INVITED COMMENTARY

The Importance of Managing Acute Pain in the Neonatal Intensive Care Unit Context

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The significance of infant pain has evolved dramatically over the last few decades. Fifty years ago, it was common practice during infant surgeries to use paralytic drugs instead of anesthetics, grounded in the incorrect assumption that infants were incapable of experiencing pain [1]. This practice persisted until the combined efforts of pioneering basic and clinical researchers, alongside parental outcry, catalyzed a shift towards the acceptance of pain in infants. Scientific evidence confirmed that neonates possessed the anatomical and neurophysiological systems essential for pain perception, demonstrated both in animal and human subjects [2]. The history of incredulous neglect of infant pain underscores the importance of the present randomized control trial by Devi, et al. [3]. Early exposure to repetitive pain and distress has profound implications for brain development, pain processing, and stress response. Preterm infants in neonatal intensive care units (NICU), approximately 10% of all infants born globally [4], frequently endure between 12-17 painful procedures a day [5].

Experiencing pain in the NICU holds far-reaching implications, profoundly impacting the health and biopsychosocial development of premature infants [6]. Prolonged or recurrent pain during this crucial phase can disrupt neurodevelopment, potentially leading to cognitive, emo-tional, and behavioral challenges later in life. Physiological responses, including altered heart rate, blood pressure, and hormonal levels, can disrupt body systems. In addition, heightened pain sensitivity may endure, influencing pain perception throughout childhood and beyond. Moreover, the stress of NICU-related pain can dysregulate an infant's stress response system, impacting stress management and emotio-nal well-being [6]. These effects extend to behaviors like irritability, disrupted sleep, feeding difficulties, and strained parent-infant interactions. Importantly, unaddressed pain might also contribute to other chronic health conditions such as respiratory issues, further underscoring the urgency of evidence-based pain assessment and management in the NICU for short-term and long-term well-being [7].This concern gains particular significance in light of research which delves into the nuanced aspect of 'iatrogenically prolonged' pain experiences stemming from repetitive medical procedures in the NICU [8-10]. The cumulative burden of these interventions must be acknowledged [11], and may be a distinct pain state whereby the infant is 'chroni-cally pained' through a continuing barrage of acutely painful procedures before having resolved the pain from the last acutely painful procedure. These implications under-score the importance of mitigating the effects of both acute and prolonged pain for the overall health trajectory of preterm neonates [8]. One of the most common repetitive acutely painful procedures for infants in the NICU is the heel prick procedure.

Included in this issue of *Indian Pediatrics* is a randomized controlled trial [3] comparing neonatal procedural pain response across various heel prick devices. This article provides valuable insight into blood draw procedures in the NICU, by assessing pain responses in 180 clinically stable, non-ventilated neonates randomized to either an automatic lancet, a manual lancet, and a 26-gauge hypodermic needle. The heel pricks were conducted with reduced light and noise, and having oral dextrose administered 2-minutes prior to the prick as per standard of care. The authors concluded that the three devices elicit similar pain responses (using the well-validated Premature Infant Pain Profile-Revised); however, the use of hypodermic needles led to a higher number of painful squeezes during the procedure and longer cerebral oxygenation normalization time. This was contrary to other findings in the literature, which demonstrated a clear superiority for the automatic lancet, over both manual lancet and needle for heel pricks. Notable structural differences with the lancing instruments available within India were noted as a mitigating factor. Another notable feature of the article was the use cerebral oxygenation as an outcome measure showing that needles were less optimal. This article draws our attention on an important aspect of pain management – procedural interventions that can reduce the pain burden. It serves as a reminder to clinicians to think about the multifaceted ways to manage pain.

Within the 5Ps of pain management (physical, pharmacological, procedural, psychological, and process) [7], discovering and utilizing the least painful tools is a critical procedural component to contemplate [3]. In addition, to pharmacological strategies such as sweetening agents and topical anesthetics, there are an abundance of no-cost non-pharmacological interventions that have been shown to support infant pain management in the NICU. The 2023 Cochrane Review on non-pharmacological strategies for managing infant and young child procedural pain reviews 138 studies examining 24 separate techniques. While 12 strategies were focused specifically on preterm infants and most showed evidence of moderating pain, the unfortunate situation is that not one strategy is backed with a 'high certainty' in the evidence because of the rampant challenge of bias in trials due to methodological concerns (or in the older literatures, poor reporting of methodology) [9]. Nonetheless, non-pharmacological strategies are critical due to the frequency of acutely painful procedures experienced in the NICU. Given the low/no-cost of these strategies and possibility to utilize parent caregivers in these strategies (e.g., skin-to-skin care, facilitated tucking, non-nutritive sucking) these approaches should be prioritized, particularly in low-resource medical environments. The current article's content and quality contribute to a much-needed body of lower-risk of bias literature on procedural pain in neonates [3].

The significance of neonatal pain needs to be reflected in an appropriate body of high-quality research on measures and practices to protect their wellbeing. Through the generation and integration of clinically relevant pain research on NICU pain, such as the present trial [3], the impact of repeated painful procedures can become moderated to better optimize the development and well-being of vulnerable preterm infants.

Funding: None; *Competing interests*: None stated.
Published online: Sep 11, 2023; *PII*: S097475591600572

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