Prophylactic antibiotics cannot prevent endoscopic retrograde cholangiopancreatography-induced cholangitis: a meta-analysis

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CRD summary
This review evaluated efficacy of prophylactic antibiotics for prevention of post-endoscopic retrograde cholangiopancreatography (ERCP) cholangitis or sepsis. The authors concluded that prophylactic antibiotics could not significantly prevent post-ERCP cholangitis in unselected patients and should not be routinely recommended. Without further details on study quality and given the other methodological concerns, it is difficult to judge the reliability of these conclusions.

Authors' objectives
To assess the efficacy of prophylactic antibiotics for the prevention of post-endoscopic retrograde cholangiopancreatography (ERCP) cholangitis/sepsis.

Searching
MEDLINE, EMBASE, The Cochrane Library and Science Citation Index were searched up to June 2007 without language restriction. The search terms were not reported. Major international conference proceedings were handsearched. Reference lists of relevant publications were screened.

Study selection
Randomised controlled trials (RCTs) that evaluated prophylactic antibiotics in patients who underwent ERCP were eligible for inclusion. The review outcomes were post-ERCP cholangitis or sepsis.

Included studies evaluated a number of prophylactic antibiotics: cefotaxime, cefonicid, piperacillin, cefuroxime, ceftazidime, clindamycin and gentamicin. It was unclear whether the control arm of included studies used placebos. Most included studies administered antibiotics intravenously 15 minutes to one hour before ERCP. The definition for the outcome of cholangitis/sepsis varied in included studies. The included studies were published between 1990 and 2006. Most included studies were published in Europe.

The authors stated neither how the papers were selected for the review nor how many reviewers performed the selection.

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

Data extraction
Data were extracted on the number of patients who experienced an event using a prespecified data extraction form. Relative risks (RRs) with 95% confidence intervals (CIs) were calculated.

Two reviewers independently extracted the data.

Methods of synthesis
The studies were combined in meta-analyses. A random-effects model was used in the presence of statistical heterogeneity; otherwise a fixed-effects model was employed. Pooled RRs with 95% CIs were calculated. Statistical heterogeneity was assessed using Cochran Q and \( I^2 \) statistics. Publication bias was visualised using funnel plots. Sensitivity analyses were performed to examine the influence of antibiotic administration route and patients' characteristics (unselected patients versus those with suspected biliary obstruction).

Results of the review
Seven RCTs (n=1,389) were included in the meta-analysis. Sample size varied from 61 to 551. Follow-up duration in the included RCTs was not reported.

Compared with controls, prophylactic antibiotics were associated with a non-significant reduction in post-ERCP cholangitis/sepsis (RR 0.58, 95% CI 0.22 to 1.55; seven RCTs). Statistical heterogeneity was observed in the outcome of post-ERCP cholangitis/sepsis ($I^2=49.3\%$, $p=0.07$).

Sensitivity analyses did not materially affect the results. Evidence of publication bias was found according to visual scanning of funnel plots.

**Authors' conclusions**
Prophylactic antibiotics could not significantly prevent post-ERCP cholangitis in unselected patients.

**CRD commentary**
This review's inclusion criteria were clear. Several relevant databases were searched. Efforts were made to find published and unpublished studies without language restriction, which minimised potential for publication and language biases. Publication bias was assessed and possible evidence of publication bias was found, although use of funnel plots to assess publication bias in a small number of studies might not be appropriate. Steps were taken to minimise bias by having more than one reviewer independently undertake data extraction; it was unclear whether the process of study selection was also performed in duplicate. There was no formal validity assessment. Statistical heterogeneity was assessed and appropriate statistical methods were used to pool the results. Without further details on study quality and given the other methodological concerns, it is difficult to judge the reliability of the authors' conclusions.

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

**Practice:** The authors stated that prophylactic antibiotics should not be routinely recommended before ERCP.

**Research:** The authors stated that further RCTs that included patients with predicted incomplete biliary drainage were required to assess effectiveness of prophylactic antibiotics in this setting.

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