Update in
Anaesthesia

Pediatric Neuraxial Anesthesia and Analgesia

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Abstract

Neuraxial anesthetic techniques are generally safe and effective in children of all ages. Spinal anesthesia may reduce the risk of early post-operative apnea in neonates and former premature infants and is an alternative to general anesthesia in resource-limited settings. Epidural anesthesia may facilitate early tracheal extubation in neonates and is a useful adjunct to multimodal analgesia to spare opioids and enhance recovery in the post-operative period. A large prospective study of >40,000 neuraxial anesthetics demonstrated the safety of epidural catheter placement in children under general anesthesia. Serious complications from pediatric neuraxial anesthesia are rare as demonstrated in case series and the Pediatric Regional Anesthesia Network database.

Key words: analgesia; epidural; anesthesia; spinal; infant; child

INTRODUCTION

Neuraxial anesthesia has been performed safely in pediatric patients for over a century, starting with successful reports of spinal anesthesia by Bier in an 11-year-old child for thigh tumor resection in 1898 and by Bainbridge in a 3-month-old infant for strangulated hernia in 1900[1-2]. Caudal epidural blockade was the next advancement, and by 1954 neuraxial anesthesia had expanded to include a case series of lumbar epidural anesthetics for inguinal hernia repair in infants and children[2]. As the safety of general anesthesia improved, interest in pediatric neuraxial anesthesia waned until a resurgence in the mid 1980s when spinal anesthesia was touted as a safe alternative to general anesthesia to reduce the risk of post-operative apnea for premature infants ≤60 weeks post-menstrual age (PMA).

Spinal Anesthesia

The Vermont Infant Spinal Registry demonstrated spinal anesthesia (SA) in high-risk infants is safe and practical with high anesthetic success rate (95.4%) and low rates of complications of hypoxemia, bradycardia, and postoperative apnea[3]. The 2015 General Anaesthesia Compared to Spinal Anesthesia Consortium (GAS) study compared general anesthesia (GA) to SA and found awake SA to reduce the risk of post-operative apnea within the first 30 minutes in infants ≤60 weeks PMA with no change in incidence of post-operative apnea from 30 minutes to 12 hours[4]. Proponents of neuraxial anesthesia have concerns about the neurotoxicity of GA and its effects on long-term neurodevelopmental outcomes. They advocate for SA as an alternative to minimize or eliminate exposure to potential GA neurotoxicity for procedures less than 90 minutes' duration. While the GAS study demonstrates no impact on 5-year neurodevelopmental outcomes from a single brief <1 hour GA, risks of exposure to longer and/or repeated GA are unknown[5].

Additional benefits of SA over GA in resource-limited settings include reduced need for tracheal intubation in patients with preexisting respiratory difficulties, avoidance of respiratory depressant effects of GA and opioids particularly in premature infants and patients with limited pulmonary reserve, shortened hospital stay, faster OR turnover time, and reduced cost[1].

Epidural Anesthesia and Analgesia (EAA)

While SA can be used as a stand-alone technique, EAA is typically used in combination with intravenous and inhaled anesthetic agents to attain intense anesthetic depth and block the surgical stress response. When an indwelling thoracic or lumbar epidural catheter is placed, EAA can extend analgesia into the postoperative period. There are no large randomized controlled trials in neonates comparing epidural to intravenous postoperative analgesia, but several case series have examined epidural techniques' benefits. In 1998 Bösenberg reported the use of lumbar/thoracic epidural analgesia for major surgery in 237 neonates and ex-premature infants. Due

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to unavailability of infusion equipment, the majority of epidurals were managed postoperatively with intermittent dosing, an effective strategy for resource-limited settings. Bösenberg reported a low rate of complications and advantages including reduced need for post-operative intubation, muscle relaxation, and opioids[6]. A 2009 case series of 40 infants by Shenkman et al. reported benefits of early tracheal extubation in the operating room and good postoperative analgesia using continuous epidural anesthesia for major surgery[7]. Caudal epidural anesthesia/analgesia is the subject of a separate article and is not included in this review.

Advantages:

The advantages of SA or single-injection epidural anesthesia include risk reduction in patients with known or positive family history of malignant hyperthermia and patients with neuromuscular disorders who have restricted cardiopulmonary function. The advantages of EAA with an indwelling catheter are particularly effective for extensive thoracic, intraabdominal-pelvic and lower extremity orthopedic procedures. The postoperative analgesia provided by continuous infusion of a local anesthetic can avoid or minimize use of opioids and related side effects such as nausea, vomiting, ileus, and respiratory depression.

