

Epidural Analgesia in Infants and Children

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Epidural analgesia has widespread use in infants and children for postoperative pain management and for certain chronic pain conditions such as cancer pain and complex regional pain syndrome. While epidurals can provide excellent analgesia in pediatric patients, they do require specific expertise in both the techniques of placement and in the management. Pediatric-specific protocols and guidelines can increase the success of placement, optimize efficacy of management and increase overall safety. Pediatric-specific epidural protocols are directed at how to confirm correct catheter placement, which type of age-specific infusion to use and how much is safe, and how to treat side effects.

There are relatively few absolute contraindications for using epidural analgesia. Lack of parental or patient consent and infection at the insertion site are absolute contraindications. Relative contraindications are:

- Coagulopathy. Usually epidural analgesia is avoided in patients who have an ongoing coagulopathy however, data suggest a relatively low complication rate in performing lumbar punctures in cancer patient with mild thrombocytopenia. Epidural analgesia may be performed in select cases with infusion of platelets, fresh frozen plasma, or other blood products just prior to placement such as in cancer pain emergencies.
- Anatomic anomalies. Epidural analgesia is often avoided in patients with spina bifida and other lumbosacral anomalies due to technical difficulties with placement, disruption of the epidural space and erratic local anesthetic spread. Radiographs that confirm normal anatomy of spine and epidural space at the entry site may allow safe placement of epidural catheters. A neurologic exam should be documented prior to placement. Local anesthetic spread may be very unpredictable and careful dosing and monitoring is indicated.
- Hypovolemia. Epidural analgesia should not be performed in cases of severe ongoing blood loss and hypovolemia. Mild to moderate hypovolemia should be corrected prior to placement.

A unique difference between adults and children in placing epidural catheters is that most epidurals are placed after induction of general anesthesia, since most children will not tolerate needle procedures while awake. Although the safety track record of placement of epidural needles and catheters has been good in several published pediatric case series, there remains some controversy regarding the risk-benefit ratio, especially in thoracic epidural placement. It is generally accepted among experienced anesthesia providers that careful placement of a lumbar epidural catheter in an anesthetized child can be safer than an attempt in an uncooperative moving child. There is more controversy over direct needle placement of thoracic epidurals in anesthetized children, particularly in infants. As an alternative to direct thoracic needle placement in infants, a common technique is to advance an epidural catheter

from the caudal space to the desired thoracic surgical dermatome. Several studies have shown success in placing thoracic epidurals using this technique. Typically a blunt tip epidural needle is used to gain access to the caudal space. There are some concerns about using a sharp tip needle or angiocath to gain access for fear of inadvertent vascular puncture or needle puncture of the rectum or other nearby structures. Once the caudal space is safely entered, a 20 gauge epidural catheter is advanced to the desired surgical dermatome. Our preference at Children's Hospital Boston is to encourage some method of objective confirmation of catheter position since failure rates as high as 30% have been reported used a "blind" technique. There are three methods to confirm correct catheter position: 1) radiographic confirmation 2) electrical nerve stimulation using Tsui's technique and 3) ultrasound.

Confirming epidural catheter location can be accomplished by injecting a small amount of contrast dye such as Omnipaque-180® and obtaining a chest radiograph to locate the epidural catheter tip. Alternatively, the epidural catheter can be advanced cephalad to the thoracic level under direct visualization using continuous fluoroscopy. It is necessary to use a radio-opaque (wire-wrapped) catheter when using this technique. Electrical stimulation technique uses a saline-filled, wire wrapped catheter to which a small current is applied. Twitches are seen at the myotomal level of the catheter tip in a current range generally between 2 and 15 mA. As the epidural catheter is advanced cephalad, a progression of twitches is seen: ankle flexion with the catheter at the lumbosacral junction, knee extension at the midlumbar region, hip flexion when the catheter is upper lumbar, abdominal musculature contractions above T12, intercostal muscle contractions when the catheter is midthoracic, and hand twitches if the catheter reaches C8-T1. This technique can detect subarachnoid catheter placement since a catheter in the subarachnoid space will result in twitching in a broad distribution at very low current (< 0.5-1 mA.) Studies in adults suggest that epidural catheters tip located on the ipsilateral side of the surgical site results in improved effectiveness of epidural analgesia. Both techniques of radiographic confirmation and electrical nerve stimulation can detect epidural sidedness. Ultrasound guidance can be used to place and confirm epidural catheters in neonates and younger infants; this technique requires significant experience in ultrasound techniques. Neuraxial structures such as ligamentum flavum, dura, epidural space, and distance from skin to epidural space can be clearly visualized, in part because of incomplete ossification of the vertebrae in neonates and younger infants. In clinical areas outside of the operating room, it is sometimes necessary to check position of an epidural catheter when patient appears to be uncomfortable despite adequate epidural infusion rates. This can be particularly challenging in neonates and preverbal children. One method is to inject a small amount of radio-contrast dye which can be detected on chest radiograph. Another method is to use a "chloroprocaine test." Using chloroprocaine rather than amide local anesthetics to test previously placed epidural catheters is based on the rationale that since most patients will have received amide local anesthetics intraoperatively, additional amide local anesthetics to test the epidural catheter may cause serum amide local anesthetic levels to reach toxic levels. Injecting approximately 0.5 ml/kg of chloroprocaine (to a maximum dose of 15 ml for patients > 50kg) incrementally into the epidural catheter should result in a sensory and motor block if the catheter is in the epidural space. If the patient is hypertensive and tachycardic due to pain, then vital signs should return to baseline if the patient experiences improved analgesia with the chloroprocaine test dose, thereby supporting correct placement in the epidural space.

