Research Article

Journal of Clinical Pediatrics (ISSN 2995-6560)

Clinical Limitations of Non-pharmacological Comfort Tools for Needle Sticks in Neonatal Intensive Care Units (NICU)

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Received Date : April 28, 2024
Accepted Date : April 29, 2024
Published Date : May 29, 2024

ABSTRACT

During a neonate's stay in the neonatal intensive care unit (NICU), they will undergo many painful, but necessary, procedures to deliver treatment and to monitor physiological status. Many of these methods will involve skin breaks by a needle. While pharmacological analgesics are available for larger procedures like surgeries and intubation, the volume of painful procedures neonates must endure makes the use of pharmacological analgesics impractical for every painful procedure. Due to their immature nervous system, preterm neonates have limited ability to modulate pain. Recent studies have demonstrated that repeated pain endured during the neonatal period is associated with long-term neurological deficits. Over the past decades, studies have begun to quantify the effectiveness of non-pharmacological comfort tools (nonnutritive sucking, swaddling, oral sucrose, ShotBlocker, etc.) in reducing neonatal pain during needles sticks. However, while these tools may be present for providers in the NICU, there are various clinical components that may limit a neonate's ability to receive these important non-pharmacological tools during a needle stick. This review analyzes the conditions where a neonate would not be able to receive a non-pharmacological comfort tool and should serve as a resource for NICUs attempting to implement guidelines for non-pharmacological comfort tool use. Future research should investigate non-pharmacological tool compatibility with various neonatal conditions for the equitable use of pain management strategies in NICU settings.

Impact :

- Increase in commonly used diagnostic tools and treatment types in neonatology over last century have led to increased volume of routine painful procedures involving skin breaks for neonates.
- High incidence of neonatal pain is associated with poor long-term neurological deficits, necessitating the use of non-pharmacological comfort tools during needle stick procedures.
- While growing evidence shows non-pharmacological comfort tool efficacy in reducing pain, no review has been done on the various clinical conditions that hinder a neonate's ability to receive non-pharmacological comfort tools during painful procedures.

Keywords : Neonatal pain, NICU painful procedures, needle sticks, non-pharmacological analgesics, pain management, newborns, comfort measures.

INTRODUCTION

Needle Stick Uses and Prevalence in NICUs

The advent of new diagnostic tools in medicine during the cell biology boom of the 20th century brought to many clinics increased utility in skin breaking procedures to collect and analyze blood. In the 1960s an American physician named Robert Guthrie developed a screening test for PKU at birth for a neonate - a simple heel prick that gave up a drop of blood.1 Over time, needle sticks became an integral part of neonatal medicine and were used to diagnose a variety of conditions through the detection of biomarkers, such as glucose, carbon dioxide, Interleukin-6, and angiopoietins.

Over the 20th century, needle sticks started to be used for other purposes in neonatology, such as the delivery of the hepatitis B and respiratory syncytial virus vaccines and the Vitamin K intramuscular injection. Today, a neonate admitted to the NICU can expect approximately 7-17 painful procedures a day, many of which involve a skin break, over an average of 8 days of stay.[2]

These diagnostic tests and injections have partly contributed

to a nearly 90% reduction in mortality rate for infants in the United States over the last century.[3]

History of Neonatal Pain Perceptions

The understanding of neonatal pain has significantly progressed since the first papers were published on it nearly 175 years ago. Early research into the dynamics of early life and pain considered neonates to be less sensitive to painful stimuli directly after birth and thus, it was encouraged that surgery, if needed, should be done soon after birth without analgesics.[4] Even small needle sticks were described as unbothering to newborns, leading to misconceptions on their ability to feel pain for decades.[5] These notions of a neonate's lack of pain sensitivity persisted until the mid-to-late 20th century when studies started acknowledging that neonates do, in fact, perceive pain at a young age during procedures as minute as a heel stick.[6,7,8] Since the late 20th century, pain research in neonates has begun to discover that not only do neonates feel pain, but that they are more sensitive to it than older aged children and adults which can lead to long-term neurological deficits.[9]

Neonatal Age and Pain Response

During the viable gestational period of 24 weeks to 43 weeks, the neonatal nervous system is immature which significantly affects neonatal interactions with external stimuli. In the peripheral nerves, neonates have a lower threshold for pain that worsens with sequelae.[10] They also have larger receptive fields in their peripheral nerves than older children and adults creating an amplified sensation on the skin from a stimuli.[11] In addition to the area of pain being larger in a neonate compared to an adult for a given stimuli, the pathways involved in modulation are also different. After peripheral nerves encounter a stimuli, an ascending signal to the brain receives and perceives the pain and a descending pathway modulates the pain to allow a response to the stimuli.[12] But in neonates, even months after birth, their ascending pathways for pain are far more developed than their descending pathways allowing them to perceive but not modulate pain effectively.[13]