Contraindications:

Neuraxial anesthesia should be absolutely avoided in patients with:

1. Presence of local infection at the needle insertion site
2. Uncorrected hypovolemia or hemodynamic instability
3. Increased intracranial pressure
4. Allergy to the intended local anesthetic
5. And parent or child refusal

Neuraxial anesthesia is relatively contraindicated with patients with:

1. Inherited or acquired coagulation abnormalities due to risk for epidural hematoma (e.g. hemophilia, patient receiving coumadin or heparin, etc.)
2. Presence of systemic infection
3. Anatomic abnormalities such as spina bifida or tethered cord
4. Progressive neurologic disorders
5. And stenotic valvular heart lesions

As with adult patients, epidural catheter placement in adolescents may be performed on awake or lightly sedated patients. In young children and anxious adolescents, epidural catheter placement is commonly performed under GA. A study of >100,000 pediatric regional blockades including almost 40,000 neuraxial blockades demonstrated the safety of neuraxial anesthesia under GA. Neurological and cardiovascular complications were rare with rates similar to those of adult studies[8].

Anatomy and Physiology:

The subarachnoid space is filled with cerebrospinal fluid (CSF) and is present between the arachnoid mater adherent to the deep surface of the dura and the pia mater adherent to the surface of the spinal cord. The conus medullaris terminates at L3 in infants <1 year. Due to differential growth of the spinal cord and vertebrae, the spinal cord will ascend to its adult position of L1-L2 by 1 year of age[9]. Due to the more caudal position of the conus medullaris, spinal anesthesia in infants is performed at the L4-L5 or L5-S1 levels. To determine the level of insertion for SA, palpate the iliac crests to locate the intercristal line (imaginary line drawn between the iliac crests)(Figure 2). The intercristal line, which transects the L4 vertebral body in adults, transects L5 in infants and L5 or S1 in neonates[10-12]. CSF volume also varies by age and necessitates larger spinal doses in infants due to a larger CSF volume of distribution of local anesthetics. CSF volume is approximately 10mL/kg in neonates, 4mL/kg in infants and toddlers, and 2mL/kg in older children and adults[12].

The epidural space is a potential space containing fat, blood vessels, lymphatics, and spinal roots located between the ligamentum flavum lining the bony spinal canal posteriorly and the dura mater anteriorly. The epidural space can be accessed by passing through the ligamentum flavum at thoracic and lumbar levels or the sacrococcygeal ligament of the sacral hiatus in the caudal region (Figure 1). Epidural landmarks include the intercristal line for lumbar epidurals as well as an imaginary line drawn between the inferior scapular borders which transects the T7 or T8 spinous process and serves as a landmark for thoracic epidurals. The distance from skin to epidural space varies by age. Below 6 months, skin to epidural distance is 5-12mm and does not correlate with weight. From 6 months to 10 years, the distance is approximately 1mm/kg[13]. A thinner ligamentum flavum yields a subtler loss of resistance during insertion of epidural needles in young children, although a more compliant epidural space eases insertion of the epidural catheter[2,14].

