Meta-analysis of the use of glyceryl trinitrate ointment after haemorrhoidectomy as an analgesic and in promoting wound healing

Ratnasingham K, Uzzaman M, Andreani SM, Light D, Patel B

CRD summary
This review concluded that glyceryl trinitrate ointment used after a haemorrhoidectomy had a significant pain-relieving effect three to seven days postoperatively and significantly improved wound healing at three weeks. Differences between trials and the low number of small trials analysed should be taken into consideration when interpreting the authors’ conclusions.

Authors’ objectives
To investigate the effectiveness of glyceryl trinitrate ointment post-haemorrhoidectomy as an analgesic and in wound healing. The adverse effect of headache was also explored.

Searching
PubMed, EMBASE, CINAHL, DARE, ACP, LILACS and Cochrane Library were searched (1966 to May 2010) for articles (including conference abstracts) published in any language. Search terms were reported. References of retrieved articles were also examined for additional articles.

Study selection
Double-blinded, randomised controlled trials (RCTs) of patients (of any age and gender) who underwent open/closed conventional haemorrhoidectomy and that compared glyceryl trinitrate ointment with placebo were eligible for inclusion. Eligible trials also had to assess pain using a visual analogue scale (VAS) on day one and/or day three and/or day seven postoperatively. Trials that used the ‘procedure for prolapsed haemorrhoids’ or transanal haemorrhoidal dearterialisation, or that included patients with other concomitant anal disease, or that used other forms of glyceryl trinitrate or haemorrhoidectomy (including lateral sphincterotomy) were excluded.

The included trials compared 0.2% glyceryl trinitrate ointment with Vaseline or paraffin placebo. The surgical technique used in included trials was the Ferguson or Milligan-Morgan haemorrhoidectomy. The mean age of included patients ranged from 33 to 54 years across treatment groups. The primary endpoints reported were symptomatic pain relief using VAS; secondary endpoints were side effects and wound healing at three weeks.

Two reviewers performed study selection and disagreements were resolved by consensus.

Assessment of study quality
The authors did not report that study quality was assessed. However, only double-blinded randomised trials were eligible for inclusion; allocation concealment, method of randomisation and whether the trial was double blinded were reported.

Data extraction
Odds ratios (ORs) and associated 95% confidence intervals (CIs) were calculated for healing and headaches; mean difference and 95% confidence intervals were calculated for pain score. For the outcome wound healing, only full epithelialisation was considered as healed.

The number of reviewers that extracted data was not reported.

Methods of synthesis
Odds ratios and weighted mean difference (WMDs), with 95% confidence intervals, were pooled in a random-effects meta-analysis. No measures of heterogeneity were reported.
Results of the review
Five RCTs were included in the review (n=333 patients; range 30 to 102).

Glyceryl trinitrate ointment use was associated with a statistically significant reduction in postoperative pain (on the VAS) on day three (WMD -1.51, 95% CI -2.87 to -0.16; five RCTs) and on day seven (WMD -1.66, 95% CI -2.98 to -0.33; four RCTs) compared with placebo, but there was no significant difference between groups on day one.

Glyceryl trinitrate ointment use was also associated with a statistically significant improvement in wound healing after three weeks (OR 3.57, 95% CI 2.06 to 6.21; three RCTs). There was no significant difference in the incidence of headaches between the glyceryl trinitrate and placebo groups.

Authors' conclusions
Glyceryl trinitrate ointment used post-haemorrhoidectomy had a significant analgesic effect in the intermediate time period (days three to seven) and significantly improved wound healing at three weeks.

CRD commentary
The research question was supported by well-defined inclusion criteria. Several relevant databases were searched without language restrictions. It appeared that conference abstracts (studies that were not fully published) were eligible for inclusion. Two reviewers were involved in study selection; it was unclear whether similar steps to reduce reviewer error and bias were employed in the data extraction process.

Trial quality was not systematically assessed, but only double blinded RCTs were included and all of these trials reported allocation concealment, suggesting that they were of reasonable quality. It did not appear that between-trial heterogeneity was assessed, but the forest plots suggested possible heterogeneity for pain scores. The meta-analyses generally included small numbers of trials with few participants; several outcomes had wide confidence intervals.

The authors' conclusions reflect the evidence presented, but the heterogeneity and the low numbers of small trials should be taken into consideration when interpreting their conclusions.

Implications of the review for practice and research
Practice: The authors stated that patients can be given glyceryl trinitrate ointment post-haemorrhoidectomy to aid pain relief, though some may encounter headaches which should be dealt with using simple analgesics.

Research: The authors stated that a large, multi-centre double blind RCT of the effects of 0.2% glyceryl trinitrate ointment for post-haemorrhoidectomy patients and measuring anal pressure and blood flow is needed.

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