HHS Public Access

Author manuscript

Crit Care Nurs Clin North Am. Author manuscript; available in PMC 2019 December 01.

Published in final edited form as:

Crit Care Nurs Clin North Am. 2018 December ; 30(4): 549–561. doi:10.1016/j.cnc.2018.07.013.

Neonatal Pain: Perceptions and Current Practice

Mallory Perry, BSN, MS, RN, CPN,
School of Nursing, University of Connecticut, Storrs, CT, U.S.A., 231 Glenbrook Road, Storrs, CT 06269-4026

Zewen Tan [Undergraduate Honors Student],
School of Medicine and School of Nursing, University of Connecticut, Storrs, CT, U.S.A., 231 Glenbrook Road, Storrs, CT 06269-4026

Jie Chen, BS, MSN, RN,
School of Nursing, University of Connecticut, Storrs, CT, U.S.A., 231 Glenbrook Road, Storrs, CT 06269-4026

Tessa Weidig [Undergraduate Honors Student],
School of Nursing, University of Connecticut, Storrs, CT, U.S.A., 231 Glenbrook Road, Storrs, CT 06269-4026

Wanli Xu, PhD, MS, RN, and
School of Nursing, University of Connecticut, Storrs, CT, U.S.A., 231 Glenbrook Road, Storrs, CT 06269-4026

Xiaomei S. Cong, PhD, RN*
School of Nursing, University of Connecticut, Storrs, CT, U.S.A., 231 Glenbrook Road, Storrs, CT 06269-4026

SYNOPSIS

Neonates may experience more than 300 painful procedures and surgeries throughout their hospitalization. Prior to 1980, there was a longstanding misconception that neonates do not experience pain. Current studies demonstrate that not only do neonate's experience pain, but due to their immature nervous systems, they are hypersensitive to painful stimuli. Poorly treated pain during the neonatal period may lead to negative long-term consequences. Proper assessment of a neonate's pain is vital. Standardized pain scales allow for consistency between providers and individualized treatment plans for neonates. The use of non-pharmacological treatments such as, nonnutritive sucking, facilitated tucking, kangaroo care, swaddling and heel warming may all be beneficial in alleviating a neonate's pain. Pharmacological treatments in the neonate have been

*CORRESPONDING AUTHOR: Xiaomei S. Cong, PhD, RN., Associate Professor, Director, Center for Advancement in Managing Pain, School of Nursing, University of Connecticut, Storrs, CT, U.S.A., 231 Glenbrook Road, Storrs, CT 06269-4026, xiaomei.cong@uconn.edu.

DISCLOSURE STATEMENT:
The authors have nothing to disclose.

well established and may include, but are not limited to opioids and non-opioid analgesics. Pharmacological and non-pharmacological interventions can be used in conjunction with each other to increase the efficacy of analgesia.

Keywords

Pain; Neonatal care; non-pharmacologic intervention; pharmacologic intervention; barriers

Introduction

The knowledge of pain in neonates has increased dramatically in the past three decades. It has been well established that newborns can detect, process, and respond to painful stimuli.[1] Preterm infants are even more hypersensitive to pain and at greater risk for pain due to immature pain inhibition mechanisms at birth.[2] Excessive, prolonged painful events in the neonate causes adverse physiological effects in all major organ systems, which can be life threatening and have long-term effects.[3] However, interventions to alleviate neonatal pain remain inadequate and inconsistently applied. Only half of the painful procedures performed in neonates were treated, with a wide variation of pain management practice among facilities and areas.[4] Gaps exist in knowledge, evidence, and practice in neonatal pain assessment and management, which may lead to challenges in managing the pain. The purpose of this article is to address gaps and provide a review of clinical recommendations of pain management from an historical and developmental perspective of neonatal pain.

Mysteries about Neonatal Pain

While the field has seen many innovations, research on neonatal pain has been lacking. In 2015, an Oxford research team found evidence that babies experience pain similarly to adults.[5] The MRI scans of ten infants and adults provided a painful stimulus were compared. Results revealed that 18 of 20 brain regions active in adults experiencing pain were also active in newborns. Moreover, infant's brains showed the same level of response as adults' when exposed to a stimulus one-fourth as strong.[5] These results directly contradict the popular belief that neonates are incapable of perceiving pain.[8] Several underlying hypotheses can explain this misunderstanding. Neonates were thought to be incapable of interpreting pain due to their inability to create memories.[1] Combined with fears of the side effects of anesthesia, neonatal physicians performed surgeries such as circumcision without analgesia until the 1990s.[6] As the Oxford research results suggest, infants do feel pain and experience it more intensely than adults. The implications of this on neonatal development is staggering, considering the logistics of the neonatal intensive care unit (NICU). Annually, 15 million premature babies are born worldwide and each may experience 300 painful surgeries during their hospitalization.[7,8] Thus, it is vital that repeated stress and insults be addressed.[4]

Developmental Aspect of Neonatal Pain

Whether or not full-term and preterm newborns have the required anatomy and physiology to sense pain contributed to the mystery. A neonate's ability to sense pain occurs with key neurodevelopment. The first step of pain sensation involves nociceptors, the nerve endings

that signal pain. Cells surrounding nociceptors release pain-signaling chemicals that respond to painful stimuli.[9] In the presence of painful stimuli, a nociceptor transforms the painful signal into an impulse, propagating along an aggregation of neurons to the dorsal horn, where sensory information is received.[10] At this point, the impulse separates: one returns to the initial site of pain to set off a reflexive reaction, the other reaches the thalamus. The thalamus localizes the pain of the stimuli. The brain is now equipped with information on the pain and how it can be prevented.[11]

