a clinical follow-up period of at least 24 hours were eligible for inclusion in the review. Eligible studies had to report the primary outcome of the incidence of post-ERCP pancreatitis (abdominal pain associated with an amylase level at least two times higher than the upper normal limit). Secondary outcomes included post-ERCP hyperamylasaemia (an amylase level greater than the upper normal limit), severe post-ERCP pancreatitis, abdominal pain and adverse events.

Included studies octreotide dosages ranged from 0.1mg to 2.0mg (67% used dosages <0.5mg and 33% used dosages ≥0.5mg). Most studies administered doses subcutaneously; the others used intravenous administration or both. Most of the included patients received octreotide before and after ERCP and were not at high risk of post-ERCP pancreatitis.

The authors did not state how papers were selected for review.

Assessment of study quality
Two reviewers independently assessed methodological quality of the trials using the Jadad scale of randomisation, blinding and withdrawals. Trials that scoring at least 3 points (out of a possible 5) were considered high quality. Disagreements were resolved by discussion.

Data extraction
Data were independently extracted by two reviewers using a standardised form. Studies were categorised into two groups dependent on the total dosage of octreotide (<0.5mg and ≥0.5mg). Odds ratios with 95% confidence intervals (CIs) were calculated.

Methods of synthesis
Studies were grouped by outcome and pooled odds ratios with 95% CIs calculated using the DerSimonian Laird random-effects model where there was significant heterogeneity; otherwise, the general inverse variance fixed-effect model was used. The number needed to treat (NNT) was reported. Statistical heterogeneity was assessed using the $\chi^2$ statistic and $I^2$ statistic.

Subgroup analyses were performed according to: route of administration (intravenous versus subcutaneous); treatment timing (before ERCP versus before and after ERCP); study size (≥100 versus <100); and pre-ERCP risk for post-ERCP pancreatitis.
Sensitivity analyses were carried out to assess effects of publication type, study quality, method of statistical pooling and study size. Publication bias was assessed using a funnel plot.

**Results of the review**
Eighteen RCTs (n=3,983) patients were included in the review. Jadad scores ranged from 1 to 5: two studies scored 5 points; two scored 4 points; five scored 3 points; three scored 2 points; and six scored 1 point. Only seven out of 18 studies reported using adequate allocation concealment methods. Nine studies were double-blinded, four were single-blinded and five were open label trials. Only seven studies clearly reported study dropouts. Sample sizes ranged from 40 to 1,199.

There was no significant difference between doses of octreotide less than 0.5mg versus control for the incidence of post-ERCP pancreatitis (11 RCTs). Incidence of post-ERCP pancreatitis was significantly lower for octreotide doses of at least 5mg versus control (OR 0.45, 95% CI 0.28 to 0.73, I²=0%, NNT=25; six RCTs). There was a statistically significant difference in incidence of post-ERCP hyperamylasaemia in favour of octreotide versus control for all doses (OR 0.79, 95% CI 0.68 to 0.93, NNT=20, I²=14%; 13 RCTs) and for doses of 0.5mg or more octreotide versus control (OR 0.63 95% CI 0.45 to 0.88, NNT=16, I²=0%; four RCTs), but not for doses of less than 0.5mg octreotide (nine RCTs). There were no significant differences between octreotide and control for the incidence of severe post-ERCP pancreatitis (five RCTs) and abdominal pain (four RCTs). No significant heterogeneity was reported.

Several sensitivity analyses and subgroup analyses were reported in the review, but none of the analyses significantly altered the findings.

Two RCTs reported adverse event data. No significant differences were reported between octreotide and control groups. Events were generally mild or dissipated spontaneously.

The authors reported funnel plots for assessment of publication bias, but did not interpret these data.

**Authors' conclusions**
Octreotide was effective in prevention of post-ERCP pancreatitis and hyperamylasaemia, but only at doses of at least 0.5mg. The optimal route and timing of administration were unclear.

**CRD commentary**
This review answered a clearly defined research question and searched a number of relevant databases. Searches were not limited by language, which minimised risk of language bias. There was a risk of publication bias as no specific attempts were made to locate unpublished data and it appeared that only published studies were included. The authors assessed the risk of publication bias using funnel plots, but did not interpret these data and given the small numbers of included studies these assessments were unlikely to be reliable. Some attempts were made to reduce risks of reviewer error and bias during data extraction and quality assessment; it was unclear whether similar precautions were taken during study selection. Risk of bias within individual studies was assessed using appropriate criteria. Study quality appeared to be generally low, which may have affected the reliability of the data. Appropriate methods were used to pool data. Both clinical and statistical heterogeneity between studies were taken into account and investigated in additional analyses; although some of these analyses may not be reliable due to the small number of included studies. Overall, the authors' conclusions appeared to be supported by the data presented, but the poor quality of many of the studies suggests that the findings may not necessarily be reliable.

**Implications of the review for practice and research**
The authors did not state any implications for practice and further research.

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None.

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