Continuous Epidural Analgesia in Neonates and Infants: Strategy for Success or Recipe for Disaster?

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Disclosures: This presenter has no financial relationships with commercial interests.

Stem Case and Key Questions Content
A 2-month old 4 kg infant is scheduled to undergo thoracotomy for resection of a paraspinal mass. The prenatal course and delivery were unremarkable. Vital signs are within normal limits. The intraoperative anesthesia plan includes inhalational induction, general anesthesia with endotracheal intubation and ICU recovery.

What options exist for post-operative pain? What cases are good candidates for epidural catheter insertion in neonates and infants?

The parents would like to know more about risks of epidural analgesia in “such a small” baby, how many procedures like this you have done, and if you had any complications.

What would you tell them? Are there any qualification requirements for providers who place epidural catheters in children? What approach would you take to the catheter insertion: caudal, lumbar or thoracic?

After obtaining consent for epidural, the patient is brought into the operating room, anesthetized and intubated uneventfully. Preparations are made for lumbar epidural placement. You are about to prep the skin, when the nurse informs you that chlorhexidine is not approved for patients younger than 2 months of age.

How would you ensure the safe insertion of the epidural catheter? What catheters and needles are available for pediatric patients?

After 3 attempts, the epidural space is identified at L4-5 via a midline approach using the loss of resistance to saline technique; however, there is difficulty in threading the catheter. The decision is
made to attempt instead the caudal insertion of a styletted wire-reinforced catheter, and advance the catheter tip to the thoracic level.

*How would you ensure proper positioning of the catheter tip? What would you do if despite your efforts, the catheter remained remote from the mid thoracic level?*

The epidural catheter is positioned at T8 with fluoroscopic guidance and the catheter is taped at 18 cm at skin. An epidural test dose is negative. Surgery proceeds uneventfully, until an hour later when you notice a gradual increase in the patient’s heart rate and blood pressure.

*Would you administer a bolus of local anesthetic through the epidural catheter? Would you start the epidural infusion? What local anesthetic would you use? Would you use any adjuvants?*

A 2 ml bolus of bupivacaine 0.25% and epinephrine 1:200,000 is injected via the epidural catheter. A few minutes later, the patient’s blood pressure decreases to 42/23, heart rate drops to the 80s, and soon after, the oxygen saturation decreases as well to low 80s.

*Can this be caused by local anesthetic toxicity or subarachnoid injection of local anesthetic? How would you manage such complications? What else could be causing the change in vital signs?* Following resuscitation, the patient’s vital signs return to normal. The rest of the surgery proceeds uneventfully, with anesthesia maintained with a combination of sevoflurane, fentanyl and rocuronium. At the end of the procedure, after discontinuation of inhaled anesthetics and reversal of muscular blockade, the patient continues to remain minimally responsive to stimulation and is not moving his extremities. His vital signs are: heart rate 156, blood pressure 79/41, oxygen saturation 100%, respiratory rate 25 (with controlled ventilation), and temperature 34.6°C.

*What is your differential diagnosis? Could this picture be explained by neurologic trauma caused by the epidural catheter insertion? What factors may have increased the risk of neurologic injury, or worsened the impact of trauma to the spinal cord and nerve roots?*

The patient eventually regains his strength, and is subsequently extubated and transported to the ICU in stable condition.

*What epidural infusion solution and rate would you choose for postoperative pain control?*

The epidural catheter is bolused with the epidural mix, and a continuous epidural infusion of bupivacaine 0.1% and fentanyl 2 mcg/ml at a rate of 0.4 ml/hour is initiated. After a couple of hours, you are called by the nurse because the patient is irritable. His vital signs are: blood pressure 85/49, heart rate 165, and his respiratory rate 32, and oxygen saturation 96% on 2 L/minute oxygen via nasal
cannula. The nurse is concerned that the catheter may be out because she noticed a fluid accumulation under the dressing. A few doses of intravenous morphine have been administered in the interim.

What is your evaluation and management strategy? How would you assess pain in infants? What is your plan if fussiness recurs?

