Oral Sucrose as an Attempt to Relieve Pain in the NICU

Rachel Yoo

NS 179A: Scholarly Concentration

University of California, UCI

June 8, 2016
Introduction

Background

Interpretation of pain in infants - especially in the NICU - is difficult to assess due to their inabilities to communicate verbally or demonstrate their pain (Bowden & Greenburg, 2010). Most often, healthcare providers rely on indicators such as facial activity, changes in muscle tone, and duration of sleep/wake states to assess the presence of pain (Holsti, Grunau, & Shany, 2011). In a study, a preterm infant - at less than 29 weeks old - could undergo 300 or more painful procedures over a 3-month period in the NICU (Grunau et al, 2007). With the high incidence of painful procedures occurring in the NICU, it is essential to find effective methods to decrease the associated discomfort and assist infants in gaining short and long term benefits (Kanwaljeet, Martin, & Kim, 2016). While there are a variety of methods to treat and manage pain levels in the NICU, the focus of this paper will be on one: the administration of oral sucrose. It has been proposed that sucrose has the potential of inhibiting pain transmission at the spinal level and also instigating the hypothalamus’s release of endorphins (Mitchell & Waltman, 2003). Furthermore, sucrose has been highly promoted for its ability to raise pain threshold, its analgesic properties, and its association with reduced crying time (Bowden & Greenberg, 2010). In a recent study conducted in 2013, it was discovered that 69% of 60,969 first-attempt procedures in a NICU were identified as painful (Hatfield, Meyers, & Messing, 2013). With the frequent painful procedures carried out in the NICU, the efficacy and safety behind repeated doses of sucrose need to be evaluated (Stevens et al, 2005). Furthermore, research shows that consistent high levels of pain or stress in preterm infants could lead to adjustments in neurodevelopmental problems: it is thus critical to validate the short-term and long-term impact
of sucrose because it is considered as a reliable relieving agent of pain (Grunau, 2013). While the use of sucrose is highly recommended to manage pain management in the NICU, the side effects of its repeated use has not been thoroughly investigated (Holsti & Grunau, 2010). Therefore, it is crucial to further examine the side effects associated with repeated doses of sucrose in order to prevent the infant from developing problems.

**Significance to Nursing Practice**

One case-control study and two randomized control studies are reviewed to assess whether sucrose is a legitimate method in improving pain management in the NICU. Within the NICU itself, the nurses may spend more time with the patient than the parents do. Consequently, the NICU nurses are given the responsibility of being the sole pain evaluator and advocate for these neonatal patients. As they spend increased time with the patient and learn to identify their individualistic portrayals of pain, they need a validated practice to use in order to appropriately relieve the neonates: sucrose. With the widespread popularity of sucrose administration in NICU settings, justifying if it is a viable method to relieve and control pain is essential (Holst & Grunau, 2010). Also, with a variety of other nonpharmacological interventions for pain management in the NICU - including facilitated tucking and pacifiers - increased trials to support the superiority in treatment effects of sucrose must be supported (Cignacco et al, 2012).

**Methods**

This research appraisal in accordance to the three studies that were incorporated integrated information from Cochrane Library, PubMed and CINAHL. The following phrases were implemented in the search: “nicu,” “pain management,” “infant anesthesia,” and “premature hospitalizations,” “pain guidelines.” Only articles with publication dates from 2010
to present were reviewed. Around 163 articles were found when the key terms mentioned earlier were combined in searches. In order to narrow the search down to articles that contained information regarding the administration of oral sucrose, the following key words were used in combination with each other: “oral sucrose,” “pain management,” “nicu,” and “repeated sucrose.” A minimum of six articles were found upon each combination of these key terms with some databases yielding up to 240 articles. However, the relevancy of all of these articles to the repeated use of sucrose rather than its one-time administration if questionable.

The three studies utilized for this paper were selected in accordance to their relevancy and whether the articles incorporated control groups and specific guidelines on how to assess and relieve pain in the NICU. Additionally, the sample sizes of each study were above 40 and incorporated only infants that were preterm or had a low-for-gestational age weight. All three studies assessed the use of oral sucrose as an appropriate intervention for pain management in the NICU.

**Results**

All three studies focused on the safety and efficacy of sucrose administration in neonates as a means of pain management. One study was a prospective case-control study and two were randomized control trials. Two main themes were identified: pain response and side effects.

