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# **Is Non-Nutritive Sucking An Effective Method Of Providing Analgesia To Newborns Undergoing Painful Procedures?**

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A SELECTIVE EVIDENCE BASED MEDICINE REVIEW

In Partial Fulfillment of the Requirements For

The Degree of Master of Science

In

Health Sciences – Physician Assistant

Department of Physician Assistant Studies  
Philadelphia College of Osteopathic Medicine  
Philadelphia, Pennsylvania

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## Abstract

**OBJECTIVE:** “The objective of this selective EBM review is to determine whether or not non-nutritive sucking is an effective method of providing analgesia to infants undergoing painful procedures.”

**STUDY DESIGN:** A systematic review of three blinded randomized-controlled trials (RCT’s), published from 2011 to 2013. All were published in English, one of which was translated from its original Spanish version to an English publication.

**DATA SOURCES:** Three RCT’s were found using the PubMed database and all were published in peer-reviewed journals.

**OUTCOMES MEASURED:** The incidence and severity of pain were measured during procedures using the Premature Infant Pain Profile (PIPP) and/or Neonatal Infant Pain Scores (NIPS).

**RESULTS:** The first study, Lima et al reported that during venipuncture, both nutritive and non-nutritive sucking provided lower pain response compared to the control group receiving no analgesic stimulus ( $P < 0.05$ ). When comparing the two experimental groups in Lima et al’s study, those receiving non-nutritive sucking achieved a P value of less than 0.001 and NNT was calculated to be 2 patients. The Milazzo et al study used Chi-square analysis to show that NIPS subscale scores for crying one minute after needle insertion for venipuncture were significantly lower for the group receiving sucrose and a pacifier than for the pacifier group alone ( $P = 0.022$ ), however all other subscale scoring parameters were insignificant ( $P > 0.05$ ) suggesting adequate analgesic relief in the control group. Lastly, Liaw et al, demonstrated that non-nutritive sucking during heel-stick procedures had the lowest mean PIPP scores (6.39) as compared to facilitated tucking (7.15) and the control (9.52), which received only routine care. Additionally, odds ratios for pain and severe pain in the NNS vs. control groups were 0.39 and 0.23 respectively, indicating the NNS group had a reduced change of experiencing pain.

**CONCLUSIONS:** All three RCT’s reported reduced incidence and severity of pain in these infants, thus suggesting that non-nutritive sucking does provide adequate analgesia during procedures that typically induce painful stimulation.

**KEY WORDS:** Non-nutritive sucking, pacifier, analgesia

## INTRODUCTION

Nociceptive pain is caused by an injury to body tissues and it allows the body to sense harmful stimuli.<sup>1</sup> It is commonly perceived as sharp, aching, or throbbing.<sup>1</sup> Nociceptors are peripheral receptors located predominantly in the skin, mucosa, and cornea.<sup>2</sup> Upon activation, they transmit noxious stimuli through the spinothalamic tract.<sup>2</sup>

Until the early 1990s, the medical community did not widely accept the fact that newborns could perceive this type of pain.<sup>3</sup> It was previously thought that a newborn's nervous system was not properly developed and that they did not have the capability of remembering the feeling of pain.<sup>3</sup> At that time, invasive procedures were carried out without sedation or anesthesia.<sup>3</sup> Nowadays, it is well known that nociceptors begin to develop in utero by 7 weeks gestation and are completed by 20 weeks.<sup>2</sup> The use of proper analgesia is paramount during invasive procedures because nociceptive stimulation in infants causes increased intracranial pressure and oxygen desaturation, both of which increase the risk for short and long-term brain damage.<sup>4</sup>

The relevance of this topic to medicine and society as a whole cannot be understated. There are approximately 4 million births annually in the United States, of which nearly 450,000 are premature.<sup>5</sup> It is estimated that as many as 13 million preterm infants are born worldwide each year.<sup>4</sup> Newborns often undergo painful procedures shortly after birth, however these procedures are much more common in premature infants due to the resources required for their survival.<sup>4</sup> In the U.S. alone, the total estimated cost for preterm infant care is over \$26 billion.<sup>5</sup> This figure does not include individuals receiving ongoing care for conditions that were diagnosed previously at birth.<sup>5</sup> It is impossible to calculate the total cost and effects of preterm birth on society. Aside from the initial birth, long-term health problems and lifelong disabilities

lead to repeated hospital visits for various reasons, ranging from infection to treatment side effects.<sup>5</sup>

