

eNeonatal Review

Jointly Presented by The Johns Hopkins University School of Medicine and The Institute for Johns Hopkins Nursing

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The use of sucrose analgesia in neonates has been well studied for various procedures, e.g., circumcision, heel stick, and percutaneous phlebotomy. For many NICU clinicians, the use of oral sucrose with or without other consoling techniques is common. Recently published work expands the procedures for which sucrose analgesia has been found successful and further identifies the patient population best served by this practice. Yet, despite these evidence-based findings, widespread clinical acceptance has been slow.

In this issue, we overview this newly reported evidence regarding the effectiveness of neonatal sucrose analgesia, and report on how it can be translated into multidisciplinary methodology and optimization strategies for successful implementation.

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This Issue

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At the conclusion of this activity, participants should be able to:

- Identify the proven uses for sucrose analgesia in neonates;
- Describe the various options for delivering sucrose analgesia to neonates;
- Discuss ways of developing a sucrose analgesia policy in neonatal care.

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Commentary

Admission of a sick newborn into a care setting is often associated with frequent painful diagnostic and therapeutic procedures. The etymology of pain comes from the Latin word *poena*, which translates as "a personal fine or penalty". The Stedman's Online Medical Dictionary defines pain as: "An unpleasant sensation associated with actual or potential tissue damage and mediated by specific nerve fibers to the brain where its conscious appreciation may be modified by various factors."^[1] It was once believed that neonates did not have the components required to experience pain. However, it is now known that by 28 weeks of fetal development the anatomic and hormonal ingredients exist for pain perception.^[2] Indeed, it is thought that neonatal pain sensitivity is high, in that neonates are less effective in blocking painful stimuli than adults.^[3]

The AAP recognizes that detection and management of pain in neonates is needed but acknowledges pain treatment remains limited.^[4] While the newborn is dependent upon caregivers (largely nurses) to dutifully assess and manage pain, the recognition and severity of pain has been helped by the introduction of standardized assessment tools, e.g., the Premature Infant Pain Profile (PIPP)^[5]. Nurses caring for newborns should assess pain as a routine part of daily care in a hospital setting. The effectiveness of a pain management plan involves customization to individual patient needs, planning of care interventions, and coordination of personnel.^[6] This approach is especially helpful with sick preterm infants, where, without care coordination, handling can occur over 200 times a day, resulting in only brief intervals between stimulation.^[7]

In the last decade, oral sucrose was generally found to decrease physiologic (blood pressure, heart rate, SpO₂ and vagal tone) and behavioral (the mean percent time crying, total cry duration, duration of burst cry, and facial action) pain in neonates undergoing heel stick or venepuncture.^[8-10] Gastric or parenteral administration of sucrose has not shown similar analgesic effect.^[11] While the effectiveness of oral sucrose can be enhanced by stimulating the newborn to suckle, the calming mechanisms underlying suckling remain unclear.^[12]

As the articles reviewed herein show, in particular the experience at the Children's Hospital of Boston as reported by Morash & Fowler, a defined policy can be an extremely beneficial pain management technique. For dosing with oral sucrose to be effective, the pain evoking procedure should be nonacute and episodic. In that regard, sucrose analgesia has been found helpful in neonatal care during bladder catheterization, eye exams, heel stick, immunization, lumbar puncture, nasogastric tube insertion, suture removal, and venipuncture. The

administration of sucrose requires a physician or nurse practitioner order, but, as the primary caregiver, the nurse can take the lead in raising awareness among NICU personnel and implementing a physician-ordered policy. To optimize analgesic effect, oral sucrose should be administered a few minutes in advance of anticipated, nonacute pain; however, clinicians should note that the use of oral sucrose may be contraindicated in infants with hyperglycemia.

The finding (reviewed herein) by Trotter et al — that in both Australia and the U.K., the majority of neonatal caregivers stated they were aware of the benefits of sucrose for neonatal painful procedures, but this knowledge for the most part had not been put into practice — is particularly troubling. Given that the positive findings for sucrose analgesia span nearly two decades, why the disparity between the evidence-base and a broad acceptance into clinical practice? Perhaps, in part, it is a perceived failure owing to lack of coordinating care, personnel and timing. Perhaps sucrose analgesia is regarded as too simple and inexpensive, and therefore does not have the "advertising" profile of exotic and expensive therapies.