Each stage of the nociceptive pain pathway develops at different times. At seven weeks gestation, nociceptive nerve endings begin to develop circumorally. Nociceptive development is complete at twenty weeks around body linings and the extremities.[12] However, without any link to the spinal column, the nociceptor signals are not functional and of limited use. The pathway between the nociceptive nerve endings and dorsal horn begins in week thirteen and is functional by week thirty.[13] With this pathway, the fetus is able to reflexively withdraw from painful stimuli but does not possess the cognitive capacity to process information regarding the pain or its source. Cortical pain perception develops after week twenty-four of gestation, when the thalamic track completes its connection to the dorsal horn. In short, a neonate will be able to localize the pain and make reflexive movements to try and avoid it after week twenty-four, thus completing the nociceptive pain pathway.

Another important component of the pain pathway is the myelin sheath and its role in pain modulation. The myelin sheath works as an electrical insulator, increasing the speed of a signal from the peripheral to central nervous system. Myelination develops after twenty-five weeks of gestation and is complete by week thirty-seven.[14] It was previously thought that unmyelinated axons were unable or too slow to transfer electrical impulses. Recent consensus is that unmyelinated neurons are fully capable of transferring a signal, although at a slower rate.[15] Pain modulation is also critical in the management of pain. Descending signal pathways protrude into the dorsal horn where pain transmission is thought to be halted by the release of endogenous opioids or the activation of the inhibitory pathways. Both of these mechanisms are much more prevalent in the adult than the neonate.[16] Thus, preterm infants may actually have a 30-50% lower pain threshold than adults and a lower pain tolerance than older children.[17] Therefore, unrelieved and repetitive painful events can result in adverse physiological effects in all major organ systems including brain structure. These can be life threatening and have long-term cumulative effects including altered neurobehavioral development.[8,17]

Neonatal Pain Assessment

Pain assessment in neonates is notoriously difficult because of their physical, cognitive, and behavioral development. The use of pain assessment scales provides consistency between nurses and other clinicians, and provides an accurate measure for the presence of pain, stress, or discomfort. These scales not only quantify pain, but can provide an accurate depiction of the effect of non-pharmacological and pharmacological management interventions on a neonate’s pain.

It is crucial to identity any potential source of pain to facilitate pain assessment.[18] Nurses should be aware that even simple procedures and daily care, such as routine heel sticks or tape removal can be painful and stressful and can result in altered pain perception and development in the future.[4] Recent evidence have supported that prolonged exposure to painful/stressful events are detrimental to the immature nervous system, and influence the early programming of neuro-immune system in this vulnerable population.[8,19] The majority of existing instruments focused on measuring the short-term acute pain based on physiological and behavioral cues. However, few instruments are available to measure persistent pain/stress in preterm infants. A recently developed tool, Accumulated Pain/Stressor Scale (APSS)[20] could serve as an assessment scale to measure severity and acuity levels of painful/stressful procedures that hospitalized neonates undergo during a certain period of time.

Cong et al.[18] summarized the characteristics of many of these scales. Table 1 summarizes several commonly used neonatal pain assessment scales. Based on their psychometric properties and purpose of usage, the NFCS,[21] Neonatal Pain, Agitation, and Sedation Scale (N-PASS),[22] COMFORTneo scale,[23] Neonatal Infant Pain Scale (NIPS),[24] and FLACC scale[25] are recommended for daily pain assessment. The PIPP-R (for neonates)[26] is recommended for pain measurement in research studies (Table 1). Pain assessment should take place routinely, while the frequency of assessment is consistent with the goal of treatment.[27]

Biopsychometric approaches to pain assessment include heart rate variability,[27] skin conductance measurements,[28] and brain-oriented techniques including electroencephagrahpy, near-infrared spectroscopy, and magnetic resonance imaging.[29] These technologies make it possible to improve the accuracy of pain measurement in neonates to provide clinicians with more variety of interventions and better decision making of pain management. Further research is needed to integrate these technologies into routine pain assessment in neonates.

Neonatal Pain Management: Prevention and Non-pharmacological Interventions

Painful/stressful procedures, the total amount and duration of noxious stimuli to which the infant is exposed must be limited to those absolutely necessary in diagnostic or therapeutic management.[30] Non-pharmacological interventions are valuable strategies that can reduce neonatal pain directly by blocking nociceptive transduction/transmission or by activation of descending inhibitory pathways. Noninvasive techniques such as sweet-tasting substances, kangaroo care (KC), breast milk and breastfeeding, non-nutritive sucking (NNS), swaddling, and facilitated tucking have been shown to be effective in soothing infants undergoing painful/stressful procedures (Table 2).

