

Pain and the Neonatal Brain: History, Outcomes, and Strategies for Improvement



Patients in the NICU are among the most delicate residents in the hospital, yet studies have shown as many as 17 painful procedures being performed on neonates each day.¹ Many painful procedures are related to blood draws for lab tests used to monitor patients and titrate support. However, more frequent blood draws lead to increased instances of pain, which can result in both short- and long-term adverse outcomes for these fragile patients. It is essential to the quality of life and long-term outlook of these preterm infants that a comprehensive approach is taken to address pain in the NICU setting.

Neonates and pain: a history²

Prior to the 21st century, the pain experience in neonates was largely unrecognized and even denied among medical professionals. During these times, it was widely believed that infants were less evolved humans than those who were grown, and therefore could not experience pain at the same level as a more mature person. Because of this long-held belief, there was skepticism of data that suggested that infants do feel pain. Infant responses to pain were brushed off as physiological or behavioral reflexes rather than legitimate painful events for the child. This view was held so firmly that infant surgery was routinely performed without the aid of anesthesia until the late 1980s.

This mindset was only changed once new information came to light. When newborns and neonates were subjected to painful stimuli, clinicians observed and began documenting crying and other response behaviors. For invasive procedures, accumulating data showed that hormonal-metabolic responses to pain were significantly reduced when the neonates were given minimal anesthesia. The acknowledgment of neonatal pain led to the further observation of the effects of early-stage pain and paved the way for advances in neonatal pain management.

How often are preterm infants exposed to pain?

NICU patients require extensive testing and frequent handling that can leave infants distressed, exhausted, and in significant amounts of pain. It has been demonstrated that neonates endure 12 or more daily painful procedures on average, with individual patients enduring as many as 51 painful procedures in one day.³ Heel punctures are responsible for 61-87% of invasive procedures performed on these infants⁴ and are mostly taken to test for blood gases and pH levels, which help clinicians titrate patient care and ventilatory support.



Heel punctures comprise 61% to 87% of the invasive procedures performed on ill infants.⁴

How do neonates process pain?

It is important to note that while we often think of pain in the short-term, frequent instances of pain in neonatal patients can have long-lasting effects. When in pain, infants may experience an increase or variability in heart rate, blood pressure fluctuations, a decrease in oxygen saturation, and a higher secretion of stress hormones.⁵ While many medical professionals prior to the 20th century denied the existence of pain in infants, one study by M. Fitzgerald concluded that infants are more sensitive to pain as they do not have the developmental competencies to comfort themselves during the painful event.⁶



Increasing evidence suggests that pain is a central factor that predicts dysmaturation, especially in babies born very preterm and in those with many early exposures to pain.¹²



Looking at the long-term effects of pain on neonates gives further reason for concern. Pain in the first few days of life has been shown to magnify pain responses to later stimuli.⁷ Essentially, more early skin breaks and other painful experiences have been linked to a list of negative outcomes. When tested at 8 and 18 months, infants with a high number of neonatal skin breaks showed lower mental development indexes.⁸ Greater numbers of invasive procedures in the early days of life were associated with reduced white matter and lower IQ,⁹ and cumulative neonatal pain-related stress was associated with changes in brain activity and negatively correlated with visual perceptual abilities at school-age.¹⁰

Overall, more invasive neonatal procedures have been associated with smaller amygdala and thalamus volumes and, in turn, related to poorer cognitive, visual-motor, and behavioral outcomes.¹¹ In a 2020 review article featured in *Pediatric Research*, the authors noted, “Increasing evidence suggests that pain is a central factor that predicts dysmaturation, especially in babies born very preterm and in those with many early exposures to pain.”¹²

What can be done?

As described by Hall et al.,² solving the issue of pain and related sequelae in the NICU involves two key pillars: reductions in painful events and a quality approach to neonatal pain. Most of the steps needed to be successful in these efforts are proactive rather than reactive.

The authors note, “Perhaps the most effective method to eliminate neonatal pain is to reduce the number of procedures performed and episodes of patient handling,” and recommend six approaches to pain reduction:

- Reduce bedside interruptions as much as possible by performing multiple interventions at once (clustered care),
- Anticipate testing needs to minimize the frequency of blood draws,
- Use devices that can perform several analyses from one blood sample
- Place peripheral or central lines (with adequate analgesia) in patients who require many heel sticks per day
- Consider implementing noninvasive monitoring such as transcutaneous PaCO₂ and/or NIRS to avoid the need for blood sampling
- Consider non-invasive therapeutic approaches for analgesia

Most NICUs have already incorporated one or more of these strategies, but a comprehensive approach is required to truly make an impact.

Pain control programs should be introduced into care plans and closely followed to avoid both the short- and long-term effects that early-stage pain can have on developing infants. The success of a pain control program revolves around education, documentation, and proactive approaches. Clinicians should recognize neonatal pain as a valid concern and perform routine assessments with validated tools that detect neonatal pain. The approach should involve all care team members and require continuous auditing to ascertain appropriate pain treatments. By utilizing the tools and approaches outlined above, Hall and his team of NICU professionals were able to decrease the number of painful procedures to less than two per day in neonates between 27 and 32 weeks old.²



Perhaps the most effective method to eliminate neonatal pain is to reduce the number of procedures performed and episodes of patient handling.²



Noninvasive monitoring as a tool for pain reduction

In the NICU, the most effective way to reduce pain is to reduce painful events, and the most common painful event neonates experience is blood sampling. Since most blood draws occur because of the need to measure blood gases, utilizing transcutaneous CO₂ monitoring offers an opportunity to maintain continuous visibility to important parameters while reducing painful events¹³ – and potentially avoiding the associated negative outcomes for these vulnerable patients.



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