Management of pain in the neonatal unit: options, challenges and controversies

Awareness of the importance of pain in newborn babies has increased during recent years, but it remains a challenging area of clinical practice. This article reviews current knowledge, addresses some of the challenges and controversies surrounding neonatal pain and suggests an approach to pain management in the neonatal intensive care unit.

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Key points

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1. Pain management is a crucial part of neonatal intensive care.
2. Assessment of chronic pain in babies is particularly challenging.
3. A range of pharmacological and non-pharmocological pain-relieving measures is available for use in babies.
4. The aim of pain management should be to achieve maximum comfort for babies, while minimising adverse effects of treatment.

Pain is unavoidable in modern neonatal intensive care. Advances in obstetric and early neonatal care have led to the survival of increasing numbers of sick and preterm infants of gestational age as low as 23 weeks. For these tiny patients, life-saving therapy means that a wide range of stresses associated with diagnostic, therapeutic and nursing interventions are all part of day-to-day life. There is no doubt that our knowledge and expertise in managing these babies has grown, but how have we progressed in the management of pain that they experience on a daily basis?

It is only a few years since it was common practice to give no analgesia to newborn babies, as they were thought to be developmentally too immature to process information about painful stimuli. We have come a long way since then and today it is widely, if not universally, accepted that even very preterm neonates are sufficiently developed, anatomically and physiologically, both to perceive and to respond to pain[1]. However, results of a recent Canadian survey comparing practice today with that of 12 years ago suggested that, although attention to pain has improved, the management of procedural pain in most centres, continues to fall short of current recommendations[2]. In all branches of medicine and nursing we strive to keep patients comfortable and pain free, and so perhaps we should ask ourselves why it is so difficult for us to get this right in the smallest and most vulnerable of our patients.

Why are babies so challenging?

Pain management in the newborn is complicated for a number of reasons, not least of which is their inability to describe their pain. The experience of pain is subjective and in adults and older children, we rely on self-report to allow us to identify and quantify pain and to monitor the effectiveness of pain-relieving interventions. Since this is impossible in babies, we will never know precisely how the newborn baby perceives painful conditions or invasive interventions. However, it is reasonable to suppose that experiences reported as painful or distressing by articulate adults, would be similarly perceived by a preverbal infant. We have turned therefore to interpretation of infant behaviour to assist us in detecting their pain. However, the behavioural repertoire of the neonate is very limited and there is no single response or behaviour that we can attribute, with certainty, to the presence of pain. The situation becomes even more complex if we attempt to distinguish between different types of pain and quantify the severity. Finally, we still have much to learn about infants' responses to pain and about the risks and benefits of different methods of pain relief and how they are affected by gestation, postnatal age and severity of illness.

The effects of neonatal pain

From a purely humanitarian perspective, treating pain in newborn babies is a desirable aspiration, but appropriate pain management is important for a number of reasons other than the avoidance of distress and suffering. Many researchers have now described long-term adverse effects following prolonged or repeated exposure to pain in the neonatal period. Studies in both animals and humans have shown altered behavioural responses to

pain and these may persist through childhood and perhaps longer[3-8]. Interestingly, there appears to be a difference between term and preterm infants in their later responses following painful experiences in the neonatal period. Studies have shown that term-born infants who had circumcision without analgesia, and infants exposed to multiple heel pricks for measurement of blood sugar levels had exaggerated behavioural responses to later immunisation[7-8]. In contrast, preterm infants who experienced neonatal intensive care were reported by their parents to be less sensitive to pain than their peers[6]. These effects are likely to be as a result of stressful procedures occurring during a critical period of anatomical and physiological development of the brain and nervous system[9].

Assessment of pain

Most research in neonatal pain assessment has centred mainly on acute pain. There are now more than 40 clinical tools available to allow assessment of the presence and severity of pain associated with invasive procedures[10]. Most use a scoring system; some are used clinically at the cot side while others are more frequently used in research studies. Behavioral indicators and in particular, facial expressions, appear to be the most specific indicators of pain and have been included in most tools[11,12]. Some have combined these with physiological indicators such as heart rate and oxygen saturation to develop multidimensional scores[13].

In contrast, there are relatively few validated tools designed for measurement of the ongoing or 'chronic' pain that might be experienced during prolonged mechanical ventilation or inflammatory conditions such as necrotising entero-colitis. It may be that responses to this sort of pain are different from those to acute pain or indeed that responses may change with the duration and progression of pain, but they have been much less studied. The lack of such tools probably reflects our poor understanding of these responses to chronic pain and the difficulties associated with observation and interpretation of an infant's condition over a prolonged period of time rather than in relation to a short-lived painful intervention[14]. To date, the EDIN (Echelle Douleur Inconfort Nouveau-Né)[15], the N-PASS (Neonatal Pain, Agitation and Sedation Scale)[16], and the COMFORTneo[17] are the only ones in existence and none is widely used.

There are, however, inherent difficulties in using pain scores. Physiological indicators such as increase in heart rate or blood pressure lack specificity for pain and may often occur as a result of other conditions; different methods of securing endotracheal tubes may distort or obscure facial features, limiting their use in ventilated babies. In addition, it is difficult to differentiate between pain and agitation and the effects of analgesia versus sedation, especially in critically ill infants in whom severity of illness may further complicate assessment.

Research to identify novel methods of detecting and quantifying chronic pain in neonates is ongoing. Investigators continue to build on the knowledge of behavioural responses[14,18]. It is likely that, in coming years, the use of non-invasive techniques, such as near infrared spectroscopy, may provide greater insight into more specific pain indicators[19].