The administration of sucrose to neonates has been a well-researched area. A single dose of sucrose, was found to be effective and safe for alleviating procedural pain in neonates.[30,31] The exact analgesic mechanism of sucrose on infant pain is not entirely understood.[31,32] Several animal studies have been conducted, though a main supporting hypothesis for

sucrose efficacy is through activation of endogenous opioids. In activating endogenous opioids, an anti-nociceptive response ensues thus attenuating nociceptive signals at the dorsal horn level.[33] However, evidence is still limited regarding the efficacy and safety (e.g., long-term neurobehavioral outcomes) of repeated use of sucrose across repeated procedural pain for neonates. Daily repeated use of sucrose (e.g., > 10 doses/day) in young preterm infants (e.g., <31 weeks gestational age) may lead to poor neurologic development.[31]

KC is skin-to-skin contact between an infant and parent. KC has been shown to alleviate both physiologic and behavioral responses in neonates during painful procedures.[34,35] KC works as an analgesic intervention through multi-sensory stimulations including emotional, tactile, proprioceptive, vestibular, olfactory, auditory, visual, and thermal stimulations in a unique interactive style. Various durations of KC have been found to be effective on reducing pain in neonates when KC is provided for 10-15 minutes,[36] 30 and 80 minutes,[34,37] or 3 hours[38] before and through the procedural pain. In addition to reducing behavioral and physiological pain responses, studies have also shown that hormonal markers including cortisol, β-endorphin and oxytocin levels being changed in infants when receive KC,[34,39] which may explain the endogenous analgesic effect of KC in neonates.

NNS is the introduction of an oral stimulant, such as pacifier or nipple, without providing nutrition. In neonates, NNS can be used with or without the addition of sucrose, both of which have individual benefits. In the absence of sucrose, NNS remains a beneficial non-pharmacological method of analgesia in neonates. It has been proven to significantly reduce crying and pain response during procedures that cause mild to moderate pain, such as heel sticks and circumcision.[40,41] Though beneficial, the efficacy ends as soon as the pacifier is removed from the infant's mouth, which can in turn lead to a rebound distress response.[33]

Formula, expressed breast milk, and breastfeeding have been used for reducing infant pain. Both formula and breast milk could significantly reduce procedural pain in neonates, even though to a lesser extent as compared to sucrose.[42-44] Infants receiving breastfeeding during a painful procedure have been found to demonstrate a significantly lower increase in heart rate, reduced crying, and lower pain scores compared to other non-pharmacological interventions, such as swaddling, holding, and NNS.[45]

Facilitated tucking (FT) is a specific way of gently holding an infant in a flexed position. It requires minimal physical adjustment and is even safe to use in mechanically ventilated neonates.[46] FT also reduces pain in neonates during painful procedures. Though beneficial, some studies indicate that it is not as efficacious as NNS.[41] Therefore, the combination of NNS and FT may be more beneficial than using FT alone.[46]

Swaddling neonates involves wrapping the neonate firmly in a blanket or other restrictive devise. Studies investigating the analgesic properties have shown that it is effective after a painful procedure, in regard to autonomic stability and recovery. Prior research indicates that swaddling may not be effective for neonates younger than 31 weeks gestational age, though research performed by Huang et al,[47] has provided contradictory results.[48] Within the study, the efficacy of swaddling was seen across all age groups pertaining to oxygen saturation recovery.

Heel warming is often utilized during the preparatory phase prior to a heel stick. By warming the neonate's heel, there may be a reduced pain response related to the decreased need for squeezing related to increased blood flow to the area. An early study did not find a difference in infant pain perception or an improvement in analgesic effect using heel warming.[49] Conversely, a recent study found heel warming to decrease pain response during heel sticks and improve recovery time in oxygen saturation.[50] More randomized clinical trials must be performed to make a definitive conclusion as to whether or not heel warming is beneficial in providing analgesic relief.

Combining several methods of non-pharmacological therapies via multisensory stimulation have proven to be most effective in providing analgesic effects.[51] The combination of oral sucrose-FT, sucking-oral sucrose, and NNS-oral sucrose-FT have been most effective in reducing neonate crying and fussiness during routine care.[52] Use of a combination of non-pharmacological interventions can achieve greater effectiveness of pain reduction, therefore is highly recommended in neonatal pain management.[30]

Neonatal Pain Management: Pharmacological Interventions

Careful consideration must be taken in administering analgesics to neonates and infants in the NICU. This is due in part to the difficulty of pain assessment, variability in individual metabolisms, neurodevelopment and drug clearance rates; all of which can lead to adverse events and side effects.[53] Pharmacological therapy should be administered in a stepwise approach. The type of pain that the neonate is experiencing (i.e., procedural vs. disease process) will determine the type of analgesia best suited. Below defines the different types of pharmacological analgesic therapies, which may be frequently used within the NICU.

Opioids must be carefully administered and monitored in the neonate due to underdeveloped renal function, which results in decreased clearance due to the glomerular filtration rate (GFR). Decreased GFR, decreased protein binding, immature hepatic function and a blood brain barrier, in combination with prematurity and subsequent illness may lead to altered opioid pharmacokinetics and possible respiratory depression in neonates.[54] Morphine is often used as the first choice of opioid analgesia in critically ill neonates, despite its known tolerance in the neonate.[55] It is broken down and metabolized within the liver, though due to its water solubility it has the potential to cross the neonate's blood brain barrier leading to respiratory depression.[54,56] Due to these potentially life-threatening side effects, reduced morphine doses are necessary. There is significant evidence of opioid tolerance in neonate's, which increases the need for vigilance and individualized care plans for neonates on morphine therapy. Several other opioids may be used in neonates such as fentanyl and ketamine. Administration of opioids may be done via intermittent and/or continuous intravenous injections, oral, or rectal preparations.