Preterm infants staying in neonatal intensive care units may undergo more than 10 invasive procedures daily for the first 2 weeks of life.<sup>4</sup> These procedures include heel-stick, venipuncture, intravenous catheter insertion, arterial punctures, suctioning, and gavage tube insertion.<sup>6</sup> During an acute painful episode, an infant will modify its psychological, behavioral, and physiological parameters to stop or limit the duration of the pain.<sup>3</sup> These parameters can be measured by clinicians and an objective pain score can be achieved.<sup>3</sup>

Early exposure to repeated procedural pain is a main factor contributing to negative physiological, cognitive, behavioral, and psychological consequences in infants.<sup>4</sup> This is because premature infants are more vulnerable to pain than older children due to their reduced pain threshold, pain sensitization from procedures, and inability to adequately modulate pain and maintain homeostasis.<sup>4</sup> Short term consequences of such poor pain control include irritation, change in sleep patterns, decreased appetite, and negative effects on the mother-newborn relationship.<sup>3</sup>

The recognition of pain effects in the neonatal period has accelerated the search for pharmacological and non-pharmacological mechanisms capable of reducing or eliminating the pain.<sup>3</sup> Pharmacological management includes the use of opioid narcotics and/or other sedatives given intravenously.<sup>4</sup> Another frequently studied pharmacological method is the oral administration of sucrose solutions, which is thought to reduce pain by releasing endogenous opioids.<sup>6</sup> Non-pharmacological methods that have also been commonly studied are nutritive sucking (NS) via breast or bottle-feeding and the use of facilitated tucking, otherwise known as swaddling.<sup>4</sup>

Previous studies have shown that nociceptive pain in preterm infants may not be effectively managed with opiates.<sup>4</sup> Additionally, most clinicians consider these drugs unacceptable due to the increased potential for adverse effects and toxicity.<sup>4</sup> This means that non-pharmacological methods are preferred and while nutritive sucking and swaddling have been shown effective at reducing pain, they can't eliminate it all together.<sup>4</sup>

Sucking is a normal reflex that begins to develop around 29 weeks gestation and is usually fully coordinated by 32-34 weeks.<sup>7</sup> This behavior has been shown to help infants self regulate their emotions, relax and focus their attention, and provides comfort and security to those in distress.<sup>7</sup> The sucking mechanism has been hypothesized to produce analgesia by stimulating orotactile and mechanoreceptors in the mouth to modulate nociceptive transmission and by activating the infant's endogenous non-opioid system.<sup>4</sup>

Non-nutritive sucking (NNS) is most commonly represented by the use a pacifier, but it also can be achieved by having the infant suck on a digit or other objects without the presence of any liquid.<sup>3</sup> NNS is a benign intervention and it is easily accessible to clinicians during procedural interventions.<sup>4</sup> Previous studies have shown great efficacy of NNS that was combined with other therapies like swaddling and sucrose solutions, therefore the use of NNS alone could be the predominant force driving that analgesic effect.

## **OBJECTIVE**

The objective of this selective EBM review is to determine whether or not non-nutritive sucking is an effective method of providing analgesia to infants undergoing painful procedures.

## **METHODS**

The population in these studies included term and preterm infants with medical requests to undergo invasive procedures that typically induce a pain response. The intervention used in

all three studies was NNS with a pacifier or via the use of a gloved finger. These NNS groups were compared to groups receiving 24% oral sucrose solution, nutritive sucking via maternal breastfeeding, tucking/swaddling methods, verbal/tactile reinforcement, or those receiving no intervention at all. All outcomes measured were patient-oriented evidence that matters (POEMs), including the incidence and severity of pain. This review includes three blinded randomized control trials.

