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StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-.

Pediatric Regional Anesthesia

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Last Update: April 7, 2022.

Continuing Education Activity

Pain relief in children undergoing surgery is often an unmet critical need. Landmark guided blocks can be associated with an untoward incidence of adverse events. The advent of the ultra-sonogram (USG) in the operating room has resulted in a paradigm shift, with many practitioners adapting regional modalities for pain relief, even in small children. The margin for error is much smaller in children compared to adults and is even smaller in infants. The USG has helped navigate this challenging landscape, enabling safe administration of regional anesthesia. Regional blocks have formed an integral part of a number of enhanced recovery protocols in children, resulting in better, faster recovery and better satisfaction. This activity provides an overview of the specific principles guiding regional anesthetic practice in pediatrics and the role of the interprofessional team in the management of patient recovery after pediatric surgeries.

Objectives:

- Summarize the differences in anatomy, physiology, and pharmacology in pediatrics that make the practice of regional anesthesia unique.
- Outline the indications for performing pediatric regional anesthesia.
- Review the possible complications of regional anesthesia in children along with measures to prevent them.
- Describe the overall preparation and techniques of regional blocks in children used by the interprofessional team to better patient outcomes.

Access free multiple choice questions on this topic.

Introduction

In recent times, advances in regional anesthesia, accelerated by the advent of the ultrasonogram (USG), have revolutionized perioperative pain management. A number of plane blocks and deep blocks that were non-existent previously have been made possible by the USG. But the utilization of regional blocks in pediatrics is much lower than in adult anesthesia due to the fear of adverse events fueled by misunderstandings and misconceptions.

A large body of high-quality evidence is being published testifying towards the safety of regional practice in children. This has the potential to enhance, fasten recovery in children, and as a result, decrease health care costs. Regional anesthesia also holds significance in the current era of the opioid epidemic. This review will provide an overview of the principles and practices of pediatric regional anesthesia.

Anatomy and Physiology

Neuraxial regional techniques, especially caudal and epidural, are the most common regional techniques performed in children. The anatomy of the vertebra and the relative position of spinal cord placement in the vertebral canal varies with age. Classical literature states that spinal cord ends (conus medullaris) as low as the L3 vertebra in infants, compared to L1 in adults.[1] Adult levels are reached at about 6 years of age. Recent imaging studies have revealed a median level of L2 for termination of the spinal cord in infants.[2] This is essential to know during neonatal/infant spinal anesthesia administration when the subarachnoid space is accessed from L4-5 or L5-S1 space compared to L2-3, L3-4 space in adults. The intercristal line serves as the landmark to identify the lumbar vertebral level. This corresponds to L3-L4 in adults, while it corresponds to L4-L5 in neonates.[3] The spine has a single curve at birth. Cervical and lumbar lordosis develop as the infants achieve milestones of head support and sitting. Adult configuration is usually achieved by 1 year. Bones, including vertebrae, are not completely ossified at birth. They are cartilaginous and offer little resistance to needle advancement. Needles passed through non-ossified bones can potentially injure the ossification nuclei.

The dural sac may extend down to S3-S4 in neonates and infants, compared to S1 in adults. Because of this, caution has to be exercised during the caudal block to prevent inadvertent dural puncture. The sacral hiatus is covered by the sacrococcygeal ligament. This space is wide open in infants, toddlers, and smaller children, allowing easy access into the epidural space. Ossification and eventual closure of the hiatus, as well as the changing axis of the coccyx, make the caudal block challenging in older children and adults. Epidural fat is very fluid up to 8 years of age, aiding the extensive spread of the LA in children below this age. The spinous processes are more parallel and horizontal, allowing easier midline access into the neuraxis. The CSF volume in a neonate is about 4 mL/kg, compared to the adult volume of 2 mL/kg, and a greater proportion of this CSF volume lives in the spinal subarachnoid space compared to adults. This is significant during neonatal/infant spinal anesthesia. The local anesthetic (LA) injected is immediately diluted by the greater spinal CSF volume, necessitating a greater dose of local anesthetic (up to 1 mg/kg of 0.5% bupivacaine) for the spinal block.[4] The duration of action of the spinal anesthetic is also significantly shorter compared to adults. Hence it is only suitable for brief procedures.