Non-opioid analgesics include multiple analgesic modalities, such as acetaminophen, non-steroidal inflammatory drugs (NSAIDs), benzodiazepines, local and regional anesthetics. Benzodiazepines, such as midazolam and lorazepam, are often used in neonates to induce sedation and muscle relaxation. They have a limited analgesic effect, though in conjunction

with other analgesic modalities, such as morphine, sedation is oftentimes improved, but due to adverse side effects caution must be taken in administering to neonates.[53]

Regional anesthetics (i.e., lidocaine) are often the analgesic of choice among neonates undergoing circumcision, as a dorsal penile block. Epidural anesthesia may also be helpful in surgical pain experienced by neonates. The use of epidural anesthesia may significantly decrease a neonate's surgical stress response as well as decrease the reduce the need for mechanical ventilation during the postoperative period.[57]

Local topical anesthetics are helpful in alleviating pain, specific to pain that is induced by breaking of the skin barrier (i.e. lumbar puncture). Though this is true, topical anesthetics such as EMLA (eutectic mixture of local anesthetic) has been least effective in circumcision and heel sticks. In addition, the time of onset for topical anesthetics is often much longer than those which are regional in nature, 60-90 minutes.[58] EMLA may be helpful in producing an analgesic response during intravenous catheter insertion (peripheral and/or arterial), as well as lumbar puncture and screening for retinopathy of prematurity.[51]

Barriers and Perceptions about Neonatal Pain

Neonatal pain management has been an enigma since 1980 when neonatal pain was first acknowledged.[59] Managing neonatal pain is a primary responsibility of neonatal nurses. Among NICU nurses, there was consensus that nurses were responsible for preventing neonate's pain. However, they also expressed that their physician counterparts did not value pain management as much as NICU nurses.[60] The commonly held paradigms about pain in the neonatal population by nurses directly influences critical decisions during neonatal care. Understanding these perceptions has only recently become a focus of nursing research and has taken on several common themes.

Neonatal nurses in the United States, the United Kingdom and China were surveyed about their current knowledge of and beliefs about neonatal pain, assessment, intervention, and protocol, as well as barriers to and strategies for improvement. It was found that nurses were generally knowledgeable about pain in neonates.[61,62] Chinese nurses held a belief that there was no difference between neonate, older child and adult pain, indicating a knowledge gap.[63] Traditionally, Western nurses felt more comfortable using pharmacologic interventions, while Chinese nurses believe that non-pharmacologic interventions are efficacious for pain treatment.[62,63] Nurses in the UK reported that they were more concerned with under-medication for pain than over-medication.[62] Less than half of the Chinese nurses knew of the pain management protocols in their unit and the majority of American, UK and Chinese nurses felt that the protocols were unclear and not based on the evidence of neonatal pain research.[61-63] . This leads to the conclusion that there is an important gap in the way in which nurses evaluate and manage neonatal pain.

Narrative data collected from American, UK, and Chinese nurses revealed the barriers to pain management were lack of time, knowledge, and trust in the tools used, the latter two likely contributing to reported fear and reluctance to change current practice.[62,63] It was

suggested that education and utilization of research along with improved communication would improve pain management.

Summary

Neonatal infants, especially preterm infants are most likely to experience a great number of repeated and prolonged painful events in the NICU that can lead to deleterious consequences, including neurodevelopmental impairment as a result. Appropriate steps have been taken to ensure a paradigm shift regarding neonatal pain, its processing and management. A deeper understanding of the pain sensory mechanism and its ramifications is necessary for a more accommodating neonatal healthcare practice. Non-pharmacologic interventions, especially those incorporating parental involvement (e.g., KC) are highly recommended. To discover new and creative approaches to address the challenge of infant pain is a primary nursing focus. According to the clinical, ethical,[64] and policy statements,[4,65,66] developing optimal assessment and treatment techniques to reduce neonatal pain is an important topic and challenge for neonatal caregivers. Even though there are gaps in knowledge, practice, attitudes, and policy regarding infant pain, health care providers should implement pain management programs to assess, prevent and relieve pain in neonates using non-pharmacological and pharmacological strategies.

References

1. Anand KJ, Hickey PR. Pain and its effects in the human neonate and fetus. N Engl J Med. 1987; 317(21):1321–1329. [PubMed: 3317037]
2. Fitzgerald M, Beggs S. The neurobiology of pain: developmental aspects. Neuroscientist. 2001; 7(3):246–257. [PubMed: 11499403]
3. Grunau RE, Holsti L, Haley D, et al. Neonatal procedural pain exposure predicts lower cortisol and behavioral reactivity in preterm infants in the NICU. Pain. 2005; 113(3):293–300. [PubMed: 15661436]
4. Committee On F, Newborn Section, On A, Pain M. Prevention and Management of Procedural Pain in the Neonate: An Update. Pediatrics. 2016; 137(2):e20154271. [PubMed: 26810788]
5. Goksan S, Hartley C, Emery F, et al. fMRI reveals neural activity overlap between adult and infant pain. Elife. 2015; 4
6. Lippmann M, Nelson RJ, Emmanouilides GC, Diskin J, Thibeault DW. Ligation of patent ductus arteriosus in premature infants. Br J Anaesth. 1976; 48(4):365–369. [PubMed: 776196]
7. Holsti L, Grunau RE, Shany E. Assessing pain in preterm infants in the neonatal intensive care unit: moving to a ‘brain-oriented’ approach. Pain Manag. 2011; 1(2):171–179. [PubMed: 21874145]
8. Cong X, Wu J, Vittner D, et al. The impact of cumulative pain/stress on neurobehavioral development of preterm infants in the NICU. Early Hum Dev. 2017; 108:9–16. [PubMed: 28343092]
9. Osterweis, M, Kleinman, A, Mechanic, D, editors. Pain and Disability: Clinical, Behavioral, and Public Policy Perspectives. Washington (DC): 1987.
10. Brown AG. The dorsal horn of the spinal cord. Q J Exp Physiol. 1982; 67(2):193–212. [PubMed: 6281848]
11. Ab Aziz CB, Ahmad AH. The role of the thalamus in modulating pain. Malays J Med Sci. 2006; 13(2):11–18. [PubMed: 22589599]
12. Hatfield LA. Neonatal pain: What’s age got to do with it? Surg Neurol Int. 2014; 5(Suppl 13):S479–489. [PubMed: 25506507]

