Journal of Clinical and Nursing Research, 2026, Volume 10, Issue 2
http://ojs.bbwpublisher.com/index.php/JCNR
Online ISSN: 2208-3693
Print ISSN: 2208-3685

Advances in Research on Procedural Pain Management in Neonates

Na Wang, Wenjie Wang*

Nursing Department, Taihe Hospital, Hubei University of Medicine, Shiyan 442000, Hubei, China

**Author to whom correspondence should be addressed.*

Abstract: Neonatal procedural pain is one of the most frequent clinical challenges in the NICU. It not only causes acute physiological stress but also possibly has long-term neurodevelopmental adverse effects. In recent years, with a change in pain concept and advancement in evidence-based medicine, strategies for managing neonatal procedural pain have been becoming increasingly systematic and individualized. By reviewing domestic and international research progress, this article summarizes the current status of procedural pain occurrence, pain assessment tool application and timing, and non-pharmacological and pharmacological interventions in clinical practice, including healthcare professional education and training; it aims to provide a reference for clinical practice and further improve the quality of neonatal pain management.

Keyword: Neonate; Intensive care unit, Neonatal; Procedural pain; Review

Online publication: Mar 10, 2026

1. Introduction

Pain is generally considered the fifth vital sign and is defined as an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage. Neonates, especially preterm and critically ill infants who need NICU care, inevitably undergo many diagnostic, therapeutic, and nursing procedures during hospitalization due to their medical condition and treatment requirements [1]. Thus, procedural pain in the neonatal period occurs with great frequency and intensity. Studies suggest that neonates demonstrate increased sensitivity to painful stimuli and a low pain threshold [2]. Repeated and/or severe pain may cause not only acute physiological changes, such as tachycardia and desaturation, but can also disrupt the neuroendocrine system [3]. Such disturbance may lead to irreversible, long-term adverse effects on neurobehavioral development, including cognitive dysfunction and disturbed sensory processing [4]. Therefore, it is a medical imperative that neonatal pain, particularly procedural pain, should be managed both scientifically and systematically in order to enhance patient outcomes and quality of life [5]. This article attempts to present the recent research advances related to the occurrence, assessment methodology, non-pharmacological and pharmacological interventions, and education of

neonatal procedural pain in order to provide clinical guidance.

2. Occurrence of neonatal procedural pain

Procedural pain refers to acute pain induced by medical diagnostic, therapeutic, and nursing interventions. Advances in medical technology have improved the survival rates of preterm infants or neonates requiring special monitoring, but this also implies that these infants encounter a greater number of painful diagnostic and care procedures during hospitalization [6]. Diagnostic procedures (e.g., heel lance, ophthalmological examination), therapeutic procedures (e.g., intravenous cannulation, endotracheal intubation, oropharyngeal/nasal suctioning), and nursing care (e.g., respiratory therapy, adhesive tape removal) can all elicit procedural pain. Data indicate that hospitalized neonates may experience procedural pain 7 to 17 times daily. Preterm infants in Europe and America experience an average of 50 to 90 procedural pain events during their hospital stay [7]. In China, the median number of painful procedures received daily by NICU infants is 20. Alarmingly, these procedures result in severe pain in up to 70.37% of cases. This poses a dual threat to the developing neonate: it can cause intense physiological stress responses and unstable vital signs in the short term; in the long term, it may increase the risk of adverse neurodevelopmental outcomes by altering the development and plasticity of neural pathways [8].

3. Factors influencing neonatal procedural pain

Studies have shown differences in the frequency of procedural pain among infants grouped by gestational age (GA) and postnatal age (PNA). Specifically, early preterm infants experience higher frequencies than late preterm infants, who in turn experience more than term infants [9]. Infants on their first day of life have higher frequencies than those aged 2–4 days, who subsequently have higher frequencies than those aged ≥ 5 days. Infants with birth weights between 1000–2000 g experience procedural pain more frequently than those weighing 2001–2500 g, who in turn experience more than those weighing > 2500 g. Infants requiring respiratory support have a higher frequency of procedural pain compared to those without. Furthermore, infants diagnosed with Neonatal Respiratory Distress Syndrome (NRDS), sepsis, or intraventricular hemorrhage (IVH) experience procedural pain more frequently than those without these diagnoses [10].

Factors contributing to the intensity of procedural pain include higher gestational age, which has also been associated with higher pain scores. Greater numbers of painful procedures are associated with higher intensity, particularly with invasive, technically difficult, and lengthy procedures. The two most common painful procedures are oropharyngeal/nasal suctioning and heel lance. The most painful procedures are ophthalmological examination and the placement of a PICC. Neonates also demonstrate increased pain scores during active, alert wake states compared with sleep states. Future research must investigate the reduction or avoidance of factors known to contribute to neonatal procedural pain and comfort measures for infants, in a way that minimizes the numerous noxious stimuli neonates endure [11].

