The Efficacy of Non-Pharmacological Pain Management Methods Amongst Premature Neonates in the Neonatal Intensive Care Unit (NICU)

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THE EFFICACY OF NON-PHARMACOLOGICAL PAIN MANAGEMENT METHODS AMONGST PREMATURE NEONATES IN THE NEONATAL INTENSIVE CARE UNIT (NICU)

by

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ABSTRACT

The purpose of this study was to conduct an integrated review of the literature examining the use of non-pharmacologic pain management strategies in premature neonates and to explore the relationship between health outcomes and time to discharge from the neonatal intensive care unit (NICU). Non-pharmacologic pain management strategies include human touch, facilitated tucking, non-nutritive sucking, and kangaroo care. A systematic review of the literature was conducted from multiple online databases. Peer reviewed, English-language articles containing the keywords 'pain management', 'neonatal intensive care unit', and 'non-pharmacologic' were included for synthesis. Exclusion criteria included articles with a focus on infants not admitted to the NICU and infants with a gestational age greater than 37 weeks. Results revealed positive outcomes when alternative pain-relieving methods, rather than drug therapy, were used in the NICU. A majority of articles suggest facilitated tucking is very successful in lowering a preterm infant’s pain. However, facilitated tucking alone was significantly less effective in relieving procedural pain compared to facilitated tucking in combination with oral sucrose administration. Kangaroo care and gentle human touch also proved to reduce physiologic and behavioral signs of pain in neonates. The literature reveled an overall positive outcome when non-pharmacologic pain interventions are used in the NICU, with some behavioral interventions showing better efficacy than others at relieving neonatal pain. None of the reviewed articles explored the relationship between reduced length of stay and parameters assessing health outcomes based on pain control in neonates. The literature indicated nurses play a significant role in the use of pain-relieving methods in neonatal populations. Implications for future research that focuses on successful behavioral-based pain management strategies that assist in refining neonatal pain
relief would be of great benefit to improving health outcomes related to infant survival after discharge from the NICU.
DEDICATION

To Robert and Christina Martinez for always supporting and encouraging me to reach my highest potential.
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# TABLE OF CONTENTS

INTRODUCTION ........................................................................................................................................... 1

BACKGROUND .................................................................................................................................................. 2

Pain in the Premature Neonate .................................................................................................................. 2

Outcome Measures of Pain in the Premature Neonate ........................................................................... 2

Non-Pharmacological Pain Management Methods ................................................................................. 3

Summary ...................................................................................................................................................... 4

PROBLEM.................................................................................................................................................... 6

PURPOSE...................................................................................................................................................... 7

METHOD....................................................................................................................................................... 8

RESULTS ....................................................................................................................................................... 9

Facilitated Tucking ...................................................................................................................................... 9

Kangaroo Care ............................................................................................................................................. 10

Gentle Human Touch .................................................................................................................................. 13

Non-nutritive Sucking ............................................................................................................................... 14

The Comparison of Two Non-Pharmacologic Pain Interventions ......................................................... 15

Non-pharmacologic in Combination with Pharmacologic Strategies ......................................................... 15

DISCUSSION ............................................................................................................................................... 18

The Efficacy of Non-Pharmacologic Pain Management Methods Available for Use ..................... 18
The Role of the Nurse in the Management of Pain ................................................................. 20

The Role of the Parent in the Management of Pain ............................................................... 20

The Importance of Personalizing Nursing Care in the Neonatal Intensive Care Unit (NICU) 21

LIMITATIONS .................................................................................................................................. 23

RECOMMENDATIONS ..................................................................................................................... 25

Research ........................................................................................................................................ 25

Education ....................................................................................................................................... 25

Nursing Practice .............................................................................................................................. 26

Conclusion ...................................................................................................................................... 27
INTRODUCTION

Each year, approximately 10 to 15 percent (half a million) of babies born in the United States (US), are admitted to the neonatal intensive care unit (NICU) immediately after birth for conditions related to prematurity (born before 37 weeks gestation), heart problems, birth defects, breathing irregularities and infections, among others (Peterson-DeGroff, 2015). It has been found that Neonates undergo as many as one hundred painful procedures in the first two weeks of life (Herrington & Chioto, 2014). The effects that routine, painful procedures have on the physiological development of an infant from admission to discharge are poorly understood and warrant further investigation.

Procedures performed on neonates can range from causing minor, temporary discomfort, such as simple heel sticks and venipuncture to more invasive treatments, such as intubation and nasogastric tube insertion. Acute and prolonged pain is also experienced during the neonatal period due to the healing process involved with various types of procedures, such as chest tube placement and surgical incision sites. It is the responsibility of the health care team to ensure that proper methods are used to protect the infant and to make painful experiences as tolerable as possible. However, the long-term effects of painful stimuli in early life and the efficacy of methods to reduce undesirable outcomes due to pain in the neonate are challenging.
BACKGROUND

Pain in the Premature Neonate

The central and peripheral nervous system of preterm neonates is immature at birth and responds differently to pain during the early weeks of life. “Preterm neonates are more sensitive to pain and have a greater response to stress than infants born at full term” (Grunau, 2013). Preterm infants have a low pain threshold and a more pronounced reflex response to touch than a full term baby. Pain has a negative impact on neonatal growth and development, and therefore has a greater significance in the neonatal population compared to any other age related demographic variables. Procedural pain in preterm infants is associated with abnormal brain development (Grunau, 2013). The use of opioids and pain relief drug therapy in neonate pain management may not be the optimal solution for pain control. Narcotic analgesic agents have demonstrated negative effects on the developing organs and tissues of preterm neonates. Alternative methods of pain control should be utilized to decrease the risk of short and long-term injury. Opioids may be effective for pain relief in preterm neonates, but the consequences of dependence and withdrawal, as well as the increased demands of the neonate to metabolize opiate based drug therapy, needs to be measured against the benefits. Although pharmacologic and non-pharmacological pain management methods are necessary to provide pain relief in the NICU, it is important to understand the critical issues that arise with the use of narcotic analgesics in the neonatal population (Anand, 2007).

Outcome Measures of Pain in the Premature Neonate

Pain is a subjective measurement and is typically assessed through verbal communication
with the person that is undergoing the painful experience. The neonate lacks the ability to verbally communicate their level of pain. Variations in the physiologic response due to an underdeveloped neurologic system contributes to the need for a better understanding of the methods that relieve pain in preterm infant encounters and potentially ease the traumatizing experiences that occur in the NICU. The outcome measures used in the articles synthesized included the Premature Infant Pain Profile (PIPP), Neonatal Infant Pain scale (NIPS), Bernese Pain Scale for Neonates, heart rate variability (HRV), and various other combinations of physiological markers.

