Early endoscopic retrograde cholangiopancreatography versus conservative management in acute biliary pancreatitis without cholangitis: a meta-analysis of randomized trials

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CRD summary
This well-conducted review concluded that early endoscopic retrograde cholangiopancreatography in patients with acute biliary pancreatitis without cholangitis was an unnecessary and invasive procedure that did not lead to significant reductions to risk of overall complications or mortality. These conclusions should be considered with caution due to possibility of clinical and statistical heterogeneity within the data.

Authors' objectives
To compare early endoscopic retrograde cholangiopancreatography with conservative management in patients with acute biliary pancreatitis (ABP) without cholangitis.

Searching
MEDLINE, EMBASE and unspecified Cochrane databases were searched to March 2007. Search terms for each database were reported. No language restrictions were applied. Identified articles and reviews were handsearched for additional citations.

Study selection
Studies were eligible for this review if they used randomisation to allocate patients with acute biliary pancreatitis but no acute cholangitis to one of the following treatment groups: early endoscopic retrograde cholangiopancreatography within 72 hours with or without endoscopic sphincterotomy; and conservative treatment with selective endoscopic retrograde cholangiopancreatography with or without endoscopic sphincterotomy. The outcomes of interest were rates of mortality and overall complications.

Included studies were all randomised controlled trials (RCTs) of patients with acute biliary pancreatitis without acute cholangitis; where trials included patients with acute cholangitis these data were presented separately. Only one trial was multicentre and the rest were single centre. Trials used different criteria to establish cholangitis (bilirubin levels, Charcot's triad or not stated). Early endoscopic retrograde cholangiopancreatography was given either within 48 hours or 72 hours of admission or onset. Patient ages in the early endoscopic retrograde cholangiopancreatography groups ranged from 20 to 90 years and in the conservative treatment groups from 15 to 96 years. The balance of females ranged from 52% to 69% in the early endoscopic retrograde cholangiopancreatography group and from 56% to 75% in the conservative treatment group. Trials reported mortality rates and overall complications; the latter was defined differently in each included study.

Study selection was performed by two reviewers working independently. Any discrepancies were resolved by discussion.

Assessment of study quality
Methodological quality was assessed using the 5-point Jadad scale on the basis of random allocation, masking of patients and dropouts/withdrawals. Three additional criteria were also used: allocation concealment, blinding of end point assessment and was at least 90% of the data reported (all items answered as yes or no). The authors did not report how the validity assessment was carried out.

Data extraction
Overall rates of mortality and complications were extracted for each study. Where no events were observed in both treatment groups, an event fraction (0.001) was added to the early endoscopic retrograde cholangiopancreatography group so that these data could be included in the pooled analyses. Data was extracted independently by two reviewers.

Methods of synthesis
Meta-analysis was performed using the Mantel-Haenszel method to pool data and calculate risk ratios (RR) and risk differences (RD) with associated 95% confidence intervals (CI) for mortality and overall complication rates. Additional analyses were conducted based on patients with predicted severe or mild acute biliary pancreatitis. Funnel plots were used to assess publication bias.

**Results of the review**

A total of three RCTs were included (total n=450); 230 patients were allocated to early endoscopic retrograde cholangiopancreatography with or without endoscopic sphincterotomy and of these 214 received successful endoscopic retrograde cholangiopancreatography; 220 patients were allocated to conservative treatment of which 30 received successful endoscopic retrograde cholangiopancreatography. Two trials scored 2 out of 5 and one scored 3 out of 5 on the Jadad quality scale. No publication bias was reported.

Early endoscopic retrograde cholangiopancreatography did not significantly reduce the risk of overall complications in ABP patients (RR 0.76, 95% CI 0.41 to 1.40). No significant difference in mortality between treatment groups was noted (RR 1.13, 95% CI 0.23 to 5.63). The risk ratios translate into very small non-significant reductions in absolute risk for complications and a non-significant increase in mortality. Stratification for predicted severity of ABP did not significantly alter these results.

**Authors' conclusions**

Early endoscopic retrograde cholangiopancreatography in patients with predicted mild and severe acute biliary pancreatitis without cholangitis was an unnecessary and invasive procedure, and did not lead to significant reductions to risk of overall complications or mortality.

**CRD commentary**

This review addressed a clear clinical question with appropriate inclusion criteria. The searches covered the main medical databases without restricting by language, but were unlikely to have identified any grey literature, thus risking publication bias. The methods used were clearly reported, use of multiple independent reviewers for screening/selection and data extraction was likely to have minimised reviewer error and bias. Methodological quality was suitably assessed and commented on within the review. The analysis appeared appropriate, although statistical heterogeneity was not assessed and there may have been clinical variation between the studies. The authors' conclusions should be considered with caution due to possibility of clinical and statistical heterogeneity within the data.

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

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

**Research:** The authors recommended that an adequately powered RCT should be carried out to explore the impact of early endoscopic retrograde cholangiopancreatography on patients with predicted severe acute biliary pancreatitis. In such studies patients with acute cholangitis should be excluded, timing of the intervention should be clearly stated and stratification for the presence or absence of cholangitis should be carried out.

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