Regardless, neonates in our care should have access to all possible analgesic interventions, without the onus of a personal fine or penalty.

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NEONATES AND INFANT PAIN THRESHOLD WITH SUCROSE ANALGESIA

Rogers AJ, Greenwald MH, Deguzman MA, Kelley ME, Simon HK. **A randomized, controlled trial of sucrose analgesia in infants younger than 90 days of age who require bladder catheterization in the pediatric emergency department.** Acad Emerg Med 2006;13(6):617-22.

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Rogers et al recently reported the results of a randomized, double-blinded study of perceived pain in infants undergoing bladder catheterization. The study group of 80 infants were <90 days of age but at birth were at least 34 weeks' gestational age. All infants were admitted and treated in the Emergency Department, where the attending pediatrician determined that a urine sample was required for diagnostic evaluation. The infants received 2 minutes before urethral catheterization either a 2cc oral bolus of a 24% sucrose solution or a placebo solution (indistinguishable in color, smell and viscosity) 2 minutes before urethral catheterization. If more than one procedure was to be performed, the enrolled infants had bladder catheterization as the first noxious procedure of their visit. No other specific comfort measures were used as part of the study, except in cases where, per parental request, pacifiers were given to some infants. Pain responses were assigned via the DAN scoring system — a 10-point scale using cry, facial expression, and limb movements to quantify the responses to pain, with 10 representing maximal response.

A subgroup of 33 infants were <30 days old (i.e., neonates), and this age group demonstrated less pain response to bladder catheterization and faster return to baseline behavior than infants receiving placebo. The older subgroups did not show a convincing analgesic effect to oral sucrose. Infants in the separate age groups were not randomized and their numbers were relatively small, so the study did not have the power to demonstrate a conclusive negative effect within the age subgroups. Additionally, multisensorial stimulation (sucrose with and without a pacifier or other methods of consoling by a caregiver, e.g., speech or touch) was balanced between groups and did not impact pain scores, but, again, the number of comparative study subjects was small. A key issue was raised (but unanswered by the authors), in their statement that: "It is possible that older infants, who on average received a smaller dose (in milligrams per kilogram), were in fact underdosed and therefore did not show an analgesic response." That consideration aside, this well designed protocol adds bladder catheterization to the list of noxious procedures where oral sucrose has been shown to mitigate pain in neonates.

VARYING PRACTICE OF PAIN RELIEF FOR NEONATES

Gray PH, Trotter JA, Langbridge P, Doherty CV. **Pain relief for neonates in Australian hospitals: a need to improve evidence-based practice.** *J Paediatr Child Health* 2006;42(1-2):10-3.

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This concise study addressed neonatal pain relief practices in a large sampling of hospitals in Australia with the aim of determining the extent of variation among centers. The authors conducted a telephone survey of 212 (99.1%) of the 214 hospitals in Australia which performed more than 200 deliveries/year. The most senior person available to care for newborns was interviewed with a standardized set of questions as part of a national quality assurance activity. This allows the authors to capture a snapshot of current neonatal pain management practices across the country.

Among their findings were that only 10% of centers used sucrose analgesia in advance of a heel stick, and only 11% of units surveyed administered sucrose before venepuncture – in other words, there was little or no analgesia of any kind for these two pain evoking procedures. Even more disconcerting was the finding that only 3 of the survey respondents were doctors, the other 199 being midwives or nurses as the most senior person caring for newborns. While sucrose analgesia is physician ordered, it should be argued that nurses, in that they have the most one-on-one care time, can be the neonate's pain management greatest advocate.

The majority of respondents "stated they were aware of the benefits of sucrose for neonatal painful procedures." While the authors admonished "that the knowledge for the most part has not been put into practice", they rationalized that other proven neonatal therapies (e.g., vitamin A in preterm infant, heat loss prevention during newborn stabilization, and prophylactic surfactant in those at risk for RDS) were also not widely used. Sadly, while the results reflect that caregiver pain management knowledge is not being put into practice, the authors note that their findings were similar to those in the United Kingdom ([Rennix et al. Arch](#)

[Dis Child Fetal Neonatal Ed, 2004](#)). They emphasize that sucrose analgesia is inexpensive and simple, but too often overlooked as an analgesic for painful procedures in neonatal care. In summary, their efforts at collecting quality assurance data are commendable, as is their concluding sentence, "It is imperative that the gap between research findings and clinical practice with regard to neonatal analgesia be addressed."