The Premature Infant Pain Profile (PIPP) is a 7-indicator composite measure used to assess acute pain in the premature infant population. The profile is composed of 3 facial actions (brow bulge, eye squeeze, and nasolabial furrow), heart rate, oxygen saturation, gestational age, and behavioral state (Johnston et al., 2008). In comparison to other outcome measures, the PIPP proves to be one of the most reliable and valid acute infant pain measures available. (Stevens et al., 2010). There is documented evidence supporting the use of NIPS in the identification of pain in infants through the observation of behavioral cues (Backus, 1996). The Bernese Pain Scale for Neonates (BPSN) consists of 9 physiological and behavioral indicators. The 9 include heart rate, oxygen saturation, grimace, body movements, crying, skin color, sleeping patterns, respiration, and consolation (Cignacco et al., 2008). According to research, BPSN is a valid and reliable tool for the assessment of pain in neonates (Cignacco et al., 2004).

Non-Pharmacological Pain Management Methods

Facilitated tucking is a non-pharmacological pain management method that can be done
by healthcare professionals or involve the parent. Facilitated tucking is performed by holding the infant’s extremities in a flexed position close to the midline of the body. This position mimics the in utero positioning and it is hypothesized that this will reduce the pain response in the neonate.

Non-nutritive sucking is not associated with feeding but rather is the sucking patterns used by infants to self-calm (Medical Dictionary for the Health professions and Nursing, 2012). It is thought that using this method during nursing procedures such as venipuncture and NG tube suctioning will soothe and calm the baby and therefore reduce the pain response.

Gentle human touch (GHT) consists of therapeutically touching a neonate with the fingertips placed above the eyebrow line of the infant and the palm touching the infant’s crown, while the other hand is gently rested on the lower abdomen (Bijari et al., 2012). It is important that the hands used to perform GHT are properly warmed before the method is administered. Since touch is one of the first strong positive senses in neonate, gentle human touch enhances sensory maturation and promotes more optimal behavioral organization (Bijari et al., 2012).

Kangaroo care is a method of pain management that involves skin-to-skin contact between the infant and the chest of the mother or father (“Kangaroo Care”, 2015). Studies have found that skin-to-skin holding reduces crying in response to painful stimuli by stabilizing heart rates, respiratory rates, and improving oxygen saturation rates (Kostandy et al., 2008).

Summary

Approximately 13 percent of all pregnancies result in premature birth and the newborns
are admitted to the NICU shortly after birth for life-saving care (Herrington & Chioto, 2014). This represents a substantial number of infants that undergo painful procedures and it is vital to understand more about non-pharmacologic pain management methods in the NICU that have successful outcomes related to growth and development. Nurses play a pivotal role in ensuring comfort of a patient. A NICU nurse must observe and assess the behaviors of neonates closely due to their inability to verbally communicate specific needs. It is within the nurse’s scope of practice and responsibility to deliver pain relieving drug therapy based on the subjective and objective data gathered from the neonate. It is important to note that there are alternative methods to ease the pain the neonate is experiencing without increasing the risk of harm to other immature organ systems. Specific methods for non-pharmacologic pain management to relieve or minimize pain in premature neonates include: facilitated tucking, non-nutritive sucking, gentle human touch, and kangaroo care. These methods have been shown to be beneficial in minimizing or relieving pain but research is needed to determine their true effectiveness with regard to short- and long-term health outcomes.
PROBLEM

Non-pharmacologic pain management strategies in premature neonates are poorly understood and their effectiveness with regard to growth and development outcomes continues to be elusive. Premature neonates exhibit severe adverse effects when subjected to pain (Grunau, 2013). This review of the literature will establish a better understanding of which non-pharmacologic pain management strategies can decrease length of stay due to fewer complications; therefore improving health outcomes in premature neonates. It is expected that non-pharmacologic pain management strategies will be more effective at decreasing the risk of abnormal neurologic development due to adverse painful stimuli. Understanding which non-pharmacologic pain management strategies have the greatest efficacy enables the nurse to personalize care directed to the neonatal population and therefore potentially reduce poor health outcomes.
PURPOSE

The purpose of this study is to review current research examining the use of non-pharmacologic pain management strategies and to provide a better understanding of the adverse effects of acute pain in the premature neonatal population and review current research examining the use of non-pharmacologic pain management strategies in premature neonates and evaluate which of these strategies have the greatest efficacy in order to personalize care directed to the premature neonatal population and reduce poor health outcomes. It is proposed that specific non-pharmacologic interventions can be used to improve pain management in premature neonates, thereby optimizing health status outcomes. The secondary purpose of this review will be to discuss potential future research that focuses on the integration of successful non-pharmacologic pain management strategies into nursing education that assists in improving premature neonatal health initiatives.
METHOD

A search of the current literature was conducted using the EBSCOhost, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Education Information Resource Center (ERIC), MEDLINE, and Psych INFO databases. The search was limited to peer-reviewed articles published and written in the English language. All articles were cross-referenced for relevance with the key word search. The initial search included the keywords ‘pain management’, ‘neonatal intensive care unit (NICU)’, and ‘non-pharmacologic’. Exploration of non-pharmacologic pain management therapy inclusion criteria using complimentary therapies was focused on specific terms related to human touch, facilitated tucking, non-nutritive sucking, and kangaroo care. Exclusion criteria included research articles with a focus on pharmacologic pain management, infants not admitted to the NICU, maternal postpartum outcomes, and infants with a gestational age greater than 37 weeks. The data extracted from the articles was compared to all available research on the topic to synthesize an educational answer to how important these management methods to premature neonates. From the overall analysis of the search articles a conclusion was synthesized on the efficacy of pain management options in the premature neonatal demographic.

Initial searches revealed 60 results, with 32 of the studies excluded immediately for not meeting the inclusion criteria. 24 studies were selected for additional review, with 12 studies selected for inclusion in this synthesis. Inclusion criteria were articles written in the English language and published in professional journals from 2003 to the present. These articles are peer reviewed and available in full text. 10 studies were excluded for not being available in full text. The remaining two studies were excluded due to irrelevance to topic being considered.
RESULTS

Thirteen studies were included in this review of literature that explored the efficacy of non-pharmacologic pain management interventions in the neonatal intensive care unit. All studies were published in the past thirteen years. Four randomized crossover trials, four randomized controlled trials, two quasi-experimental studies, one short-term longitudinal study, one experimental pilot feasibility study, as well as one single blind crossover design were included in synthesis. All studies were peer reviewed and one study included a questionnaire.