Throughout the night, due to patient’s irritability the epidural infusion rate is increased to 0.8 ml/hour. On postoperative day 2, the tip of the epidural catheter is noted to be at the C7 level on the chest X-ray. The patient is hemodynamically stable, and comfortable, but the apnea monitors have gone off a few times, and the patient required stimulation in order to resume breathing.

What can explain the apparent migration of the epidural catheter? Are certain catheters more likely to migrate than others? How do you secure the epidural catheter in order to prevent migration? Would you pull back the catheter and re-tape it, or remove the catheter?

The epidural catheter is removed, and the patient’s pain is further controlled with a combination of opioids, ketorolac and acetaminophen. Everybody seems relieved that the epidural is out.

What intraoperative and postoperative strategies could increase the safety of the continuous epidural anesthesia in infants and small children? Are there any requirements in terms of qualification, experience, and immediate availability for the anesthesia providers following these patients in the post-operative period? What can be done to increase the competence and comfort level of the ICU staff in taking care of small children with epidural catheters?

Model Discussion Content
Despite the multiple benefits of central axial blocks, continuous epidural analgesia (CEA) in infants and neonates remains controversial. The advantages of CEA include decreased intraoperative requirements of anesthetics, better control of surgical stress response compared with opioids, earlier tracheal extubation, and return of gut function, improved postoperative analgesia, decreased ICU stay and length of hospitalization.

However, the use of CEA in neonates and infants has been questioned by some (1). In addition, in the context of current advances in surgical laparo- and thoracoscopic surgery, the use of CEA may decrease, with consequent decrease in opportunities for providers to maintain their expertise.
Indications
CEA has been used successfully in open thoracic surgery (e.g. tracheo-esophageal fistula, congenital diaphragmatic hernia, PDA ligation, Blalock shunt), and major intra-abdominal surgery (omphalocele, gastroschisis, intestinal atresia, tumors, cysts, bladder extrophy, malrotation).

Other pediatric pain control modalities include transverse abdominal plane (TAP) blocks, single-shot or continuous paravertebral nerve block, intercostal blocks, interpleural paravertebral block, and wound-infiltration techniques.

Contraindications for CEA include local skin infection, meningitis, bacteremia, neurologic disease, spinal or vertebral abnormalities, and non-consenting parents. Coagulopathy is a contraindication; however coagulation tests in neonates may be abnormal despite clinically adequate coagulation.

Anatomical considerations
In neonates and infants, the conus medullaris is located at L3, the intercristal line bisects the L5 vertebra, and the sacral hiatus is located more cephalad than in adults increasing the risk for dural puncture. The loosely packed epidural fat and lack of lumbar lordosis allow for relatively easy advancement of catheters from the caudal to the lumbar and thoracic levels. In infants up to the age of 6 months, the vertebral column remains cartilaginous, and epidural catheters can be visualized with ultrasonography. There is a subtler “give” as the ligamentum flavum is pierced. As a general rule the epidural space is found at 1 mm/kg of body weight. The bolus and infusion doses should be based on ideal body weight.

Pharmacological considerations
Neonates have reduced levels of plasma alpha1-acid glycoprotein (AAG) and albumin and therefore reduced binding of amide local anesthetics (LA), and an increased risk of LA toxicity. The hepatic metabolism of amide LA does not mature until 6 months of age. Pharmacokinetic studies in neonates show a significant increase in plasma bupivacaine levels after 48 hours of continuous epidural infusion. Esther LAs such as chloroprocaine are rapidly cleared even in young infants.

Risks associated with epidural analgesia
Some consider the risk of CEA too great in infants for use by individuals who do not have the requisite expertise, even despite the advent of ultrasound (1). However, data from the U.K. National epidural audit shows that CEA in neonates can be safely performed outside of major pediatric centers (2). The Pediatric Regional Anesthesia Network (PRAN) study (3) found no complications with long-term consequences, and identified short-term consequences such as catheter dislodgement or kinking, accidental dural puncture (0.9%), intravascular injection (2%) and local site infection (11%).

1. **Neurologic:** In the U.K. audit (2), of the 10,633 pediatric epidurals, there were 6 events of neurological injury, of which only one lasted over 12 months (cauda equina syndrome related to a drug infusion error). However catastrophic neurologic injury can occur as shown in a recent report of 4 cases from institutions where pediatric epidurals are placed regularly (4). Animal data suggest that manipulation with large bore styletted catheters in the epidural space can cause detectible damage to the spinal cord.

