Glyceryl trinitrate for prevention of pancreatitis after endoscopic retrograde cholangiopancreatography: a meta-analysis of randomized, double-blind, placebo-controlled trials

Bai Y, Xu C, Yang X, Gao J, Zou DW, Li ZS

CRD summary
The review concluded that prophylactic glyceryl trinitrate was useful for prevention of post-ERCP pancreatitis, but research was needed on optimal dosage, route and timing of administration. This was a generally well-conducted review and the authors' conclusions are likely to be reliable.

Authors' objectives
To assess the prophylactic efficacy of glyceryl trinitrate on post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis compared with placebo.

Searching
PubMed, EMBASE, the Cochrane Library, Science Citation Index and Google Scholar were searched to January 2009; search terms were reported. Major conference abstracts and reference lists from included studies were searched.

Study selection
Randomised controlled trials (RCTs) that compared prophylactic glyceryl trinitrate with placebo in patients undergoing ERCP were eligible for inclusion. Trials also had to report the incidence of post-ERCP pancreatitis.

Most studies were of patients with biliary disease. Glyceryl trinitrate doses ranged between 0.1mg and 15mg by a variety of routes (topical, sublingual, transdermal and intravenous).

It appeared that two reviewers independently selected studies for inclusion.

Assessment of study quality
Two reviewers independently assessed study quality based on criteria of allocation sequence, allocation concealment and double blinding. Studies were classed as having a low (all three criteria met), moderate (one or more of the criteria partly met) or high (one or more of the criteria not met) risk of bias. Disagreements were resolved by discussion.

Data extraction
Two reviewers independently extracted data in order to calculate risk ratios (RR) with 95% confidence intervals (CI).

Methods of synthesis
Pooled risk ratios with 95% CIs were calculated using a random-effects model. Number needed to treat (NNT) was calculated. Subgroup analyses examined study quality and route of administration. Statistical heterogeneity was assessed using the Q and I² statistics. The authors stated that publication bias was assessed using a funnel plot, but no results were presented.

Results of the review
Eight RCTs (n=1,920) were included in the review. Sample sizes ranged from 74 to 806 participants. All trials reported adequate double blinding. Two studies had unclear allocation concealment and two had unclear reporting of generation of allocation sequence. Five trials had a low risk of bias and three trials had moderate or high risk of bias. Six trials reported use of a sample size calculation.

Incidence of post-ERCP pancreatitis was significantly lower for patients who took glyceryl trinitrate (RR 0.61, 95%CI 0.44 to 0.84; eight RCTs; I²=0%; NNT=26 patients); sensitivity analysis suggested the result was not significantly influenced by study quality. Transdermal (three RCTs) and sublingual (two RCTs) administration were associated with statistically significantly reduced rates of pancreatitis, but topical (two RCTs) administration was not. Results of post-
hoc analyses were reported.

**Authors’ conclusions**

Prophylactic glyceryl trinitrate was useful for prevention of post-ERCP pancreatitis, but the optimal dosage, route, and timing of administration needed further clarification before the treatment came into routine clinical use.

**CRD commentary**

The review addressed a clear question supported by suitable inclusion criteria. A search was conducted for both published and unpublished studies (details of the conference abstracts searched were not given). It was unclear whether there were any language restrictions, so the possibility that relevant studies were missed could not be ruled out. Suitable methods were used to reduce risks of reviewer error and bias throughout the review process. An assessment of study quality was made and used in interpreting the review results. Study details were tabulated (details of participant populations were very basic). Appropriate methods were used to pool data and assess heterogeneity. Overall, this appears to be 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, in spite of the results of the review, it was too early to recommend routine clinical administration of glyceryl trinitrate before ERCP due to uncertainties about optimal dosage, route and timing of administration.

**Research:** The authors stated that a head-to-head trial that compared sublingual and transdermal administration of glyceryl trinitrate was needed, but studies of dosage and administration strategies were required before any large scale RCT is conducted.

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