**Pain Response**

Two of the three studies focused on improved pain responses observed through the implementation of pain scores: both demonstrated significant improvements. Cignacco et al. (2011) used the *Behavioral Bernese Pain Scale for Neonates* (B-BPSN) and *Physiological Bernese Pain Scale* for neonates (P-BPSN) to assess pain response. Facilitated tucking (FT) did
not succeed in reducing pain as much as sucrose alone: B-BPSN (M_{FT} = 7.01 \pm 3.59 \text{ vs. } M_S = 5.58 \pm 2.95, \ p = .01) \text{ and P-BPSN } (M = 2.72 \pm 1.98 \text{ vs } M=5.58 \pm 2.95, \ p = .0002). \text{ The combination of FT and sucrose was the most effective in decrease pain levels: B-BPSN } (M_C = 5.49 \pm 2.95, \ p = .007) \text{ & P-BPSN } (M_C = 2.03 \pm 1.73, \ p = .003). \text{ Stevens et al. (2005) had similar results in a reduction of pain scores with sucrose administration. Significant differences were seen among its three groups: standard care, water plus pacifier, and sucrose plus pacifier. The pain responses in this study were measured using the Premature Infant Pain Profile (PIPP). The PIPP scores associated with the combination of sucrose and pacifiers was significantly lower } (P=0.03) \text{ than the standard care group } (P=0.01) \text{ that did not use either sucrose or pacifiers. However, this study The study did not include means & standard deviations for PIPP scores.}

\textbf{Side Effects of Sucrose}

Two of the studies consistently found that there was no significant difference in side effects or neurological risk factors associated with sucrose administration in neonates. Linhares et al. (2014) evaluated the potential side effects of sucrose on pain relief which was focused on factors both during hospitalization and after discharged, including parenteral feeding, duration of orogastric tube use, weight at 38 weeks postconception, weight at discharge, weight gain between birth and 38 weeks postconception, weight gain between birth and discharge, and feeding patterns. No significant differences were found in any of the parameters (ps >0.05), demonstrating that no adverse side effects were found with the administration of sucrose. Similarly, Stevens et al. (2005) showed no significant differences in neurological risk status and clinical outcomes as evidenced in both groups: Group A included immediate adverse events, such as heart rate <100 and >240, oxygen desaturation <85%, apnea > 15 seconds, and choking
while Group B incorporated long-term adverse events such as hyperglycemia >10.0 mmol, oral infection, necrotizing enterocolitis or intraventricular hemorrhages of grades 3 or 4, and death ($p > 0.05$).

**Discussion**

The study design of the studies was both a strength and weakness: the strength lies within the two studies that were randomized controlled trials, or RCTs. The weakness is design of the remaining study, which was a prospective case-control study. RCTs - often considered the “gold standard” - highlight outcomes of specific interventions with its emphasis on cause-and-effect relationships and ability to reduce allocation bias (Barton, 2000; Sullivan, 2011). While case-control studies are relatively quick and inexpensive to conduct, reduced precision in data collection and possible flaws in either the sampling design and implementation may occur (Wacholder, 2009).

Sampling methods was a strength observed in the 3 studies. Although Linhares et al. (2014) does not specify how its subjects were assigned to the sucrose and control groups, 17 out of 18 participants in its sucrose group correlated to data belonging to a previously published RCT examining the same interventions of repeated sucrose administration. Cignacco et al. (2011) performed block randomization using the Statistical Package for Social Sciences, or SPSS, and Stevens et al (2005) used central randomization and allocation concealment from a computer-generated table of random numbers only available to the neonatal pharmacist. In addition, all 3 studies applied both inclusion and exclusion criteria with zero to only a handful of drop outs. Cigancco et al. (2011) had 1 participant who had incomplete data because the fifth heel stick was missed while Stevens et al. (2005) had 2 drop outs for unknown reasons.
Sample size was a weakness among all studies. Linhares et al. (2014) had 43 subjects, Cignacco et al. (2011) had 71 subjects, and Stevens et al. (2005) had 66 subjects. Small sample sizes make it more difficult to identify confounding factors and their associated effects on the population; the risk of not accomplishing a study’s purpose is also increased (Zodpey, 2004).

Another weakness identified in the 3 studies was the inconsistency or lack of blinding subjects and interventionists. Linhares et al (2014) did not have its interventionists blind both groups of subjects. While Cignacco et al. (2011) blinded its pain rater to the phases of the procedure - baseline, heel stick, and recovery - it could only partially blind the raters: they could clearly observe whether the subject was receiving facilitated tucking, sucrose, or both. Similarly, Stevens et al. (2005) partially blinded its pain raters to only the 2 study groups that used pacifiers due to the actual pacifier’s visibility; the standard care group did not receive any pacifiers.

