Prophylactic antibiotic administration reduces sepsis and mortality in acute necrotizing pancreatitis: a meta-analysis

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Authors' objectives
To evaluate the role of prophylactic antibiotics that can achieve minimum inhibitory concentration in necrotic pancreatic tissue in patients with acute necrotising pancreatitis (ANP).

Searching
MEDLINE was searched from 1966 to January 2000 using the keywords 'pancreatitis', 'pancreatitis, acute necrotizing' and the textword 'acute pancreatitis' combined with 'antibiotics' (keyword and textword). Official proceedings of all major North American and European meetings were searched. Dual publications were excluded. If more than one version of the same trial had been retrieved, only the most recent data would have been used. There does not seem to have been any language restrictions.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were included.

Specific interventions included in the review
Antibiotics used to prevent the complications (local and systemic infections) of ANP were eligible for inclusion in the review. The included trials used imipenem (500 mg, three times daily) or cefuroxime (1.5 g, three times daily). The control groups in these trials received no antibiotic prophylaxis. Another included trial seems to have compared a combination ofloxacin (200 mg, twice daily) and metronidazole (500 mg, twice daily) with a control group which received no antibiotic prophylaxis.

Participants included in the review
People diagnosed with ANP. In two included trials, the patients had severe acute pancreatitis but no pancreatic necrosis on computed tomography. Publications that included patients without ANP or were without a control group receiving no antibiotic prophylaxis were excluded.

Outcomes assessed in the review
The included studies had to report the rates of local pancreatic infections, sepsis and mortality in each treatment arm.

How were decisions on the relevance of primary studies made?
Both authors independently reviewed each study.

Assessment of study quality
The authors do not state that they assessed validity.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the reviewers performed the data extraction.

The data were extracted into the following categories: study details; antibiotic prophylaxis and dose; sample size; and results.

Methods of synthesis
How were the studies combined?
The pooled relative risk reduction (RRR), absolute risk reduction (ARR) and number-needed-to-treat (NNT) were calculated, along with 95% confidence intervals (CIs), for pancreatic infection, sepsis and mortality. The NNTs were rounded to the nearest whole number.

How were differences between studies investigated?
The Breslow-Day test for homogeneity (see Other Publications of Related Interest) was applied to ensure that the trials were appropriate for pooling.

Results of the review
Three RCTs (n=160) were included.

No significant heterogeneity was found (p=0.70).

Local pancreatic infection: the RRR was 31% (95% CI: -14, 60), the ARR was 12% (95% CI: -2.4, 26.4), and the NNT was 8 (95% CI: number-needed-to-harm 41, NNT 4).

Sepsis: the RRR was 46% (95% CI: 15, 70), the ARR was 21.1% (95% CI: 6.5, 35.6), and the NNT was 5 (95% CI: 3, 15).

Mortality: the RRR was 72% (95% CI: 40, 100), the ARR was 12.3% (95% CI: 2.7, 22), and the NNT was 8 (95% CI: 5, 37).

Authors’ conclusions
This meta-analysis supported the use of prophylactic antibiotics in patients with ANP. All patients with severe pancreatitis should be evaluated with a rapid bolus, contrast-enhanced computed tomography scan to look for pancreatic necrosis. Patients with pancreatic necrosis should be started on prophylactic antibiotics that have proven efficacy to prevent infection in ANP. This should reduce the morbidity associated with this condition. Furthermore, the results suggest that it should only be necessary to treat approximately eight patients to prevent one death.

CRD commentary
The review question was not stated clearly but the study selection criteria were clear. The literature search was restricted to one database (MEDLINE), and while no language restrictions were imposed, this restriction to MEDLINE may have led to some studies being missed. No attempt was made to locate unpublished material. Conference proceedings were searched but the authors do not state which conferences these were. No attempt was made to assess validity. Some details of the review process were given. The individual studies are not reported in much detail, in particular, with regard to the participants and control groups. The methods of pooling seem appropriate.

The pooled results showed a significant reduction in the risk of sepsis and mortality (but not pancreatic infection) in the antibiotic group. However, the authors’ conclusions should be treated with some caution owing to limitations in the search, the absence of a validity assessment, and the fact that the results came from only three RCTs with a total of 160 participants.

Implications of the review for practice and research
Practice: The authors state that all patients with severe pancreatitis should be evaluated with a rapid bolus, contrast-enhanced computed tomography scan to look for pancreatic necrosis. Patients with pancreatic necrosis should be started on prophylactic antibiotics that have proven efficacy to prevent infection in ANP.

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

Reviewer’s comment: Further research, in the form of a large multicentre RCT, seems warranted to confirm the findings of this review.

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Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
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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.