All studies in this review were researched using PubMed by the author. Keywords used in searches were “non-nutritive sucking”, “pacifier”, and “analgesia.” All 3 articles were printed in the English language, one of which (Lima et al) was translated from its original Spanish publication to an English version. All studies were published in peer-reviewed journals between 2011 and 2013, and each was selected based on its relevance to the topic as well as patient-oriented outcome. Inclusion criteria were RCTs published after 1999 that included stable term and preterm infants with a medical necessity for invasive procedures. Exclusion criteria were infants with opiate or sedative exposure and those with any condition that can disrupt or alter the pain response.<sup>3,4,6</sup> Statistical analysis was used for each study to determine their significance by P values, number needed to treat (NNT), Confidence Intervals (CI), Odds Ratio (OR), Generalized Estimating Equation (GEE), Chi-squared ( $X^2$ ), and SPSS software analysis.<sup>3,4,6</sup>

**TABLE 1 – Demographics of included studies.**

Study	Type	# Pts	Age (days)	Inclusion Criteria	Exclusion Criteria	W/D	Interventions
Liaw (2012)	RCT	34	3 – 28	Preterm Infants meeting the following: 1) gestational age 29-37 wks and post-menstrual age 30-38.5 wks  2) post-birth age 3-28 days  3) stable condition	Infants with any of the following: congenital anomalies, neurologic impairment, documented sepsis, surgery, severe growth restriction at birth, substance-abusing mother, or any condition requiring the use of sedatives, muscle relaxants, anti-epileptics, or analgesics.	0	Pacifier use (NNS) vs. Facilitated tucking during heel-stick procedures
Lima (2013)	RCT	64	0 - 10	Newborn infants with a medical request for venipuncture	All newborns suffering from neurological damage, head/neck malformations, heart diseases, and those with absent motion or sucking reflexes.	0	Breastfeeding vs. Gloved Digit sucking (NNS) vs. no intervention during venipuncture
Milazzo (2011)	RCT	47	> 2	Preterm infants meeting the following: 30-36 wks gestation, 48 hours of age, NPO status, and medical requirement for arterial puncture	Infants with any of the following: intubation, narcotic analgesia since admission, and/or fetal exposure to maternal opioids	2	24% oral sucrose solution vs. sole use of a pacifier (NNS) prior to arterial puncture

## **OUTCOMES MEASURED**

All outcomes measured in these studies were patient-oriented evidence that matters using either the Premature Infant Pain Profile (PIPP) or Neonatal Infant Pain Scores (NIPS). The PIPP scoring system includes 7 parameters: 3 behavioral (brow bulge, eye squeeze, and nasolabial furrow), 2 physiologic (heart rate and O<sub>2</sub> saturation), and 2 contextual (gestational age and sleep/wake state).<sup>4</sup> The NIPS system utilizes 6 parameters: facial expression, cry, breathing patterns, arm position, leg position, and state of arousal.<sup>3,6</sup>

The Lima et al and Milazzo et al studies both used the NIPS system to analyze their trials. The difference between the two was that Lima et al dichotomized their data to deduce the incidence of pain during venipuncture, while Milazzo et al used NIPS criteria to rate the severity of the infants' pain at the time of arterial puncture and one minute after. Meanwhile, Liaw et al applied PIPP criteria to their analysis of the severity of pain during heel-stick procedures.

## **RESULTS**

This EBM review analyzed three blinded randomized control trials. Lima et al and Milazzo et al both used NIPS criteria to report their results as dichotomous data, however their control and experimental groups differed so data will be presented separately below. Dichotomized data was further calculated with numbers needed to treat (NNT). Liaw et al's study did not dichotomize any results and data could not be further dichotomized, therefore no NNT calculations were made.

In the Lima et al study, 64 newborns with medical requests for venipuncture were randomly divided into three groups. Group 1 consisted of 20 newborns that received NS, while group 2 also had 20 newborns that received NNS.<sup>3</sup> Group 3, the control, consisted of 23 newborns that did not receive any stimulation.<sup>3</sup> Gestational age and gender analysis showed no

statistical significance among the three groups.<sup>3</sup> NIPS was used to evaluate their response during the procedure.<sup>3</sup> Data was dichotomized to determine the incidence of pain based on NIPS scoring.<sup>3</sup> A score of 3 or less indicated the absence of pain, while scores ranging from 4 to 7 indicated the presence of pain.<sup>3</sup> The prevalence of pain was significantly lower in groups 1 and 2 when each was compared to group 3, with p values of 0.001 and <0.001 respectively.<sup>3</sup> When groups 1 and 2 were compared to one another, there was no significant difference in pain prevalence ( $P > 0.05$ ).<sup>3</sup> Treatment calculations showed a low NNT of 2 (see table 2), so for every 2 patients treated with NNS one more would experience no pain during venipuncture when compared to those receiving no stimulation.