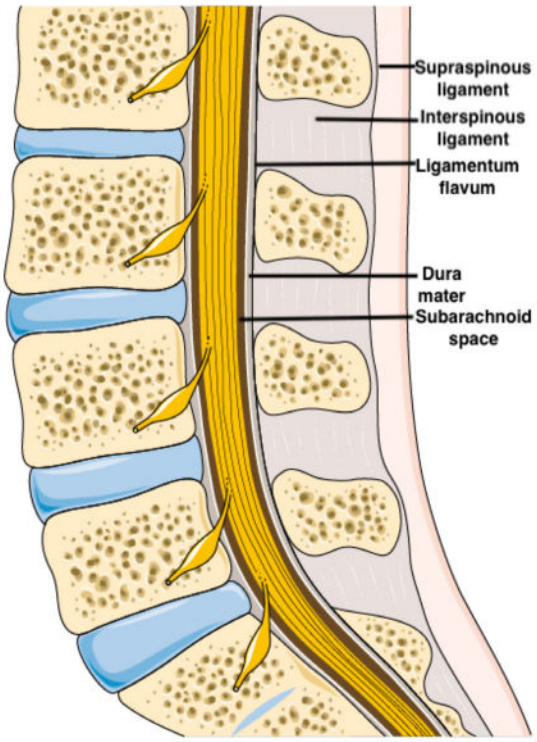

Figure 1: Anatomy of the lumbar epidural space

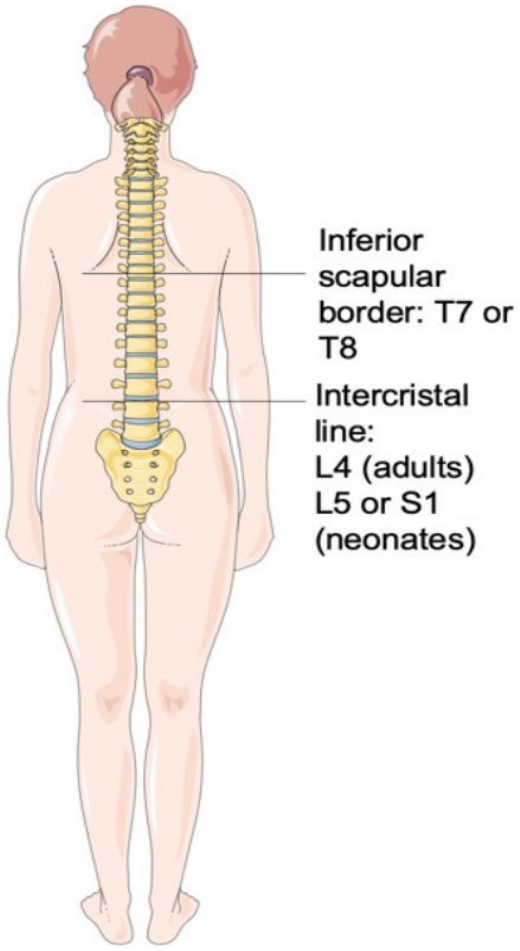

Figure 2: Anatomic landmarks for epidural insertion sites

In older children and adults, neuraxial anesthesia attenuates sympathetic tone leading to vasodilation, hypotension, and bradycardia. Bradycardia is especially likely when anesthetic level rises to high thoracic levels > T2-4 where the cardioaccelerator fibers originate. In infants and some toddlers in whom the parasympathetic nervous system predominates, neuraxial anesthesia is associated with hemodynamic stability. In Bosenberg's case series, 0 of 234 neonates had a change in systolic blood pressure >20% from baseline and 15 of 234 required administration of Atropine for heart rate <100 beats per minute[6]. As in adults, hypotension is treated with a fluid bolus and vasoactive drugs such as intravenous epinephrine.

Management of Patients Receiving Neuraxial Anesthesia:

Pre-procedure consent should be obtained from the guardian and assent from the patient when appropriate. Coagulation studies including platelet count, INR (International Normalized Ratio), and PTT (Partial Thromboplastin Time) should be obtained in patients with risk for coagulopathy such as personal history of spontaneous bleeding or prolonged surgical bleeding, family history of coagulopathy, or cirrhosis. Children with an INR ≤1.4 who are not on warfarin are not at increased risk of spinal bleeding and may safely undergo neuraxial anesthesia or removal of a catheter in accordance with ASRA (American Society of Regional Anesthesia) guidelines[15]. If a patient is on warfarin, it should be discontinued for 5 days and INR is allowed to normalize to <1.2. A consensus threshold for thrombocytopenia has not been established, but expert opinion generally supports the following thresholds: platelet count ≥100,000-150,000/μL (baseline risk of spinal bleeding, neuraxial anesthesia may be safely performed), 75,000-100,000/μL (low bleeding risk if stable platelet count and absence of clinical bleeding), 50,000-75,000/μL (increased bleeding risk, risk may be acceptable if benefit of neuraxial anesthesia outweighs risks and provided that platelet function is normal), and <50,000/μL (high bleeding risk, acceptable only in limited circumstances). Coagulation studies are not indicated for routine neuraxial anesthesia in healthy children. Children receiving anticoagulant medications should follow ASRA or ESA (European Society of Anaesthesiology) guidelines[15-16]. NPO guidelines should be followed as for general anesthesia.