Pharmacological differences from adults result from different anatomy at the neuronal level. Myelination is incomplete at birth; this can take up to 12 years to complete. Due to this reason, a dilute local anesthetic will be able to provide a denser block with a fast onset of action. However, the duration of effect may be shorter than in adults because of greater systemic absorption secondary to greater cardiac output and decreased LA trapping in the immature sheath.

Amide local anesthetics are bound to plasma proteins, namely alpha-acid glycoprotein and albumin. The free fraction of the LA contributes to systemic toxicity. Infants have low levels of binding proteins, resulting in greater levels of unbound LA. Adult levels are reached by 1 year of age. CYP450 enzymes necessary for the metabolism of amide local anesthetics are immature in neonates.[5] Ester local anesthetics are metabolized by plasma esterases. Esterase activity is lower in neonates.[6] All these enzyme activities gradually increase through the first year of life. Immature metabolism, greater free fraction of LA due to lower levels of binding proteins, coupled with greater systemic absorption and immature blood-brain barrier could lead to increased susceptibility to LA systemic toxicity (LAST).[7][8] This is especially true in neonates. Cardiac and central nervous system toxicities in neonates can occur concomitantly, unlike in adults, in whom convulsions typically precede arrhythmia. In addition, since blocks are done under GA for children, neurological symptoms of LA toxicity can be masked by the anesthetic agents. It is prudent to reduce the maximal allowable dosage of LAs by at least 30% in infants below 6 months.[9]

Physiological differences between children and adults exist in pain perception itself, mainly due to the ongoing development and maturation of central and peripheral nervous systems. The receptive field of neurons may be greater in children, leading to poor pain localization.[10] The descending inhibitory pathways are immature, and this could allow unmodulated nociceptive inputs. Thus, contrary to the classical belief that infants do not perceive pain, pain perception is very much intact after 25 weeks of gestation.[10] The neurohormonal stress response to acute pain and risk of chronic pain and behavioral problems secondary to acute pain warrant meticulous and pre-emptive management of acute pain in infants and children. Regional modalities play an important role in aiding this.

Indications

Regional analgesic techniques are indicated whenever possible for the management of postoperative pain. Several regional techniques are also used to treat various cancer and non-cancer chronic pain conditions. Regional techniques form an integral part of a number of enhanced recovery protocols and aid in minimizing the requirements of opioids to control postoperative pain. Adequate management of acute pain is essential to prevent transition to chronic pain.[11]

Contraindications

Contraindications to pediatric regional anesthesia are similar to those in adults.[12] Absolute contraindications include patient or parent refusal and local anesthetic allergy. True allergic reactions to LAs are relatively rare. Most of the "allergies" reported by the patient include reactions to preservatives such as metabisulfite and methylparaben. Some are symptoms of overdose toxicity. Relative contraindications include infection at the needle insertion site, coagulopathy, sepsis, septicemia, and pre-existing neurologic deficit. Patients receiving anticoagulation medications can be managed according to the American Society of Regional Anesthesia and Pain Medicine (ASRA) guidelines.[13]

Hemodynamic instability might be a limiting factor for performing a neuraxial technique. The risk of acute compartment syndrome (ACS) after trauma surgeries of extremities has been considered a relative contraindication to regional block, as a nerve block can mask pain, which is the most common presenting symptom of ACS. But this is not true, and there is evidence to the contrary.[14]

When low concentration LA is used for the block, progressive increase in pain and increasing analgesic requirements can still point towards ACS. Other symptoms include paresthesia, swelling, and reduced perfusion. Major vertebral anomalies can frequently be present in children undergoing major urology, lower limb orthopedic reconstruction procedures. Therefore, caution is necessary when a neuraxial block is considered for these children. In addition, pre-existing neurological deficits might be considered a relative contraindication due to concern for the progressive deficit. Children with these conditions should be assessed on a case-by-case basis to evaluate the benefits and risks of performing the block.

Equipment

Age-appropriate equipment is key to the safe and successful performance of regional procedures in children. Smaller gauge, shorter needles are essential for neuraxial procedures. Short block needles can be used for peripheral nerve blocks. A majority of the complications reported in the French-Language Society of Paediatric Anaesthesiologists (ADARPEF) could be attributed to inappropriate equipment.[15]

Chlorhexidine is the most common skin disinfectant used prior to regional blocks. Chlorhexidine has prolonged residual action and helps prevent bacterial colonization of continuous catheters.[16] Povidone-iodine can be used in children allergic to chlorhexidine. It should be allowed to dry after application and thoroughly wiped off using alcohol before needle insertion, as it can cause aseptic chemical meningitis.[17] Also, prolonged skin contact with povidone-iodine can cause irritation.[18]

Ultrasonogram (USG) has become a piece of integral equipment in the anesthesiologist's toolbox. It helps in the precise localization of the nerves and administration of very small LA doses to block nerves safely and effectively. It has also paved the way for a range of plane blocks, including transversus abdominis plane block and erector spinae plane block. In addition, appropriate pediatric size probes with a smaller footprint facilitate better visualization and block placement.