An understanding of age-related differences in local anesthetic pharmacology is necessary in choosing safe and effective epidural solutions. Neonates have reduced levels of

albumin and α -1-acid glycoprotein and therefore reduced protein binding of amide local anesthetics and other protein-bound drugs. Preterm infants have even lower levels of α -1-acid glycoprotein than term infants making them particularly susceptible to local anesthetic toxicity. Decreased levels of serum proteins lead to increased unbound, pharmacologically active drug and increased CNS and cardiotoxicity. Neonates and young infants have delayed maturation of hepatic enzyme systems involved in drug metabolism. Drugs that undergo liver metabolism such as opioids and amide local anesthetics have a prolonged elimination half-life, resulting in a narrow therapeutic index. The hepatic conjugation oxidation system in infants does not mature to adult functional levels until approximately 6 months of age. Pharmacokinetic studies in neonates receiving continuous bupivacaine infusions have shown a continuous rise in plasma bupivacaine levels after the first 48 hours. In the case of lidocaine, the predominant hepatic metabolite, MEGX, can accumulate in neonates with resultant risk of seizures. The limitations in safe local anesthetic infusion rates for amide local anesthetics have led to the use of chloroprocaine epidural infusions in neonates and younger infants. Although infants have reduced levels of plasma cholinesterase, ester local anesthetics are still rapidly cleared even in young infants.

Continuous epidural analgesia in infants and children generally consists of dilute solutions of local anesthetics combined with fentanyl, hydromorphone, and/or α 2 agonists such as clonidine. Bupivacaine is the most commonly used amide local anesthetic for epidural analgesia because it has a long duration of action with slightly greater selectivity of sensory block compared to motor block. Pharmacokinetic studies of bupivacaine in children over the age of 6 months have reported good safety for infusion rates below 0.4 mg/kg/hr with plasma bupivacaine levels in a safe range of 2-3 μ g/ml. For children less than 4-6 months of age, we restrict the dose of bupivacaine to 0.2 mg/kg/hr. Pharmacokinetic studies in neonates have shown that epidural bupivacaine infusion rates greater than 0.2 mg/kg/hr result in a continuous rise in serum bupivacaine levels after the first 48 hours with the potential for reaching toxic levels. Ropivacaine is along-acting amide local anesthetic shown in adults to have less CNS and cardiac toxicity and slightly more sensory selectivity when compared to bupivacaine. Pharmacokinetic studies in infants and children receiving single boluses of epidural ropivacaine show that clearance is reduced in infants. Overall, infusion rates of 0.4 mg/kg/hr in older infants and children and 0.2-0.3 mg/kg/hr in younger children appear to be safe. Chloroprocaine can be used in neonates and young infants to avoid concerns of decreased metabolism and clearance associated with amide local anesthetics. Chloroprocaine is rapidly metabolized in neonates and young infants with an elimination half-life of approximately 6 minutes and studies have shown good analgesia with no signs of neurotoxicity.