Facilitated Tucking

Two studies focused on the efficacy of facilitated tucking in the Neonatal Intensive Care Unit (NICU). The two specific nursing procedures implemented in the studies were endotracheal/pharyngeal suctioning and venipuncture.

Premature infants needing endotracheal and pharyngeal suctioning in a randomized crossover trial underwent the procedure using both facilitated tucking by parents’ and routine care within a 2-day interval (Axelin et al., 2005). Without facilitated tucking, the infants had a median Neonatal Infant Pain Scale (NIPS) score of 5 (Axelin et al., 2005). We can see the effectiveness of facilitated tucking when it is done during the suctioning procedure by the lower median NIPS score of 3 (Axelin et al., 2005). The study concluded that facilitated tucking is a safe and effective pain management method during suctioning of a preterm infant (Axelin et al., 2005). Given that the parent is willing and able, there is the added benefit of increased bonding between parent and infant when the parent is given an active role in the pain management of their preterm infant. Although even if the parent is unable or not willing to participate, this pain
management method can still be carried out by a nurse or other licensed professional to relieve the infant’s pain during the suctioning procedure. Each parent completed a questionnaire on their perception of the procedure and nineteen out of twenty parents preferred facilitated tucking during suctioning compared to routine care (Axelin et al., 2005).

Participants in a quasi-experimental study were divided into control group and treatment group, the control group was exposed to venipuncture under the normal NICU routine while the treatment group received facilitated tucking during the venipuncture procedure (Lopez et al., 2014). The treatment group displayed lower Premature Infant Pain Profile (PIPP) scores during venipuncture than that of the control group with mean score of 9.68 in the treatment group and 10.47 in the control group that received routine care (Lopez et al., 2014). This shows a significant decrease in the pain experienced by the neonate that received facilitated tucking during venipuncture.

Kangaroo Care

Four studies focused on kangaroo care and it’s efficacy in the NICU to reduce pain in preterm infants. These four studies show the efficacy of kangaroo care in reducing the pain of heel stick procedures in the NICU. Given the results of the articles, kangaroo care proves to be an effective alternative to pharmacologic pain management and standard care in not only affecting the behavioral responses to pain but also reducing the autonomic pain response in preterm neonates. Kangaroo care is also a potentially beneficial strategy for promoting the health of the family.

Preterm infants in Canada were recruited to participate in a single-blind randomized
A crossover trial in which the infants underwent a heel lance procedure while being held in skin-to-skin kangaroo care position with their mother (Johnston et al., 2008). The control group was in a prone position and swaddled in a blanket in the incubator during the heel lance procedure (Johnston et al., 2008). Mean Premature Infant Pain Profile (PIPP) scores were significantly lower in the kangaroo care position ninety seconds post-heal lance at 8.871 versus the control group in which the mean PIPP was 10.677 (Johnston et al., 2008). Although there is a significant difference at ninety seconds post-heal lance, the kangaroo care condition at thirty and sixty seconds post-heal lance was not significant (Johnston et al., 2008). Despite this, the time it took the infants to return to baseline heart rate post procedure was significantly shorter for the treatment group at one-hundred and twenty three seconds versus one hundred and ninety three seconds for the control condition (Johnston et al., 2008). It is concluded in this article that kangaroo care is a safe and effective pain management method that increases the ability of the mother to be involved in the pain control of the infant facilitating a bonding experience (Johnston et al., 2008).

A randomized control trial studied the effectiveness of kangaroo care in lowering the pain response to a heel stick procedure in the NICU (Gao et al., 2015). The infants were separated into a control group and a treatment group. Both groups received a heel stick without intervention to give a baseline for each infant to the observers of the recordings (Gao et al., 2015). After the initial heel stick, three more were done to each infant within a two-week period in which the treatment group received kangaroo care and the control group remained prone in the incubator as per protocol (Gao et al., 2015). The kangaroo care condition revealed significantly lower heart rates and a shorter duration of crying and grimacing than the incubator group (Gao et
al., 2015). In the control group, the heart rates of the infants remained significantly faster in the recovery phase than those of the kangaroo care group (Gao et al., 2015). This article concludes that kangaroo mother care may be a safe analgesic alternative in preterm infants during nursing procedures in the NICU (Gao et al., 2015).

In a similar study, a single blind crossover design was used to determine the efficacy of kangaroo care during heel stick procedures in the NICU (Johnston et al., 2003). Again, the infants recruited were separated randomly into two groups, a treatment group and a control group (Johnston et al., 2003). The treatment group received kangaroo care for thirty minutes prior to the heel stick and throughout the procedure (Johnston et al., 2003). The Premature Infant Pain Profile (PIPP) scores across the first 90 seconds of the heel-lancing procedure were significantly lower in the kangaroo care condition by two points (Johnston et al., 2003). Given this data, the article concludes that kangaroo care is an effective pain-reducing alternative to usual nursing protocols during heel stick procedures in the NICU (Johnston et al., 2003).

A slightly different approach was taken in the randomized crossover trial done in 2012 by Xiaomei Cong et al. The purpose of this trial was to determine the effects that longer kangaroo care (thirty minutes) and shorter kangaroo care (fifteen minutes) have on autonomic responses in preterm infants before and throughout heel stick procedures (Cong et al., 2012). As previously determined, kangaroo care is effective at reducing the pain responses of premature infants during heel stick procedures but this trial shows not only the behavioral responses but also the autonomic responses through heart rate variability and the effect that kangaroo care has on these responses (Cong et al., 2012). Heart rate changes from baseline to heel stick phases of the
procedure were significantly less in the thirty-minute kangaroo care treatment group as opposed to fifteen-minute kangaroo care and standard incubator care (Cong et al., 2012). In incubator care, low frequency power significantly increased from baseline to heel stick and dropped from heel stick to recovery phase but in the two kangaroo care conditions, no changes across the study phases were found (Cong et al., 2012). This shows that kangaroo care has a significant effect on reducing autonomic pain responses in preterm infants. Longer kangaroo care for thirty minutes greatly affected the infants sympathetic and parasympathetic responses during heel stick compared to incubator care in which these responses are not significantly affected (Cong et al., 2012). This suggests that kangaroo care is a safe and effective intervention in the NICU that has a profound effect on reducing not only behavioral responses to pain but also autonomic pain responses.

**Gentle Human Touch**

One article reviewed tested the efficacy of gentle human touch on reducing pain responses on an infant during heel stick procedures.