Personnel

Anesthesiologist trained in regional anesthesia for pediatric patients should perform the block. Inexperience is highly correlated with a greater incidence of complications associated with pediatric regional anesthesia. Facility and personnel, including trained nursing staff, are essential for monitoring after the procedure, during recovery from the block.

Preparation

Pediatric blocks are generally placed under general anesthesia (GA), unlike in adults, where blocks are preferably placed when the patient is awake. This is because patient cooperation can be challenging with children, and communication and feedback of paresthesia after contact with a nerve or intraneural injection are sub-optimal at best. Identification of signs and symptoms of LA systemic toxicity is challenging even in awake children. On the other hand, the risk associated can be greater in terms of injury to structures, secondary to sudden movements. According to the data from the Pediatric Regional Anesthesia Network (PRAN), 93.7% of pediatric blocks are performed under GA.[19] The risk of complications associated with an awake block was higher than blocks performed under GA (OR: 2.93; 95% CI, 1.34 to 5.52; $P < 0.01$). The only common situations when awake blocks are performed include adolescents who are able to cooperate for the block placement and infants undergoing brief procedures under awake spinal anesthesia. General anesthesia (GA), with or without neuromuscular blockade (NMB), provides excellent conditions for USG guided regional blocks in children.[14] NMB can be avoided if a nerve stimulator is to be used.

USG use has significantly increased in the last decade to aid visualization of the nerve or plane for block placement, needle path, and the deposition of the LA. There has also been a decrease in the use of nerve stimulator-guided/landmark techniques for block placement. The anatomical variations in growing children make landmark-guided approaches less reliable, especially when the margin of safety is narrow. USG facilitates reduction in the doses of LA required to achieve adequate sensory and motor block required for the intra- and postoperative analgesia. With the increasing use of USG over the years, the incidence of neurological complications with peripheral nerve blocks in children has been decreasing. A good quality USG with appropriate presets for neurological (for nerve blocks) or musculoskeletal (for plane blocks) is recommended. The most useful transducer probes for pediatric regional anesthesia are linear arrays, which have a smaller footprint and a broad range of frequency (6 to 13 MHz) to image both superficial and deep structures. Curved array probes might be required for adolescents and obese patients for deep blocks.

Optimal positioning of the patient and ergonomic placement of the USG and the operator are necessary to facilitate successful block placement. A time-out should be performed to confirm the patient, confirm allergies, type of block, consent for the block, and confirm laterality. This is essential, especially when the patient is under GA. Sterile precautions include sterile skin preparation and draping, sterile ultrasound probe cover, hand washing, sterile gloves, and sterile equipment for the block. Chlorhexidine is the most commonly used agent for skin disinfection. Povidone-iodine can be used in patients with chlorhexidine allergy. Maximal doses of LA should be calculated beforehand, and the doses required should be drawn out, along with the appropriate additive medication. Blunt tip echogenic needles should be used for most peripheral nerve blocks. Sharp tip needles could facilitate the easy placement of plane blocks such as TAP blocks. Blunt, curved tip Tuohy needles of appropriate length are used for epidural placement. Tuohy, butterfly, or angiocath needles can be used for a caudal block. A small-bore (25G) 1 inch-long spinal needle can be used for infant spinal blocks.

Technique

It is ideal to use USG for peripheral nerve blocks, to visualize nerves, and monitor drug spread. An in-plane approach should be used whenever possible to visualize the entire length of the needle, including the tip. For plane blocks, normal saline can confirm the correct plane and hydro-dissect the plane before injecting the medication.