Neuraxially administered opioids have a synergistic analgesic effect when combined with local anesthetics. Due to the hydrophilic nature of hydromorphone, there is a slight preference to using hydromorphone for postoperative analgesia for surgical procedures involving multiple dermatomes. Because of the higher cephalad spread of hydromorphone and greater risk of respiratory depression, the use of hydromorphone should be restricted to infants over the age of 6 months. Fentanyl and hydromorphone are the most commonly used opioid in epidural analgesia. Morphine offers no particular advantage over hydromorphone and is associated with higher incidence of side effects, especially pruritus. All neuraxially administered opioids can cause side effects including nausea, vomiting, respiratory depression, urinary retention, pruritus, sedation, and constipation. The incidence of vomiting in patients receiving epidural fentanyl has been reported to be between 28% and 52% depending on the

population studies and the concentration of fentanyl. Kehlet and others have advocated multimodal approaches to postoperative analgesia that emphasize opioid-sparing in part because of the detrimental impact of opioid side effects on postoperative recovery. Opioid side effects occur by action at both peripheral and central sites. For example, opioid-induced nausea and vomiting involve activation of receptors in the brainstem and in the gastrointestinal tract. Pediatric-specific epidural management protocols allow for the rapid institution of opioid side effect treatments.

Clonidine is often added to epidural infusions as an adjuvant to improve analgesia without worsening pruritus, nausea, vomiting, and respiratory depression associated with opioids. Studies of caudal clonidine administered with bupivacaine showed prolongation of analgesia by 50-75% when compared with epidural bupivacaine alone. Pharmacokinetic studies of single-dose epidural clonidine in children show great variation in plasma concentration and a wide range for time for absorption from the epidural space. Single-doses of epidural clonidine above 1 µg/kg have shown prolongation of analgesia but greater incidence of sedation. Combining epidural clonidine with opioids frequently results in prolonged sedation, especially if doses above 1 mcg/kg are used. Our practice for children 1 year of age and older is to use 0.5-1 µg/kg (to a maximum dose of 15 µg) for single-shot caudal blocks and 0.12-0.16 µg/kg/hr for continuous epidural infusions. Children younger than 1 year should receive reduced dosages.

The published literature suggests that epidural complications are very rare however may result in serious morbidity and mortality. There are few published prospective trials on the safety of epidural blockade in children and a relatively small number of retrospective case and series reports. A retrospective study of the morbidity of regional anesthesia in 24,000 infants and children showed an overall complication rate of 1.5 adverse events /1000 procedures. The complications included: a) 8 dural punctures resulting in 4 spinal anesthetics and 2 post puncture headaches b) 6 intravascular injections with 2 patients experiencing cardiac dysrhythmias due to overdose of a mixture of bupivacaine and lidocaine in infants and 2 patients experiencing seizures c) 2 patients experienced transient parenthesis and d) 1 patient experienced delayed postoperative apnea due to an overdose of epidural morphine.

In a recent retrospective study of 10,000 epidural catheters used in over 7700 children, Sethna et al identified 13 cases of infections all of which occurred between days 3 and 11 after epidural catheter insertion... Of the 13 cases of infections, there were 9 cases of cellulitis, 2 cases of paravertebral muscular infections, 1 epidural inflammation, and 1 patient had an epidural abscess. The incidence of infection was significantly higher in patients treated for chronic pain ($7/216 = 3.2\%$) compared to postoperative pain ($6/10,437 = 0.06\%$) ($P < 0.0001$.) Surgical drainage of subcutaneous pus was performed in 3 patients and medical therapy was administered in the remainder of patients; all patients recovered without sequelae.

Because most epidural anesthesia techniques are performed in anesthetized or heavily sedated children, monitoring during the procedure is critical and every effort should be made to adhere to strict aseptic technique and basic principles of regional anesthesia. Careful monitoring during continuous infusions is also warranted. Caudal catheters have a higher incidence of colonization rate than lumbar or thoracic catheters. Tunneling caudal catheters may reduce colonization rates by almost 50%.

Epidurals can provide excellent and safe analgesia in infants and children for a variety of painful conditions. It is necessary to understand the pharmacokinetics of epidurally administered local anesthetics, opioids, and adjuvants in choosing the most appropriate

epidural infusion. Neonates in particular have reduced clearances of amide local anesthetics and have increased risk of respiratory depression from neuraxially-administered opioids. Although epidural complications rates are very low, monitoring is crucial both during catheter placement and during continuous infusions. Vigilance is important for the early diagnosis of epidural catheter-related soft tissue and epidural infections.