In the feasibility pilot study eleven infants received heel sticks with and without gentle human touch to determine the effectiveness of gentle human touch in reducing pain response in premature infants (Herrington and Chiodo, 2012). When the infants did not receive gentle human touch they had decreased respiration, increased heart rate, and increased cry time during the heel stick procedure while the infants who received gentle human touch during the heel stick procedure did not show reduced respiratory rate, increased heart rate, or increased cry time (Herrington and Chiodo, 2012). There were no profound differences noted between the GHT and
non-GHT groups in oxygen saturation during the heel stick procedure (Herrington and Chiodo, 2012). Although given the heart rate, respiratory rate, and cry time data, gentle human touch is a simple non-pharmacologic therapy that can be used by nurses and even families to reduce the pain response of a preterm neonate to heel sticks in the NICU.

**Non-nutritive Sucking**

One article reviewed tested the efficacy of non-nutritive sucking on reducing pain responses on an infant during NG tube feeding.

The short-term longitudinal experimental design assesses how non-nutritive sucking (NNS) using a pacifier affected physiological and behavioral outcomes of preterm infants (Kamhawy et al., 2014). There was a control group receiving routine care and a treatment group who received non-nutritive sucking during the routine nasogastric feed (Kamhawy et al., 2014). Significantly higher oxygen saturation occurred during and after nasogastric tube feeding for the intervention infants as compared to the control group (Kamhawy et al., 2014). Although no significant group differences were shown in the heart rate data, the NNS group started nipple feeding 5 days earlier than the control infants (Kamhawy et al., 2014). The treatment group was discharged at a younger average post-menstrual age than the control group and were heavier at discharge (Kamhawy et al., 2014). While uncomfortable, nasogastric tube feeds are not normally considered a painful procedure. The article concludes that non-nutritive sucking positively affects the physiological and behavioral outcomes of preterm infants and therefore it is suggested that non-nutritive sucking could be just as effective in reducing pain responses in the NICU.
The Comparison of Two Non-Pharmacologic Pain Interventions

One prospective randomized controlled crossover trial compares the efficacy of two non-pharmacological interventions; non-nutritive sucking (NNS) and facilitated tucking (FT) with routine care. Each preterm infant participating in the study were in need of three separate heel sticks done on different days and were randomly assigned to a sequence of three treatments (Liaw et al., 2012). During heel stick procedures, infants received routine care, non-nutritive sucking, and facilitated tucking and had mean PIPP scores of 9.52, 6.39, and 7.15, respectively (Liaw et al., 2012). Infants receiving non-nutritive sucking and facilitated tucking had significantly lower mean pain scores during the procedure than when they were exposed to routine care (Liaw et al., 2012). Both of these interventions effectively lowered pain during the heel stick procedure. Non-nutritive sucking had a greater effect on the PIPP score than facilitated tucking (FT) but FT proved to reduce stress-related behaviors as well and show a much broader effect on pain management through higher oxygen saturation levels and lower heart rate (Liaw et al., 2012).

Non-pharmacologic in Combination with Pharmacologic Strategies

Three studies included in synthesis explored the effectiveness of non-pharmacologic pain management methods in combination with pharmacologic methods.

A randomized control trial assessed the analgesic effect of pharmacologic (sucrose, water) and a non-pharmacologic measure (pacifier) in preterm infants and determined whether there is any synergism between the pain relief of these two methods (Elserafy et al. 2009). The lowest pain scores occurred with the use of 24% sucrose solution combined with a pacifier
(Elserafy et al. 2009). The pain score was 0.7 higher on the PIPP scale when sterile water was used in combination with non-nutritive sucking via pacifier (Elserafy et al. 2009). These results show that the synergistic effect of the combination of sucrose and non-nutritive sucking proved to be clinically effective in relieving the pain of simple nursing procedures.

A randomized controlled trial tested the comparative effectiveness of a non-pharmacologic pain-relieving intervention and a pharmacologic intervention administered alone or in combination across time for repeated heel sticks in preterm infants (Cignacco et al., 2012). During heel stick, the infants receiving only facilitated tucking had significantly higher BPSN scores than the combination group and sucrose group (Cignacco et al., 2012). In the recovery phase it proved beneficial to use both in conjunction with each other with a significantly lower BPSN score in the combination group during recovery than that of each method used alone (Cignacco et al., 2012). Facilitated tucking alone was significantly less effective in relieving procedural pain but when combined with sucrose the methods have an added benefit in lessening BPSN scores in the recovery phase (Cignacco et al., 2012).

The third randomized control trial compared the effectiveness of combinations of non-nutritive sucking, oral sucrose, and facilitated tucking with routine care during heel-stick procedures (Liaw et al., 2012). The outcome measure for this study was a state-coding scheme. The three combinations of oral sucrose-facilitated tucking, non-nutritive sucking-oral sucrose, and oral sucrose-facilitated tucking-non-nutritive sucking more effectively reduced occurrences of infant crying and arousal when compared to routine care during heel-stick (Liaw et al., 2012). The most effective combination of the three proved to be non-nutritive sucking-oral sucrose and facilitated tucking with a 52.8% more quiet-sleep occurrence (Liaw et al., 2012). Combining
these two non-pharmacologic interventions with the pharmacologic intervention of sucrose not only preserved infant’s sleep but also reduced agitation during heel stick procedures (Liaw et al., 2012).
DISCUSSION

Based on the review of the literature on non-pharmacologic pain interventions in the Neonatal Intensive Care Unit (NICU) four areas related to nursing care were identified. These are the efficacy of non-pharmacologic pain management interventions available for use in the NICU, the role of the nurse in pain-management of the preterm population, the role of the parent in the management of pain in the NICU, and the importance of personalizing nursing care in the preterm neonate population to reduce poor health outcomes.