A loss of resistance (LOR) technique is used to locate the epidural space. The ligaments offer resistance to the injection of Normal Saline, which is suddenly lost as the needle tip enters the epidural space. Saline is preferred to air for loss of resistance because of the risk of air embolus when air is used.[14] Needle direction should be horizontal for the lumbar level, and a cephalad tilt is required for a thoracic epidural. The paramedian approach increases the chance of success for thoracic epidural placement. The median approach is acceptable for lumbar epidural placement. The use of epinephrine-containing test doses in pediatrics is another controversial issue.[14] The hemodynamic response to epinephrine-containing test dosing is attenuated in children under GA. Because of this reason, an increase in T-wave amplitude is more reliable compared to heart rate or blood pressure response. However, a test dose is not an alternative to slow incremental injection of LA, after negative aspiration, with continuous EKG monitoring.

Caudal is performed in the lateral position. The sacral hiatus is bound on both sides by the sacral cornua. It forms the apex of an equilateral triangle formed by the posterior superior iliac spine. It is covered by the sacrococcygeal membrane, which offers a feeling of a 'pop' as the needle is inserted at a 45-degree angle to the skin. The anatomical differences should be taken into account during caudal for infants. 0.5 mL/kg of LA volume is required for sacral coverage, 1 mL/kg for lumbar, lower thoracic coverage, 1.25 mL/kg for mid-thoracic coverage.[20] In children, determining the local anesthetic volume only according to the targeted level when applying caudal anesthesia may cause the block time to be too short. Considering the elimination time of the local anesthetic as well as the block level, it may be necessary to administer a higher volume of local anesthetic. Drugs used include bupivacaine (0.25%), levobupivacaine (0.25%) and ropivacaine (0.2%). Additives like clonidine or opioids can be used. Spinal anesthesia for infants can be performed in a sitting or lateral position. 0.5% bupivacaine at doses up to 1 mg/kg up to 5 mg can be used. Clonidine can be used as an additive at doses up to 1 mcg/kg to prolong the duration of surgical anesthesia. The infant should be maintained in a flat position to prevent cephalad spread and a total spinal. Spinal block induces sympathetic blockade, and hemodynamic changes are typically absent in infants due to their immature sympathetic nervous system.

Ideal body weight is used for the calculation of the maximal allowable dose of local anesthetic. This is 3mg/kg for bupivacaine, levobupivacaine, and ropivacaine, 5 mg/kg for lidocaine without epinephrine, and 7 mg/kg for lidocaine with epinephrine for bolus dosing. Toxicities of different local anesthetic drugs are additive. If a maximal dose of one LA has already been used, a different LA should not be used. Infants less than 6 months require at least a 30% reduction in the maximal doses due to increased free fractions and decreased elimination. An epidural infusion dose of 0.4 to 0.5 mg/kg/hr is used for bupivacaine (0.25%), levobupivacaine (0.25%) and ropivacaine (0.2%); this is reduced to 0.25 mg/kg/hr for infants less than 6 months. Chloroprocaine (2%) is a rapid, short-acting ester LA used in infants at a dose of 8 to 10 mg/kg/hr. It is rapidly metabolized and eliminated by plasma esterases.[21]

The initial manifestations of LA systemic toxicity (LAST) are usually neurological, potentially ranging from tremors, twitching, or seizures. This is usually followed by cardiovascular manifestations, namely, high degree block, QRS widening, ventricular tachycardia, fibrillation, and cardiac arrest. In children, the neurological manifestations can be masked by the GA, and cardiac manifestations are noticed first or in conjunction with neurological signs. Management follows advanced life support to ensure oxygenation, ventilation, and cardiovascular support.[22] It is essential to ensure normothermia, oxygenation, normocapnia, normokalemia, and avoid acidosis. Intralipid may be required as a rescue agent in cases of intractable cardiac arrest. The initial bolus dose is 1.5 mL/kg of 20% intralipid, followed by an infusion of 0.25 to 0.5 mL/kg/min. Repeat bolus doses at 1 to 1.5 mL/kg may be administered up to a maximum of 3 mL/kg.[22]

Additive medications are used to prolong the duration of analgesia for single injection central neuraxial and peripheral blocks.[23] Clonidine and dexmedetomidine are the most commonly used agents at a dose of 1 to 2 mcg/kg. Opioids like morphine, fentanyl can be used, but their neuraxial use has been associated with the risk of respiratory depression and other adverse effects like pruritus and urinary retention. Ketamine 0.5 mg/kg, dexamethasone, and epinephrine are other agents used as additives. Liposomal bupivacaine is a long-acting, slow-release formulation with an apparent duration of action of up to 72 hours. But a recent review of literature has raised questions about the clinical usefulness of liposomal bupivacaine, given its high cost.[24]

Complications

The Pediatric Regional Anesthesia Network (PRAN) is a collaborative group of several pediatric hospitals that acts as a registry for regional procedures in children.[19] In 2018, they reported the data collected between 2007 and 2015, which included 104,393 blocks placed on 91,701 pediatric patients.[19] The most common single injection block was caudal, and the most common single-shot peripheral nerve block was a femoral block. The majority of the catheters placed were central neuraxial (Epidural/caudal: 73%). The most common adverse events observed were benign failures related to catheters (4%), including dislodgement, occlusions, and disconnections.

