

# Commentary

## Pain relief in Neonates: No Doubt it's a Duty

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### Introduction

Pain is the most common complaint for which a patient presents to a physician. Pain management in neonate warrants special consideration because the present knowledge of developmental neuro-physiology has been enriched. With the advancement of various surgical techniques and improved peri-operative care, more and more sick neonates undergo surgery and optimum peri-operative pain management may improve outcome.

### Why should pain in neonate be treated?

Neonates in a hospital are routinely subjected to various degrees of painful procedures from very early in their lives ranging from venipuncture to major surgery. Apart from ethical reasons and expectation of the parents, there are several long term and short term effects of poorly managed acute pain in neonate.

Neonates, even the premature ones feel pain and elicit stress response. This was first scientifically described in a landmark study by Anand et al<sup>1</sup> in 1987. Blunting the stress response with fentanyl was associated with improved outcome. Subsequently in 1992, Anand et al<sup>2</sup> showed that management of postoperative pain after cardiac surgery by potent opioids was associated with improved outcome. The stress response, activated by afferent neuronal impulses from the site of injury, was found to be greater in magnitude but shorter in duration in neonates compared with adults during the same surgeries. The stress response initiates a series of metabolic changes leading to catabolism of protein, fat and carbohydrate. In premature or sick infants, this might cause metabolic acidosis, hypoglycemia, hyperglycemia and electrolyte imbalances leading to increased morbidity and mortality<sup>3</sup>.

Altered and heightened pain responses in subsequent painful procedures are most common long term effect<sup>4</sup> and this may persist till adolescent life. A proper analgesic regimen may prevent heightened pain response. Behavioral response may also be altered by stress exposure in the Neonatal Intensive Care Unit (NICU)<sup>5</sup>. Current consensus is that neonatal pain must be managed regardless of their age and severity of coexisting illness<sup>6</sup>.

### Neonates feel more pain than their older counterpart

Clinical and laboratory investigations of neonatal pain suggest that preterm neonates have an increased sensitivity to pain<sup>7</sup>. Anatomic studies have shown that the density of nociceptive nerve endings in the skin of newborns is similar to or greater than that in adult skin<sup>8</sup>. Lack of myelination was suggested as an argument to support the hypothesis that neonates are not capable of perceiving pain. However, nociceptive impulses in the peripheral nerves are conducted through unmyelinated (C- fibers) and thinly myelinated fibers (A- fibers)<sup>9</sup>. Lower pain threshold and the lack of inhibitory controls contribute to hypersensitivity in the most premature neonate. Repeated tactile stimulation leads to a significant lowering of the threshold (sensitization) in neonates up to 35 weeks postconceptional age<sup>10</sup>. The low pain threshold in preterm neonates is accentuated by an increased excitability of nociceptive neurons in the dorsal horn of the spinal cord after exposure to any painful stimulus (wind-up phenomenon). In neonate, prolonged activity in the nociceptive pathways may be perceived as chronic noxious stimulation.

### Strategy

Appropriate pain management plan should be formulated and communicated to the parents to minimize their anxiety. Unnecessary laboratory investigations should be avoided to minimize pain associated with invasive procedures. Fasting period beyond the stipulated guidelines should not be extended to avoid unnecessary discomfort. Patient's present clinical conditions, presence of other co-existing medical illness, nature of the surgical procedure to be done and the area where the neonate will be managed in the postoperative period should be taken into consideration.

For blood sampling, heel is preferable, as it is less painful and mother should be encouraged to breast feed the baby whenever feasible or sucrose solution should be used. However topical local anesthetic cream (Eutectic mixture of local anesthetic; EMLA) may be used during venous/ arterial puncture and peripherally inserted central catheter (PICC) insertion in neonates aged more than 26 weeks and it is safe in single dose<sup>11</sup>. Neonates undergo a variety of surgeries ranging from simple herniotomy to major thoraco-abdominal

surgery. The analgesic regimen should also vary according to the severity of surgical trauma and depends upon where the baby is being managed in the postoperative period.

The options of postoperative pain management range from simple analgesics like paracetamol to central neuraxial block like caudal or epidural. However, anesthesiologist should remember that a neonate is not a 'small child'. There is immense anatomical and physiological uniqueness in a neonate that affects the pharmacodynamics and pharmacokinetic characteristics of drugs to a considerable extent.