Premedication can be given as indicated. For patients undergoing awake neuraxial procedures, topical anesthesia such as EMLA (Eutectic Mixture of Lidocaine and Prilocaine) 5% cream or tetracaine 4% gel (Ametop or AnGel) should be applied to the anticipated needle puncture site. Consider use of lidocaine 4% cream in premature and term infants under 1 month of age due to risk for methemoglobinemia with use of EMLA 5% cream and tetracaine 4% gel[17]. Obtain intravenous access prior to induction of neuraxial anesthesia to allow the rapid administration of vasoactive agents or intralipid in the event of peri-neuraxial hemodynamic instability or accidental systemic toxicity. Calculate the maximum allowable dose of local anesthetic (Table 1), the anticipated spinal (Table 3) or epidural (Table 4) bolus dose, and the epidural test dose, if indicated. There are no controlled trials to guide dosing in awake infants and children, and all dosing recommendations are based on observational studies. The dosing guide for spinal anesthesia in awake infants or sedated older children is based on targeting a T4 sensory dermatome for indicated surgical procedures below the T10 spinal segment. Epidural dosing is based on multiple studies that retrospectively estimated the dosing regimens by assessing the regression of sensory dermatomes after patients awaken from general anesthesia. Most recommended dosing regimens are estimated on the maximum allowable dose of local anesthetic given to children under general anesthesia (Table 1).

Table 1: Maximum recommended dose of local anesthetics for epidural administration[14]

Local anesthetic	Maximum dose (mg·kg-1)*	Duration (min)
Bupivacaine or levobupivacaine	2.5	80-600
Ropivacaine	3	120-240
2-Chlorprocaine	11 (without epinephrine) 14 (with epinephrine)	30-60
Lidocaine	5 (without epinephrine) 7 (with epinephrine)	90-200

Intra-Procedure

Ensure all supplies are gathered at the bedside and perform a "time-out" checklist prior to beginning the neuraxial blockade. Apply standard ASA monitors. Position the patient in a lateral or seated position, as desired. Ensure the spine is flexed into a C-shape while the head is extended to maintain a patent airway. Some advocate seated or reverse Trendelenburg lateral positioning for neonatal SA to maximize hydrostatic pressure and enhance CSF efflux from small diameter spinal needles[12,14]. An assistant should be available to aid in positioning, patient monitoring, and airway management. Use universal infection precaution for procedural sterility and follow standard practice for skin preparation. Skin antiseptic solution should be allowed adequate drying time for effectiveness, for example chlorohexidine gluconate requires a minimum of 3 minutes.

Spinal anesthesia in infants is typically performed with a 22g (Quincke tip) or 25g (pencil tip) spinal needle. Smaller needles can delay CSF efflux rate but significantly reduce the incidence of post-dural puncture headaches in children. Pencil tip needles are not used in infants due to difficult placement of the side opening into the narrow subarachnoid space and low CSF pressure causing very slow flow of CSF into the needle hub. Blunt tip needles should be used in infants and toddlers when possible and are associated with lower rates of post-dural puncture headaches.

The spinal needle should be inserted with stylet until increased resistance is felt with engagement of ligamentum flavum. A stylet is used to prevent iatrogenic implantation of skin and subcutaneous tissue that may introduce infection or grow over time into spinal epidermoid tumors. The needle is advanced slowly until a "pop" is felt. After stylet removal, free flow of clear CSF indicates correct placement in the subarachnoid space. The weight-based dose of local anesthetic is then slowly injected. (Table 3) 1-mL syringes are preferred for measuring a unit dose of local anesthetic and avoiding errors. The duration of action of spinal anesthesia can be prolonged with the addition of adjunctive agents such as epinephrine, opioids, or clonidine in older children.

Baricity of the local anesthetic injected into subarachnoid space combined with patient positioning will affect the desired anesthetic height attained. Hyperbaric solutions are heavier than CSF and spread in the direction of gravity. A hyperbaric spinal dose in a child who remains seated will spread in a caudate direction resulting in coverage of primarily sacral dermatomes, a "saddle" blockade. If a higher dermatome is desired, the child should be quickly placed supine after a hyperbaric dose is administered to allow more even spread in the cranial-caudate dimension. On the other hand, a hypobaric [lighter than CSF] spinal dose will primarily spread in the opposite direction to gravity in a seated or lateral decubitus child. The spread of isobaric [of equal density to CSF] spinal doses is less affected by patient position/gravity and will concentrate at the site of injection.