4. Assessment of neonatal procedural pain

Because neonates cannot express pain verbally, their pain assessment requires a comprehensive analysis of behavioral and physiological parameters. Timely and accurate pain assessment is, therefore, important for the implementation of effective pain management. Pain assessments in neonatal units worldwide range from a low of

6% to a high of 50.3%, while in China, the rate stands at 39.02% [12,13].

Clinically, it is advisable to employ validated multidimensional pain assessment scales in order to effectively integrate behavioral, physiological, and contextual elements for the improvement of accuracy in assessment. The assessment should include: origin of the pain, intensity of pain, site of pain, periodicity, duration, associated symptoms, and the impact of the pain on sleep, development, and physical functioning [3,5,14].

Scales with good reliability and validity that can accurately differentiate pain levels include the Neonatal Pain, Agitation and Sedation Scale (N-PASS), the Neonatal Infant Acute Pain Assessment Scale (NIAPAS), the CRIES scale (Cries, Requires Oxygen, Increased Vital Signs, Expression, Sleeplessness), the Behavioral Indicators of Infant Pain (BIIP), the revised Premature Infant Pain Profile (PIPP-R), the Douleur Aiguë du Nouveau-né (DAN), and the Neonatal Infant Pain Scale (NIPS). The aforementioned pain assessment scales were all developed from abroad, but at the present time, only the N-PASS, NIAPAS, and BIIP have standardized versions translated into Chinese. Looking at the balance between having good measurement properties and the need to minimize the assessment burden on clinicians, the Chinese version of N-PASS is recommended as the first-line tool in assessing the degree of neonatal procedural pain [15]. Regarding the frequency and timing of procedural pain assessment, various studies suggest that these assessments should be done before, during, and after an anticipated painful procedure. Assessment every 4 hours is a suggested frequency. This helps in the early detection of pain; thus, the effectiveness of an intervention may be assessed and management plans revised [16].

5. Management of painful procedures in neonates

Painful procedures should not be combined with other procedures that can cause exacerbation of pain. Whenever possible, the number of painful procedures should be minimized. On average, it is noted that arterial blood sampling and peripheral intravenous cannulation have the highest failure rates, with 4 or more attempts per procedure. Therefore, personnel performing these skills must be appropriately trained, have passed competency evaluations, and use the skill frequently to ensure accuracy in their technique to minimize the number of failed and repeated procedures. Non-pharmacological interventions should be provided before all painful procedures. Providing non-pharmacological interventions during various points surrounding a procedure, such as 2 minutes before and during and 2 minutes after a heel lance, is more effective than providing a single intervention [17,18].
Clinicians should pay particular attention to procedures that have been associated with the highest frequency and intensity of pain, for example, oropharyngeal/nasal suctioning, heel lance, ophthalmological examination, and PICC placement [19]. For these procedures, non-pharmacological interventions for pre-emptive analgesia are recommended in advance, with careful consideration given to combined pharmacological intervention when necessary to reduce pain and discomfort. For heel lance during blood sampling, automated heel incision devices are preferred over manual lancets, and the use of blade-type lancets is preferred over needle-type lancets. For peripheral arterial or venous puncture, precise technique is very important, and the use of smaller-gauge catheters, for example, 24–26 G, is advisable whenever possible. Similarly, for intramuscular and subcutaneous injections, needles with as small a gauge as possible should be chosen. To minimize the pain intensity of lumbar puncture, comfortable positions, such as the flexed lateral, knee-chest, or head-elevated position, should be adopted [20–23].

6. Non-pharmacological interventions for neonatal procedural pain

Non-pharmacological interventions are widely used due to safety, efficacy, and practicality. Providing a pacifier for non-nutritive sucking produces calming and distracting effects and is known to be effective in alleviating procedural pain among term infants. Non-nutritive sucking is suggested for mild, moderate, and severe pain, as well as for persistent pain in neonates in the "Expert Consensus on Neonatal Pain Assessment and Analgesia Management (2020 Edition)" in China [24,25]. Sucrose or glucose solution given via syringe, dropper, or pacifier can also relieve neonatal procedural pain. Kangaroo Mother Care (KMC), which involves placing the diaper-clad infant in an upright position against the bare chest of the mother or another relative at approximately a 60° angle to maximize skin-to-skin contact, provides warmth and security. KMC is recommended for preventing and alleviating neonatal procedural pain. Maintaining the infant in a flexed lateral position from 15 minutes before to 15 minutes after a painful procedure can also help prevent and relieve procedural pain. Additionally, breastfeeding (especially direct breastfeeding by the biological mother), maternal voice, olfactory stimulation, gentle touch, and music therapy have all demonstrated favorable effects on procedural analgesia [26,27].