Paracetamol has long been known to be an effective analgesic in pediatric populations. Its efficacy in mild to moderate pain in neonate is now well documented<sup>12</sup>. It may be used in oral or per rectal route; however, for severe pain it may be used in intravenous route for its opioid sparing effects. But, at this moment, the use of intravenous paracetamol in preterm neonates with a postconceptual age (PCA) of less than 32 weeks may not be justified before further pharmacokinetic/pharmacodynamic studies are conducted<sup>13</sup>.

Robust data on use of NSAIDs in neonates are lacking till today. In the absence of prospective randomized controlled trials, at this time routine use of NSAIDs in neonates cannot be recommended<sup>14</sup>.

Opioids are the mainstay of pain management following major surgery including in neonatal population. Morphine is the most commonly used opioid in the postoperative period and fentanyl is also being increasingly used. However, opioids exhibit narrow therapeutic window between analgesic doses and the dose that may cause respiratory depression. Neonates receiving opioids should have continuous pulse oximetry monitoring and should be managed in a setting where rapid intervention for airway management is possible, because respiratory-rate monitoring alone may be an inadequate predictor of impending apnea<sup>15</sup>.

Epidural analgesia has been investigated as a modality of pain relief after major surgery. The most important consideration in central neuraxial block in neonates is the safety and possibility of inadvertent injury to the developing spinal cord. Serious complications including neurologic injury has been reported in neonates and many authors have mentioned that only experienced pediatric anesthesiologist should perform central neuraxial block in neonate<sup>16</sup>.

## Conclusion

Despite various opinions regarding methods of optimum postoperative pain management in neonate, there is little doubt that neonates feel more pain than their older counterpart. Intravenous opioids with the use of morphine or fentanyl remains the most common modality of neonatal pain management and the role of paracetamol in decreasing opioid requirement seems to be promising. Though ketorolac appears to be safe, larger studies are required before its routine use can be recommended. Epidural analgesia/anesthesia when

performed in experienced hand is quiet safe and poses several benefits over systemic opioids. Where technical and logistic feasibility is present, it may be a logical option as a part of balanced anesthesia technique.

