

Academy of Breastfeeding Medicine
Annotated Bibliography:
MANAGEMENT of PAIN and STRESS in the BREASTFEEDING NEONATE

Breastfeeding as Analgesia

Reference	Content	Level of Evidence*
Phillips RM. Analgesic effects of breast-feeding or pacifier use with maternal holding in term infants. <i>Ambulatory pediatrics</i> . 2005;5(6):359.	Infants undergoing heel lance were breastfed (n= 32), held by mother holding a pacifier in baby's mouth (n= 25) or held by research assistant holding a pacifier in baby's mouth (n= 25). Fewer breast-feeding infants cried than infants using a pacifier while held by nonmothers both during the procedure (69% vs 100%) and after the procedure (28% vs 60%). Those infants crying during the procedure cried for less time if held by their mothers either breast-feeding (33%) or using a pacifier (45%) than those using a pacifier while being held by nonmothers (66%).	I
Shendurnikar N. Analgesic effects of breastfeeding on heel lancing. <i>Indian pediatrics</i> . 2005;42(7):730.	Compared 50 infants that were breastfed to 50 infants that were swaddled (n=100 infants during heel lance. Pain scores in breastfed group were significantly lower compared to swaddled babies.	I
Gradin M. Feeding and oral glucose - additive effects on pain reduction in newborns. <i>Early Human Development</i> . 2004;77(1-2):57.	120 term infants were randomized to one of the following groups: I) Breast-fed and 1-ml placebo; II) Breast-fed and 1-ml 30% glucose; III) Fasting and 1-ml placebo; IV) Fasting and 1-ml 30% glucose. Premature Infant Pain Profile (PIPP) score was significantly lower in the infants receiving glucose, than in those not given glucose. PIPP score was lower in group II (median 7) than in group I (md 10). There was a similar difference between group IV (md 9) and group III (md 11). The median crying times during the first 3 min in groups I, II, III, and IV were 63, 18, 142 and 93 s, respectively.	I
Upadhyay A. Analgesic effect of expressed breast milk in procedural pain in term neonates: A randomized, placebo-controlled, double-blind trial. <i>Acta pædiatrica</i> . 2004;93(4):518.	Infants tasting breastmilk (n= 40) were compared to infants given distilled water (n= 41) prior to venepuncture. Duration of crying in breastfed group was significantly shorter in the breastfed group (38.5 s) compared to control group (90 s). Change in heart rate was significantly lower (129 bpm at 3 minutes post-venepuncture) and returned to baseline sooner in the breastfed group compared to the control group (145 bpm at 1 minute).	I
Carbajal R. Analgesic effect of breast feeding in term neonates: Randomised controlled trial. <i>BMJ</i> . 2003;326(7379):13.	Infants undergoing venepuncture were breastfed (n= 44), held in mother's arms without being breastfed (n= 45), given sterile water but not held (n= 45), or given 30% glucose followed by a pacifier but not held (n= 45). PIPP scores for breastfed, held in mother's arms, placebo and glucose were 1, 10, 10 and 3, respectively. The difference between the breastfed and glucose groups was not found to be significant.	I