Good quality of data collection was a major strength in all 3 studies. Linhares et al (2014) reviewed medical charts using protocol for data collection by trained researchers, which was then further analyzed with SPSS and the Shaprio-Wilk test to confirm proper data distribution. Both Cignacco et al. (2011) and Stevens et al. (2005) implemented videotaping by trained individuals using standard protocols. Cignacco et al. (2011) enforced a protocol that each video be documented on when it started and finished, be at least 3 minutes, and reviewed by trained study nurses prior to being shown to 4 nurses for assessment of pain responses. Additionally, Stevens et al. (2005) had its data verified and double entered into its database; this was followed by logic checks that indicated an error rate in data entry of <1%. The videotaping in both studies confirms high-quality data collection in both studies. Further, the young age of all subjects - all under 37 weeks GA - resulted in overall compliance during both interventions and data collections.
Overall, all 3 studies demonstrated that sucrose administration is a reliable, safe method to manage pain in neonates as seen by lower pain scores and a minimal number of adverse effects. Despite flaws identified in the studies, the supported use of sucrose to relieve pain validates its continued use in medical settings. This conclusion is relevant to neonates born greater than 26 and less than 30 weeks GA or with low birth weight of less than 1500 grams. born preterm or with low births weight. Considering the exclusion criteria for all 3 studies, this cannot be applied to patients with the following criteria: major congenital anomalies, umbilical catheter in first 2 weeks of life, intraventricular hemorrhage, pH less than 7.0, pain expression impairments, surgical procedures, and a history of opioids or sedatives.

Implications

All three studies conducted by Linhares et al. (2014), Cignacco et al. (2012), and Stevens et al. (2005) validated the efficacy and safety of sucrose administration in decreasing neonatal pain. Sucrose - combination with either facilitated tucking or pacifiers - both yielded no significant adverse events and proved to be even more effective when combined with either pacifiers or facilitated tucking. Moreover, lengthy exposure to pain increases neonatal morbidity and affects pain reaction as they enter infant-hood (Mancuso & Burns, 2009). Prolonged neonatal pain has also been linked to abnormal brain development, potentially stunting head and body growth early in life (Grunau, 2013). For moderately preterm infants, the average cost of a 17-day stay in the NICU is $31,000 (Kirkby, Greenspan, Kornhauser, & Schneiderman, 2007). Improved neonatal outcomes could result in shorter hospital stays, which decrease costs. By standardizing the sucrose administration - along with facilitated tucking or pacifiers - as an intervention for
neonatal pain, nurses are provided with a consistent, legitimate platform to utilize: this will help reduce both the number of long-term, negative outcomes and expensive medical fees.

A crucial gap in evidence that exists within the studies is the developmental trajectory in the neonates after they are discharged. Monitoring health status post-discharge for one or two years is necessary to assess the long-term effects of repeated sucrose administration. Evaluating this population of sucrose-exposed neonates until they at least exit the stage of infancy - or until they are 2 years old - could possibly yield significant data. Moreover, whether this intervention could be applied to the population outlined by each study’s exclusion criteria or not should further be explored. The following lists some but not all of the characteristics of neonates that were excluded from the studies: neonates with major congenital anomalies, intraventricular hemorrhage (grade III/IV), hypo/hyperglycemia, or life-threatening malformations.

**Conclusion**

All three studies demonstrated that sucrose administration was able to effectively decrease neonatal pain levels without any significant adverse effects. By implementing this tool, healthcare providers will be able to help prevent long-term adverse outcomes in neonates as well as decreasing medical costs. Further research is needed to assess the longitudinal effect of sucrose on neonatal developmental outcomes in diverse populations.

**Abstract**

**Introduction** Nurses often find it difficult to accurately assess a neonate’s pain level due to their inability to communicate their pain using verbal language. Despite this barrier, it is essential to accurately interpret their pain signals and respond accordingly with the proper interventions. This literary review evaluates the effect of sucrose administration on neonatal pain levels.
Methods PubMed and CINHAL were extensively reviewed to obtain three studies. One prospective case-control and two randomized controlled trial studies were selected based on specific criteria that they were published during or after 2005.

Results All three studies confirmed that sucrose administration decreased neonatal pain levels without no serious adverse effects. Moreover, interventions combining sucrose with either facilitated tucking or pacifiers proved to be more effective than sucrose alone.

Discussion Good sample methods and high-quality data collection were both significant strengths among the three studies. A weakness in the external validity was the small sample size, which limited the generalization of results.

Conclusion Sucrose administration for neonatal pain is an extremely helpful and useful intervention that should be emphasized within a nurse’s scope of practice. Further research could be done to evaluate developmental impacts and to encompass a broader population with other medical conditions.
References


