Pain management during eye examinations for retinopathy of prematurity in preterm infants: a systematic review
Sun X, Lemyre B, Barrowman N, O'Connor M

CRD summary
The review concluded that sucrose was at least partially effective at reducing pain during an eye examination for retinopathy of prematurity screening in premature infants. This conclusion is supported by the results presented, but the evidence came from a few small trials and this should be taken into account when interpreting review findings.

Authors’ objectives
To determine the efficacy and tolerance of pharmacological and non-pharmacological pain management for newborn infants undergoing a screening eye examination for retinopathy of prematurity.

Searching
MEDLINE, EMBASE, CINAHL and Cochrane Central Register of Controlled Trials (CENTRAL) were searched without language restriction up to October 2008; search terms were reported. Unpublished studies and abstracts were not included.

Study selection
Randomised controlled trials (RCTs) and quasi-randomised controlled trials of pharmacological (sucrose administered via oral syringe or nasogastric tube, and topical anaesthetic eye drops) and non-pharmacological (swaddling, developmental care and non-nutritive sucking) interventions provided before or during the eye examination in premature infants meeting criteria for retinopathy of prematurity screening and less than 44 weeks corrected gestational age were eligible for inclusion.

Pharmacological interventions included oral sucrose (24 to 33%, 0.1 to 2mL) and proparacaine (hydrochloride salt in ophthalmic solutions at 0.5%, 1 to 2 drops). Comparators were placebo (sterile water and saline). Most of the trials using sucrose also used topical anaesthetic eye drops, with or without a pacifier. Non-pharmacological trials used: Newborn Individualized Developmental Care and Assessment Program (NIDCAP) compared with standard care; and swaddling, pacifier (with sucrose soaked gauze) plus being held by a nurse compared with no treatment. Gestational age at trial entry ranged from less than 28 weeks to less than 32 weeks. Birth weight was less than 1500g in most trials. Infant pain was measured using the Premature Infant Pain Profile (PIPP), behavioural scores, and changes in physiological parameters.

Three reviewers independently selected studies for inclusion in the review.

Assessment of study quality
Three reviewers independently assessed the methodological quality of the included trials using the following criteria: allocation concealment, adequate randomisation, blinding of intervention, and blinding of outcome.

Data extraction
Three reviewers independently extracted data from the included trials.

Methods of synthesis
Where possible, trials were combined in a meta-analysis using a random-effects model. Summary estimates were reported as weighted mean differences (WMD) and their associated 95% confidence intervals (CI). Results for one cross-over trial were adjusted in order to allow for inclusion in the meta-analysis. Statistical heterogeneity was assessed using the $X^2$ and $I^2$ tests.

Results of the review
Eight trials were included in the review (n=330 infants). Four trials reported adequate randomisation; seven trials
reported allocation concealment, blinding of intervention and outcome assessment.

**Sucrose as the intervention** (four trials): A reduction in mean Premature Infant Pain Profile (PIPP) scores (indicating significantly less pain during eye examination) was found with oral sucrose compared with placebo (WMD 1.38, 95% CI 0.41 to 2.35; I²=25%).

**Topical anaesthetic as the intervention** (two trials): Results were inconsistent. One trial found a significant reduction in PIPP scores with proparacaine compared with saline, while the other trial found no significant between proparacaine and placebo saline in vital signs or behaviour.

**Non-pharmacological interventions** (two trials): In one trial, Newborn Individualized Developmental Care and Assessment Program (NIDCAP) was associated with better behavioural scores compared with standard care, but no significant differences were found for vital signs or PIPP scores. In the other trial, no statistically significant differences were found between developmental care (swaddling, pacifier and held by nurse) and standard care for vital signs or behaviour.

**Authors’ conclusions**
Sucrose reduced pain during eye examination, whereas the efficacy of proparacaine was not consistent. However, the Premature Infant Pain Profile scores remained relatively high in all trials, indicating a need for further research in order to delineate better pain reduction strategies.

**CRD commentary**
The objective of the review was clearly stated and the inclusion criteria defined. Searches were conducted without language restriction, although only trials published in full were included, raising the possibility of publication bias. Measures were taken to minimise the possibility of error and/or bias in study selection, data extraction and quality assessment.

The methodological quality of the included trials was assessed using appropriate criteria and the results presented. Appropriate methods appear to have been used to pool trials and assess heterogeneity.

The authors’ conclusions are supported by the results presented, but the evidence came from a few small trials and this should be taken into account when interpreting review findings.

**Implications of the review for practice and research**
**Practice:** The authors did not state any implications for practice.

**Research:** The authors stated that further research considering repeated doses of sucrose and topical anaesthetic eye drops or systemic pain reducing measures is needed.

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