The Efficacy of Non-Pharmacologic Pain Management Methods Available for Use

Given the amount of painful procedures that a premature neonate undergoes in the NICU environment (Herrington & Chioto, 2014), the detrimental effects of pain in this population (Grunau, 2013), and the adverse effects of pharmacologic interventions (Anand, 2007), it is necessary to explore the efficacy of additional interventions available. Throughout all the literature, each non-pharmacologic intervention proved to be effective in reducing the pain response elicited by the preterm neonate. Facilitated tucking lowered the mean Neonatal Infant Pain Scale (NIPS) score by 2 points and the mean Premature Infant Pain Profile (PIPP) score by 0.79 points. Kangaroo care lowered the Premature Infant Pain Profile (PIPP) score by 1.806 in one study and 2 points in a secondary study. The infants receiving kangaroo care had lower heart rates during the procedure and the heart rates returned to baseline 70 seconds faster than those of the control group. The duration of cry and grimace was shorter when kangaroo care was implemented. Kangaroo care also proved to have a significant effect on reducing the autonomic pain responses in preterm infants exemplified by Heart Rate Variability (HRV) indices. Through the HRV study it is shown that kangaroo care for at least 30 minutes before and during the heel
stick procedure had a profound impact on the infants sympathetic and parasympathetic responses compared to standard incubator care. Gentle Human Touch (GHT) showed no evidence of decrease respiratory rate, increased heart rate, or increase cry time in contrast with the control group that received standard care during the procedure. There were no noted differences in oxygen saturation between the GHT group and the non-GHT group. Infants who received non-nutritive sucking during and after nasogastric tube feed displayed higher oxygen saturation levels than the control group. There was no significant data to support that non-nutritive sucking lowers heart rate during procedures although there is much data to support that non-nutritive sucking has a profound impact on good health outcomes in the NICU. The treatment group transitioned to nipple feeding five days earlier than the control group and weighed more at discharge. Non-nutritive sucking leads to an earlier average postmenstrual discharge age than infants who did not receive non-nutritive sucking. While this data is greatly in support of routine use of non-nutritive sucking with tube feeding preterm infants, it can be suggested that this intervention can be used to reduce pain experienced by the neonate during painful procedures and can lead to better health outcomes. Non-nutritive sucking is tested deeper in a study that compares the method to the use of facilitated tucking. Non-nutritive sucking lowered mean PIPP scores by 3 points in comparison to the control group and therefore was more effective at reducing PIPP scores than facilitated tucking in which the score was lowered by just over 2 points. It is concluded that the infants’ pain after receiving non-nutritive sucking decreased by 77% in comparison to routine care and decreased by 72% with facilitated tucking compared to routine care.

Although all interventions prove to be effective at reducing pain responses to a certain degree, more research is needed that compares the efficacy of the interventions to each other. More
research is also needed that compares the non-pharmacologic interventions directly to pharmacologic interventions to determine the true efficacy in comparison and therefore make a more educated decision when weighing the risk and benefits of pharmacologic interventions with non-pharmacologic methods.

The Role of the Nurse in the Management of Pain

Nurses play a vital role in the management of pain of their patients and the role is even bigger in the underdeveloped premature neonatal population. Infants cannot voice what they need to be said therefore the nurse must prove to be the advocate and voice of the client. The nurses’ goal of pain management in neonates is to minimize the experience of pain and maximize the neonate’s capacity to cope with and recover from the many painful procedures in the NICU (Nicolet et al., 2010). The nurse must maintain a balance between pain relief and adverse effects of analgesics. This requires that the nurse have knowledge and feel comfortable providing pharmacologic interventions as well as non-pharmacologic interventions (Nicolet et al., 2010). It is the responsibility of the nurse to determine when a procedure is eliciting pain that requires pharmacologic interventions and when a procedure elicits a mild enough form of pain to use non-pharmacologic approaches. Some instances may require the combination of pharmacologic and non-pharmacologic interventions and in other instances the nurse may decide to implement a combination of multiple non-pharmacologic interventions to more effectively protect the infant from the adverse effects of pain.

The Role of the Parent in the Management of Pain

When a neonate is born prematurely and admitted to the neonatal intensive care unit
(NICU) it can be devastating to the family. The NICU environment can severely limit the ability of the parents’ to bond with the child in the critical first days of life. Most parents will experience feelings of guilt and helplessness when their newborn must undergo so many painful procedures in the NICU. Non-pharmacologic interventions have a secondary benefit to pain management; these interventions provide an opportunity for the family to be involved in the pain management of the child. The family can be taught the techniques in order to properly provide gentle human touch, facilitated tucking, and kangaroo care and therefore a bonding experience can be facilitated through simple pain management strategies. It is suggested that interventions such as kangaroo care are significantly more effective when the mother or guardian is the one providing the interventions therefore benefiting not only the mother but the neonate as well and promotes the health of the family. In a study that allowed one parent to be involved with the pain management of the neonate during endotracheal and pharyngeal suctioning, nineteen out of twenty parents preferred facilitated tucking during suctioning compared to routine care (Axelin et al., 2005).

The Importance of Personalizing Nursing Care in the Neonatal Intensive Care Unit (NICU)

The preterm neonate can suffer from various medical conditions that range greatly in severity; no two cases are identical requiring personalization of care. The personalization of nursing care in the neonatal intensive care unit is vital in order to provide the best health outcomes to each individual infant. To accomplish this, the nurse must provide a thorough assessment of each patient in the NICU and use discretion in deciding the best pain management approaches for that specific individual. This requires knowledge of the developmental stages of the premature infant based on gestational age and how this can affect the infant’s response to
pain. No two infants are the same; the nurse must assess how well each patient tolerates each nursing procedure and decide what methods can be used to provide the most comfort to the infant while causing the least harm. With the amount of procedures each neonate in the NICU undergoes, the nurse should be aware of the current research regarding the effectiveness of pain management and be prepared to personalize the care for that patient.
LIMITATIONS

While there is much research on pain management in the neonatal intensive care unit, most of the articles that fit the search criteria were unavailable for this review of literature. Search results revealed a large number of articles that explored the efficacy of a specific non-pharmacologic intervention but only one of the studies reviewed compared the use of two interventions to each other. The studies used many different outcome measures making it difficult to compare the results of multiple studies. Inclusion and exclusion criteria are subjective in nature, and thus limit this review of literature.

Many of the studies were limited by location and small sample sizes affecting the validity of the results. The largest sample size of the studies reviewed was 110 subjects from a medical center in Taiwan (Liaw et al., 2012) with the smallest sample size included in synthesis being 11 subjects (Herrington and Chiodo, 2012). The majority of studies were done in small, specifically-targeted populations limiting the generalizability of the findings. Many of the studies used recorded footage to assess the pain response of the infant, which creates a further limitation for comparison due to technology as a confounding factor. Infant behavioral responses could have been influenced by environmental, internal stimuli or disease severity (Liaw et al., 2012). A variety of studies do not use each infant as their own control creating a limitation on the research as neonates respond to painful procedures differently. Further limitations include the use of different healthcare professionals performing the nursing procedures. With multiple techniques comes variability of amounts of pain inflicted on each neonate.

Due to the acuity of the premature population admitted to the NICU, response rates and
retention of participants further limit findings. Retention of subjects was particularly difficult in
the studies that included a parent. One study had a refusal rate of 32 percent with the main reason
for refusal being that the mothers felt too stressed to participate and did not want to see their
baby in pain (Johnston, 2008).
RECOMMENDATIONS

Research

The literature review suggests that non-pharmacologic interventions demonstrate a reduction in the short-term pain response but further research should be conducted to evaluate the long-term pain effects (Lopez, 2014). The research reviewed in this investigation revealed the parent’s perception and the nonverbal response of the neonate but lacked substantial data on the nurse’s perspective of the interventions. Studies are needed to evaluate nurses’ perspectives in order to determine the practicality of the interventions used and how they can be implemented into routine nursing practice.