7. Pharmacological interventions for neonatal procedural pain

For procedures that are expected to cause moderate-to-severe pain, or where non-pharmacological approaches are insufficient, careful use of pharmacological analgesia is warranted. Studies have demonstrated that the application of EMLA cream (2.5% lidocaine + 2.5% prilocaine) reduces pain during venipuncture, percutaneous central venous catheter placement, and peripheral arterial puncture, but is ineffective for heel lance. In neonates undergoing venipuncture, the combination of EMLA cream with oral sucrose results in better analgesia [28–30]. In infants who are already intubated or receiving mechanical ventilation and who demonstrate agitation during other painful procedures, appropriate sedation and analgesia should be provided. During the use of systemic analgesics, therapy should be individualized based on the condition of the neonate. Healthcare providers should closely monitor the therapeutic response and side effects, and continuously assess changes in the infant's vital signs [31,32].

8. Summary

Neonatal procedural pain management is an important aspect of improving NICU care quality and ensuring the safety and health of infants. With the continuous evolution of pain management concepts and evidence-based medicine, managing neonatal procedural pain has become more systematic and individualized. This article systematically reviewed the latest research progress in the occurrence, influencing factors, assessment methods, and non-pharmacological and pharmacological interventions for neonatal procedural pain, emphasizing scientific and systematic management. Non-pharmacological interventions are an effective measure; however, the implementation in hospitals is not the same. Pharmacological interventions have more risks and potential harm, and their application should be carefully managed. In the future, studies should further develop the following: first, enhancing assessment to make procedural pain assessment more accurate and timely; second, enhancing the study and application of non-pharmacological interventions, finding particular and practical ways of non-pharmacological analgesia; third, optimizing the protocol for pharmacological intervention, developing medicinal forms and administration routes that are more appropriate for neonates to reduce the incidence of adverse reactions; and fourth, enhancing pain management knowledge education and training for parents to improve their involvement.

Neonatal procedural pain management is a complicated but crucial topic that requires cooperation between related healthcare professionals. Only through unremitting efforts in research and practice can better and safer pain management be offered to neonates, which will promote healthy growth and development.

Funding

National Health Commission Hospital Management Research Institute 2024 Medical Quality (Evidence-Based) Management Research Project (Project No.: YLZLXZ24G090)

Disclosure statement

The authors declare no conflict of interest.

References

[1] Rogers M, Kuo P, 2020, Pain as the Fifth Vital Sign. Journal of the American College of Surgeons, 231(5): 601–602.

[2] Raja N, Carr D, Cohen M, et al., 2020, The Revised International Association for the Study of Pain Definition of Pain: Concepts, Challenges, and Compromises. Pain, 161(9): 1976–1982.

[3] Shen Q, Zheng X, Shi Y, et al., 2023, Evidence-Based Guidelines for Neonatal Pain Management in China (2023). Chinese Journal of Contemporary Pediatrics, 25(2): 109–127.

[4] Li L, Ren X, 2021, Research Progress on Procedural Pain in Preterm Infants and the Application of White Noise. Modern Clinical Nursing, 20(1): 79–84.

[5] Fu L, Xie Y, Wang Y, et al., 2024, Evidence Summary for Auditory Stimulation Intervention on Neonatal Procedural Pain. Journal of Nursing, 31(9): 42–47.

[6] Wang Y, Li Y, Sun J, et al., 2019, Investigation on the Status of Procedural Pain in Neonates in Neonatal Intensive Care Unit. Journal of Nursing Science, 34(11): 20–23.

[7] Ancora G, Lago P, Garetti E, et al., 2019, Evidence-Based Clinical Guidelines on Analgesia and Sedation in Newborn Infants Undergoing Assisted Ventilation and Endotracheal Intubation. Acta Paediatrica, 108(2): 208–217.

[8] Roofthooft D, Simons S, Anand K, et al., 2014, Eight Years Later, Are We Still Hurting Newborn Infants? Neonatology, 105(3): 218–226.

[9] McPherson C, Miller S, El-Dib M, et al., 2020, The Influence of Pain, Agitation, and Their Management on the Immature Brain. Pediatric Research, 88(2): 168–175.

[10] Sellam G, Cignacco E, Craig K, et al., 2011, Contextual Factors Influencing Pain Response to Heelstick Procedures in Preterm Infants: What Do We Know? A Systematic Review. European Journal of Pain, 15(7): 661–665.