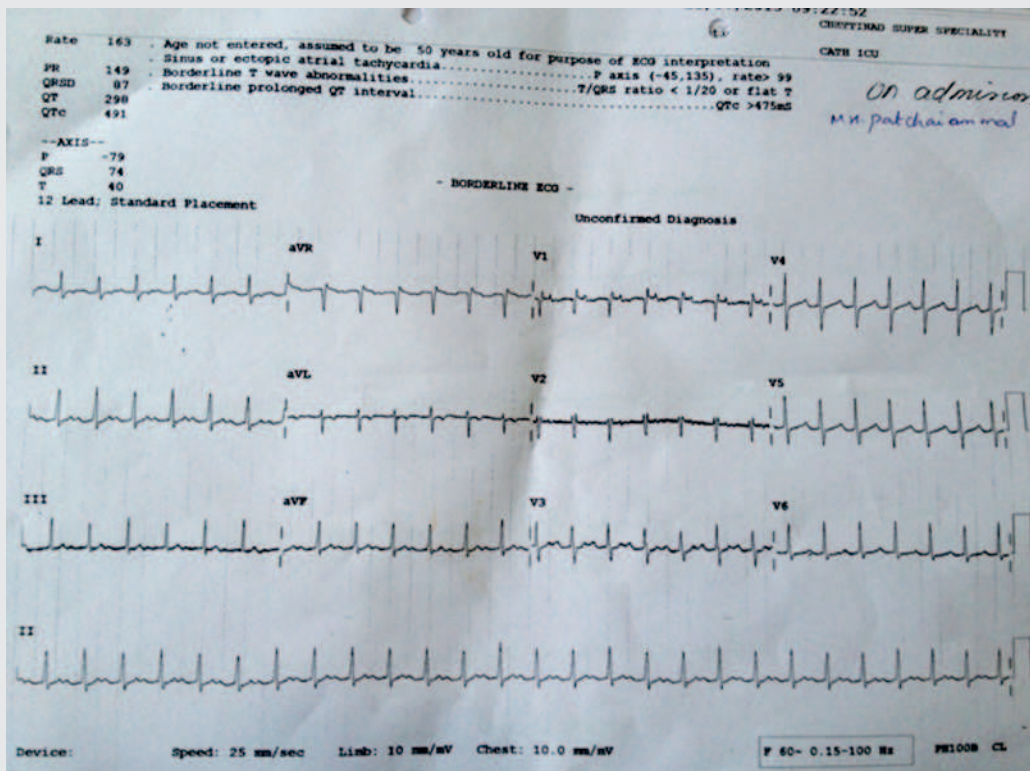
## References

- 1) Anand KJ, Sippell WG, Aynsley-Green A. Randomised trial of fentanyl anaesthesia in preterm babies undergoing surgery: effects on the stress response. *Lancet*. 1987 Jan 31;1(8527):243-8.
- 2) Anand KJ, Hickey PR. Halothane-morphine compared with high-dose sufentanil for anesthesia and postoperative analgesia in neonatal cardiac surgery. *N Engl J Med*. 1992;326:1-9.
- 3) Goldman RD, Koren G. Biologic markers of pain in the vulnerable infant. *Clin Perinatol* 2002;29:415-25.
- 4) Grunau RE, Oberlander TF, Whitfield MF, Fitzgerald C, Lee SK. Demographic and therapeutic determinants of pain reactivity in very low birth weight neonates at 32 weeks' postconceptional age. *Pediatrics*. 2001;107:105-12
- 5) Grunau RE, Holsti L, Haley DW, Oberlander T, Weinberg J, Solimano A, et al. Neonatal procedural pain exposure predicts lower cortisol and behavioral reactivity in preterm infants in the NICU. *Pain*. 2005;113:293-300
- 6) Anand KJ; International Evidence-Based Group for Neonatal Pain. Consensus statement for the prevention and management of pain in the newborn. *Arch Pediatr Adolesc Med*. 2001;155:173-80.
- 7) Anand KJ. Clinical importance of pain and stress in preterm neonates. *Biol Neonate*. 1998;73:1-9.
- 8) Gliess J, Stuttgen G. Morphologic and functional development of the skin. In: Stave U, editor. *Physiology of the Perinatal Period*, Vol. 2. New York: Appleton-Century-Crofts; 1970. pp 889-906.
- 9) Bouza H. The impact of pain in the immature brain. *J Matern Fetal Neonatal Med*. 2009;22:722-32.
- 10) Grunau R. Early pain in preterm infants. A model of long-term effects. *Clin Perinatol*. 2002;29:373-94
- 11) Taddio A, Ohlsson A, Einarson TR, Stevens B, Koren G. A systematic review of lidocaine-prilocaine cream (EMLA) in the treatment of acute pain in neonates. *Pediatrics*. 1998;101:E1.
- 12) Ceelie I, de Wildt SN, van Dijk M, van den Berg MM, van den Bosch GE, et al. Effect of intravenous paracetamol on postoperative

- morphine requirements in neonates and infants undergoing major noncardiac surgery: a randomized controlled trial. JAMA. 2013;309:149-54
- 13) Van den Anker JN, Tibboel D. Pain relief in neonates: when to use intravenous paracetamol. Arch Dis Child. 2011;96:573-4.
- 14) Aldrink JH, Ma M, Wang W, Caniano DA, Wispe J, Puthoff T. Safety of ketorolac in surgical neonates and infants 0 to 3 months old. J Pediatr Surg. 2011;46:1081-5.
- 15) Anand KJ, Hall RW, Desai N, Shephard B, Bergqvist LL, Young TE, et al. NEOPAIN Trial Investigators Group. Effects of morphine analgesia in ventilated preterm neonates: primary outcomes from the NEOPAIN randomised trial. Lancet. 2004;363(9422):1673-82.
- 16) Bösenberg AT, Jöhr M, Wolf AR. Pro con debate: the use of regional vs systemic analgesia for neonatal surgery. Paediatr Anaesth. 2011;21:1247-58.

### Diagnose the Condition

55 years old post menopausal female is known case of RHD – Severe MS, S/P CMV (2009), S/P BMV at CHRI on regular follow up, presented to us with complaints of Acute onset of palpitation. ECG taken taken is given below.



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