Role of antibiotics in acute pancreatitis: a meta-analysis

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Authors' objectives
To determine the role of antibiotics in preventing infectious complications in acute pancreatitis.

Searching
MEDLINE was searched from 1966 to June 1997, with search terms including 'pancreatitis', 'antibiotics' and 'randomised studies'. The bibliographies of identified trials, and other recent publications on the treatment of pancreatitis, were reviewed.

Study selection
Study designs of evaluations included in the review
Randomised prospective trials.

Specific interventions included in the review
Systemic and oral antibiotics were compared with standard care (pain medication, nasogastric suction, intravenous hydration, and nutritional support, and some studies used atropine or antiprotease drugs). The antibiotics studied included: ampicillin (500 mg to 1 g every 6 hours, 1 g every 6 hours); ceftazidime (2 g every 8 hours, intravenously); amikacin (7.5 mg/kg every 12 hours); flagyl (500 mg every 8 hours plus 500 mg twice daily); imipenem (500 mg every 8 hours); cefuroxime (1.5 g/day intravenously); ofloxacin (200 mg twice daily); colistin sulfate (200 mg orally every 6 hours and daily enema); amphotericin (500 mg orally every 6 hours and daily enema); norfloxacin (50 mg orally every 6 hours and daily enema); and cefotaxime (500 mg every 8 hours, intravenously).

Participants included in the review
Patients with acute pancreatitis (ETOH, idiopathic, gallstones, trauma, and other) of varying severity, as determined by Ranson score, Imrie score and Balthazar grade. Average age ranged from 35.7 to 55.5 years, and in the majority of the studies there were a higher percentage of men.

Outcomes assessed in the review
The outcome of interest was mortality.

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
The studies were critically reviewed using a 10-point scale proposed by Solomon and McLeod (see Other Publications of Related Interest no.1). The studies were critically reviewed by two independent investigators. Inter-observer agreement was assessed by the intra-class correlation (see Other Publications of Related Interest no.2).

Data extraction
Pertinent results including demographic data (age and sex), methods, and end points including death were extracted and coded by two of the authors, and any differences were arbitrated by a third investigator.

Methods of synthesis
How were the studies combined?
Treatment effects across multiple studies were summarised by calculating the Mantel-Haenszel statistic (see Other Database of Abstracts of Reviews of Effects (DARE)
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Publications of Related Interest no.3) as well as the standard error and corresponding 95% confidence intervals (CIs). The authors used a fixed-effect model for the meta-analysis to calculate log odds ratios (ORs) and 95% CIs.

How were differences between studies investigated?
Homogeneity was assessed by calculating the Q statistic. Sensitivity analysis was performed when appropriate.

Results of the review
Eight prospective randomised trials (n=514). None of the trials were blinded.

The average study quality score was 7.5 with an intra-class correlation of 0.41 (P<0.0001).

The Mantel-Haenszel log OR, which summarises the mortality data across all 8 trials was -0.77 (95% CI: -0.14, -1.40, P=0.016). The probability of dying was 6.6% in the antibiotic-treated patients compared to 13.3% in the patients. The homogeneity of variance, Q, was 3.60 (P=0.82).

Removing the study by Luiten et al., which used systemic and oral antibiotics, gave a Mantel-Haenszel log OR of -1.16 (95% CI: -0.19, -2.15, P=0.016) and Q was 3.19 (P=0.78). Removing the trial by Sainio et al. gave a log OR of -0.56 (95% CI: 0.12, -1.24, P=0.10).

Three trials using ampicillin were analysed as a separate group. The combined log OR was 0.40 (95% CI: -1.71, 2.52, P=0.71) and Q was 0.20 (P=0.91).

Analysis of 4 studies using broad-spectrum antibiotics in patients with severe pancreatitis gave a Mantel-Haenszel log OR of -1.38 (95% CI: -0.32, -2.44, P=0.008) and Q of 1.41 (P=0.70). Patients who received antibiotics had a 5.3% probability of dying compared to a 18.2% incidence in the control group.

Authors’ conclusions
Strong consideration should be given to treating patients with severe pancreatitis with broad-spectrum antibiotics, such as imipenem or one of the fluoroquinolones, which have been shown to achieve therapeutic concentrations in pancreatic tissue.

CRD commentary
Overall, the methodological quality of this review was mixed. The inclusion criteria were acceptable but the authors could have carried out a more extensive literature search: by limiting the search to MEDLINE there is the possibility that a number of studies may have been missed. Validity assessment was good as each study was independently and systematically assessed by two reviewers. A number of study details were lacking from the tables, in particular straightforward sample sizes. Pooling of the results appeared to be appropriate and a number of subgroup analyses were undertaken. Heterogeneity was assessed and not found to be significant.

The authors conclusions should be interpreted with caution due to the small number of studies included in the meta-analysis and the limitations described. The main conclusion of the review is based on data from only 4 trials with a combined total of 314 patients.

Implications of the review for practice and research
Practice: The authors state that strong consideration should be given to treating patients with severe pancreatitis with broad-spectrum antibiotics, such as imipenem or one of the fluoroquinolones, which have been shown to achieve therapeutic concentrations in pancreatic tissue. Patients with an Imrie or Ranson score greater than or equal to three, or a Balthazar grade of D or greater, should be considered for prophylaxis.

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

PubMedID
10457308

Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
Acute Disease; Anti-Bacterial Agents /therapeutic use; Bacterial Infections /drug therapy; Humans; Pancreatitis /complications /drug therapy

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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.