The overall incidence of neurological complications was 2.4 per 10,000 blocks. These were mainly sensory issues that were resolved in less than 3 months. None of the patients had permanent motor deficits. There was no difference in neurological complications between neuraxial vs. peripheral nerve blocks. There was no difference in the incidence of complications between caudal vs. lumbar vs. thoracic epidural blocks. The risk of neurological complications was similar between single injection vs. continuous catheter techniques.[19]

The incidence of severe LA systemic toxicity (cardiac arrest/seizures) was 7 per 10,000 blocks. Most of them were in infants, less than six months, after a bolus dose of LA. One epidural abscess was reported (incidence of 0.76 per 10,000), which required intervention but resolved without any residual nerve damage. 53 per 10,000 blocks were complicated by cutaneous infections, which was more common with neuraxial catheters compared with peripheral catheters. There were no hematomas reported with neuraxial blocks. Inadvertent dural puncture incidences were 66, 86, and 10 per 10,000 for thoracic, lumbar, and caudal approaches, respectively. 14 out of 10,000 patients who received opioids through a neuraxial catheter experienced respiratory depression. The prospective study of around 30,000 pediatric regional blocks by the French-language Society of Paediatric Anesthesiologists similarly found a very low incidence of complications, none of which resulted in any sequelae.[15]

Clinical Significance

Several benefits to regional modalities for postoperative analgesia have been documented in the literature. Most of this evidence comes from adult literature.[25][26] Intraoperative neuraxial anesthesia and postoperative epidural analgesia have been shown to have mortality benefits. The sympathetic blockade offered by a thoracic epidural can favorably affect the myocardial oxygen supply-demand balance, protecting from ischemic events and arrhythmias.

Uncontrolled pain after abdominal surgeries can impair respiration, resulting in atelectasis and pneumonia. Epidural analgesia for major abdominal procedures offers excellent pain relief and minimizes the incidence of postoperative pulmonary complications. Epidural also facilitates the quicker return of gastrointestinal motility after major abdominal surgeries, both by its direct analgesic action and indirectly by minimizing opioid requirements. Neuraxial analgesia attenuates neurohumoral stress response to pain and subsequently the postoperative hypercoagulable state, decreasing the incidence of thromboembolic complications. Other benefits include decreased opioid requirements and reduced incidence of opioid adverse effects like sedation, nausea, and vomiting.[21][12]

Enhancing Healthcare Team Outcomes

Regional modalities can significantly decrease the requirements of opioids for surgical pain relief. This is noteworthy in the face of a nationwide opioid epidemic. Adequate management of acute surgical pain also halts transition to chronic pain, which significantly impairs quality of life and results in long-term opioid use. In addition, regional anesthesia is an integral component of many enhanced recovery strategies aimed to accelerate postoperative recovery and minimize the length of hospital stay. This ultimately translates to improved patient and parent satisfaction and decreased healthcare costs for the system.

Regional anesthesia for pediatric patients requires the efforts of an interprofessional healthcare team that includes the clinician, NPs and PAs, anesthesiologists and nurse anesthetists, and OR nursing staff, coordinating their activities and monitoring patient response to achieve optimal outcomes with minimal adverse events. [Level 5]

Nursing, Allied Health, and Interprofessional Team Interventions

Successful performance and optimal outcomes for regional anesthesia require multidisciplinary, collaborative teamwork. Communication between the surgeon and anesthesiologist, buy-in from the surgeon, and appropriate monitoring and nursing facilities are imperative. For instance, a patient with a lumbar epidural catheter might require a urinary catheter, which calls for coordination between the surgical, anesthesia, and nursing teams.