Management of pain

Of course, prevention is better than cure and it is clear that we must avoid non-essential painful procedures. Limiting invasive interventions to the absolute minimum required for the safe medical management of the baby is central to good clinical practice. Nevertheless, there are frequent occasions when invasive procedures are clinically indicated even though they may be potentially distressing for the infant. The choice of procedure or methods used may be important. For example, venepuncture appears to be less painful than heel prick and heel prick using a spring-loaded mechanical device is less painful than using a manual lancet[20].

A number of non-pharmacological measures have been studied, as well as drug therapies, and all may be useful in managing pain. These are summarised below.

Behavioural and environmental (non-pharmacological) measures

Skin-to-skin contact between mothers and babies (kangaroo care) has been shown to be effective in reducing pain responses associated with heel prick. Breastfeeding during a painful procedure has also been reported to have analgesic effects[21]. It is difficult to be sure how much is contributed by each of the individual components involved in breastfeeding – milk, holding, comforting and suckling. One randomised placebo-controlled trial found that breast milk significantly decreased pain responses and crying time associated with venepuncture in term neonates[22]. Animal studies have suggested that analgesic effects of milk may be opioid mediated and related to the sugar content[23]. For mothers who feel able to be present when their baby is having a painful procedure these may be appropriate, simple and safe options for pain relief. However, parents are not always present to comfort or feed babies during invasive interventions and, understandably, many prefer to avoid watching painful procedures. Other behavioural measures that can be administered by staff caring for babies have therefore been studied.

The simplest interventions that have been shown to promote physiological stability during painful procedures are handling techniques such as containment, swaddling and facilitated tucking[24]. Non-nutritive sucking on a dummy/pacifier, either alone or in combination with sucrose, has also been the subject of research and has been shown to reduce pain responses[25]. Concerns have been raised about the possibility of non-nutritive sucking adversely affecting the establishment of breastfeeding in preterm babies. A recent study found no evidence to support withholding dummies/pacifiers on these grounds[26].

Pharmacological measures

Sucrose

Sucrose has been extensively studied[27]. For many years sweet solutions have been known to have a calming effect in crying babies. The mechanism of action of sucrose has not been fully defined, but it may be mediated by the activation of endogenous opioids; sweet taste appears to be important. A Cochrane Review concluded that intraoral sucrose reduces procedural pain in neonates[28]. It has been shown to decrease the duration of crying and reduce behavioural responses in babies having heel prick or venepuncture and, for these procedures, is more effective than the use of topical local anaesthetic creams[29]. A wide range of volumes and concentrations has been investigated and the optimal dose has not yet been determined; doses between 0.012g-0.12g were effective[28]. The analgesic effect of sucrose appears to peak at around two minutes after administration into the mouth and last for several

minutes. Most work has been done in infants of more than 27 weeks' gestation. No adverse effects have been reported with administration of single doses of sucrose.

Studies of the long-term effects are very few, and only one has studied neurodevelopmental outcomes[30]. This study showed worse motor development and attention at 36-40 weeks of gestation in babies born at <31 weeks of gestation who had repeated sucrose doses. Potential mechanisms for effects of sucrose on development have been suggested[31] and further work is needed to assess the long-term effects of sucrose therapy.

A recent study by Slater et al measured brain and spinal cord activity in babies given sucrose and showed that, although sucrose reduced observed pain behaviour in these babies, it did not have any significant effect on spinal pain reflexes or activation of pain networks in the brain[32]. This led the authors to question whether sucrose is, in fact, an effective analgesic or whether its only effect lies in the blunting of behavioural responses.

Although these studies raise questions about both the efficacy and safety of sucrose, the evidence is insufficient to inform practice and therefore sucrose currently remains one of the treatments of choice for the pain of minor invasive procedures.

Opioid analgesia

Opioids are the most extensively studied pharmacological analgesic agents used in neonatal intensive care and morphine is probably the most commonly used. It is a potent analgesic, suitable for severe or prolonged pain and also has sedative properties, which can be desirable in some babies. Opiates also carry with them undesirable effects such as hypotension[33,34], decreased gut motility[35] and increased duration of ventilation[36]. The effects of morphine on acute procedural pain in preterm ventilated neonates have been studied and morphine does not appear to provide adequate analgesia[37]. Routine pre-emptive use of continuous opiate analgesia in sick, ventilated preterm neonates is not recommended[38]. Opiate withdrawal is well recognised in older children and adults and in infants exposed to drugs *in utero*. Withdrawal following therapeutic doses of opiates has been little studied in neonates, but signs consistent with withdrawal have been observed in babies after a relatively short duration of treatment[39].

Paracetamol

Paracetamol is commonly used in term babies thought to have acute pain following an invasive procedure or traumatic delivery. Until recently, it has been used less frequently in preterm infants in the UK. An intravenous preparation is available that is suitable for intermittent administration in ventilated neonates. However, its safety and efficacy have not been fully evaluated in the preterm population[40] and pharmacokinetic studies are ongoing.

Conclusion

It is now widely accepted that pain relief is a crucial part of the management of babies in the neonatal unit. There are a large number of different measures for pain control available, ranging from simple holding techniques to potent analgesic medications. In all decision-making it is important to ensure that the chosen treatment or preventive measure is appropriate for the type of procedure and degree of discomfort likely to be experienced. It is always preferable to start with simple measures first and, in some cases, drug therapy can be avoided altogether. Should medication be required, the safest strategy, as with any drug, is to use the minimum dose that is effective in achieving the desired response. There are risks and benefits to all therapies and these must be fully considered, with the aim of maximising comfort while minimising adverse effects.

Achieving optimum pain management in neonatal intensive care is challenging, particularly with respect to chronic pain, which is extremely difficult to assess and quantify. Our knowledge remains limited and further work is needed to explore infant responses to pain further, to maximise efficacy and safety of treatment, and to optimise short- and long-term outcomes for babies.

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