Due to the variety of outcome measures used, there is a need for more studies directly comparing the efficacy of the interventions to each other. It is established in research that each intervention is effective to a degree but there is a need for further research to determine which intervention is the most effective. Also, since preterm neonates suffer from a plethora of medical issues, further research is needed on the efficacy of these interventions when used on patients with similar medical diagnoses.

Education

Education of nurses is essential for the successful implementation of non-pharmacologic pain management interventions in the NICU. Nurses cannot provide quality care if they are not educated on the proper techniques to do so. Nurses must be taught the various
techniques in order to make an educated and personalized decision on the pain management needed for that patient. If these techniques are not performed properly, such as the use of cold hands or excessive pressure, the interventions could cause pain rather than relieve it. This can be avoided if thorough education is offered. For many of these interventions, a parent can be involved in the pain management process but proper education and instruction of the parent is needed. This falls under the responsibility of the nurse therefore the nurse must be knowledgeable and comfortable with the techniques in order to instruct properly.

**Nursing Practice**

Research findings have many implications for nursing practice. As nurses it is our responsibility to be knowledgeable about evidence-based practices and up to date on the current research in order to provide the highest quality of care possible. Research supports the use of non-pharmacologic interventions in the NICU and suggests that these interventions have the potential to minimize and relieve pain during nursing procedures and improve infant health outcomes. As patient advocates, nurses can develop protocols and integration of these interventions to enhance the comfort of the neonate and prevent adverse health outcomes in relation to untreated pain during procedures as well as the use of opiates.
Conclusion

Non-Pharmacologic pain management interventions have the potential to not only provide optimal comfort in the NICU but also personalize care directed to the neonatal population and therefore potentially reduce poor health outcomes. Studies support the use of these non-pharmacologic interventions and it is the nurse’s responsibility to incorporate these interventions in their care to provide the best quality care available. Multiple studies show the efficacy of each non-pharmacologic intervention but more research is needed comparing the interventions to each other as well as the comparison of pharmacologic interventions with non-pharmacologic interventions. The limited studies synthesized in this literature review support the use of combining interventions for optimal pain relief outcome. Further research regarding the efficacy of these interventions in direct relation to each other will facilitate implementation of the most effective intervention in clinical practice.
APPENDIX: Table of evidence
<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Study Design and Purpose</th>
<th>Sample Size</th>
<th>Intervention Protocol</th>
<th>Screening Measures</th>
<th>Outcome Measures</th>
<th>Key Findings and Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Axelin et al. (2005)</td>
<td>Finland</td>
<td>Randomized Crossover Trial</td>
<td>N=20</td>
<td>Baseline video was recorded 2 minutes before the actual suctioning procedure. After 2 minutes a nurse will put saline in both nostrils and suction the mouth, throat, and endotracheal tube of the intubated patients. The video continued recording until the infant was calmed down. Each preterm infant underwent endotracheal/pharyngeal suctioning for clinical purposes using either the facilitated tucking by parents’ or control care within a 2-day period.</td>
<td>The infants were less than or equal to 37 weeks gestation age at birth with no major congenital anomalies and a need for endotracheal/pharyngeal suctioning. No analgesics were received for 4 hours before the procedure and one parent of each infant participated in the study.</td>
<td>The primary outcome measure is the Neonatal Infant Pain Scale (NIPS) score. The highest NIP score was used to represent the maximum pain during the procedure. Two independent scorers rated NIPS scores from videotapes in 1-minute sections. Heart rate and oxygen saturation were recorded. Parents also completed a questionnaire about</td>
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Cignacco et al. (2012) conducted a Randomized controlled trial in Switzerland to test the comparative effectiveness of a non-pharmacologic pain-relieving intervention and a pharmacologic intervention administered alone or in combination across time for NICU patients. The study included $n=71$ infants with gestational age between 24 0/7 and 32 0/7 weeks with an anticipated clinical need of at least 5 routine capillary blood samples within 2 weeks after birth. Infants excluded if they had severe intraventricular hemorrhage, life-threatening malformations/disorders affecting cardiovascular or brain. Sucrose administered orally 2 minutes before the heel stick. FT was started at the beginning of the baseline phase and continued through all phases.

Nicu's patient's gestational age between 24 0/7 and 32 0/7 weeks with an anticipated clinical need of at least 5 routine capillary blood samples within 2 weeks after birth. Bernese Pain Scale for Neonates was used to measure outcomes. Three BPSN scores were calculated (1) the total, (2) behavioral and, (3) physiologic. Scores include measurement of heart rate, respiratory rate, oxygen saturation, grimace, body movements, crying, skin color, sleeping.

During heel stick phase, the FT group had higher B-BPSN and P-BPSN scores than the sucrose and combination groups. During recovery the combination group had significantly lower B-BPSN scores than both other groups. Findings show that either oral sucrose alone or oral sucrose in combination with FT remains effective in reducing heel stick-related pain over time in preterm infants during the critical phase of the first 14 days of NICU stay. Although still effective, FT alone appears to be less effective than in combination with sucrose. Results indicate that the combination of sucrose and FT may have additive pain-relieving effects during the recovery phase. No sign
Cong et al. (2012) Connecticut

<table>
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<tr>
<th>Study</th>
<th>Design</th>
<th>Participants</th>
<th>Intervention</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Randomized crossover trial</td>
<td>Mother-infant dyads were randomly assigned to 1 of the 3 sequences of interventions. Sequence A was kangaroo care for 30 minutes before and throughout heel stick (KC30), kangaroo care for 15 minutes before and throughout heel stick (KC15), and then standard incubator care. Sequence B was KC15, incubator care, and then KC30. Sequence C was incubator care, and then KC30.</td>
<td>The participants were patients in a level III NICU who were between 28-31 weeks gestational age and less than 14 days old. These infants were cared for in an incubator and had mothers older than 18 years of age. Infants were excluded if they had congenital anomalies, grade III or IV intraventricular hemorrhage, surgical procedure, pH&lt;7.0 or any problem that could impair pain expression.</td>
<td>The measure of kangaroo care’s pain reduction ability can be established by determining the kangaroo care’s effects on autonomic responses through heart rate variability (HRV). The HRV is used to determine the frequency content of the fluctuating heart rate.</td>
<td>Heart rate changes from baseline to heel stick were significantly less in 30 minute kangaroo care and 15 minute kangaroo care than incubator care and more infants had heart rate decreases in incubator care than in the two kangaroo care conditions. In incubator care, low frequency power and high frequency power significantly increased from baseline to heel stick and dropped from heel stick to recovery; in the two kangaroo care conditions, no changes across study phases were found. During heel stick low frequency and high frequency power significantly decreased resulting in higher low frequency power decrease than high frequency power decrease in both kangaroo care; heart rate variability (HRV) was significantly higher in the two kangaroo care groups compared to incubator care.</td>
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(15 minutes) before and throughout heel stick compared with incubator care.