Other areas include the timing of postoperative anticoagulation therapy and the use of ancillary medications as part of enhanced recovery after surgery protocols. The American Society of Regional Anesthesia (ASRA) has published guidelines on the performance of regional techniques in patients receiving anticoagulant medications. Prophylactic anticoagulant therapy is commonly used in the postoperative period to prevent thromboembolic complications. A detailed description of anticoagulant management in patients receiving regional blocks is beyond the scope of this article. Still, a thorough knowledge of this is essential for safe clinical practice. The readers are referred to the American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines (fourth edition) for a detailed description.[13]

Nursing, Allied Health, and Interprofessional Team Monitoring

Post-operative monitoring should be tailored to the kind of regional technique performed, in addition to monitoring for recovery from GA. For an epidural, this means hemodynamic monitoring to avoid hypotension, checking ability to void, prevent urinary retention, and also monitor the level of blockade. Continuous catheters should be monitored for dislodgement, disconnection, leakage, the integrity of the sterile occlusive dressing, and signs of infection.

Motor recovery should be monitored and documented for all regional blocks. In cases of same-day surgery, discharge should be permitted only after motor power has been at least partially restored. This reduces the incidence of falls and subsequent injuries. The sensory blockade should be monitored, and pressure points should be padded to prevent pressure-related injuries. Patients who have received neuraxial opioids should be monitored overnight for respiratory depression in the hospital.

Review Questions

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References

1. Shin SK, Hong JY, Kim WO, Koo BN, Kim JE, Kil HK. Ultrasound evaluation of the sacral area and comparison of sacral interspinous and hiatal approach for caudal block in children. Anesthesiology. 2009 Nov;111(5):1135-40. [PubMed: 19809281]
2. Willschke H, Bosenberg A, Marhofer P, Willschke J, Schwindt J, Weintraud M, Kapral S, Kettner S. Epidural catheter placement in neonates: sonoanatomy and feasibility of ultrasonographic guidance in term and preterm neonates. Reg Anesth Pain Med. 2007 Jan-Feb;32(1):34-40. [PubMed: 17196490]
3. van Schoor A, Bosman MC, Bosenberg AT. The value of Tuffier's line for neonatal neuraxial procedures. Clin Anat. 2014 Apr;27(3):370-5. [PubMed: 23408712]
4. Kokki H. Spinal blocks. Paediatr Anaesth. 2012 Jan;22(1):56-64. [PubMed: 21899656]
5. Tanaka E. In vivo age-related changes in hepatic drug-oxidizing capacity in humans. J Clin Pharm Ther. 1998 Aug;23(4):247-55. [PubMed: 9867310]
6. Zsigmond EK, Downs JR. Plasma cholinesterase activity in newborns and infants. Can Anaesth Soc J. 1971 May;18(3):278-85. [PubMed: 5578586]
7. Booker PD, Taylor C, Saba G. Perioperative changes in alpha 1-acid glycoprotein concentrations in infants undergoing major surgery. Br J Anaesth. 1996 Mar;76(3):365-8. [PubMed: 8785135]
8. Mazoit JX, Dalens BJ. Pharmacokinetics of local anaesthetics in infants and children. Clin Pharmacokinet. 2004;43(1):17-32. [PubMed: 14715049]