**Table 2** – Absence of pain during venipuncture of infants receiving NNS vs. those receiving no treatment in Lima et al’s study.

<b>CER (no stimulation)</b>	<b>EER (NNS)</b>	<b>RBI</b>	<b>ABI</b>	<b>NNT</b>
17.4%	76.2%	338%	58.8%	2 patients

CER – control event rate, EER – experimental event rate, RBI – relative benefit increase,

ABI – absolute benefit increase, NNT – number needed to treat

In the Milazzo et al study, 47 premature infants with a medical necessity for arterial puncture were examined. The minimum sample size was 39 subjects, as determined with power analysis for chi-square tests using a calculated effect size of 0.5 based.<sup>6</sup> An intent-to-treat analysis was used in this study.<sup>6</sup> Infants assigned to the experimental group received 0.5 mL of 24% oral sucrose solution followed by a pacifier, while infants in the control group received pacifier only.<sup>6</sup> Gestational age was not found to be significantly different between the sucrose and NNS groups ( $33.7 \pm 1.0$  and  $33.9 \pm 1.1$  weeks, respectively).<sup>6</sup>

Before the procedure began, 87% of subjects had a total NIPS score of 0 and the remainder had low scores ranging from 0 to 3. At the time of needle insertion and 1 minute

after, Chi-square analysis showed that the change in NIPS subscale for crying was significantly lower in the experiment sucrose group ( $X^2 = 9.30$ ,  $df = 2$ ,  $P = 0.006$ ).<sup>6</sup> However, no significant difference was found between the 2 groups in all other NIPS subscale parameters (all  $P$  values  $> 0.05$ ).<sup>6</sup> Physiological changes (HR and SpO<sub>2</sub>) were found to be similar in both groups immediately following needle insertion and one minute after completion, analysis of variance found no statistical differences ( $P > 0.05$ ).<sup>6</sup>

Treatment calculations (see table 3) were low with a NNT of 3. So, for every 3 patients treated with 24% oral sucrose, one more would have a reduced incidence of increased crying during and after arterial puncture. However, this number is blunted by the fact that no other NIPS parameters changed between this sucrose group and those receiving only NNS.

**Table 3** – Changes in NIPS crying immediately after needle insertion in those receiving 24% sucrose + NNS vs. NNS only in Milazzo et al's study.

CER (NNS)	EER (sucrose + NNS)	RBI	ABI	NNT
39.1%	79.1%	102%	40%	3 patients

CER – control event rate, EER – experimental event rate, RBI – relative benefit increase,

ABI – absolute benefit increase, NNT – number needed to treat

Lastly, in the Liaw et al study, 34 preterm infants with a medical need for heel-stick procedures were studied. Study power was calculated by determining the effect size of 0.51, based on mean PIPP scores of the control and NNS groups (9.52 and 6.39 respectively) and the SDs (4.95 and 3.35 respectively), and the correlation ( $r = 0.375$ ) of PIPP scores between the two groups.<sup>4</sup> So, power for 34 preterm infants with an effect size of 0.649 and significance level of 0.05 was 95.5%.<sup>4</sup>

Each infant received 3 heel-sticks and was randomly assigned using a random table format to a sequence of 3 treatments, two of which were pain-relief interventions (NNS and

facilitated tucking) and the other of which was the control condition receiving routine care only.<sup>4</sup> Each treatment condition was performed on a different day to avoid any carry-over of treatment effects.<sup>4</sup> The carry-over effect was analyzed by comparing scores from each treatment in the 3 differing sequences and pain scores were found to have no significant difference between the sequences with all P values being greater than 0.05.<sup>4</sup>