Table 1
Recommended Epidural Infusion Rates

Solution	(mL/kg/hr)*		
	<1 month	1-4 months	>4 months**
Bupivacaine 0.1% +/- Fentanyl 2mCg/mL +/- Clonidine 0.4 mCg/mL	Rarely used	0.2	0.4
Ropivacaine 0.1% +/- Fentanyl 2 mCg/mL +/- Clonidine 0.4mCg/mL	Rarely used	0.3	0.4-0.5
Bupivacaine 0.1% + Hydromorphone 10mCg/mL	Rarely used	Rarely used	0.3-0.4
Ropivacaine 0.1% + Hydromorphone 10 mCg/mL	Rarely used	Rarely used	0.3-0.4
Chloroprocaine 1.5% + Fentanyl 0.2 mCg/mL +/- Clonidine 0.04 mCg/mL	0.5 (mid thoracic) 0.6-0.7 (lumbar and low thoracic)	0.5 (mid thoracic) 0.6-0.7 (lumbar and low thoracic)	Rarely used Rarely used

*Infusion rates and solutions should be modified according to clinical circumstances. Little information is available on how best to adjust these rates based on degrees of prematurity. Rates shown reflect upper end of usual infusion rates, based largely on both systemic accumulation of local anesthetics and on expected extent of sensory and/or motor blockade. Solutions containing hydrophilic opioids such as hydromorphone may pose a higher risk for delayed respiratory depression, so appropriate frequency of observation and continuous electronic monitoring is recommended. Higher concentrations of opioids may be considered for selected patients who are opioid tolerant.

**Weight scaled infusion rates should plateau at values recommended for patients weighing around 45 kg, such as maximum infusion rates for larger patients should rarely exceed 15mL/hr.

Table 2
Management of Common Opioid Side Effects

Side effect	Comments	Drug dosage
Nausea	Consider switching to different opioid Use antiemetics Exclude other processes (e.g., bowel obstruction)	Ondansetron 10-30 kg: 1-2 mg intravenously q 8 h >30 kg: 2-4 mg intravenously q 8 h Naloxone infusion 0.25-1 mcg/kg/h Metoclopramide 0.1-0.2 mg/kg PO/intravenously q6 h
Pruritus	Exclude other causes (e.g., drug allergy) Consider switching to different opioid Use antipruritics	Nalbuphine 10-20 mg/kg/dose intravenously q 6 h Naloxone infusion 0.25-1 mcg/kg/h
Sedation	Add nonsedating analgesic (e.g., ketorolac) and reduce opioid dose Consider switching to different opioid	Methylphenidate 0.05-0.2 mg/kg PO Bid (morning and midday dosing) Dextroamphetamine 5-10 mg every day
Constipation	Regular use of stimulant and Stool softener laxatives	Naloxone infusion 0.25-1 mcg/kg/h Ducosate Child: 10-40 mg PO daily Adults: 50-200 mg PO daily Dulcolox Child: 5mg PO/PR daily Adult: 10mg PO/PR daily Methylnaltrexone dosing is extrapolated from adults

Bid, twice a day; PO, orally; PR, rectally; q, every

References

Giaufre, E., Dalens, B., and Gombert, A. Epidemiology and morbidity of regional anesthesia in children: a one-year prospective survey of the French language society of pediatric anesthesiologists. *Anesthesia & Analgesia* 1996; 83:904-912.

Greco C, **Berde CB**. Acute Pain Management in Children. In: Bonica's Management of Pain, 4th edition. J. Ballantyne, J. Rathmell, S. Fishman, editors, LWW, Philadelphia, 2010. Chapter 50. 681-698.

Greco, C. and C. Berde (2005). "Pain management for the hospitalized pediatric patient." *Pediatr Clin North Am* **52**(4): 995-1027, vii-viii.

McCann, M., Sethna, N., Mazoit, J., Sakamoto, M., Rifai, N., Hope, T., Sullivan, L., Auble, S., and Berde, C. The pharmacokinetics of epidural ropivacaine in infants and young children. *Anesthesia & Analgesia* 2001; 93:893-897.

Sethna, N., Clendenin, D., Athiraman, U., Solodiuk, J., Rodriguez, D., and Zurakowski, D. Incidence of epidural catheter-associated infections after continuous epidural analgesia in children. *Journal of Anesthesiology* (in press).