13. Kostovic I, Rakic P. Developmental history of the transient subplate zone in the visual and somatosensory cortex of the macaque monkey and human brain. J Comp Neurol. 1990; 297(3): 441–470. [PubMed: 2398142]
14. Hasegawa M, Houdou S, Mito T, Takashima S, Asanuma K, Ohno T. Development of myelination in the human fetal and infant cerebrum: a myelin basic protein immunohistochemical study. Brain Dev. 1992; 14(1):1–6. [PubMed: 1375444]
15. Dubin AE, Patapoutian A. Nociceptors: the sensors of the pain pathway. J Clin Invest. 2010; 120(11):3760–3772. [PubMed: 21041958]
16. Fitzgerald M, Walker SM. Infant pain management: a developmental neurobiological approach. Nat Clin Pract Neurol. 2009; 5(1):35–50. [PubMed: 19129789]
17. Slater R, Fabrizi L, Worley A, Meek J, Boyd S, Fitzgerald M. Premature infants display increased noxious-evoked neuronal activity in the brain compared to healthy age-matched term-born infants. Neuroimage. 2010; 52(2):583–589. [PubMed: 20438855]
18. Cong X, McGrath JM, Cusson RM, Zhang D. Pain assessment and measurement in neonates: an updated review. Adv Neonatal Care. 2013; 13(6):379–395. [PubMed: 24300956]
19. Ranger M, Grunau RE. Early repetitive pain in preterm infants in relation to the developing brain. Pain Manag. 2014; 4(1):57–67. [PubMed: 24641344]
20. Xu W, Walsh S, Cong XS. Development of Accumulated Pain/Stressor Scale (APSS) in NICUs: A National Survey. Pain Manag Nurs. 2016
21. Grunau RE, Craig KD. Pain expression in neonates: facial action and cry. Pain. 1987; 28(3):395–410. [PubMed: 3574966]
22. Hummel P, Puchalski M, Creech SD, Weiss MG. Clinical reliability and validity of the N-PASS: neonatal pain, agitation and sedation scale with prolonged pain. J Perinatol. 2008; 28(1):55–60. [PubMed: 18165830]
23. van Dijk M, Roofthooft DW, Anand KJ, et al. Taking up the challenge of measuring prolonged pain in (premature) neonates: the COMFORTneo scale seems promising. Clin J Pain. 2009; 25(7):607–616. [PubMed: 19692803]
24. Lawrence J, Alcock D, McGrath P, Kay J, MacMurray SB, Dulberg C. The development of a tool to assess neonatal pain. Neonatal Netw. 1993; 12(6):59–66.
25. Crellin DJ, Harrison D, Santamaria N, Babl FE. Systematic review of the Face, Legs, Activity, Cry and Consolability scale for assessing pain in infants and children: is it reliable, valid, and feasible for use? Pain. 2015; 156(11):2132–2151. [PubMed: 26207651]
26. Stevens BJ, Gibbins S, Yamada J, et al. The premature infant pain profile-revised (PIPP-R): initial validation and feasibility. Clin J Pain. 2014; 30(3):238–243. [PubMed: 24503979]
27. Cong X, Cusson RM, Walsh S, Hussain N, Ludington-Hoe SM, Zhang D. Effects of skin-to-skin contact on autonomic pain responses in preterm infants. J Pain. 2012; 13(7):636–645. [PubMed: 22595172]
28. Tristao RM, Garcia NV, de Jesus JA, Tomaz C. COMFORT behaviour scale and skin conductance activity: what are they really measuring? Acta Paediatr. 2013; 102(9):e402–406. [PubMed: 23782068]
29. Hartley C, Slater R. Neurophysiological measures of nociceptive brain activity in the newborn infant--the next steps. Acta Paediatr. 2014; 103(3):238–242. [PubMed: 24180281]
30. IASP IAftSoP. Acute pain management in newborn infants. Pain Clinical Updates. 2011. http://www.iasp-pain.org/AM/AMTemplate.cfm?Section=IASP_Press_Books2&CONTENTID=15068&SECTION=IASP_Press_Books2&TEMPLATE=/CM/ContentDisplay.cfm
31. Gao H, Gao H, Xu G, et al. Efficacy and safety of repeated oral sucrose for repeated procedural pain in neonates: A systematic review. Int J Nurs Stud. 2016; 62:118–125. [PubMed: 27474944]
32. Stevens B, Yamada J, Ohlsson A, Haliburton S, Shorkey A. Sucrose for analgesia in newborn infants undergoing painful procedures. Cochrane Database Syst Rev. 2016(7):CD001069.
33. Gibbins S, Stevens B. Mechanisms of sucrose and non-nutritive sucking in procedural pain management in infants. Pain Res Manag. 2001; 6(1):21–28. [PubMed: 11854758]

