Prophylactic antibiotic treatment in acute necrotizing pancreatitis: results from a meta-analysis
Xu T, Cai Q

CRD summary
This review found that use of prophylactic antibiotics reduced the risk of pancreatic or peri-pancreatic infections, but was not associated with a reduction in mortality or surgical intervention. The review was generally well conducted, but the results should be treated with caution given the relatively small number of trials and their small sample size.

Authors' objectives
To assess the long-term efficacy of prophylactic antibiotic treatment for acute necrotizing pancreatitis.

Searching
PubMed, EMBASE and the Cochrane Central Register of Controlled Trials (CENTRAL) were searched until December 2007. Search terms were reported. A manual search of the bibliography of the retrieved articles was also performed. No language restrictions were enforced.

Study selection
To be selected studies had to be a randomized trial, with placebo or untreated controls, in patients with severe confirmed necrotizing pancreatitis, within 120 hours of onset of symptoms. No exclusion criteria were specified, but studies were excluded on the grounds of inappropriate antibiotic use (non-pancreatic tissue penetration), non-intravenous administration of antibiotics, two or more antibiotics assessed, or insufficient data.

Mean age of patients in included trials ranged between 38.7 and 60 years. Half of the trials evaluated carbapenem antibiotics. Duration of antibiotic use varied between five and 21 days.

The decision to include trials was made independently by two researchers, with discrepancies resolved in common.

Assessment of study quality
Trials were assessed for quality using the Jadad five point quality scale by two authors separately and discrepancies resolved by consensus. Trials with a quality score of 3 or more were considered as of high quality.

Data extraction
Relative risks (RRs) were calculated for dichotomous outcomes using data on numbers of participants and events. Group means and standard deviations were used to calculate the mean difference for continuous outcomes.

Data were independently extracted by two researchers and disagreements resolved by consensus.

Methods of synthesis
The pooled relative risks or weighted mean differences (WMDs) were calculated using a fixed-effect meta-analysis for all endpoints. Heterogeneity was assessed using the $\chi^2$ and $I^2$ statistics. Each endpoint was also stratified by carbapenem versus other antibiotics in subgroup analyses.

Results of the review
Eight randomised controlled trials (RCTs) were included (n=540 patients, range 26 to 114). Two trials were considered of low quality.

There was no evidence that antibiotic prophylaxis reduced mortality (RR 0.76, 95% CI 0.50 to 1.18) or surgical intervention (RR 0.90, 95% CI 0.66 to 1.23) for acute necrotizing pancreatitis. Antibiotic prophylaxis significantly reduced pancreatic or peri-pancreatic infection (RR 0.69, 95% CI 0.50 to 0.95). Antibiotic therapy significantly
reduced the length of hospital stay (WMD 5.64 days, 95% CI 0.27 to 11.01), but this result was only based on three trials. There was no evidence of statistical heterogeneity in the outcome assessments.

In the subgroup analysis, carbapenem antibiotics were associated with significant reductions in pancreatic and non-pancreatic infections, but other antibiotics were not.

**Authors’ conclusions**
Prophylactic antibiotic treatment was associated with a significant reduction of pancreatic, peri-pancreatic or non-pancreatic infection and hospital length of stay, but not with death or surgical intervention in acute necrotizing pancreatitis.

**CRD commentary**
The review clearly stated the objectives and search methodology. It was not clear if any attempt was made to assess publication bias, so bias could not be ruled out. Although a quality scale was used to score the individual trials, no sensitivity analysis on quality was performed. Appropriate methods were used to minimise risk of errors and bias during the review process.

Adequate details of the included trials were included. Trials were synthesised by meta-analysis and some sources of heterogeneity were investigated.

The review was generally well conducted, but the results should be treated with caution given the relatively small number of trials and their small sample size.

**Implications of the review for practice and research**
**Practice**: The authors stated that prophylactic antibiotic treatment is suggested to prevent infection, possibly focusing on carbapenem, in line with published guidelines on infected pancreatic necrosis.

**Research**: The authors stated that areas for further research include: the type of nutritional support; the timing of initiation and duration of antibiotic treatment; and the selection of patients at high risk for infected pancreatic necrosis.

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