The Hierarchy of Evidence

The Hierarchy of evidence is based on summaries from the National Health and Medical Research Council (2009), the Oxford Centre for Evidence-based Medicine Levels of Evidence (2011) and Melynyk and Fineout-Overholt (2011).

I  Evidence obtained from a systematic review of all relevant randomised control trials.

II Evidence obtained from at least one well designed randomised control trial.

III Evidence obtained from well-designed controlled trials without randomisation.

IV Evidence obtained from well designed cohort studies, case control studies, interrupted time series with a control group, historically controlled studies, interrupted time series without a control group or with case-series

V Evidence obtained from systematic reviews of descriptive and qualitative studies

VI Evidence obtained from single descriptive and qualitative studies

VII Expert opinion from clinicians, authorities and/or reports of expert committees or based on physiology


<table>
<thead>
<tr>
<th>Reference (include title, author, journal title, year of publication, volume and issue, pages)</th>
<th>Evidence level (I-VII)</th>
<th>Key findings, outcomes or recommendations</th>
</tr>
</thead>
</table>
| Stevens, B., Yamanda, J., Lee G., & Ohlsson, A. Sucrose for analgesia in newborn infants undergoing painful procedures. Cochrane Database if Systematic Reviews, 2013, Issue 1 Art. No.: CD001069.DOI:10.1002/14651858.CD001069.pub4. | I | Systematic review of 57 RCT’s in which neonates term (29) preterm (27) or both (1) received sucrose for procedural pain.  
Sucrose is safe and effective for reducing procedural pain from single events  
Sucrose is most effective for heel lancing and has some effectiveness for venipuncture.  

**Optimal dosing yet to be established, inconsistency in effective sucrose dosing evidence:**  
- Recommended use of sucrose 0.012 to 0.12 g (0.05ml to 0.5ml of 24% sucrose) be administered **approximately two minutes prior** to single heel lances and venipunctures in neonates.  
- **The peak effect appears to occur at two minutes and lasts approximately four minutes;** the analgesic effect may wear off for prolonged procedures.  
- Small doses of 24% sucrose (0.01 to 0.02 ml) are efficacious in very-low birthweight infants while larger doses (0.24 to 0.50 ml) reduce crying time in term infants.  
- **Sucrose was effective** in reducing crying behaviours, grimacing, and vagal tone. Unidimensional, multidimensional and composite pain scores were reduced during heel lance with **volumes and concentrations ranging from 0.5 to 2 mL of 12% to 50% solution.**  