34. Cong X, Ludington-Hoe SM, Walsh S. Randomized crossover trial of kangaroo care to reduce biobehavioral pain responses in preterm infants: a pilot study. Biol Res Nurs. 2011; 13(2):204–216. [PubMed: 21196428]
35. Boundy EO, Dastjerdi R, Spiegelman D, et al. Kangaroo Mother Care and Neonatal Outcomes: A Meta-analysis. Pediatrics. 2016; 137(1)
36. Johnston CC, Filion F, Campbell-Yeo M, et al. Kangaroo mother care diminishes pain from heel lance in very preterm neonates: a crossover trial. BMC Pediatr. 2008(8):13.
37. Cong X, Ludington-Hoe SM, McCain G, Fu P. Kangaroo Care modifies preterm infant heart rate variability in response to heel stick pain: pilot study. Early Hum Dev. 2009; 85(9):561–567. [PubMed: 19505775]
38. Ludington-Hoe S, Hosseini R, Torowicz DL. Skin-to-skin contact (Kangaroo Care) analgesia for preterm infant heel stick. AACN Clin Issues. 2005; 16(3):373–387. [PubMed: 16082239]
39. Vittner D, McGrath J, Robinson J, et al. Increase in Oxytocin From Skin-to-Skin Contact Enhances Development of Parent-Infant Relationship. Biol Res Nurs. 2018; 20(1):54–62. [PubMed: 29017336]
40. Golianu B, Krane E, Seybold J, Almgren C, Anand KJ. Non-pharmacological techniques for pain management in neonates. Semin Perinatol. 2007; 31(5):318–322. [PubMed: 17905187]
41. Liaw JJ, Yang L, Katherine Wang KW, Chen CM, Chang YC, Yin T. Non-nutritive sucking and facilitated tucking relieve preterm infant pain during heel-stick procedures: a prospective, randomised controlled crossover trial. Int J Nurs Stud. 2012; 49(3):300–309. [PubMed: 22001561]
42. Collados-Gomez L, Ferrera-Camacho P, Fernandez-Serrano E, et al. Randomised crossover trial showed that using breast milk or sucrose provided the same analgesic effect in preterm infants of at least 28 weeks. Acta Paediatr. 2017
43. Blass EM. Milk-induced hypoalgesia in human newborns. Pediatrics. 1997; 99(6):825–829. [PubMed: 9164777]
44. Ou-Yang MC, Chen IL, Chen CC, Chung MY, Chen FS, Huang HC. Expressed breast milk for procedural pain in preterm neonates: a randomized, double-blind, placebo-controlled trial. Acta Paediatr. 2013; 102(1):15–21. [PubMed: 23057434]
45. Shah PS, Herbozo C, Aliwalas LL, Shah VS. Breastfeeding or breast milk for procedural pain in neonates. Cochrane Database Syst Rev. 2012(12):CD004950.
46. Hartley KA, Miller CS, Gephart SM. Facilitated tucking to reduce pain in neonates: evidence for best practice. Adv Neonatal Care. 2015; 15(3):201–208. [PubMed: 26002861]
47. Huang CM, Tung WS, Kuo LL, Ying-Ju C. Comparison of pain responses of premature infants to the heelstick between containment and swaddling. J Nurs Res. 2004; 12(1):31–40. [PubMed: 15136961]
48. Cignacco E, Hamers JP, Stoffel L, et al. The efficacy of non-pharmacological interventions in the management of procedural pain in preterm and term neonates. A systematic literature review. Eur J Pain. 2007; 11(2):139–152. [PubMed: 16580851]
49. Barker DP, Willetts B, Cappendijk VC, Rutter N. Capillary blood sampling: should the heel be warmed? Arch Dis Child Fetal Neonatal Ed. 1996; 74(2):F139–140. [PubMed: 8777665]
50. Shu SH, Lee YL, Hayter M, Wang RH. Efficacy of swaddling and heel warming on pain response to heel stick in neonates: a randomised control trial. J Clin Nurs. 2014; 23(21–22):3107–3114. [PubMed: 24476226]
51. Krishnan L. Pain relief in neonates. J Neonatal Surg. 2013; 2(2):19. [PubMed: 26023439]
52. Liaw JJ, Yang L, Lee CM, Fan HC, Chang YC, Cheng LP. Effects of combined use of non-nutritive sucking, oral sucrose, and facilitated tucking on infant behavioural states across heel-stick procedures: a prospective, randomised controlled trial. Int J Nurs Stud. 2013; 50(7):883–894. [PubMed: 23068310]
53. Hall RW, Shbarou RM. Drugs of choice for sedation and analgesia in the neonatal ICU. Clin Perinatol. 2009; 36(2):215–226. vii. [PubMed: 19559316]
54. Bhalla T, Shepherd E, Tobias JD. Neonatal pain management. Saudi J Anaesth. 2014; 8(Suppl 1):S89–97. [PubMed: 25538531]
55. Hall RW. Anesthesia and analgesia in the NICU. Clinics in Perinatology. 2012; 39(1):239–254. [PubMed: 22341549]

