Efficacy of sweet solutions for analgesia in infants between 1 and 12 months of age: a systematic review

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CRD summary
The authors concluded that sucrose or glucose solution given before immunisation moderately reduced the incidence and duration of crying in infants aged one to 12 months. Evidence appeared to support the authors’ conclusions, but the small number of trials in each pooled analysis should be taken into account when interpreting review findings.

Authors’ objectives
To evaluate the effectiveness of sweet solutions as analgesia during immunisations in infants aged one to 12 months.

Searching
MEDLINE, EMBASE, CINAHL, PsycINFO and all EBM Reviews were searched from inception to March 2009. Search terms were reported. Reference lists from articles, personal files and recent proceedings of relevant conferences were screened. No language restrictions were applied.

Study selection
Randomised controlled trials (RCTs) that evaluated the effects of sucrose, glucose or other sweet solutions administered orally during immunisations in infants beyond the neonatal period (corrected for gestational age) up to 12 months were eligible for inclusion. The main outcomes assessed in the review were cry behaviours.

Most of the included trials evaluated sucrose solution (concentrations ranged from 12 to 75%); other trials evaluated glucose solution (30 or 40% concentration). Most trials administered 2mL or less of the sweet solution two minutes before immunisation. Two trials used co-interventions (topical anaesthetic or non-nutritive sucking plus parental holding). Most trials used either water or no treatment as the control (water was the most common). Most trials described participants as healthy infants aged one to 12 months undergoing one, two, three, four or multiple immunisations. Included trials assessed a variety of outcomes including cry behaviours, pain scale scores and physiological measures; trials used a variety of measures of pain outcomes.

The authors did not state how papers were selected for the review.

Assessment of study quality
Two reviewers independently assessed trial quality using methods of the Cochrane Collaboration. Criteria included randomised generation, allocation concealment, blinding, incomplete reporting of outcome data, selective reporting of outcomes and other sources of bias. Disagreements were resolved by consensus or through consultation with a third reviewer.

Data extraction
Two reviewers independently extracted outcome data for cry behaviours, pain scale scores and physiological measures using relative risks (RRs) for dichotomous data and mean differences for continuous data.

Methods of synthesis
Where possible, data were pooled using a random-effects meta-analysis. Pooled relative risks and 95% confidence intervals (CIs), risk differences (RD) and numbers needed to treat to benefit (NNTB) were calculated for dichotomous data; weighted mean differences (WMD) with 95% confidence intervals were calculated for continuous data. Heterogeneity was assessed using I^2. Potential sources of significant heterogeneity were explored.

Where meta-analysis was not possible, trials were combined in narrative synthesis.
Results of the review
Fourteen RCTs were included in the review (n=1707 infants). Sample size ranged from 40 to 323 infants.

Trials were generally of high-quality. Twelve trials reported allocation concealment. In all but two trials, knowledge of the allocated intervention was adequately prevented; in the other two trials, the outcome assessor was blinded. All but one trial adequately dealt with incomplete data. Three trials were at risk of other sources of bias including small sample size, use of different co-interventions in treatment and control groups and possible lack of blinding.

Sucrose or glucose solutions were associated with a significant reduction in the proportion of crying time after immunisation (WMD -10%, 95% CI -18 to -2%; three trials; n=150 infants), a significant reduction in the reported incidence of crying after immunisation (RR 0.80, 95% CI 0.69 to 0.93; three trials; n=243 infants; NNTB 6, 95% CI 3 to 20) and a non-significant reduction in crying duration (WMD -16 seconds, 95% CI -32 to 0.08; six trials; n=716 injections). A high degree of heterogeneity was found for crying duration ($I^2$=88%).

Authors’ conclusions
Sucrose or glucose given before immunisation moderately reduced the incidence and duration of crying in infants aged one to 12 months.

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

Trial quality was assessed; the results were reported in full. Adequate information was provided about the included trials. Appropriate methods were used to combine trials; where heterogeneity was found, potential sources were explored. Differences between trials were discussed. The authors acknowledged that the use of co-interventions in two trials meant that the effects of sweet solutions could not be analysed separately.

Evidence appeared to support the authors’ conclusions, but the small number of trials in each pooled analysis should be taken into account when interpreting review findings.

Implications of the review for practice and research
Practice: The authors stated that the use of sucrose, glucose and other pain reduction strategies should be employed during immunisations and other painful procedures. For multiple immunisations, sweet solutions should be given throughout the procedure.

Research: The authors stated that further research is required to compare different concentrations of sucrose and glucose and to compare single versus divided dosing during prolonged painful procedures.

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