This lack of neurological development not only exposes neonates to increased pain acutely during a painful procedure but can affect their long-term neurological function. Repeated pain during the immediate postnatal period has been shown to decrease cortical thickness and connectivity in language and cognitive domains.[14,15] Decreases in brain volume are also associated with low IQ in adulthood.[16]

Recent studies have displayed the utility in using non-pharmacological comfort tools during needle stick procedures in neonates; these tools can be split into three groups: oral measures, comfort positions, and physical distractions.[17] While there are no national or international guidelines currently in place for the use of non-pharmacological comfort tools during painful procedures in NICUs, the mounting evidence of their utility and the consequences of not addressing neonatal pain will likely lead to their official implementation into routine clinical care. This review aims to identify the complex clinical conditions that limit certain populations of neonates from receiving these important comfort tools during painful procedures and to be a resource for institutions implementing non-pharmacological comfort tools in their NICUs.

NON-NUTRITIVE SUCKING (NNS)

NNS involves the offering of a pacifier or gloved finger to the neonate to mimic the act of breastfeeding without the presence of nutrients. Often offered in the conjunction with oral sucrose, NNS is a well-studied non-pharmacological comfort tool in neonates and has been shown in randomized controlled trials to be effective in both term and preterm infants.[18,19,20] Despite its efficacy, problems arise in its ubiquitous use as an comfort tool for all neonates undergoing needle sticks as NNS is a learned skill for neonates and there are various conditions in which a neonate may not be able to accept a pacifier or gloved finger during a painful procedure.[20]

Oral and Facial Malformations

Oral and facial malformations are relatively common defects (~1:700 live births) that neonatologist encounter.[21] Some examples of these conditions are cleft palate, cleft lip, and micrognathia.[22,23] While surgical options are available to correct these conditions, surgery usually does not occur until the baby is almost one year of age.[22,24] In the case of a cleft lip, the upper lip and/or the soft palate are separated due to a failure of fusion of the frontonasal and maxillary processes during pregnancy.24 A gap across the upper lip severely limits the ability to latch during oral feeding making the act of NNS a difficult task.[25]

Facial palsy, either congenital or acquired, is another relatively common facial malformation in neonates (~1:555) where facial nerves lack total neurological excitability leading to decreased facial motor skills and facial droop.[26] Lack of control of facial muscles makes coordination of the mouth difficult for a sustained suck reflex, which is central to the skill of NNS.[27] Neonates with this condition will find it difficult to accept and maintain NNS for the duration of a painful procedure; this was demonstrated in studies which assessed the ability of an infant to perform NNS before, during, and two minutes after the procedure. [19]

While muscular, nervous, and soft tissue conditions present challenges for sustaining NNS for extended periods of time, bony structural malformations, such as micrognathia, might create difficulties for the neonate to accept NNS on the basis

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of the size and shape of the pacifier.[28] The mandible size of an infant with micrognathia ranges based on severity of the condition but can cause feeding difficulties due to limited jaw strength and abnormal oral positioning.[29] The size of a pacifier may also vary due to the heterogeneity of mouth sizes in neonates with normal oral cavity development. The current use and advertisement of pacifiers is categorized by the size of pacifiers for various age groups.[30] However, a study out of Switzerland in 2022 has refuted the current pacifier design as not anatomically fitting to neonates.[31] Oral and facial heterogeneity and malformations can limit the ability of a neonate to sustain NNS.

Neurological Conditions

Approximately 18% of neonates admitted to the NICU have congenital or acquired neurological conditions, and this incidence is higher in preterm infants.[32,33] These conditions range in their acuteness, mortality, and symptoms. Even mild neurological conditions, such as hypoxic ischemic encephalopathy, hypotonia, and poor neurological development, may present poor suck reflex.[34,35] Some of these conditions may not have clear symptoms and may be undiagnosed during the first days of life, and providers may not consider an underlying neurological condition as a cause for poor NNS skills.

Additionally, neonates born to mothers who used prescribed or illicit opioids during pregnancy showed limited ability to perform a suck and swallow reflex.[36] For these patient populations, non-pharmacological comfort tools in the first day of life are an imperative tool during painful procedures due to their withdrawal symptoms. However, due to their limited ability to suck and swallow, the use of NNS and oral sucrose may be limited in these infants.