2. **Local anesthetic toxicity** can be caused by either intravascular injection of LA, or by excessive bolus or infusion doses. Cardiac dysrhythmia and apnea are more likely presentations in neonates and infants than convulsions. Agitation, restlessness and myoclonic movements may be confused for unrelieved pain. Intravenous intralipid (20% in a dose of 1-1.5 ml/kg every 3-5 min for a total dose of 3 ml/kg, followed by an infusion at a rate of 0.25 - 0.5 ml/kg/min) can be lifesaving.

The inadvertent intravascular administration of an epinephrine test dose (0.5-1 mcg/kg epinephrine) is signaled by an increase in the heart rate, hypertension or changes in T-wave appearance on the electrocardiogram. A negative test dose reduces, but does not eliminate the possibility of intravascular injection.

3. **Infectious:** Catheter tip colonization occurs in 20-37% of caudal catheters, whereas it is seen in only 4 % of catheters placed from the lumbar approach. The UK prospective audit reported 2 epidural abscesses and a child with meningismus. The risk of infection can be decreased by subcutaneous tunneling of the catheter. Alcohol-based chlorhexidine disinfectants are more effective than providone iodine for reducing skin colonization. Although cases of severe arachnoiditis potentially related to the used of chlorhexidine for skin disinfection have been reported, a recent retrospective study showed no
adverse effects after neuraxial anesthesia with chorhexidine antisepsis (5). Because of limited safety data, chlorhexidine is not approved in children less than 2 months of age.

4. **Catheter migration**: Migration of epidural catheters may occur in 40% or more cases, and it may result in perforation of dura, intravascular migration, high thoracic or cervical administration of epidural solution, or catheter dislodgement. Cephalad migration may occur after change from prone or lateral to supine position. Compared to firm inelastic epidural catheters, the more stretchy and elastic Arrow Flex-Tip catheter may be more likely to migrate in active patients by gripping motion of ligamentum flavum (6). Leakage around the catheter can loosen the sterile dressings and cause premature removal of the catheters. Techniques of catheter fixation proved to decrease leakage or migration include use of Dermabond®, Mastisol®, Steri-strips®, commercial fixation devices, and catheter tunneling.

5. **Hemodynamic effects and total spinal anesthesia**
Due to the lack of sympathetic system maturity, cardiovascular stability is maintained even following high thoracic anesthesia in neonates and infants. Hypotension should prompt anesthesiologists to rule out total spinal anesthesia, intravascular injection, hypovolemia, decreased cardiac contractility, or excessive depth of anesthesia.

**Techniques**
The midline approach is recommended for small children. Loss of resistance to saline is almost universally recommended due to the risk of embolism and neurologic injury with air injection.

**Caudal approach:**
For caudal approach, recommended needles are Crawford or a regular 18 G intravenous catheter. Due to the lack of lumbar lordosis in non-walking infants, it is easy to advance the tip of the catheter up to the thoracic level. Because catheters threaded from the caudal space do not behave in a predictable way, placement verification is necessary.

**Lumbar approach:**
Lumbar-to-thoracic catheter placement is rarely successful, and this route is less preferred in
neonates. For lumbar catheters, analgesia in the thoracic area may be improved by increasing the volume of epidural infusion or administering morphine epidurally.

Thoracic approach:
Due to a higher risk in neonates and small infants with this approach, direct thoracic epidural placement should be reserved for anesthesiologists very experienced with this technique.

Methods of verification of catheter tip position

1. Radiographic: The use of a radio-opaque catheter facilitates the placement of the catheter tip, whereas the injection of contrast through the catheter helps identify the subdural and intravascular placement, and predict analgesic coverage. The disadvantages are cost, and radiation and contrast exposure.
2. Nerve stimulation-guided (Tsui technique): As the catheter is advanced, the operator is able to follow the muscular response. This technique can also detect subarachnoid placement.
3. Ultrasound-guided: This method provides real-time visualization the catheter tip during the cranial advancement of the catheter. However, the technique is demanding, requiring the help of an “experienced third arm”, and it is difficult to find good working space during the performance of the block.