incubator care, KC30, and then KC15. IV intraventricular hemorrhage, signs of heel tissue breakdown or inflammation, or required oxygen and respiratory support. Low frequency (LF) primarily represents sympathetic activity with some parasympathetic activity, while the high frequency (HF) is related to respiratory sinus arrhythmia and reflects parasympathetic activity. The LF/HF ratio reflects the balance of sympathetic and parasympathetic activities and is a recommended indicator of painful events shortly after birth. Frequency were significantly higher in incubator care than in kangaroo care for 30 minutes. Longer kangaroo care significantly affected infants; sympathetic and parasympathetic responses during heel stick compared with incubator care. Therefore kangaroo care is a safe and effective intervention in the NICU that has a significant effect on reducing autonomic pain responses.
Elserafy et al. (2009)
saudi arabia
randomized controlled trial
To assess the analgesic effect of pharmacologic (sucrose, water) and a non-pharmacologic measure (pacifier) in preterm infants

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Participants</th>
<th>Procedures</th>
<th>Outcomes</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elserafy et al. (2009)</td>
<td>Randomized controlled trial</td>
<td>n=36 preterm infants</td>
<td>36 preterm infants were randomly allocated to six different regimens during a stay in intensive care of up to 15 days. These six different regimens were: sterile water with pacifier, sterile water without pacifier, sucrose with pacifier, sucrose without pacifier, pacifier alone, and the control group that received</td>
<td>Infant behavioral state was measured using the Anderson Behavioral State Scoring System (ABSS). This system has 12 categories from very quiet sleep to hard crying.</td>
<td>The use of 24% sucrose solution combined with pacifier resulted in the lowest pain score of all groups for all measurements from zero to ten minutes. Although non-nutritive sucking (pacifier) did prove effective without sucrose it was not as effective as it was in combination with sucrose. Therefore, there is a synergistic effect between both interventions.</td>
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<td></td>
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<td>Pain scores were measured with the Premature Infant Pain Profile (PIPP).</td>
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and to find whether there is any synergism between these intervention in relieving pain during the painful procedures.

| Gao et al. (2015) | Randomized controlled trial | n=80 | The procedure of each heel-stick included three phases; baseline, blood collection, and recovery. Both the control group and the treatment group received the first heel stick with no intervention. During the next three heel sticks, the treatment group received kangaroo care 30 minutes prior to the procedure and | Preterm infants were recruited from the level III NICU and had a gestational age of less than 37 weeks. Inclusion criteria included that they are cared for in an incubator, were anticipated to have at least four routine Crying, grimacing, and heart rate in response to pain were evaluated at each phase by three trained independent observers who were blinded to the purpose of the study. | Between-group comparison revealed that preterm infants’ heart rate was significantly lower, and the duration of crying and facial grimacing were both significantly shorter in the kangaroo mother care group than the incubator group. No significant within-group difference was found in heart rate between the baseline phase and recovery phase through repeated heel sticks for Kangaroo Mother care group. In contrast, |
Premature infants ranging from 27-34 weeks gestational age were recruited and randomized. The control phase the infants were prone in the incubator as per normal protocol. Capillary blood draws within 2 weeks, not scheduled to receive paralytic or analgesic medications 48 hours prior to study session. Infants were excluded if they had congenital anomalies, grade III or IV intraventricular hemorrhage, signs of heel tissue breakdown or inflammation, or required oxygen and respiratory support.

The control group remained prone in the incubator as per normal protocol. The group experienced significant within group differences in heart rate between baseline and recovery through repeated heel sticks. The effect of kangaroo mother care analgesia remains stable in preterm infants over repeated painful procedures and given the many invasive procedures that are a part of clinical care in preterm infants and that most mothers prefer to provide comfort to their infants, this could be a safe analgesic alternative to pain management.

<p>| Herrington and Chiodo (2012) | Experimental pilot feasibility study using repeated-measures | n=11 | In the intervention phase, all infants received gentle human touch (GHT) during the heel stick procedure while in the control phase the infants were | Premature infants ranging from 27-34 weeks gestational age were recruited and randomized. The Heart rate, respiratory rate, oxygen saturation and cry were measured continuously beginning at baseline and | Infants who did not receive GHT had decreased respiration, increased heart rate, and increased cry time during the heel stick. In contrast, infants who received GHT did not have decreased... |</p>
<table>
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<tr>
<th>crossover study design</th>
<th>placed side-lying and supported with blanket rolls to create a “nest confinement” which is the standard of care in the NICU. To rid the experiment of the bias that the presence of another person may be the cause of comfort to the infant, hands were placed inside the incubator during the non-GHT heel sticks but not in contact with the infant in any way.</th>
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<tr>
<td>To evaluate the efficacy of the non-pharmacologic pain management technique of gentle human touch (GHT) in reducing pain response to heel stick in premature infants in the neonatal intensive care unit (NICU)</td>
<td>infants were hemodynamically stable, not requiring blood pressure support medications, with mild to moderate respiratory distress, who did not require increasing levels of support during the period of data collection.</td>
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<tr>
<td>continuing through heel warming, heel stick, and recovery phases.</td>
<td>respiration, elevated heart rate, or increased cry time during the heel stick. No significant differences were noted in oxygen saturation in either group. It is concluded that gentle human touch is an easy and simple non-pharmacologic therapy that can be used by nurses and families to reduce pain of heel stick procedures in premature infants in the NICU.</td>
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<tr>
<td>Study</td>
<td>Design</td>
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<tr>
<td>Johnston et al. (2003) Canada</td>
<td>Single blind crossover design</td>
</tr>
<tr>
<td>Johnston et al. (2008) Canada</td>
<td>Single blind randomized crossover trial</td>
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Mother care is efficacious in diminishing pain response to heel lance in very preterm neonates. Position and swaddled in a blanket in the incubator during the heel lance procedure. The infants were within 10 days of birth and received an Apgar score of at least 6 at 5 minutes. The infant could not have any major congenital anomalies, could breathe unassisted, and had no suffered grade III or IV intraventricular hemorrhage. The secondary outcome was the time it took for the infant to recover, when the heart rate returns to baseline. The infants had a gestational age between 30 to 34 weeks at birth, were on room air with a nasogastric feeding tube, and did not have any major congenital anomalies, could breathe unassisted, and had no suffered grade III or IV intraventricular hemorrhage. During 10 days the behavioral responses were videotaped and the physiological responses such as heart rate and oxygen were highly significantly lower across all points in time reaching a two-fold difference by 120 seconds post-lance and heart rate was significantly lower across the first 90 seconds in the kangaroo mother care condition. Very preterm neonates appear to have endogenous mechanisms elicited through skin-to-skin maternal contact that decrease pain response but not as powerfully as in slightly older preterm neonates. The shorter recovery time in kangaroo mother care is clinically important in helping maintain homeostasis.