**Further investigation required:**  
- The repeated administration of sucrose in neonates  
- The use of sucrose with other interventions e.g. NNS and kangaroo care  
- The minimal effective dose of sucrose during a single painful procedure  
- Sucrose use in extremely preterm, unstable, ventilated neonates ( or a combination)  
- The effectiveness of sucrose for longer procedures such as ROP examinations, bladder catheterisation, venipuncture and circumcision.  
- The effect of repeated sucrose administration on immediate (pain intensity) and long-term (neurodevelopmental) outcomes  
- No studies reported on long-term neurodevelopmental outcomes |
<table>
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<tr>
<th>Harrison, D., Yamada, J., Adams-Webber, T., Ohlsson, A., Beyene, J., Stevens, B.</th>
<th>Systematic review of RCT’s, 7 Published and 1 unpublished, in which children aged one year to 16 years, received a sweet tasting solution or substance for needle-related procedural pain. Efficacy of sweet tasting solutions or substances for reducing needle-related procedural pain in children beyond one year of age:</th>
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<td>• The evidence is insufficient and conflicting in determining the analgesic effects of sweet tasting solutions or substances during acutely painful procedures in young children (one to four years of age) • There is no evidence of analgesic effects of sweet taste in school-aged children.</td>
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<tr>
<th>Beuno, M., Yamada, J., Harrison, D., Khan, S., Ohlsson, A., Adams-Webber, T., Beyene, J., and Stevens, B. (2013). A systematic review and meta-analyses of non-sucrose sweet solutions for pain relief in neonates. Pain Research Management, 18(3), 151-163.</th>
<th>Systematic review and meta-analyses of thirty-eight studies (3785 neonates) Glucose was investigated in 35 trials, with doses ranging from 0.2 mL to 2 mL of 5% to 50% solutions. Other solutions studied were artificial sweeteners, fructose, glycine, honey and maltitol. Efficacy and safety of sweet-tasting solutions other than sucrose during acute procedural pain in neonates:</th>
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<td>• Glucose reduces pain scores and crying during single heel lance and venipuncture. • 20% to 30% glucose solutions have analgesic effect and can be an alternative to sucrose for procedural pain reduction in healthy term and preterm neonates undergoing a single heel lance and venipuncture. Further investigation to establish the efficacy and safety of non-sucrose solutions:</td>
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<td>• Current research demonstrates considerable variability in outcome measurements, due to the volumes and concentrations of non-sucrose solutions administered • No studies measured the effects of repeated doses of glucose for procedural pain</td>
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**Breastfeeding or breast milk should be used to alleviate procedural pain in neonates:**
- In reducing procedural pain the administration of glucose/sucrose had similar effectiveness as breastfeeding
- Breast milk by syringe was not as efficacious as breastfeeding
- Effective for a single painful procedure compared to no intervention
**Future investigation required:**
- The effectiveness of breast milk for painful procedures in the preterm population
- Efficacy and safety of repeated administration of breast milk or breastfeeding for painful procedures |
| Harrison, D., Stevens, B., Bueno, M., Yamada, J., Adams-Webber, Beyene, J and Ohlsson, A. (2010) Efficacy of sweet solutions for analgesia in infants between one and 12 months of age: A systematic review. Archives of Disease in Childhood, 95(6), 406-413 | I | Systematic review of 695 studies, revealed 14 RCTs (1674 injections) meeting the inclusion criteria of sucrose, glucose or other sweet solutions administered orally during immunisations in infants beyond the neonatal period to 12 months.
**Efficacy of sweet solutions for analgesia in infants between 1 and 12 months of age:**
- Infants aged 1–12 months who had sucrose or glucose administered before immunisation have moderately reduced incidence and duration of crying
- Healthcare professionals should consider using sucrose or glucose before and during immunisation
- Use sucrose or glucose with other recommended procedural pain management strategies e.g. NNS, breastfeeding and distraction for immunisation
- Effective doses for neonates ranged between 0.05ml and 2 ml of 24% sucrose
- Infants one to 12 months, require higher concentrations of either sucrose or glucose for effectiveness compared to neonates
- Non-sucrose sweet solutions of sufficient concentration are analgesic
**Further studies in infants beyond the neonatal period required:**
- Comparison of single dose to divided doses, of sweet solution, given over the duration of a prolonged procedure
- Evaluation of different concentrations of sucrose and glucose |
**Cochrane review (Stevens, et.al., 2013) revealed a number of methodological issues:**
- small sample size, study may have been underpowered
- moderate attrition rates
- questionable methods used to measure and analyse EEG and EMG recordings
- potentially insufficient doses of sucrose (i.e. 0.5 mL) administered to full-term infants |
<table>
<thead>
<tr>
<th>Authors</th>
<th>Title</th>
<th>Page/Volume</th>
<th>Key Points</th>
<th>Reference</th>
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</table>
| Harrison, D.       | Oral sucrose for pain management in infants: Myths and misconceptions.| VII         | - Oral sucrose, when administered to both healthy and sick hospitalised infants, in small volumes, prior to acute painful procedures is a safe, effective, economic, and feasible pain reduction strategy  
- There is no evidence of increased risk of necrotising enterocolitis, dental caries, bacterial overgrowth or hyperglycemia associated with oral sucrose  
| Blass, E., & Ciaramitaro, V. | A new look at some old mechanisms in human newborns. Monographs for the Society for research in child development. 59(1). | II          | - Oral sucrose failed to calm newborn infants born to mothers on methadone, due to their low levels of circulating endogenous opioids  