Randomized controlled trials of antibiotic prophylaxis in severe acute pancreatitis: relationship between methodological quality and outcome


CRD summary
The authors concluded that there is currently inadequate evidence that antibiotic prophylaxis is effective in severe acute pancreatitis; methodological quality appears to influence the outcomes. There were some limitations to this review but, overall, the authors’ conclusions reflect the evidence presented and are likely to be reliable.

Authors' objectives
To evaluate the effectiveness of antibiotic prophylaxis in severe acute pancreatitis and to examine the influence on the results of the methodological quality of randomised controlled trials (RCTs).

Searching
MEDLINE, EMBASE and the Cochrane CENTRAL Register were searched from 1990 using the reported search strategy. No language restrictions were applied.

Study selection
Study designs of evaluations included in the review
RCTs were eligible for inclusion.

Specific interventions included in the review
Studies that evaluated intravenous antibiotic prophylaxis were eligible for inclusion. Studies that compared different antibiotic regimens or modes of administration were excluded, as were studies of selective decontamination of the digestive tract. The included studies used a variety of antibiotics, including imipenem, meropenem, cephalosporins and a combination of third-generation fluoroquinolones plus metronidazole.

Participants included in the review
Studies of patients with severe acute pancreatitis were eligible for inclusion. Some of the primary studies only included patients with alcohol-induced pancreatitis; other studies included patients with biliary and other causes. Mean prognostic Ranson scores ranged from 2.3 to 5.5. The inclusion criteria for individual studies were reported.

Outcomes assessed in the review
Inclusion criteria were not specified in terms of the outcomes. The review assessed infection of pancreatic necrosis and mortality.

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

Assessment of study quality
Studies were assessed using an adapted published quality assessment tool that assessed the following validity criteria: population (patient selection and patient characteristics), intervention (allocation sequence, concealment of allocation, blinding, description of intervention, and method of feeding) and the flow of participants. The maximum possible score was 17 points. Three researchers independently assessed study quality, with any disagreements resolved by consensus. Studies that scored less than 5 points were excluded from the meta-analyses.

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction. For each study included in the meta-analyses, the absolute risk reduction (ARR) and relative risk reduction (RRR) were presented with their respective 95% confidence intervals (CIs).
Methods of synthesis
How were the studies combined?
Pooled ARRs and RRRs with 95% CIs were calculated using a random-effects model for studies that scored at least 5 points out of 17 on validity criteria.

How were differences between studies investigated?
Spearman’s correlation coefficient was used to assess the relationship between study quality and outcomes.

Results of the review
Eight RCTs met the inclusion criteria. However, only six met the quality criteria and were included in the meta-analyses (n=397).

In one study the treatment groups were highly comparable. Two studies used a double-blind placebo-controlled design. Three studies did not report the feeding method. Two studies explicitly reported the flow of participants.

There was no significant difference between antibiotic prophylaxis and control in infection of pancreatic necrosis (ARR 0.055, 95% CI: -0.084, 0.194) or mortality (ARR 0.058, 95% CI: -0.194, 0.154).

No relationship was found between methodological quality and the risk of infection of pancreatic necrosis.

Studies of higher methodological quality showed a smaller effect of antibiotic prophylaxis on mortality than lower quality studies (correlation coefficient for ARR -0.841, p=0.036; correlation coefficient for RRR -0.948, p=0.004).

Authors’ conclusions
There is currently inadequate evidence that antibiotic prophylaxis is effective in severe acute pancreatitis. Methodological quality appears to influence the outcomes.

CRD commentary
The review addressed a clear question that was defined in terms of the participants, intervention and study design; inclusion criteria were not defined for the outcomes. Several relevant sources were searched, with attempts made to minimise language bias but not publication bias. Validity was assessed using specified criteria, the results were reported, and only studies meeting the minimum quality criteria were included in analyses. Appropriate methods were used to minimise reviewer error and bias in the assessment of validity, but it is unclear whether such steps were taken to minimise errors and bias in the study selection and data extraction processes. Studies were pooled using meta-analysis without prior assessment of heterogeneity, and forest plots suggested some differences between the study results. The examination of the association between study quality and outcomes was appropriately accompanied by scatter plots. There were some limitations to this review but, overall, the authors’ conclusions reflect the evidence presented and are likely to be reliable.

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

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