Prophylactic antibiotics in necrotizing pancreatitis: a meta-analysis

CRD summary
The authors concluded that prophylactic antibiotics did not reduce mortality, rate of infected necrosis or the need for surgical intervention in patients with necrotising pancreatitis, but that they did reduce the risk of non-pancreatic infections and length of hospital stay. Given the unclear quality of the included trials, the reliability of the authors’ conclusions is unclear.

Authors' objectives
To investigate the effects of prophylactic antibiotics in necrotising pancreatitis.

Searching
MEDLINE, Cochrane Central Register of Controlled Trials and the Cochrane Database of Systematic Reviews were searched to May 2007. Search terms were reported. Abstracts of conference proceedings from at least 11 relevant conferences were also searched. Bibliographies of selected studies and previously published meta-analyses were scanned.

Study selection
Randomised controlled trials (RCT) that compared treatment with prophylactic intravenous (IV) antibiotics to treatment without prophylactic antibiotics in patients with acute necrotising pancreatitis, confirmed by contrast enhanced computed tomography, were eligible for inclusion. Trials investigating head-to-head antibiotic usage, gut decontamination or timing of antibiotic administration were excluded. Outcomes of interest were infected pancreatic necrosis, mortality, number of non-pancreatic infections, surgical intervention and mean hospital stay.

Prophylactic antibiotics used in the included trials were meropenem, cefuroxime, imipenem, ciprofloxacin plus metronidazole, imipenem plus cilastatin or ofloxacin plus metronidazole, administered for between seven and 21 days (where reported). Both multi-centre and single centre trials in North American and Europe were included.

The authors did not state how the studies were selected for the review, or how many reviewers performed the study selection.

Assessment of study quality
The authors did not state that they assessed validity, but they did report on the use of placebo and blinding within the results.

Data extraction
The number of events in each group were extracted for dichotomous outcomes and used to calculate odds ratios with corresponding 95% confidence intervals. For continuous data, the mean difference between groups was extracted.

Data were independently extracted by two reviewers, with a third reviewer examining for agreement. Differences were resolved through discussion between the three reviewers. Authors were contacted for further information.

Methods of synthesis
Pooled odds ratios with 95% confidence intervals were used to combine dichotomous data. Weighted mean differences with 95% confidence intervals were used to combine continuous data. Both fixed-effect and random-effects models were used. Statistical heterogeneity was assessed using the I^2 statistic. Publication bias was assessed using funnel plots and the Harbour-Egger method.

Results of the review
Seven randomised controlled trials (RCTs) were included for the review (n=429 patients); two placebo-controlled
double-blind RCTs (n=176 patients) and five unblinded RCTs (n=253 patients).

Prophylactic antibiotics were not associated with a reduction in the risk of infected pancreatic necrosis (odds ratio 0.72, 95% confidence interval (CI): 0.45 to 1.16; seven RCTs, n=429 patients), mortality (odds ratio 0.71, 95% CI: 0.41 to 1.23; seven RCTs, n=429 patients) or surgical intervention (odds ratio 0.82, 95% CI: 0.52 to 1.30; six RCTs, n=403 patients) compared to no treatment.

Prophylactic antibiotic use was associated with a significant decrease in the incidence of non-pancreatic infections (odds ratio 0.51, 95% CI: 0.32 to 0.82; five RCTs, n=334 patients) and length of hospital stay (weighted mean difference -5.64, 95% CI: -11.01 to -0.27; three RCTs, n=153 patients).

There was no evidence of significant statistical heterogeneity for any outcomes. There was no evidence of publication bias.

**Authors’ conclusions**

Prophylactic antibiotics did not reduce mortality, rate of infected necrosis or the need for surgical intervention in patients with necrotising pancreatitis. Prophylactic antibiotics did reduce the risk of non-pancreatic infections and length of hospital stay. However, these benefits should be weighed against the risk of bacterial resistance and fungal infections.

**CRD commentary**

The review addressed a clear question. Inclusion criteria for intervention, study design, outcomes and participants were well-defined. Several relevant databases were searched. Some attempts were made to identify unpublished material and publication bias was assessed. Appropriate attempts appeared to have been made to limit language bias. Appropriate methods were used in the data extraction process to minimise reviewer error and bias; it was unclear whether these were also applied in the study selection process, so reviewer error and bias cannot be ruled out. A formal validity assessment did not appear to have been carried out, so the methodological quality of the included trials was unclear. Only limited details of the included trials were reported, leaving the reviewer to assess the quality and relevance of the included trials. Suitable methods were used to combine the trials and statistical heterogeneity was assessed. Given the unclear quality of the included trials, the reliability of the authors’ conclusions is unclear.

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

**Practice:** The authors stated that the relatively minor clinical benefits of prophylactic antibiotic use should be weighed against the risk of bacterial resistance and opportunistic fungal infection.

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

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