56. Haidon JL, Cunliffe M. Analgesia for neonates. Continuing Education in Anaesthesia Critical Care and Pain. 2010; 10(4):123–127.
57. PA L. Regional anesthesia and analgesia in the neonate. Best Pract Res Clin Anaesthesiol. 2010; 24(3):309–321. [PubMed: 21033009]
58. Anand K, Johnston C, Oberlander T, Taddio A, Lehr V, Walco G. Analgesia and local anesthesia during invasive procedures in the neonate. Clin Ther. 2005; 27(6):844–876. [PubMed: 16117989]
59. Anand K, Hall W. Controversies in neonatal pain: an introduction. Seminars in Perinatology. 2007; 31(5):273–274. [PubMed: 17905180]
60. Byrd PJ, Gonzales I, Parsons V. Exploring barriers to pain management in newborn intensive care units: a pilot survey of NICU nurses. Adv Neonatal Care. 2009; 9(6):299–306. [PubMed: 20010148]
61. Cong X, Delaney C, Vazquez V. Neonatal nurses' perceptions of pain assessment and management in NICUs: a national survey. Adv Neonatal Care. 2013; 13(5):353–360. [PubMed: 24042143]
62. Akuma AO, Jordan S. Pain management in neonates: a survey of nurses and doctors. J Adv Nurs. 2012; 68(6):1288–1301. [PubMed: 21988718]
63. Cong X, McGrath JM, Delaney C, et al. Neonatal nurses' perceptions of pain management: survey of the United States and China. Pain Manag Nurs. 2014; 15(4):834–844. [PubMed: 24508269]
64. Franck LS. A pain in the act: musings on the meaning for critical care nurses of the pain management standards of the joint commission on accreditation of healthcare organizations. Crit Care Nurse. 2001; 21(3):8, 10, 12.
65. National Association of Neonatal Nurses. Position statement on pain management in infants. Central Lines. 2000; 16(1):4–6.
66. Baker DW. Statement on Pain Management: Understanding How Joint Commission Standards Address Pain. Jt Comm Perspect. 2016; 36(6):10–12.

KEY POINTS

- Neonates are more hypersensitive to painful stimuli, due to their immature nervous system and decreased inhibition of nociceptive pain.
- Poorly treated pain in neonates may lead to lifelong consequences, including altered neurobehavioral development.
- There are more than 40 pain assessment scales in the neonate population, which may standardize assessment of pain, though also provide confusion among providers.
- Both non-pharmacological and pharmacological interventions should be used in conjunction with each other to provide a synergistic effect of pain analgesia.
- Barriers to properly managing neonate's pain include lack of time, knowledge, influx or distrust of assessment tools and disagreement between providers.

Table 1

Summary of Recommended Pain Assessment Scales for Neonates

Instrument	Items/Score Range	Clinical Utility	Reliability/Validity
NFCS - Neonatal Facial Coding System (Grunau et al., 1987)	9 items: Brow bulge, eye squeeze, naso-labial furrow, open lips, stretch mouth (vertical), stretch mouth (horizontal), lip purse, taut tongue, chin quiver Score: 0 – 9 (full-term); 0-10 (preterm)	Procedural pain; Preterm, Full-term	InterRR: 0.88 IntraRR: 0.83 Face, content, & construct validity: Yes
FLACC - Face, Legs, Activity, Cry, Consolability (Merkel, et al., 1997)	5 items: Face, legs, activity, cry, consolability Score: 0 – 10	Postoperative pain; Preverbal/nonverbal children < 7 years old	InterRR: 0.94 Content & construct vadility: Yes
COMFORTneo – modified from the COMFORT behavior scale (Van Dijk, et al., 2009)	7 items: Alertness, calmness/agitation, respiratory response (in mechanically ventilated children), crying (in spontaneously breathing children), body movement, facial tension, (body) muscle tone. Score: 6 - 30	Prolonged pain Sedation level; Preterm, Full-term 24 - 42 wks GA	InterRR: 0.79 Internal consistency: 0.84-0.88 Concurrent validity : Yes
NIPS - Neonatal Infant Pain Scale (Lawrence et al., 1993)	6 items: 5 behavioral items (facial expression, cry, arms, legs, and state of arousal) and 1 physiological item (breathing pattern) Score: 0 - 7	Procedural pain, Postoperative pain; Preterm, Full-term 26 - 47 wks GA	InterRR: 0.92 - 0.97 Internal consistency: 0.87 - 0.95 Concurrent validity: 0.53 - 0.84
N - PASS - Neonatal Pain, Agitation, and Sedation Scale (Hummel, et al., 2008)	**5 items:** 4 behavioral items (Crying/ irritability, behavior/state, facial expression, extremities/tone, and 1 physiological item (vital signs: heart rate, RR, BP, SaO 2) Score: 0 – 10	Ongoing pain (ventilation Sedation level), Procedural pain, Postoperative pain, Preterm, Full-term 23 - 40 wks GA	Internal consistency: 0.85–0.95 InterRR: 0.88–0.93 Test –retest reliability: 0.87
PIPP - Premature Infant Pain Profile(Stevens et al., 1996); **PIPP-R** - Premature Infant Pain Profile – revised (Stevens, et al., 2014)	7 items: 3 behavioral items (brow bulge, eye squeeze, nasolabial furrow), 2 physiological items (heart rate, oxygen saturation), and 2 Contextual items (gestational age, behavioral state) Score: 0 – 18 (full-term); 21 (preterm)	Procedural pain, postoperative pain; Preterm, Full-term 28 - 42 wks GA The most commonly used tools in research studies.	InterRR: 0.93-0.96 IntraRR: 0.94-0.98 Content & construct validity: Yes

Note. wks = weeks; GA = gestational age; InterRR = inter-rater reliability; IntraRR = intra-rater reliability.