Equipment
Thinner catheters are more difficult to thread than larger ones, but larger catheters may cause more trauma (7). Adult-size catheters may be too large for premature infants. The most common catheters used in neonates are a 21-G catheter (via 19-G Tuohy needle), and a 23-G catheter (via a 21-G Tuohy needle).

Loading volume
In general, the loading volume is 0.05 ml/kg/dermatome. The number of segments is counted in one direction from the catheter tip. For mid-thoracic catheters the loading volume should be reduced by 50%. Fentanyl (0.5-1 mcg/kg), morphine (10-30 mcg/kg) or hydromorphone (1-3 mcg/kg) may be administered, with the caveat that in neonates, and especially with the catheter tip at the thoracic level, they may cause respiratory depression.

Choice of infusions
Children often require LA doses near the maximum acceptable. The first step in planning an epidural infusion is to determine the maximal amount of acceptable LA that may be infused per hour. Typical infusion rates are 0.2-0.4 ml/kg/hr for lumbar catheters, and 0.1-0.15 ml/kg/hr for thoracic catheters. It may be necessary to reduce the planned concentration of a LA in order to keep the total dose to an acceptable amount.

- **Bupivacaine (0.1%)** infusions should be restricted to less than 0.2 mg/kg/hr in infants less than 4 months, and 0.4 mg/kg/hr in children older than 4 months for no longer than 48 hours.
- **Chloroprocaine (1.5% at 0.5-1 ml/kg/hr)** is particularly useful in patients requiring wide dermatomal coverage, and in patients with decreased hepatic function.
- **Ropivacaine 0.1%** causes less motor block than bupivacaine, and can be used at maximum rates of 0.3 mg/kg/hr (<4-6 months), and 0.4 mg/kg/hr (>4 months), usually for no longer than 48 hours.
- **Lidocaine** (maximum infusion rate 1 mg/kg/h) has the advantage that its plasma levels can be monitored. Rapid development of tolerance limits its use.
- **Levobupivacaine** causes less toxicity than bupivacaine, and can be used in doses similar to racemic bupivacaine.

**Opioids:** In infants, fentanyl 2 mcg/ml is usually used. Because of higher cephalad spread, the use of hydro-soluble opioids should probably be restricted to infants over the age of 6 months.

**Clonidine:** In very young infants, use of clonidine has been associated with apnea, hypotension and excessive sedation. Clonidine is rarely used in neonates. The typical dose and concentration of clonidine in epidural solutions is 0.1-0.2 mcg/kg/hr and 0.4-0.5 mcg/ml, respectively.

**Postoperative monitoring**
Assessment of pain in infants can be quite difficult. Irritability/agitation may occur despite an apparently well-functioning epidural, and may be caused by the presence of intravenous lines, nasogastric tube, urinary catheter, or even the hospital environment. Satisfactory sedation may be achieved with intravenous administration of opioids, or by adding clonidine to the epidural infusion.

The epidural catheter functionality can be tested by injecting radio-contrast dye which can be detected on chest radiograph, or by administering Chloroprocaine (3%, 0.2 ml/kg increments, up to 0.8 ml/kg total). Alternatively, lidocaine (0.5-1%, 3-5 mg/kg) may be used, but caution should be taken not to exceed maximum allowable doses for amide LAs. If pain is not well controlled, a bolus equal to the volume of a one-hour infusion may be administered and the infusion rate increased by 20%.
Strategies for success:

- choose the correct indication for CEA
- exclude contraindications
- abort catheter placement when “difficult”
- use age appropriate equipment
- verify catheter position
- scrupulous asepsis
- consider tunneling the catheter
- precautions to avoid drug errors
- use best drug, appropriate loading lose and lowest rate
- identify a maximal infusion rate
- ensure high-quality postoperative monitoring and management
- limit duration of use and remove as soon as possible
- provide training to staff
- ensure detailed protocols for postoperative management
- perform regular audits of satisfaction, efficacy and complications

Conclusions
Epidural analgesia remains one of the cornerstones of high-quality analgesia for neonates and infants undergoing major surgery. Scrupulous attention to technique and detail, prudent patient selection and systematic measures to ensure safety in the postoperative period are essential for a good outcome.

References