CAN THE USE OF ORAL SUCROSE AND A PACIFIER REDUCE THE DISCOMFORT OF EYE EXAMS?

Mitchell A, Stevens B, Mungan N, Johnson W, Lobert S, Boss B. **Analgesic effects of oral sucrose and pacifier during eye examinations for retinopathy of prematurity.** *Pain Manag Nurs* 2004;5(4):160-8.

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Many diagnostic and therapeutic procedures in the NICU are painful for the newborn, and that pain component is obvious to care givers as they witness the pain responses to their care interventions (e.g., catheterization, heel stick, and venepuncture). However, during an eye examination of the preterm infant, the primary caregiver (nurse) can allow the ophthalmologist to complete their exam with little awareness of the neonate's pain responses. Indeed, it is not unusual for the nurse to restrain the infant's arms and head, while the ophthalmologist holds open the eyelids, applies eye drops and examines the back of the eye. Mitchell et al's nursing-based study is the first to evaluate the pain response to routine eye examination for Retinopathy of Prematurity (ROP) and the effects of sucrose with a pacifier for attenuating the associated pain. This report was the result of collaboration between nursing faculty at the Universities of Louisiana and Mississippi (USA) and the University of Toronto (Canada).

30 infants were studied. Although all required an initial or follow-up eye exam for ROP evaluation, they were examined only once in the context of this study. The infants were randomized to receive either oral sucrose or water in a dosing sequence prior to and during the eye exam. Both groups of infants had a pacifier in place during the study period. Infant pain was measured using the Premature Infant Pain Profile (PIPP). (The PIPP has been validated for use with preterm infants of all gestational ages, as well as with full-term infants. PIPP scores are based on 30-second observations that compare baseline indicators to phases throughout a procedure. A score of 6 or less may indicate minimal or no pain, and a score of 12 or greater may indicate moderate to severe pain.) Although both study groups exhibited pain, the mean PIPP for the sucrose group was 8.8 versus the water group at 11.4. The 30% reduction in pain score was isolated to oral dosing of sucrose, and no untoward side effects were noted with use of sucrose.

This study highlights the impact a nursing observation can have, in that it spawned a meticulously designed study that culminated in an evidence-based change in the practice of pain management for newborns. However, a disconcerting point mentioned by the authors was that: "None of the infants in the study had previous exposure to sucrose analgesia." Since an entry criterion was a requirement of at least 72 hours of supplemental oxygen therapy, it would be very likely that these study infants would also have had heel sticks and venepunctures; yet no mention of other analgesics in the care of these study infants is made nor is there a statement that analgesia was intentionally withheld. It bears asking: was any form of analgesia provided for these painful procedures?

PROCEDURAL CONCERNS WITH ESTABLISHING A SUCROSE ANALGESIA POLICY

Morash D, Fowler K. **An evidence-based approach to changing practice: using sucrose for infant analgesia.** *J Pediatr Nurs* 2004;19(5):366-70.

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This article by Morash & Fowler provides an overview of how best evidence can be translated into practice, as was done at the Children's Hospital of Boston, and demonstrates how the efforts of nursing can be coordinated with the multidisciplinary collaboration of child life specialists, medicine, and pharmacy. The nursing research literature has established the efficacy of using sucrose as infant analgesia; however, once there is evidence that an intervention works, there remains the task of implementing the intervention into practice. The authors report on the development of a comprehensive policy and procedure for neonatal sucrose analgesia, as follows:

Policy:

- This policy applies to infants ranging in age from 27 to 44 weeks gestational age or up to 1 month of age who experience episodic, nonacute pain. Administration of sucrose requires a physician or nurse practitioner order.

Purpose:

- To provide analgesia for routine procedures that cause pain in the neonate, including heel stick, venepuncture, IV or nasogastric insertion, suture removal, lumbar puncture, urinary catheterization, and immunization.
- To expose oral mucosa to 24% sucrose for absorption. Delivery of sucrose solution to the gastric mucosa is not the desired outcome. High concentrations of sucrose in contact with oral mucosa induces the release of endogenous opioids.

Note: Hyperglycemia may occur with repeated dosing. The use of oral sucrose may be contraindicated in infants with hyperglycemia.