Table 2

Non-pharmacologic Pain Interventions and Major Effects

Interventions	Major Effects: Research Evidence	Use in Painful Procedures
Sweet-tasting solutions: Sucrose and Glucose Administration	• Decrease changes of heart rate. • Reduce crying time and facial grimacing. • Lower pain scores (PIPP, NFCS scores) • Physiological mechanism not entirely understood; may activate endogenous opioid and nonopioid pathways through orotactile and orogustatory stimulation.	• Effective and safe for single does given to full-term and preterm infants. • Use in heel stick, intramuscular injection, venipuncture, subcutaneous injections, bladder catheterization, arterial puncture, insertion of nasogastric/orogastric tubes, eye examinations, and echocardiography. • Manage short term (5-8 min) pain and usually given 2 minutes before the procedure. Administer on the infant's tongue with a pacifier, syringe, or cup. • No clear recommendation of optimal dose (a 20-fold variation in the doses used) • Recommended by IASP: 24% sucrose can be given: 24–26 wks GA: 0.1 mL 27–31 wks GA: 0.25 mL 32–36 wks GA: 0.5 mL >37 wks GA: 1 mL • Concerns: potential adverse effects for repeated, multiple dose regimens in preterm infants.
Skin-to-skin contact - Kangaroo	• Decrease changes of heart rate, respiratory rate, and oxygenation saturation.	• Effective and safe in full-term and preterm infants.
Care (KC)	• Decrease crying time and facial grimacing. • Improve behavioral states and sleep-wake patterns. • Lower pain scores (e.g., PIPP, NFCS scores) • Reduce recovery time. • Decrease cortisol concentrations • Promote autonomic maturation (e.g., heart rate variability). • Reduce parental stress, anxiety and increase competence. • Provide multi-sensory stimulation; activate β-endorphin release (endogenous opioid response) and oxytocin mechanism.	• Use in heel stick, intramuscular injection, venipuncture, and subcutaneous injections, and pre and post operation, • Use pre, during and post procedures, 10-15 min, 30 – 80 min, or 2-3 hours. • Effects last as the infant placed in the KC position and may also last after KC session.
Nonnutritive Sucking (NNS)	• Decrease changes of heart rate, respiratory rate, and oxygenation saturation. • Decrease crying time. • Decrease cortisol concentrations • Lower pain scores (e.g., PIPP, NFCS scores)	• Effective and safe in full-term and preterm infants. • Use in heel stick, circumcision, intramuscular injection, venipuncture, and subcutaneous injections, and pre and post operation, • Administer NNS at least 3 min before the procedure

Interventions	Major Effects: Research Evidence	Use in Painful Procedures
	• Mechanism of NNS on pain is unclear; may stimulate orotactile and mechanoreceptors in the mouth and regulate behavioral states.	• Effective when pacifier is in the infant's mouth; removal can lead to rebound distress. • Best used in procedures with mild to moderate pain. • Concerns: influence on initiation and sustainability of breastfeeding practice.
Formula, Breast milk, and Breastfeeding	• Decrease changes in heart rate • Reduce crying time • Lower pain scores (e.g., PIPP, NIPS, NFCS, DAN scores)	• Safe and effective for repeated administration in full-term and preterm infants. • Use in heel stick, intramuscular injection, and venipuncture. • May provide similar effectiveness to oral sucrose or glucose solutions
Facilitated Tucking (FT)	• Decrease changes in heart rate • Reduce crying time • Lower pain scores (e.g., PIPP, NIPS scores) • Reduce parental stress and increase competence when parents participate in.	• Safe and effective in full-term and preterm infants. • Use in heel stick, endotracheal suctioning, and venipuncture. • Use FT before, during, and after procedures. • Contraindication: infants with poor skin integrity (e.g., extreme prematurity or epidermolysis bullosa).
Swaddling	• Decrease changes of heart rate and oxygenation saturation. • Reduce crying time. • Lower pain scores (e.g., NIPS scores). • Shorten pain recovery time. • Reduce parental stress and increase competence when parents participate in.	• Safe and effective in preterm infants. • Use in heel stick. • Use swaddling before, during, and after procedures. • Contraindication: infants with poor skin integrity (e.g., extreme prematurity or epidermolysis bullosa).
Heel Warming	• Decrease changes of heart rate and oxygenation saturation. • Reduce crying time. • Lower pain scores (e.g., NIPS scores). • Shorten pain recovery time.	• Safe and effective in preterm infants. • Use in heel stick. • Use before heel stick.

Note: PIPP= Premature Infant Pain Profile; NFCS = Neonatal Facial Coding System; NIPS = Neonatal Infant Pain Scale; DAN = Douleur Aigue Nouveau-né score Scale; wks GA = weeks gestational age.