A meta-analysis of rectal NSAIDs in the prevention of post-ERCP pancreatitis
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CRD summary
The authors concluded that, in this meta-analysis, prophylactic rectal non-steroidal anti-inflammatory drugs were effective in preventing post-endoscopic retrograde cholangiopancreatography pancreatitis, but further studies are needed to confirm these findings before their use becomes widespread. Overall, this was a well-conducted review and the authors’ conclusions are likely to be reliable.

Authors' objectives
To evaluate the effect of prophylactic rectal non-steroidal anti-inflammatory drugs (NSAIDs) for the prevention of post-endoscopic retrograde cholangiopancreatography pancreatitis (PEP).

Searching
MEDLINE and EMBASE were searched from 1966 to December 2007. Search terms were reported. Reference lists of potentially relevant papers were screened. In addition, abstracts from meetings of the American Gastroenterologic Association, American Society of Gastrointestinal Endoscopy, American College of Gastroenterology and United European Gastroenterology Week (2002 to 2007) were searched.

Study selection
Randomised controlled trials (RCTs) were eligible if they compared the effect of rectally administered prophylactic non-steroidal anti-inflammatory drugs (NSAIDs) with placebo on the incidence of post-endoscopic retrograde cholangiopancreatography pancreatitis (PEP). The review assessed the overall incidence of pancreatitis and the incidence of moderate to severe pancreatitis.

The included trials were conducted in Iran, Mexico and Scotland. Trials evaluated 100mg rectal diclofenac given on arrival in the recovery area and 100mg rectal indomethacin given immediately before endoscopic retrograde cholangiopancreatography (ERCP). Three of the four trials did not report use of prophylactic pancreatic stents. PEP was defined as a more than a three of four-fold rise in amylase above the normal upper limit plus specified types of pain. Two trials were in high-risk patients (limited to those undergoing pancreatogram with or without cholangiography) and two recruited patients regardless of risk status; trials excluded patients with contraindications to NSAIDs.

Three reviewers independently selected studies.

Assessment of study quality
Validity was assessed using the following five criteria described by the Evidence-Based Gastroenterology Steering Group: allocation concealment of randomisation; blinding of patients and caregivers; equal co-interventions in NSAID and placebo groups; complete follow-up of study patients; and use of intention-to-treat analysis.

The authors did not state how many reviewers assessed validity.

Data extraction
Two reviewers independently extracted data and reached full agreement.

Methods of synthesis
Pooled relative risks (RR) with 95% confidence intervals (CI) were calculated using fixed-effect (Mantel-Haenszel) and random-effects models. No significant heterogeneity was found using the \( \chi^2 \) test, so results from the fixed-effect model were reported.

The number needed to treat (NNT) to prevent one episode of pancreatitis was also calculated.
Results of the review
Four RCTs were included (n=912 patients). All of the trials were considered to be of reasonable quality. Two trials met all validity criteria, one trial met four criteria, and one trial met three criteria.

Rectal non-steroidal anti-inflammatory drugs (NSAIDs) were associated with a statistically significant reduction in post-endoscopic retrograde cholangiopancreatography pancreatitis (PEP) compared with placebo (RR 0.36, 95% CI 0.22 to 0.60; four RCTs; NNT 15). No significant heterogeneity was found.

Rectal NSAIDs were associated with a statistically significant reduction in moderate to severe pancreatitis compared with placebo, zero patients in the NSAID groups versus seven patients in the placebo control groups (RR 0.10, 95% CI 0.01 to 0.76; two RCTs; NNT 39).

None of the included trials reported any adverse effects associated with rectal NSAIDs.

Cost information
The authors estimated that based on review findings, with a PEP risk of 5% there would be 38 cases of PEP per year among 750 patients undergoing ERCP. Cost savings using rectal NSAIDs were estimated at US$141,000 annually per 750 patients.

Authors' conclusions
In this meta-analysis, prophylactic rectal non-steroidal anti-inflammatory drugs were effective in preventing post-endoscopic retrograde cholangiopancreatography pancreatitis. Further studies are needed to confirm these findings before their use becomes widespread.

CRD commentary
The review question was clearly stated and inclusion criteria were appropriately defined. Several relevant sources were searched. Attempts were made to minimise publication bias, but it was not clear if attempts were made to limit language bias. Methods were used to minimise reviewer errors and bias in the selection of studies and extraction of data, but it was not clear whether similar steps were taken for the validity assessment.

Study quality was assessed and the numbers of criteria met were reported. Appropriate methods were used for the meta-analyses and heterogeneity was assessed.

Overall, this was a well-conducted review and the authors' conclusions are likely to be reliable.

Implications of the review for practice and research
Practice: The authors stated that findings from this review require confirmation in additional multicentre studies before the use of rectal NSAIDs becomes widespread.

Research: The authors stated that additional multicentre studies on the effect of rectal NSAIDs on PEP are required. The effects of rectal NSAIDs on severe pancreatitis requires further research, as does the effect of combining rectal NSAIDs with other prophylactic interventions.

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