Prematurity

It should be noted that prematurity alone has been associated with a poor suck reflex.[37] Whether neurological coordination, muscle strength, or an underlining medical condition was present or not, the suck reflex as a skill improved as infants grew older. With medical advancements, the earliest birth gestational age that an infant can survive has decreased. [38] As noted in the introduction, it is the premature infant population in particular that is the most predisposed to hypersensitivity to pain, however, this group faces many restrictions to the use of non-pharmacological comfort tools.

Intubation

Laryngoscope use and endotracheal intubation for neonates presenting with respiratory illness in NICUs is a fairly common procedure occurring for ~25% of NICU admissions.[39] During the time an infant is intubated, they may require needle sticks for blood gas monitoring, routine lab draws, etc.[40,41] Intubation covers the oral cavity of the neonate eliminating the option of a pacifier or gloved finger as a comfort tool during needle sticks.

Cardiorespiratory issues

The leading cause of NICU admissions, besides general prematurity, is respiratory distress syndrome (RDS) with a total of 10% of all babies born in the United States acquiring this condition.42 While the medical prognosis of this condition is good, neonates with RDS can be expected to be treated for a period of days to months with surfactant, supplemental oxygen, inhaled corticosteroids, etc.[43] Infants with more severe RDS have more difficulty with sustaining a suck and swallow reflex.[44] Oral feeding development and coordination is limited by respiratory distress, and this limits the use of oral sucrose as a comfort tool in this population.[45]

Additionally, congenital heart diseases (CHDs), especially cyanotic CHDs, are associated with swallowing and feeding-related difficulties. Infants with CHDs, both pre- and post-operatively, may simply be breathing too fast for it to be safe to use a pacifier or gloved finger; they may also experience fatigue while sucking. Additionally, infants with CHDs may have a higher incidence of end organ failure, resulting in neurological injury, which as described above, may limit the ability to perform the NNS skill.[46]

ORAL SUCROSE

24% oral sucrose has, in recent decades, shown promise as a non-pharmacological comfort tool in neonates.[47] As mentioned previously, oral sucrose is commonly used in conjunction with a pacifier.[48] While the mechanism of sucrose as a comfort tool is unclear, oral sucrose is a common comfort tool used in the NICU for neonates.[49] However, there are limitations to the use of oral sucrose in certain neonatal populations.

Necrotizing Enterocolitis (NEC) Risk

NEC is the leading cause of mortality in neonates, affecting approximately 8% of United States NICU admissions per year and is highly associated with prematurity.[50] Some studies have found an association between hyperosmolar oral sucrose administration and NEC in very low birth weight infants, however, other studies have found no association between NEC and oral sucrose administration.[51,52] Because the molecular etiology of NEC is poorly understood a causal link between NEC and sucrose has not been properly established, but neonatal pig model studies have found decreased carbohydrate absorption in the GI tracts of those with NEC potentially linking the two pathologically.[53] The connection between NEC, oral sucrose, and very low birth weight infants has led for calls to investigate the correlation further through

Journal of Clinical Pediatrics (ISSN 2995-6560)

research-based evidence and led institutions to recommend caregivers not provide oral sucrose for neonates at high risk for NEC.[47,54]

Hypoglycemia

Accounting for approximately 4.5% of NICU admissions in the United States, hypoglycemia in neonates is a serious, well-defined, generally acute, condition with positive outcomes.[55] Although there are multiple types of neonatal hypoglycemia (perinatal stress-induced, genetic, translational), it commonly occurs due to high levels of insulin in a neonate born to a diabetic mother.[56] Even though oral sucrose is often administered in amounts as low as 0.5 mL, studies have shown that oral sucrose can transiently increase the glucose levels of neonates born to diabetic mothers.[47,57] Current guidelines describe glucose checks, for which heel sticks are the gold standard measurement, to be done every 3 hours after birth making them a high yield patient population for painful procedures.[58] Using sucrose which is known to transiency increase glucose levels in body for a baby getting frequent needle sticks for the monitoring of glucose levels is counterintuitive and can jeopardize making accurate clinical decisions.

Cardiorespiratory issues

As described earlier, infants with cardiorespiratory issues have an underdeveloped suck and swallow reflex. Infants with CHD are more prone to developing NEC, which as described above, may be associated with the administration of oral sucrose in at-risk infants.[46] Injuries during surgery for CHDs may also result in laryngopharyngeal dysfunction, eliminating the safe use of oral sucrose in this population. This limits the use of oral sucrose as a non-pharmacological comfort tool in this population.