Dosage/Administration:

- In each 24% sucrose cup, one pacifier dip = 0.2 mL sucrose
- Preterm Infants: 27-37 weeks gestation: 0.2-0.4 mL orally per procedure (1-2 dips)
- Full Term Infants: those >37 weeks gestation up to 1 month of age: up to 2 mL orally (10 dips) per procedure

Note: As a general rule, dosing of 2cc aliquots should not exceed eight (8) in a 24 hour period.

Procedure:

1. Verify Physician or Nurse Practitioner order.
2. Dip pacifier once in 24% sucrose cup and allow infant to begin sucking 1-2 minutes before noxious procedure.
3. Allow continuous sucking on pacifier throughout the procedure. Assess infant's response to sucrose administration. Repeat dose as needed per dosing policy.
4. If infant is agitated or irritable despite maximum dosage of oral sucrose, additional comfort measures and/or analgesia are to be considered.
5. Discard unused portion of sucrose solution.
6. Document the effectiveness of analgesia using a developmentally appropriate pain assessment tool.

The authors queried four other children's hospitals (unnamed in their article) on their practices of sucrose usage for infant analgesia, which was foundation for the Policy above. The logistics of implementing a change in practice are nicely covered: collecting the evidence, obtaining consensus from the key players, obtaining approval for the policy, ordering supplies, educating staff, promoting the policy, and maintaining the enthusiasm for use of the policy. The authors note that sucrose analgesia is a "little thing that is easily overlooked". Given the concerted effort to establish the policy, it would have been helpful for the authors to have included additional information on both caregiver compliance in the frequency of, and PIPP-based success with use of, sucrose analgesia for specific procedures known to elicit pain in neonates under their care.

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Ask a Question about this Newsletter 

LAST MONTH'S Q & A September 2006 - Volume 4 - Issue 1

Last issue, we reviewed the effectiveness of sucrose analgesia in neonates, and reported on optimization strategies for successful implementation.



Commentary & Reviews:
Robert J. Kopotic, MSN, RRT, FAARC

Director of Clinical Programs
ConMed Corporation
Vital Signs Development Center

The eNeonatal Review Team asked the September faculty a few questions.



Are we doing enough to manage the pain experienced by neonates undergoing pain evoking procedures?



It appears not. Anand and Hickey (Anand KJ, Hickley PR. [Pain and its effects in the human neonate and fetus](#). N Engl J Med 1987;19;317(21):1321-9) first described the phenomenon of neonatal pain in 1987. Yet now, nearly 20 years later, Anand and other international experts have concluded that: "Despite published data on the complex behavioral, physiologic, and biochemical responses of these neonates and the detrimental short- and long-term clinical outcomes of exposure to repetitive pain, clinical use of pain-control measures in neonates undergoing invasive procedures remains sporadic and suboptimal." (Anand KJ, Johnston CC, Oberlander TF, Taddio A, Lehr VT, Walco GA. [Analgesia and local anesthesia during invasive procedures in the neonate](#). Clin Ther 2005 Jun;27(6):844-76).



Which key issues remain to be studied regarding the use of sucrose as a neonatal analgesic?



In the 2005 review by Anand et al (cited above), the authors provide a comprehensive list of questions needing further investigation, including:

- Do more intensely painful procedures require higher doses than less painful procedures?
- What is the dose-response relationship to such adverse metabolic effects as hyperglycemia and metabolic acidosis?
- Does sucrose have an interactive effect with other analgesics?
- What are the most appropriate outcome measures at the extremes of prematurity, when gestational age and severity of illness might confound the sucrose response?
- What are the long-term consequences of sucrose therapy in relation to clinical, behavioral, and neurodevelopmental outcomes?

These and other issues raised by Anand et al await further study.

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- Identify the proven uses for sucrose analgesia in neonates;
- Describe the various options for delivering sucrose analgesia to neonates;
- Discuss ways of developing a sucrose analgesia policy in neonatal care.

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- Dr. Noguee has indicated a financial relationship of grant/research support with Forest Laboratories and has received an honorarium from Forest Laboratories.
- Dr. Lawson has indicated a financial relationship of grant/research support from the NIH. He also receives financial/material support from Nature Publishing Group as the Editor of the Journal of Perinatology.
- Dr. Lehmann has indicated a financial relationship in the form of honorarium from the Eclipsys Corporation.

All other faculty have indicated that they have not received financial support for consultation, research, or evaluation, nor have financial interests relevant to this e-Newsletter.

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