Table 2: Appropriate size of epidural Tuohy needle by age[20]

Age (years)	Epidural needle gauge
0-6	20
7-10	19
>10	18 or 19

Epidural Anesthesia (Figure 3) is usually performed at lumbar or thoracic levels where the epidural space can be entered via a midline or paramedian approach. In a midline approach, the epidural needle is introduced between spinous processes and advanced through the supraspinous and interspinous ligaments before piercing ligamentum flavum to enter the epidural space. In the paramedian approach, the epidural needle is inserted lateral to the superior edge of the spinous process. The needle is directed downward at a 90-degree angle to the skin, makes contact with lamina, then is "walked off" the lamina toward the midline into the interlaminal space until it pierces ligamentum flavum and enters the epidural space. The paramedian approach is advantageous for mid to high thoracic epidurals where the spinous processes are angled steeply caudate and a midline approach is more challenging. The paramedian approach should be used cautiously in infants where incomplete ossification of the neuraxial skeleton makes identification of laminae challenging and introduces potential damage to ossification centers[9,14].

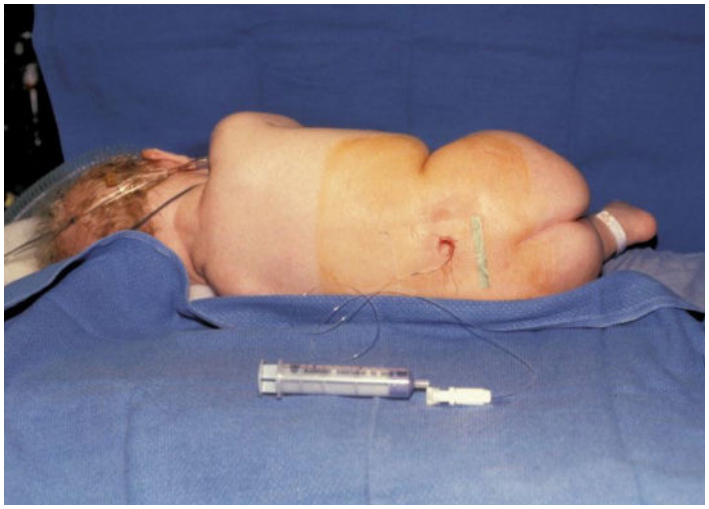

Figure 3: Epidural catheter in a neonate

An appropriately-sized styleted epidural needle such as a Tuohy or Crawford (thoracic spine) is inserted via the midline or paramedian technique until loss of resistance is attained (Table 2). When using a syringe to identify loss of resistance, saline may be preferable to air in infants as inadvertent injection of even small amounts of air into epidural veins could lead to venous air embolism[18]. The epidural catheter is inserted through the epidural needle to the desired surgical dermatome target. The epidural needle is typically inserted with bevel oriented superiorly so that the epidural catheter threads in a cranial direction. Special care should be taken to thread multiple orifice epidural catheters deep enough that all orifices lie within the epidural space. Alternatively, an open-ended epidural catheter can be used. The epidural catheter tip for post-operative analgesia is ideally placed at a vertebral level that corresponds with the surgical dermatomes. Important dermatomal reference levels include T4 (nipple line) for thoracic and upper abdominal procedures, T10 (umbilicus) for lower

Table 3: Recommended dosage of pediatric spinal anesthetics[1,12,21]

Local Anesthetic	Weight (kg)	Dosage	Mean Duration of Anesthesia (min)
Tetracaine 0.5% in 5% dextrose (hyperbaric)	<5	0.5-1mg·kg^{-1} (0.1-0.2 mL·kg-1)	90
	5-15	0.4mg·kg^{-1} (0.08 mL·kg-	
	>15	1 0.3mg·kg^{-1} (0.06mL·kg^{-1})	
Ropivacaine 0.5% (isobaric)	<5 kg	0.5-1 mg·kg-1 (0.1-0.2 mL·kg-1)	96
	≥5 kg	0.5 mg·kg-1 (0.1 mL·kg-1)	
Bupivacaine or levobupivacaine* 0.5% (isobaric or hyperbaric)	<5	0.5-1 mg·kg-1 (0.1-0.2 mL·kg-1)	80
	5-15	0.4 mg·kg-1 (0.08 mL·kg-1)	
	>15	0.3 mg·kg-1 (0.06 mL·kg-1)	

* is used off-label in the USA.

abdominal and pelvic procedures, and L1 (inguinal crease) for lower extremity procedures.

After a negative aspiration of the epidural catheter for blood, most anesthesiologists administer a test dose of 0.5mcg/kg epinephrine, typically accomplished with 0.1mL/kg local anesthetic with 1:200,000 epinephrine. A sudden increase in heart rate ≥10 beats per minute above baseline or increase in systolic blood pressure ≥15 mmHg above baseline within 90 seconds of injection is indicative of intravascular injection. The sensitivity of this test dose is increased by atropine premedication in patients receiving halothane and isoflurane (but not sevoflurane) anesthesia[19].