SHOTBLOCKER

ShotBlocker is a C-shaped plastic device that has been shown to reduce pain during intramuscular injections in children and adults.[59,60] ShotBlocker is fitted with small bumps on the bottom side of the device that are pressed onto the skin prior to injection. The device works on the "gate control theory of pain" by stimulating cutaneous nerves around the site of injection before the shot is given which is postulated to inhibit a larger pain response once the injection is delivered.[61] Studies continue to demonstrate its efficacy, and it has begun to emerge as a new tool for non-pharmacological analgesics in NICU settings.

Thigh Circumference of Low Birth Weight Infants

Currently, ShotBlocker is available in only one size (7cm x 5cm x 1cm) and has only been studied in ages as young as term infants.[62] This size, however, may not be able to conform properly to the thighs of low-birth-weight infants in NICU settings, disqualifying ShotBlocker as a readily available tool for younger gestational age babies at the time of injections. Studies of term infants' thigh circumferences reported ranges from 11cm-18cm in circumference.[63] While there is limited literature published on the thigh size of low birth weight infants, their weight can be up to eight times less than the averages for term babies making their tissue volume and thigh circumference likely considerably smaller than the 11cm-18cm range of healthy term infants.[64,65] This decreased thigh circumference is below the width of the ShotBlocker device.. Because the width exceeds the circumference of the thigh, the device will not be able to be properly placed on the leg. Further research needs to be conducted on the efficacy of ShotBlocker in varying gestational age and weight groups for neonates before this tool can be seen as an effective non-pharmacologic comfort tool for NICU admits.

PARENTAL CARE AND PHYSICAL TOUCH DURING NEEDLE STICKS

Parental presence plays an important role in early bonding with a newborn admitted to the NICU. Holding of the newborn, breastfeeding, and skin-to-skin contact (SSC) are just some of the important bonding measures that have been associated with better long term neurodevelopmental and relationship outcomes.[66,67] SSC as a comfort measure has been shown to increase oral oxytocin in neonates and reduce oral cortisol levels.[68] For painful procedures, SSC and breastfeeding have shown promise in reducing pain, but parental presence in NICU during needle sticks are confounded by many factors that limit a parent's ability to be present during these times.[69,70] Breastfeeding acts on the same analgesic mechanism discussed in NNS and oral sucrose and the large limitations of NNS and oral sucrose for an neonate also apply to breastfeeding which significant limits its functionality. The goal of this section is to address the medical and social barriers of SSC and breastfeeding for neonates during needle stick procedures.

Parental Presence Limitations

The use of SSC and breastfeeding as analgesics for needle stick procedures necessitates the parents of the neonate be present at the time of the needle stick. Many factors can affect the ability of a parent to visit their baby in the NICU: occupation type, transportation, other children at home, and parental-baby legal status are just some of the variables that could limit parental limitation at the bedside. On average, studies showed that parents were present in the NICU for an average of 4.00 days per week and 21.33 hours per week and averaged holding their baby for 2.29 days out of

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the week although studies on this topic range greatly with some reporting 14 hours of visitation per week.66,71 The low average parental visitation may not cover the times that a neonate experiences needle sticks and therefore, may limit the ability of a neonate to receive SSC or breastfeeding.[2]

Holding limitations

Both breastfeeding and SSC require the neonate to be held by parents which in most cases is feasible and encouraged in the NICU. Some neonates, however, are not suited to being held at a young age and this sub-section aims to address those instances where, even though a parent is present, holding the neonate for breastfeeding and SSC as an analgesic may not be feasible. For example, neonates in incubators are not excluded from participating in SSC with parent present, and studies have shown that SSC temperature contact from parents compensate for lower ambient humidity in the room compared to incubator.[72] However, conditions like ventilator status and overall variability in vitals are instances where holding a baby may be discouraged during NICU visitation.[71]

SWADDLE

Swaddling as a practice for comforting neonates has been used for centuries. Many variations to swaddling have limited the generalizability of its analgesic effects, but the wrapping of an infant's extremities in cloth has been shown to reduce pain and discomfort during painful procedures.[73,74] Potential risks of swaddling are increased incidence of sudden infant death syndrome (SIDS) risk if the infant is laid prone while swaddling and higher incidence of skeletal dysplasia.[75,76] Despite these risks, there are several medical conditions that neonates admitted to the NICU face which limit the use of swaddling as a non-pharmacological comfort tool for painful procedures.