Gray L. Breastfeeding is analgesic in healthy newborns. Pediatrics. 2002;109(4):590.	Full-term, breastfed infants were either given standard of care (swaddled in their bassinets) (n=15) or were held and breastfed by their mothers (n=15) during heel lance. Crying and grimacing were reduced by 91% and 84%, respectively, from control infant levels. Heart rate was also substantially reduced by breastfeeding.	I
Blass EM. Effects of colostrum in newborn humans: Dissociation between analgesic and cardiac effects. Journal of developmental behavioral pediatrics. 2001;22(6):385.	60 newborn infants received colostrum, sucrose, or water, by syringe or on a pacifier, for a total of 6 groups (n = 10 per group). Colostrum delivered via pacifier, but not via syringe, prevented rise in heart rate induced by this procedure. Infants receiving pacifier dipped in sucrose cried for 20% of the procedure compared to 80% for the colostrum group.	I
Bilgen H. Comparison of sucrose, expressed breast milk, and breast-feeding on the neonatal response to heel prick. The journal of pain. 2001;2(5):301.	130 term newborns undergoing heel prick received either 25% sucrose (n= 35), breast milk (n= 33), sterile water (n= 34), or breastfeeding (n= 28). Crying times were lowest in the sucrose group (36 s), followed by the breast-fed group (51 s) and then the breastmilk group (62 s).	I
Bucher HU. Artificial sweetener reduces nociceptive reaction in term newborn infants. Early Human Development. 2000;59(1):51.	Compared utility of an artificial sweetener (n= 20), to glycine (n= 20), expressed breast milk (n= 20), and sterile water (n= 20) in infants undergoing heel lance. Found that artificial sweetener is a suitable analgesic alternative to sucrose. Breast milk had no effect and glycine increase pain reaction in this study.	I
Uyan ZS. Effect of foremilk and hindmilk on simple procedural pain in newborns. Pediatrics international. 2005;47(3):252.	Infants undergoing heel lance were given foremilk (n= 20), hindmilk (n= 21) or sterile water (n= 21). Statistically significant differences between the three groups were not found in terms of crying time, duration of the first cry, percent change in heart rate or maximum heart rate (P = 0.19,P = 0.08,P = 0.22 and P = 0.91, respectively). There was no statistically significant difference in mean pain scores at 0, 1, 2, and 3 minutes between the three groups (P = 0.58, P = 0.55, P = 0.58 and P = 0.84, respectively).	I

Alternative to breastfeeding: Sucrose taste

Reference	Content	Level of Evidence*
Isik U. Comparison of oral glucose and sucrose solutions on pain response in neonates. The journal of pain. 2000;1(4):275.	113 term infants undergoing heel lance received 30% sucrose, 10% sucrose, 30% glucose, or water. Mean crying times were 60, 102, 95, and 105 seconds in the sucrose, 10% glucose, 30% glucose, and placebo groups, respectively. A statistically borderline difference in heart rate existed at the end of 2 minutes favoring sucrose.	I
Stevens B. The Efficacy of Developmentally Sensitive Interventions and Sucrose for Relieving Procedural Pain in Very Low Birth Weight Neonates. Nursing research [0029-6562] Stevens yr:1999 vol:48 iss:1 pg:35.	122 very low birthweight neonates undergoing consecutive heel lance received all 4 interventions in succession, serving as their own controls: (a) prone positioning; (b) pacifier with water; (c) pacifier with 24% sucrose; d) no intervention (control). The mean PIPP scores for pacifier with sucrose (7.87) and pacifier with sterile water (8.44) significantly reduced pain. Prone positioning did not decrease pain (10.3) compared to no intervention (9.80).	I