Infants receiving NNS and facilitated tucking has significantly lower mean PIPP scores (6.39 and 7.15, respectively) than those in the control group (9.52).<sup>4</sup> The calculated range for true population mean was lowest for the NNS group at 5.62 to 7.16 and the NNS group also had the narrowest 95% Confidence Interval at +/- 0.79 (see table 4). Odds ratio (OR) of pain for NNS vs control was 0.39 ( $p = 0.005$ ), indicating the NNS group had a 61% chance of decreased pain compared to the control group.<sup>4</sup> Similarly, the OR of severe pain for NNS vs control was 0.23 ( $p < 0.001$ ), indicating a 77% chance of reduced pain compared to the control.<sup>4</sup> Results (see table 5) were calculated with the Generalized Estimating Equation (GEE), which produces more efficient and unbiased estimates than ANOVA.<sup>4</sup>

**Table 4** – True Population Ranges during heel-stick for Liaw et al’s study.

Variable	n	Mean PIPP	SD	95% C.I.	True Population Range
Control	72	9.52	4.95	+/- 1.14	8.38 to 10.66
Facilitated tucking	75	7.15	3.88	+/- 0.87	6.28 to 8.02
NNS	72	6.39	3.35	+/- 0.79	5.62 to 7.16

**Table 5** – ORs for moderate pain and severe pain of NNS vs control in Liaw et al's study.

<b>Severity of Pain</b>	<b>OR</b>	<b><i>p</i></b>	<b>95% C.I.</b>
Moderate	0.39	0.005	+/- 0.20
Severe	0.23	<0.001	+/- 0.10

## **Discussion**

In the Lima et al study, both NNS and breastfeeding were shown to provide effective analgesia during venipuncture when compared to those receiving no stimulation.<sup>3</sup> Comparison data between the two groups was not significant.<sup>3</sup> Overall, absence of pain was greater in the NNS group than in those who were breastfed.<sup>3</sup> From this, we can deduce that the sucking mechanism was likely the primary source of pain relief in these infants. NNT was also low at only 2 patients, indicating great efficacy of NNS at managing procedural pain in infants.

In the Milazzo et al study, the 24% sucrose solution followed by a pacifier provided the most effective means of cry reduction in infants during arterial puncture when compared to groups receiving NNS only. The instillation of sucrose prior to the pacifier triggers the endogenous release of opioids and dopamine, which provide an additional benefit of increased focus, mood, and comfort.<sup>2</sup> However, no other NIPS subscale parameters were significantly different between the two groups ( $p>0.05$ ). The effect was likely synergistic in that both the pacifier and sucrose provided comfort. The use of a pacifier in both groups, along with this lack of change in other pain parameters, means that the sucking mechanism was the again the primary source of analgesia to these infants. In order to truly differentiate the two, this study should have kept each variable separate.

The Liaw et al study, NNS was more effective in relieving pain during heel-stick than facilitated tucking or those receiving routine care. This was based on mean PIPP scores, lower ORs, and narrow CIs. However, the control group was not monitored as closely as the other two because routine care was highly variable. Routine care was defined as providing only light touch and verbal reinforcement by the nurses.<sup>4</sup> Both of these variables can differ based on the nurse caring for each individual, with the amount and force of touch being inconsistent, as well as the tone of voice. The difference between the NNS and control groups was significant with p values  $< 0.005$  and  $< 0.001$  for moderate and severe pain, respectively.<sup>4</sup> So, although the control had some variability in their care, it was not likely relevant enough to discount the analgesic efficacy of NNS.

### **Conclusion**

Based on the studies reviewed, it can be concluded that non-nutritive sucking is an effective method of providing analgesia to infants undergoing painful procedures. Nutritive sucking (NS) may offer an additional distraction to the infant, but it did not appear to be the primary source of pain relief since both NS and NNS require the sucking reflex. As discussed previously, NS appears to activate the endogenous opioid system and opioids have been shown in prior studies to be ineffective at managing procedural pain in infants.<sup>4</sup> On the other hand, the sucking mechanism was hypothesized to produce analgesia by activating the infant's endogenous non-opioid system.<sup>4</sup> These studies have demonstrated that activating this system is the safest and most efficacious way of providing analgesia to infants and preterm infants with a medical requirement for a procedure that typically induces a pain response.

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