Of note, aspiration of the epidural catheter for blood may yield a false negative result in children due to low venous pressures and epidural venous collapse during aspiration. Furthermore, the routine administration of test dose in infants and children is controversial because of low sensitivity and specificity under GA. It is therefore recommended to include epinephrine in the epidural loading dose (Table 4). The loading dose should be administered incrementally with intermittent aspiration in 0.1-0.2mL/kg aliquots while observing for changes in heart rate and blood pressure as indicators of systemic toxicity[19]. Preservative-free adjunctive agents including fentanyl, morphine, clonidine, can be added to epidural solutions to augment analgesic properties and requires close monitoring for potential respiratory depression.

A simple estimation of the required volume of local anesthetic needed to block one spinal dermatome in older children follows:

Volume (mL per segment) = age in years / 10

with a maximum volume of 1mL/segment achieved by age 10-12 years.[20]. The total dose of local anesthetic delivered should not exceed recommended dosages as listed in Table 4. Further information about the anatomy and performance of neuraxial anesthesia can be found at **https://www.nysora.com/**.

Complications:

Serious complications from pediatric neuraxial anesthesia are rare, but can occur due to inadvertent intravascular injection of local anesthetic resulting in systemic toxicity such as seizures and cardiovascular collapse. Anesthesiologists providing neuraxial anesthesia should be familiar with guidelines for the management of local anesthetic systemic toxicity including initiation of cardiopulmonary resuscitation, use of lower doses of epinephrine (≤1mcg/kg), and administration of lipid emulsion[22]. A checklist for treatment can be downloaded at **https://www.asra.com/content/documents/asra_last_checklist_2018.pdf**.

Other serious complications include accidental intrathecal injection; high spinal anesthesia leading to hypotension, bradycardia, and even respiratory arrest; epidural hematoma that may compress the spinal

Table 4: Recommended dosage of pediatric epidural continuous infusion[21]

Local Anesthetic	Initial Bolus Dose (mL·kg^{-1})	Subsequent Bolus Dose after 2 hours (mL·kg^{-1})	Continuous Infusion (mL·kg^{-1}·hr)
Bupivacaine or levobupivcaine 0.25%*	0.5 (lumbar) 0.3 (thoracic)	0.25	<3 months: 0.08 3 months-1year: 0.12 ≥1 year: 0.16
Ropivacaine 0.2%*	0.5 (lumbar) 0.3 (thoracic)	0.25	<3 months: 0.1 3 months-1year: 0.15 ≥1 year: 0.2
2-Chlorprocaine 1.5%*	0.5		<3 months: 0.0133 3 months-1year: 0.02 ≥1 year: 0.0333

*Due to immature hepatic metabolism and low plasma levels of alpha-1 acid glycoprotein, amide local anesthetics can accumulate in infants and young children leading to high free plasma levels and toxicity. The ester 2-Chlorprocaine is preferred in this age group because it is metabolized in the plasma by pseudocholinesterase.

cord; epidural abscess; meningitis; needle-induced injury to nerve roots or the spinal cord; venous air embolism; and delayed respiratory depression from opioids. Less serious complications include post-dural puncture headache, transient neurologic symptoms from SA, unilateral or patchy epidural blockade, and cutaneous infection at the site of an indwelling epidural catheter. A Pediatric Regional Anesthesia Network trial examining more than 41,000 single-injection neuraxial blockades and 13,000 neuraxial continuous catheters identified 5 cases of severe local anesthetic toxicity, 18 cases of respiratory depression (all associated with neuraxial catheters, 15 of 18 with opioid-containing epidural solution), one epidural abscess, no epidural hematomas, and no permanent motor deficits[8].

CONCLUSION

Neuraxial anesthesia is generally safe and effective in children of all ages based on case and case-series reports and Pediatric Regional Anesthesia Network safety data. Spinal anesthesia is a safe alternative to GA in neonates and former premature infants at risk for post-operative apnea as well as in resource-limited settings. EAA may facilitate early tracheal extubation in neonates and is a useful adjunct to multimodal analgesia to spare opioids and enhance recovery in the post-operative period. There are no large randomized controlled data on the efficacy of neuraxial techniques compared to other anesthetic/analgesic modalities on alleviating pain, suppressing the neuroendocrine stress response to surgery, and improving post-surgical outcomes.

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