9. Berde C. Local anesthetics in infants and children: an update. Paediatr Anaesth. 2004 May;14(5):387-93. [PubMed: 15086849]
10. Hatfield LA. Neonatal pain: What's age got to do with it? Surg Neurol Int. 2014;5(Suppl 13):S479-89. [PMC free article: PMC4253046] [PubMed: 25506507]
11. Andreae MH, Andreae DA. Regional anaesthesia to prevent chronic pain after surgery: a Cochrane systematic review and meta-analysis. Br J Anaesth. 2013 Nov;111(5):711-20. [PMC free article: PMC3793661] [PubMed: 23811426]
12. Merella F, Canchi-Murali N, Mossetti V. General principles of regional anaesthesia in children. BJA Educ. 2019 Oct;19(10):342-348. [PMC free article: PMC7807952] [PubMed: 33456856]
13. Horlocker TT, Vandermeulen E, Kopp SL, Gogarten W, Leffert LR, Benzon HT. Regional Anesthesia in the Patient Receiving Antithrombotic or Thrombolytic Therapy: American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines (Fourth Edition). Reg Anesth Pain Med. 2018 Apr;43(3):263-309. [PubMed: 29561531]
14. Ivani G, Suresh S, Ecoffey C, Bosenberg A, Lonnqvist PA, Krane E, Veyckemans F, Polaner DM, Van de Velde M, Neal JM. The European Society of Regional Anaesthesia and Pain Therapy and the American Society of Regional Anesthesia and Pain Medicine Joint Committee Practice Advisory on Controversial Topics in Pediatric Regional Anesthesia. Reg Anesth Pain Med. 2015 Sep-Oct;40(5):526-32. [PubMed: 26192549]
15. Ecoffey C, Lacroix F, Giaufré E, Orliaguet G, Courrèges P., Association des Anesthésistes Réanimateurs Pédiatriques d'Expression Française (ADARPEF). Epidemiology and morbidity of regional anesthesia in children: a follow-up one-year prospective survey of the French-Language Society of Paediatric Anaesthesiologists (ADARPEF). Paediatr Anaesth. 2010 Dec;20(12):1061-9. [PubMed: 21199114]
16. Scott M, Stones J, Payne N. Antiseptic solutions for central neuraxial blockade: which concentration of chlorhexidine in alcohol should we use? Br J Anaesth. 2009 Sep;103(3):456; author reply 456-7. [PubMed: 19679583]
17. Doghmi N, Meskine A, Benakroute A, Bensghir M, Baite A, Haimeur C. Aseptic meningitis following a bupivacaine spinal anesthesia. Pan Afr Med J. 2017;27:192. [PMC free article: PMC5579419] [PubMed: 28904717]
18. Demir E, O'Dey DM, Pallua N. Accidental burns during surgery. J Burn Care Res. 2006 Nov-Dec;27(6):895-900. [PubMed: 17091089]
19. Walker BJ, Long JB, Sathyamoorthy M, Birstler J, Wolf C, Bosenberg AT, Flack SH, Krane EJ, Sethna NF, Suresh S, Taenzer AH, Polaner DM, Martin L, Anderson C, Sunder R, Adams T, Martin L, Pankovich M, Sawardekar A, Birmingham P, Marcelino R, Ramarmurthi RJ, Szmuk P, Ungar GK, Lozano S, Boretsky K, Jain R, Matuszczak M, Petersen TR, Dillow J, Power R, Nguyen K, Lee BH, Chan L, Pineda J, Hutchins J, Mendoza K, Spisak K, Shah A, DelPizzo K, Dong N, Yalamanchili V, Venable C, Williams CA, Chaudahari R, Ohkawa S, Usljebrka H, Bhalla T, Vanzillotta PP, Apiliogullari S, Franklin AD, Ando A, Pestieau SR, Wright C, Rosenbloom J, Anderson T., Pediatric Regional Anesthesia Network Investigators. Complications in Pediatric Regional Anesthesia: An Analysis of More than 100,000 Blocks from the Pediatric Regional Anesthesia Network. Anesthesiology. 2018 Oct;129(4):721-732. [PubMed: 30074928]
20. Wiegele M, Marhofer P, Lönnqvist PA. Caudal epidural blocks in paediatric patients: a review and practical considerations. Br J Anaesth. 2019 Apr;122(4):509-517. [PMC free article: PMC6435837] [PubMed: 30857607]
21. Gunter JB. Benefit and risks of local anesthetics in infants and children. Paediatr Drugs. 2002;4(10):649-72. [PubMed: 12269841]
22. El-Boghdadly K, Pawa A, Chin KJ. Local anesthetic systemic toxicity: current perspectives. Local Reg Anesth. 2018;11:35-44. [PMC free article: PMC6087022] [PubMed: 30122981]
23. Brummett CM, Williams BA. Additives to local anesthetics for peripheral nerve blockade. Int Anesthesiol Clin. 2011 Fall;49(4):104-16. [PMC free article: PMC3427651] [PubMed: 21956081]
24. Hussain N, Brull R, Sheehy B, Essandoh MK, Stahl DL, Weaver TE, Abdallah FW. Perineural Liposomal Bupivacaine Is Not Superior to Nonliposomal Bupivacaine for Peripheral Nerve Block Analgesia.

Anesthesiology. 2021 Feb 01;134(2):147-164. [PubMed: 33372953]
25. Bugada D, Ghisi D, Mariano ER. Continuous regional anesthesia: a review of perioperative outcome benefits. Minerva Anestesiol. 2017 Oct;83(10):1089-1100. [PubMed: 28607342]
26. Lirk P, Hollmann MW. Outcome after regional anesthesia: weighing risks and benefits. Minerva Anestesiol. 2014 May;80(5):610-8. [PubMed: 24193234]

Bookshelf ID: NBK572106 PMID: 34283472