Therapeutic Hypothermia (TH)

TH is a common practice for babies who develop hypoxic ischemic encephalopathy (HIE) after birth, a condition where oxygen supply is cut off from the fetus for a period of time. Once oxygen flow is restored, tissue damage occurs through reperfusion injury, which targets the mitochondria in cells, a site for important metabolic processes, and this leads to cell apoptosis and necrosis.[77] In developed countries, the incidence of HIE is approximately 1:500 babies and is associated with a 60% mortality rate at two years of age.78 Current treatments are limited for this condition but TH, commonly done by a cooling pad to reduce reperfusion injury through the lowering of metabolic rates, has been shown to significantly decrease death and the neurological complications of long-term survivors.[79] Literature has shown the importance in maintaining a rectal temperature of 33.0°C-34.0°C for a 72-hour period during TH, which could become difficult if the infant is swaddled.[80]

While material for swaddling and duration of time can change heat increases for the neonate, cloth swaddling is the most common. Cloth swaddling has been previously shown to increase rectal temperature by an average 0.4°C or 40% of the variation allowed for effective TH.[81] Many studies that show swaddling for analgesic purposes describe infants swaddled for at least 8 minutes.[73] These studies have only described temperature in resting infants getting swaddled, not those undergoing painful procedures. Additionally, some NICUs that do not have cooling pad equipment are advised to use passive cooling which involves no blankets covering the infant as part of the TH. More research needs to be conducted on relative temperature swings for neonates getting swaddled during painful procedures to investigate whether infants undergoing TH can be swaddled during painful procedures for pain relief.

Congenital Anomalies/Open Wounds

Each year in the United States, approximately 1,500 babies are born with spina bifida, a condition that occurs due to the incomplete closure of the spine and spinal cord.[82] Neonates diagnosed with spina bifida often undergo surgery to repair the spine in the first 24 hours of life. Lab draws are common during the pre- and post-operative periods. Guidelines for neonates prior and immediately post-spina bifida correcting surgery require laying the infant prone due to the risk of infection and pressure at the site of the lesion.[83] As discussed earlier, infants who are prone and swaddled are at an increased risk of SIDS, thus, swaddling is not an appropriate comfort tool in the setting of spina bifida and other spinal conditions.

Humidity

Swaddling in heated incubators can also cause an increase in abdominal temperatures ranging from 0.2 degrees Celsius to 0.4°C. [84,85] Research has indicated a need for lower incubator temperatures for swaddled infants, however, many institutional guidelines may not include this. Other comfort measures may be more appropriate in infants with immature thermoregulation.

CONCLUSIONS AND NEXT STEPS

Numerous non-pharmacological comfort tools are becoming readily available to NICU providers with mounting evidence of their efficacy in reducing pain during needle stick procedures. As their use becomes implemented in standard-of-care protocols, it is important for NICUs to acknowledge that many neonates, including early gestational ages who are at the highest risk of long-term damage from pain, may not be able

to receive these comfort tools due to medical conditions.

While there is literature on the efficacy of non-pharmacological comfort tools there currently is no consensus on what amount or duration of their use is needed to achieve pain relief. Does NNS require use from before through two minutes after a needle stick to have a measurable pain relief effect like some studies suggest?[19] If so, that will exclude a larger number of infants from using this tool for pain relief because they are not able to sustain NNS for such a period of time. For other tools like swaddling, if the duration of swaddle needed for pain relief is approaching 5 minutes, how much does that increase body temperature? What is the range of temperature increase across various sizes of infants for a 5-minute swaddle? There is extremely limited evidence on this even though thermoregulation is an aspect of neonatal care. For devices like ShotBlocker and Buzzy, future studies need to investigate device size relative to infant thigh size as potential limitations of their ubiquitous utilization among infants. Additionally, ShotBlocker and Buzzy act upon the gate theory of pain which has been well described for adult and pediatric nervous systems, but what about the developing preterm nervous system which have lower thresholds of pain and larger receptive fields? Is the device as effective in these neurologically immature populations?

Even more established non-pharmacological comfort tools like oral sucrose have unanswered questions on safety and applicability to preterm infants. The limited research on the correlation between oral sucrose and NEC is conflicting, in part due to a poorly defined etiology of the condition. However, there continues to be studies on the beneficial effects of oral sucrose in pain relief on neonates. Studies that investigate oral sucrose for pain relief must also correlate NEC incidence in their study population particularly for the low weight or low gestational ages. Beyond NEC risk, future studies need to address the issue of infants who are not on oral feeds receiving oral sucrose for pain relief as some institutions have strict limitations for receiving oral fluids while on nil per oral orders.[86]

As different hospitals adopt slightly different protocols of the management of their infants in the NICU, these policies may change what infants are eligible to receive the described comfort tools above. When implementing these non-pharmacological comfort tools as standard-of-care, providers must be meticulous as they look through their institutional protocols to identify what infants will not be able to benefit from certain comfort tools to make non-pharmacological pain relief as accessible to all infants as possible.

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