

## Opioid free anesthesia in a pre-term neonate: A case report

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### ABSTRACT

Opioids play a major role in the perioperative management of pain in adults and children. Though there is significant morbidity and mortality associated with overdosage of opioids, they remain the most common means of providing analgesia in the perioperative period. We report the case of a preterm neonate born with low birth weight who underwent high sigmoid loop colostomy for high anorectal malformation using opioid-free general anesthesia with supplementation with caudal block. Successful uncomplicated extubation of preterm baby was achieved with good spontaneous efforts. Opioid free general anesthesia can prevent respiratory depression and the need for postoperative mechanical ventilation even when given to preterm neonates.

**Keywords:** Anesthesia, Caudal block, Opioid, Preterm neonate.

Pain pathways are fully developed before birth and neonatal pain stimulus may lead to stress responses such as hypoglycemia or hyperglycemia, electrolyte imbalance, and metabolic acidosis. These lead to increased neonatal morbidity, poorer neurodevelopmental outcomes and even mortality [1]. Therefore, neonatal anesthesia requires adequate pain management during the perioperative period.

Opioids play a major role in the perioperative management of pain in adults and children [2]. Morbidity associated with overdosage of opioids, especially over 20ng/mL in blood, can be as high as 67% [3]. They still remain the most common means of providing analgesia in the perioperative period. A study was conducted by Sale et al in 2006 in 30 infants born prematurely under 37weeks of gestation operated for inguinal herniotomy using general anesthesia with desflurane or sevoflurane and caudal block as a mainstay for pain management thus avoiding opioids [4]. We hereby report a case of 28 weeks preterm neonate, weighing 1000gms, operated for exploratory laparotomy using opioid-free anesthesia by providing multimodal analgesia with caudal block and acetaminophen.

### CASE REPORT

A male preterm baby was born at 28weeks to Indian parents, who presented on 2<sup>nd</sup> day of life with complaints of non-passage of meconium. The baby was born of a normal vaginal delivery at home at 28 weeks of gestation. Baby's weight was 1000gms and was alert, active and afebrile. His pulse rate was 120/min, blood pressure-60/32 mm-Hg and SpO<sub>2</sub>- 93% on room air. The chest was bilaterally clear and no murmurs were auscultated.

The neonate's blood investigations showed Hemoglobin is 12g/dL., white blood cells-3400/mm<sup>3</sup>, platelet count-144,000/mm<sup>3</sup>, serum sodium-128meq/l and serum potassium- 5.6meq/l. He was diagnosed as a case of high anorectal malformation and was taken up for high sigmoid loop colostomy under general anesthesia. Risk assessment was done and duly explained to the parents in view of prematurity, low birth weight and non-availability of bed in the pediatric ICU in case of requirement of postoperative elective mechanical ventilation.

The operation theatre was prewarmed to a temperature of 26° C. The patient's limbs were covered in cotton to prevent hypothermia. A 24G intravenous (IV) access was established. The patient was operated under general anesthesia with opioid-free induction combined with regional anesthesia. The patient was pre-oxygenated with 100%O<sub>2</sub> and induced with IV thiopentone 5mg and IV atracurium 0.5mg. The airway was secured with uncuffed endotracheal tube number 2 and fixed at 8cm mark. Anesthesia was maintained with oxygen and air, 50% each, and sevoflurane 0.8%. After general anesthesia, the patient was turned lateral and a caudal block was given with a 26G hypodermic needle with 1ml of 0.25% plain bupivacaine. Ventilation was controlled to maintain an EtCO<sub>2</sub> 40-45 mm-Hg using the Jackson Rees circuit. A high sigmoid loop colostomy was performed. The patient was extubated after giving IV neostigmine 50 µg and IV glycopyrrolate 10 µg. The use of opioid was avoided during the entire procedure so as to facilitate early and easy extubation. IV paracetamol 7.5mg was given for pain relief as part of a multimodal analgesia regimen. After the return of spontaneous efforts and activity, the patient was extubated and shifted to a nursery for observation.

After 48 hours, the neonate was healthy and was shifted to the ward thereafter. The patient will be taken up for posterior sagittal anorectoplasty at 3 months of age and for the closure of stoma at 6 months of age. Informed written consent was taken by the parents regarding the case report publication.

## DISCUSSION

Pain can be managed in neonates either by using pharmacological agents like acetaminophen, non-steroidal anti-inflammatory drugs (NSAIDs) and opioids or by using regional techniques like a caudal epidural, spinal etc. or by a combination of both [5,6]. Opioid-related side effects include respiratory depression, tolerance, ileus, urinary retention and pruritus. To protect this vulnerable group from the above-mentioned side effects, we need to devise a pain management plan best suited to the individual and multimodal analgesia has to be administered. To decrease opioid-related side effects, the pain has to be managed by a variety of techniques [3].

