Use of octreotide for the prevention of pancreatic fistula after elective pancreatic surgery: a systematic review and meta-analysis

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CRD summary
This review concluded that perioperative octreotide was associated with a significant reduction in the incidence of pancreatic fistula after elective pancreatic surgery. However, the risk reduction was not associated with a similar difference in postoperative mortality. This was a well-conducted review and the authors' conclusions appear to be reliable.

Authors' objectives
To evaluate the effectiveness of octreotide for preventing postoperative pancreatic fistula after pancreatic resection.

Searching
MEDLINE, EMBASE and the Cochrane Central Register of Controlled Trials were searched from inception to September 2004. Search terms were reported. Reference lists of retrieved articles were also scanned.

Study selection
Randomised controlled trials (RCTs) in adults (aged over 18 years) undergoing elective pancreatic resection, treated postoperatively with octreotide or somatostatin compared with placebo or no intervention, were eligible for inclusion. Pancreatic resection was defined as surgery for pancreatic cancer, periampullary cancer or chronic pancreatitis. The primary outcome was the incidence of pancreatic fistula after pancreatic surgery (detailed definition given in the review). The secondary outcome was postoperative death. Trials of surgery for acute pancreatitis and pancreatic trauma, or those not specifying how fistula were detected, or those with an unspecified follow-up duration, were excluded.

Included trials evaluated octreotide doses of 100, 150, 250 or 600μg given every eight hours (apart from one trial where it was every 24 hours) for between six and eight days. Most trials were placebo-controlled, except for one trial which was a no-treatment control. Mean patient age ranged from 47 to 65 years.

Studies were selected by two reviewers independently with disagreements resolved by consensus.

Assessment of study quality
Study validity was assessed by two reviewers independently using the van Tulder quality assessment scoring system (which assigns between 0 and 19 points).

Data extraction
If a trial had multiple treatment arms, the comparison between octreotide and placebo was used where possible. The relative risk and 95% confidence interval was calculated for each trial.

Data were extracted by two reviewers independently onto pre-designed data extraction forms. Discrepancies were resolved by consensus with the senior reviewer.

Methods of synthesis
Clinical heterogeneity was assessed by considering the populations, interventions and outcomes of the included trials. Statistical heterogeneity was assessed using the $\chi^2$ test, with $p<0.10$ considered significant. If trials were considered heterogeneous, a random-effects model was used for any meta-analyses; otherwise a fixed-effect model was used. The number-needed-to-treat was calculated. If pooling was not thought appropriate, a qualitative overview was presented. Heterogeneity was explored by considering the trial characteristics and also by subgroup analyses comparing single and multicentre trials. Publication bias was assessed using a funnel plot.
Results of the review

Seven randomised controlled trials (RCTs) were included (n=1,359 patients); six trials scored 6 for quality and one trial scored 5.

**Postoperative pancreatic fistula risk:** Octreotide treatment reduced the risk of postoperative pancreatic fistula compared with placebo (relative risk 0.59, 95% confidence interval (CI): 0.41 to 0.85; p=0.004). There was some evidence of heterogeneity (p=0.07 and I²=48.7%). The numbers-needed-to-treat to prevent one patient from having a fistula was 10. Subgroup analyses showed a significant reduction with octreotide treatment in the multicentre trials (relative risk 0.46, 95% CI: 0.34 to 0.60; p<0.001) but no evidence of a difference in the two single centre studies (relative risk 1.25, 95% CI: 0.74 to 2.10; p=0.4). Splitting by the number of centres also removed the heterogeneity. There was no evidence of publication bias.

**Death after surgery:** Results for death after surgery were presented by the length of follow-up. From three trials which reported 90 day mortality, octreotide treatment showed a reduction in mortality, although it was not statistically significant (relative risk 0.62, 95% CI: 0.26 to 1.48; I²=0%). There was also no evidence of a difference for mortality at 60 days (two RCTs), 30 days (one RCT) and in hospital (one RCT).

**Authors' conclusions**

Octreotide given perioperatively was associated with a significant reduction in the incidence of pancreatic fistula after elective pancreatic surgery. This risk reduction was not associated with a similar difference in postoperative mortality. Further research is needed to confirm these results and identify subgroups who would derive most benefit from octreotide prophylaxis.

**CRD commentary**

This review had clear inclusion and exclusion criteria. A number of relevant sources were searched. It was unclear if there were any language restrictions, so some relevant studies may have been missed. However, the authors assessed publication bias and concluded that this was not an issue. Systematic review methods were performed in duplicate. Trial quality was assessed, although only a total score was given. Further details of the aspects covered by this scale and reporting of the complete data for each trial would have been helpful for readers to judge the reliability of the evidence. The methods used in the meta-analysis were appropriate. The authors gave careful consideration in the discussion to any differences between the trials. The methods and reporting of this review were good and the authors’ conclusions appear to be reliable.

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

**Practice:** The authors did not state any implications for practice.

**Research:** Further research is needed to confirm the results of this meta-analysis and to identify subgroups of patient who would gain the most benefit from octreotide given prophylactically for pancreatic surgery.

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