[11] Williams A, Khattak A, Garza C, et al., 2009, The Behavioral Pain Response to Heelstick in Preterm Neonates Studied Longitudinally: Description, Development, Determinants, and Components. Early Human Development, 85(6): 369–374.

[12] Sellam G, Engberg S, Denhaerynck K, et al., 2013, Contextual Factors Associated with Pain Response of Preterm Infants to Heel-Stick Procedures. European Journal of Pain, 17(2): 255–263.

[13] Chen M, Shi X, Chen Y, et al., 2012, A Prospective Study of Pain Experience in a Neonatal Intensive Care Unit of China. Clinical Journal of Pain, 28(8): 700–704.

[14] Slater R, Cantarella A, Yoxen J, et al., 2009, Latency to Facial Expression Change Following Noxious Stimulation in

Infants Is Dependent on Postmenstrual Age. Pain, 146(1–2): 177–182.

[15] Maxwell L, Fraga M, Malavolta C, 2019, Assessment of Pain in the Newborn: An Update. Clinics in Perinatology, 46(4): 693–707.

[16] Ishak S, Nfe F, Zakaria S, et al., 2019, Neonatal Pain: Knowledge and Perception Among Pediatric Doctors in Malaysia. Pediatrics International, 61(1): 67–72.

[17] Cravero J, Agarwal R, Berde C, et al., 2019, The Society for Pediatric Anesthesia Recommendations for the Use of Opioids in Children During the Perioperative Period. Paediatric Anaesthesia, 29(6): 547–571.

[18] National Clinical Research Center for Child Health and Disorders, 2023, Evidence-Based Guidelines for Neonatal Pain Management in China (2023). Chinese Journal of Contemporary Pediatrics, 25(2): 109–127.

[19] He B, 2017, Translation and Validation of a Neonatal Pain, Agitation and Sedation Scale, thesis, Zhejiang University.

[20] Liu R, 2016, Translation and Validation of the Neonatal Acute Pain Assessment Scale, thesis, Huzhou University.

[21] Chen Y, 2017, Validation and Applicability Study of the Behavioral Indicators of Infant Pain Scale, thesis, Hangzhou Normal University.

[22] Registered Nurses' Association of Ontario, 2022, Assessment and Management of Pain (Third Edition).

[23] Spence K, Henderson-Smart D, New K, et al., 2010, Evidence-Based Clinical Practice Guideline for Management of Newborn Pain. Journal of Paediatrics and Child Health, 46(4): 184–192.

[24] Huang H, Wen X, 2021, Research Progress on Neonatal Analgesia and the 3TSS Method. Maternal and Child Health Care of China, 36(10): 2431–2434.

[25] Yan F, Mei H, Zhang Y, et al., 2017, Reliability, Validity, and Clinical Applicability of the Revised Premature Infant Pain Profile for Repeated Painful Procedures in Preterm Infants. Chinese Pediatric Emergency Medicine, 24(10): 3.

[26] Huang H, Zhang H, Wen X, et al., 2022, Analgesic Effect of 3T Sensory Saturation Method on Procedural Pain in Preterm Infants and Its Impact on Cerebral Blood Flow and Cerebral Oxygen Saturation. Maternal and Child Health Care of China, 37(6): 4.

[27] Hummel P, Puchalski M, Creech S, et al., 2008, Clinical Reliability and Validity of the N-PASS: Neonatal Pain, Agitation and Sedation Scale with Prolonged Pain. Journal of Perinatology, 28(1): 55–60.

[28] Chinese Medical Doctor Association Neonatology Branch, 2020, Expert Consensus on Neonatal Pain Assessment and Analgesic Management (2020 Edition). Chinese Journal of Contemporary Pediatrics, 22(9): 923–930.

[29] Zeng X, Li L, Hu X, 2022, Research Progress and Implications of Kangaroo Mother Care Performed by Fathers of Preterm Infants Abroad. Chinese Journal of Nursing, 57(15): 1898–1903.

[30] Francisco A, Montemezzo D, Ribeiro S, et al., 2021, Positioning Effects for Procedural Pain Relief in NICU: Systematic Review. Pain Management Nursing, 22(2): 121–132.

[31] Lago P, Garetti E, Bellieni C, et al., 2017, Systematic Review of Nonpharmacological Analgesic Interventions for Common Needle-Related Procedure in Newborn Infants and Development of Evidence-Based Clinical Guidelines. Acta Paediatrica, 106(6): 864–870.

[32] Cheng R, Yang Y, Shi Y, et al., 2020, Expert Consensus on Neonatal Pain Assessment and Analgesic Management (2020 Edition). Chinese Journal of Contemporary Pediatrics, 22(9): 923–930.