Paracetamol (N-acetyl-p-aminophenol, acetaminophen, APAP) is the safest and a commonly used drug in infants and neonates to treat pain or to supplement opioid analgesia [5,6]. Since it had been available in oral form for a long time, its safety profile is well-known and well-studied. It inhibits prostaglandin secretion in the hypothalamus via inhibition of cyclooxygenase [7]. Hepatic toxicity from an overdose of acetaminophen and accumulation of the metabolite N-acetyl-p-benzoquinone imine (NAPQI) is very uncommon in infants because they have an immature function of P450 enzyme, specifically CYP2E1, and make much lower concentrations of this metabolite [3]. Paracetamol is commonly used to reduce opioid exposure as part of multimodal analgesia. It has analgesic, antipyretic and modest peripheral anti-inflammatory properties [8-10].

NSAIDs are important in the treatment and prevention of mild or moderate pain in children [11]. However, NSAIDs should be avoided in children less than 6 months of age because of the immature hepatic enzyme system and decreased glomerular filtration rate (GFR). NSAIDs in combination with paracetamol produce better analgesia than either alone [12]. Other contraindications include children with aspirin or NSAID allergy, those with dehydration or hypovolaemia, children with renal or hepatic failure, or those with coagulation disorders, peptic ulcer disease or where there is a significant risk of hemorrhage [11,13]. Mechanism of action is inhibition of cyclooxygenase which in turn inhibits the production of prostaglandins both in the periphery and central nervous system.

Neonates have a lower plasma clearance, a higher volume of distribution, decreased protein binding resulting in a greater free fraction and decreased renal clearance of opioids due to decreased GFR. Opioid pharmacokinetics also get altered by prematurity and acute illnesses [14-16]. Due to the immaturity of the blood-brain barrier, there is more possibility of water-soluble agents like morphine to cause respiratory depression. Due to unpredictable

pharmacokinetics and respiratory depression caused by morphine, drugs like fentanyl and remifentanyl which have fewer side effects, were brought into the picture. Since these two are metabolized by tissue esterases which are functional at birth so they were put to use. However, fentanyl and its derivatives carry risks of chest wall rigidity and bradycardia which further lead to cardiovascular and respiratory compromise [3].

Regional techniques like central neuraxial blocks, peripheral nerve blocks and local infiltration reduce anaesthetic drugs requirement, aid in postoperative pain management and subsequently reduce opioid exposure. Decreasing opioid exposure while maintaining the depth of anesthesia is desirable in neonates and infants [16]. Epidural blocks can reduce the chances of postoperative ventilation in procedures like trachea-oesophageal fistula [17]. The technical problems faced with pediatric regional anesthesia are: either inability to establish a block or failure to maintain the block. Infection, pressure area problems, peripheral nerve injury, local anaesthetic toxicity, and serious adverse effects of opioids are much rarer [18].

Caudal epidural anesthesia remains the most common technique of giving regional anesthesia to pediatric age group. This technique requires the placement of the needle through the sacrococcygeal ligament into the caudal epidural space. This technique acts as an adjunct to general anesthesia, for postoperative pain management or to replace general anesthesia. In our case, we used a single-shot technique with 0.25% bupivacaine with a dose of 1ml/kg. Other drugs like ropivacaine can also be used. The volume of the drug depends upon the height of the block required. It can vary from 0.75ml/kg- 1.5ml/kg. Lower volumes are used for surgeries involving penoscrotal region while higher volumes are used for upper abdominal and umbilical surgeries.

Care is to be taken not to exceed the toxic dose of a local anaesthetic drug used so as to avoid local anaesthetic drug toxicity. There is an increased risk of toxicity in preterm neonates because the hepatic microsomal enzyme system is not developed until 1-3 months of age. Also, there is decreased  $\alpha$ -1-acid glycoproteins as a result of which there is less binding and higher free fraction increasing the chances of toxicity [19].

We provided an effective analgesic cover combining good regional anesthesia assisted by paracetamol use, thus avoiding any serious opioid-related side-effects, even with a very low birth weight preterm baby. This helped us extubate the baby within a few minutes of ending the surgical procedure, saving post-operative morbidity to the neonate, along with valuable resources and ventilator requirements.

## CONCLUSION

Though opioids are very effective tool for analgesia, they come with a risk of serious side-effects. Avoiding them and using multimodal analgesia helped us to successfully conduct the anesthesia of preterm very low birth weight baby and have an extubated, active and pain-free baby at the end of surgery.

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