

Analgesia for skin-breaking procedures in newborns and children: What works best?

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∞ See related research papers by Farion and colleagues, page 31, and by Taddio and colleagues, page 37

Healthy newborns routinely experience acute pain during blood sampling for metabolic screening, injection of vitamin K or hepatitis vaccine, or circumcision. Children are similarly exposed to acute pain due to vaccination, invasive procedures or trauma. Acute pain caused by skin-breaking procedures can lead to physiologic instability and behavioural distress, and it has downstream effects on subsequent pain processing, development and stress responsivity.¹⁻⁵ Because of these detrimental effects, reduction or prevention of pain are worthy clinical goals that are also expected by most parents.^{6,7}

Opioids, such as fentanyl and morphine, form the mainstay of pediatric pain management, but they may not be effective against injury-induced acute pain in newborns or children.^{8,9} Accumulating data suggest that opioids lead to harmful side effects, tolerance and possibly altered brain development.¹⁰ Other analgesic and anesthetic agents also appear to increase brain cell death in animal studies,^{11,12} fuelling concerns about their use, particularly in newborns. Such concerns have led to the development of nonpharmacologic therapies such as sucrose, massage and kangaroo care for neonatal pain, and distraction techniques, hypnosis and cognitive-behavioural interventions for pediatric pain.

In this issue of *CMAJ*, 2 randomized controlled trials evaluate the efficacy of sucrose given orally and a topical coolant spray for reducing acute pain due to skin-breaking procedures. Taddio and colleagues¹³ report that sucrose reduced pain caused by venipuncture in term newborns of diabetic and nondiabetic mothers. However, sucrose did not reduce pain caused by intramuscular injections or heel lance. Farion and colleagues¹⁴ report that the use of a vapocoolant spray reduced pain caused by intravenous cannulation and was associated with increased success in the first attempt at cannulation. The interventions in both studies had a fairly modest effect size with wide confidence intervals, which implies considerable variability in the responses to skin injury and analgesia. Both trials were well designed and had several features that support the validity of their conclusions. These investigations suggest that not every type of analgesic works for every procedure, patient, disease or age group. For nonpharmacologic interventions, it is not their ease of use, low cost or fast onset that will determine their ultimate role in the treatment of pediatric pain. Instead, their use will be determined by their efficacy compared with systemic analgesics and local anesthetics.

Farion and colleagues¹⁴ describe a rapid, convenient

Key points

- In this issue of *CMAJ*, 2 randomized controlled trials evaluate the efficacy of nonpharmacologic approaches to treating the acute pain in newborns and children.
- Taddio and colleagues report that sucrose given orally reduced pain caused by venipuncture in newborns.
- Farion and colleagues report that a vapocoolant spray quickly and effectively reduced pain caused by intravenous cannulation in children.
- The results of these 2 studies will likely alter clinical practice and stimulate further research into the use of currently available nonpharmacologic analgesics in children.

method for reducing the acute pain caused by intravenous cannulation; however, the effectiveness of this method for other outpatient procedures remains to be investigated. Pain due to subcutaneous injections may be reduced by vapocoolant sprays,¹⁵ but other methods may be required to reduce pain caused by intramuscular injections or intradermal skin tests.¹⁶ The efficacy of noncommercial approaches in children, such as ice cube application, should also be investigated, particularly in resource-limited health care settings.^{16,17} The authors' finding of increased success of intravenous cannulation on the first attempt may be explained by clinical bias and the lack of successful blinding among bedside clinicians. Their findings may also be related to cold-induced vasodilation.¹⁸ This physiologic response, which differs among patients of different races and between smokers and nonsmokers, is protective against frostbite¹⁹ and may explain some of the observed variability between individual patients.

The observation by Taddio and colleagues¹³ that sucrose does not reduce pain caused by intramuscular injection or heel lance is also important for the management of acute pain in newborns. The authors postulate that sucrose is a weak analgesic, but they are unsure whether the lack of analgesia is a ceiling effect (peak of pain during the procedure), a floor effect (minimal pain from a retractable automatic lancet), an age-related effect (circulating levels of β -endorphin after birth) or a disease-related effect (pain processing in newborns

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of diabetic mothers²⁰). A host of important physiologic questions arise from these observations, which warrant further research in this area. It is debatable, however, whether the Premature Infant Pain Profile “is the best validated measure of pain in newborns;” this was not a conclusion of the Newborn Drug Development Initiative neonatal pain-control group.⁵

The availability of safe and effective nonpharmacologic analgesia that can be used repeatedly for acute pain in newborns or children would cause a paradigm shift in the management of pediatric pain. Perhaps different combinations of nonpharmacologic approaches in specific populations may be more effective than either modality alone.²¹ Another approach that has not been investigated systematically in this population is acupuncture, a well-known and effective treatment for chronic and recurrent pain in adults²² and children.²³ Therapeutic touch is another technique that could be considered for acute pain relief in newborns and children,²⁴ but its efficacy has not been investigated in these populations.

Investigators embarking on these avenues of research would do well to learn from the careful study design, concealment of allocation, selection of controls, outcome measures and study performance measures described by Taddio and colleagues¹³ and by Farion and colleagues.¹⁴ Indeed, these authors are to be commended for their innovative study designs, implementation, statistical analyses and data interpretation, which bring the highest standards of evidence-based medicine to the field of pediatric pain research. As a consequence, their conclusions will continue to provide food for thought and stimulate much additional research among clinical and basic scientists alike.

Competing interests: None declared.

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