Allen KD. Sucrose as an analgesic agent for infants during immunization injections. Archives of pediatrics adolescent medicine. 1996;150(3):270.	285 infants undergoing immunization were randomly assigned to receive no intervention, sterile water or 12% sucrose solution via syringe or pacifier. Infants who received either the sterile water or sucrose solution cried significantly less than infants who received no intervention ($F=5.92$, $P<.005$). The results suggested that in the absence of nonnutritive sucking, the actual analgesic effects of sucrose may be nonspecific.	I
Blass EM. Suckling- and sucrose-induced analgesia in human newborns. Pain. 1999;83(3):611.	40 term infants 34-55 hours old undergoing heel lance were randomized to receive I) water; II) water and pacifier; III) 12% sucrose; IV) 12% sucrose and pacifier (n=10 in each group). Cry duration during the procedure for group I, II, III and IV was 50%, 35%, 8% and 5% respectively.	I
Johnston CC. Effect of repeated doses of sucrose during heel stick procedure in preterm neonates. Biology of the neonate. 1999;75(3):160.	48 preterm infants undergoing heel lance received 24% sucrose as a single dose or 3 doses. Placebo group received 3 doses of water. Both sucrose groups had lower pain scores (single sucrose pain scores, 6.8-8.2; repeated sucrose pain scores, 5.3-6.2) than water (7.9-9.1). The repeated dose had lower scores than the single dose (6.2 vs. 8.2).	I
Stevens B. The efficacy of developmentally sensitive interventions and sucrose for relieving procedural pain in very low birth weight neonates. Nursing research. 1999;48(1):35.	122 preterm neonates undergoing heel lance were randomized to one of the following groups: prone positioning; pacifier dipped in water; pacifier dipped in 24% sucrose; no intervention (placebo). Significant pain reduction was seen in the pacifier with sucrose ($F = 24.09$) and pacifier with sterile water ($F = 9.00$). Prone positioning did not decrease pain ($F=2.24$).	I
Herschel M. Neonatal circumcision: Randomized trial of a sucrose pacifier for pain control. Archives of pediatrics adolescent medicine. 1998;152(3):279.	119 term male babies undergoing circumcision were given standard care (no treatment), dorsal nerve penile block (DNPB) or sucrose via a pacifier. The average difference in the elevation of heart rates during the circumcision operative procedure among the 3 groups were as follows: control vs DPNB, 27.1 bpm, and control vs sucrose, 9.7 bpm.	I
Abad F. Oral sweet solution reduces pain-related behaviour in preterm infants. Acta pædiatrica. 1996;85(7):854.	Preterm infants undergoing venepuncture received 12% sucrose (n=8), 24% sucrose (n=8) or water (n=12). The mean cry duration was significantly reduced in the group treated with 24% sucrose solution (19.1 s) compared to the control group. No significant difference in cry duration was observed between the 12% sucrose solution (63.1 s) and control groups (72.9s).	I
Ramenghi, LA. Reduction of pain response in premature infants using intraoral sucrose. Archives of disease in childhood, 1996, 74, 2 SUPPL., F126.	15 preterm infants undergoing heel lance were given 25% sucrose or water. Infants receiving sucrose on average cried significantly less (6%) than control infants (16%) over a period of 5 minutes.	I
Haouari N. The analgesic effect of sucrose in full term infants: A randomised controlled trial. BMJ. 1995;310(6993):1498.	60 term infants undergoing heel lance were given 12.5%, 25% or 50% sucrose. Control group received water. Concentrated sucrose solution reduces cry duration (106 seconds for 12.5% sucrose, 81 s for 25% sucrose, and 45 s for 50% sucrose) compared to water (135 s).	I

Alternative to breastfeeding: Non-nutritive suckling (NNS)

South, MMT. The use of non-nutritive sucking to decrease the physiologic pain response during neonatal circumcision: A randomized controlled trial. American journal of obstetrics and gynecology, 2005, 193, 2, 537.	Term neonates in the study all received oral Tylenol and a dorsal penile nerve block (DPNB) before circumcision. Study group (n=22) was offered the addition of NNS before the DPNB and throughout the procedure. Control group (n=22) did not receive additional intervention. NNS group, compared to the control group, had a significant decrease in crying time (4.2 vs 6.3 minutes), 90-minute post-procedure salivary cortisol level (50 vs 75 mmol/L), and post-penile clamping pain score (5.2 vs 8). group. No difference in mean heart rate during the procedure was apparent.	I
Taddio A. Pain management for neonatal circumcision. Paediatric drugs. 2001;3(2):101.	Pacifiers may decrease crying associated with painful procedure, but do not appear to affect physiological parameters.	III
Franck LS. Environmental and behavioral strategies to prevent and manage neonatal pain. Seminars in perinatology. 1998;22(5):434.	Non-nutritive suckling has been found to be antinociceptive in rats. In humans, NNS is associated with decreased restlessness, heart rate and energy expenditure, and increases in oxygenation, respiratory and gastrointestinal function.	III

Alternative to Breastfeeding: Skin to Skin Contact (SSC)