**Kamhawy et al. (2014)**

Short-term longitudinal experimental design

| n=47 | The infants were divided into treatment group and control group. The treatment group received non-nutritive sucking with a preemie Gerber pacifier during nasogastric feeding for the intervention infants. | The infants had a gestational age between 30 to 34 weeks at birth, were on room air with a nasogastric feeding tube, and did not have any major congenital anomalies, could breathe unassisted, and had no suffered grade III or IV intraventricular hemorrhage. | During 10 days the behavioral responses were videotaped and the physiological responses such as heart rate and oxygen were highly significantly lower across all points in time reaching a two-fold difference by 120 seconds post-lance and heart rate was significantly lower across the first 90 seconds in the kangaroo mother care condition. Very preterm neonates appear to have endogenous mechanisms elicited through skin-to-skin maternal contact that decrease pain response but not as powerfully as in slightly older preterm neonates. The shorter recovery time in kangaroo mother care is clinically important in helping maintain homeostasis. | Non-nutritive sucking was found to improve physiological and behavioral responses of preterm infants. Significantly higher oxygen saturation occurred during and after nasogastric tube feeding for the intervention infants as |
To assess how non-nutritive sucking (NNS) using a pacifier affected physiological and behavioral outcomes of preterm infants. Tube feeding while infants in the control group never received non-nutritive sucking. Infants were required to receive analgesics or anesthesia. Infants were excluded if they had congenital anomalies that might interfere with sucking, developed necrotizing enterocolitis or sepsis, or required surgery. Saturation were monitored. Physiological and behavioral variables for intervention and control infants were compared using repeated measure ANOVA. Compared to the control group, no significant group differences occurred in heart rate. The NNS group showed an accelerated transition to nipple feeding and had better weight gain and earlier discharge.

| Liaw et al. (2012) | Prospective Randomized controlled trial Taiwan | n= 110 | The samples of infants were randomly assigned to five combinations of non-pharmacological treatment groups. The five being: nonnutritive sucking-oral sucrose-facilitated tucking, nonnutritive sucking-oral sucrose, oral sucrose-facilitated tucking, nonnutritive sucking-oral sucrose, oral sucrose-facilitated tucking, nonnutritive sucking-oral sucrose. | Infants were level III NICU patients at a medical center in Taiwan. Gestational age is between 26-37 weeks with a postmenstrual age of 26.4-38 weeks. The infants are post birth age 2-28 days and the disease condition of the infant is acceptable. | Infant states were measured by a state-coding scheme. They included quiet sleep, active sleep, transition, quiet awake, active awake, and fussing or crying. Infant behavioral states were measured based on the guidelines for coding. | The occurrence rate of quiet sleep was significantly greater in infants receiving NNS-sucrose-FT and NNS-sucrose across all assessment phases than those receiving routine care. The infants fussy or crying state occurred significantly less often in infants receiving sucrose-FT, NNS-Sucrose, and NNS-Sucrose-FT the percentages being 77.3%, 72.1%, and 51.5% respectively. |
facilitated tucking with routine care on infants’ sleep-wake states before, during, and after heel-stick procedures.

| Liaw et al. (2011) Taiwan | Prospective, randomized controlled crossover trial | n=34 | Infants were randomly assigned to a sequence of three treatments, two of which are pain-relief interventions and one control condition. The first sequence is routine care, non-nutritive sucking, and then facilitated tucking. The second sequence being non-pharmacological interventions facilitated tucking and routine care. | Infants were 29-36 weeks gestational age and their post birth age was between 2 and 28 days old. The infants were in a stable condition. Exclusion criteria include congenital anomalies. | Pain was measured by the Premature Infant Pain Profile (PIPP). Infant behavior was studied using a behavioral coding scheme and physiological signals by electrocardiogram | Infants receiving non-nutritive sucking and facilitated tucking had significantly lower mean pain scores during heel-stick procedures than those receiving routine care. Based on odds ratios, the infants’ pain after receiving these non-pharmacological interventions decreased from 66% to 61%. Infants receiving facilitated tucking also had lower... |
Lopez et al. (2014) Malaysia Quasi-experimental study To test the effectiveness of facilitated tucking

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Participants</th>
<th>Methods</th>
<th>Outcomes</th>
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</thead>
<tbody>
<tr>
<td>Lopez et al. (2014)</td>
<td>Quasi-experimental study</td>
<td>n=42 Subjects meeting the study criteria were divided into a treatment group and control group. The treatment group received a venipuncture while being held in a tucked position while the control group</td>
<td>Preterm infants between 23-36 weeks of gestation requiring venipuncture were eligible for participation. The exclusion criteria was a mean of 9.68 in the treatment group and 10.47 in the control group.</td>
<td>The severity of pain was measured using the Premature Infant Pain Profile Score and primary outcome measure was the reduction in these frequency ratios for stress-related behaviors, abnormal heart rates, and decreased oxygen saturation than infants receiving routine care. Both non-nutritive sucking and facilitated tucking effectively reduced pain scores but non-nutritive sucking reduced PIPP pain scores more effectively than facilitated tucking. However, facilitated tucking showed broader effects not only on relieving pain, but also on enhancing infants’ physiological and behavioral stability during heel-stick procedures.</td>
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<td>tucking among babies and enlighten health professionals on a method of simple and effective pain relief.</td>
<td>received the venipuncture under the normal NICU routine.</td>
<td>include infants who were clinically unstable or who had labile physiological parameters. No infants were accepted if they received any form of sedation or analgesia.</td>
<td>scores with facilitated tucking.</td>
<td>outcome of facilitated tucking in the treatment group, seen from the PIPP score, was significantly lower than that of the control group during venipuncture.</td>
</tr>
</tbody>
</table>
LIST OF REFERENCES