Ludington-Hoe SM, Hosseini R, Horowicz D. Skin to Skin Contact (Kangaroo Care) Analgesia for Preterm Infant Heel Stick. AACN. 2005;16(13):373.	23 preterm infants were randomized to one of two sequences: A) 3 hours of SSC with heel stick during SSC followed by 3 hours in the warmer with heel stick in warmer; B) 3 hours in warmer with heel stick in warmer followed by 3 hours in SSC with heel stick during SSC. Crying times were significantly shorter during SSC heel stick (4.98 s for group A, 5.09 s for group B) than during warmer heel stick (45.69 s, 39.25 s).	I
Johnston CC. Kangaroo Care Is Effective in Diminishing Pain Response in Preterm Neonates. Archives of pediatrics adolescent medicine. 2003;157(11):1084.	37 preterm infants received skin-to-skin contact 30 minutes before and throughout the duration of a heel lance procedure. 37 preterm infants in the control group were in the prone position in the isolette. Premature Infant Pain Profile scores 90 seconds after the heel lance were significantly lower in the skin-to-skin group (10.3) compared to the control group (12.1).	I
Gray L, Watt L, Blass EM. Skin-to-skin contact is analgesic in healthy newborns. Pediatrics. 2000;105(1):110.	Newborns were assigned randomly to either being held by their mothers in whole body, skin-to-skin contact (n=15) or to no intervention (n=15) during a heel lance procedure. Crying and grimacing were reduced by 82% and 65%, respectively, from control infant levels during the heel lance procedure.	I

Comparison studies

Carbajal R. Randomised trial of analgesic effects of sucrose, glucose, and pacifiers in term neonates. BMJ. 1999;319(7222):1393.	150 term infants undergoing venepuncture received 30% sucrose, 30% glucose, pacifier alone, 30% sucrose and pacifier, water or no treatment (n= 25 in each group). All groups had significantly lower pain scores compared to the water group. The sucrose with pacifier group (1 on a scale of 10) had the lowest overall pain score, followed by the pacifier group (2), sucrose and glucose groups (both 5), and lastly the water and no treatment groups (both 7). Differences between groups were	I
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	found to be significant.	
Ors R. Comparison of sucrose and human milk on pain response in newborns. European journal of pediatrics. 1999;158(1):63.	Newborns (n= 102) undergoing heel lance given sucrose, human milk or sterile water. Median crying times were 36, 52, and 62 seconds in the sucrose, placebo and human milk groups, respectively. Recovery times were 72, 112 and 124 seconds in the sucrose, milk and placebo groups, respectively. Differences between groups were statistically significant.	I
Bucher. Artificial sweetener reduces nociceptive reaction in term newborn infants. Early Human Development. 2000;59(1):51.	Eighty healthy term infants were randomly assigned to one of four groups: 2 ml sweetener, glycine, expressed breast milk or water was given before a heel prick. Newborns who received the sweetener recovered quicker from the procedure (27 seconds) than the infants allocated to the three other groups (52 seconds for breast milk group, 75 s for glycine group, 51s for water group).	I
Blass EM. Effects of colostrum in newborn humans: Dissociation between analgesic and cardiac effects. Journal of developmental behavioral pediatrics. 2001;22(6):385.	10 infants undergoing heel lance quasi-randomized to each of the following groups (60 total): 1) water via syringe, 2) colostrum via syringe, 3) sucrose via syringe, 4) water on pacifier, 5) colostrum on pacifier, 6) sucrose on pacifier. Colostrum did not reduce cry duration compared to the water group (control). However, sucrose did significantly reduce cry duration compared to the control group.	I

Areas needing further research: The analgesic effects of breastmilk and other non-pharmacologic agents need to be studied in relation to procedures other than heel lance and venepuncture (such as circumcision and immunization). More studies need to be done in premature infants in the NICU to determine efficacy in this population.

US Preventive Services Task Force Ranking of Evidence from Scientific Studies

- I Evidence obtained from at least one properly randomized controlled trial.
- II-1 Evidence obtained from well-designed controlled trials without randomization.
- II-2 Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one center or research group.
- II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could be regarded as this type of evidence.
- III Opinions of respected authorities, based on clinical experience, descriptive studies and case reports; or reports of expert committees.