Principles of Regional Anaesthesia in Children

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Published 22 November 2022

KEY POINTS

- Understanding the difference in anatomy, physiology and pharmacology between adults and children is essential when performing paediatric regional anaesthesia (PRA).
- PRA techniques help ensure optimal analgesia, early ambulation and earlier discharge from hospital.
- PRA can be performed safely under general anaesthesia or deep sedation.
- Ultrasound guidance reduces the risk of inadvertent vascular, nerve or organ injury.
- To avoid life-threatening local anaesthetic systemic toxicity, the maximum recommended dose of local anaesthetic should be calculated prior to administration.

INTRODUCTION

Paediatric regional anaesthesia (PRA) helps to ensure optimal analgesia. It is opioid sparing and has beneficial effects on the autonomic, metabolic and immunological systems.[1] Regional anaesthesia is a useful adjunct that can reduce the dose of general anaesthetic agents required, and in some cases may be used as a sole anaesthetic technique or with minimal sedation (for example, spinal anaesthesia).[1,2] An appreciation of the differences in the anatomy, physiology, pharmacology and controversies associated with regional anaesthesia in children compared with adults is required prior to performing PRA to ensure it is performed safely and effectively.

ANATOMICAL DIFFERENCES

Central Nervous System

During normal development, the rate of growth of the vertebral column exceeds that of the spinal cord. This has clinically significant implications for the relationship between surface landmarks and anatomy when performing central neuraxial blocks in paediatric patients. The changes in the central nervous system with increasing age are outlined in Table 1.[2-4]

Peripheral Nervous System

The differences between children and adults are outlined in Table 2.[2,5]

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Structure	Neonate	12-mo-old	Adult	Clinical Implication
Spinal cord				
Termination of conus medullaris	L3 or L4	L1	L1	• In neonates and infants, SAB should be performed at L4 or below to avoid direct trauma to spinal cord.
Termination of dural sac	S3 or S4	S2	S2	• In neonates, there is a higher risk of dural puncture. Frequent aspiration while injecting small aliquots of LA and US-guidance may help to reduce this risk.
Bone				
Tuffier line	L5-S1	L5-S1	L4-L5	• In all age groups, surface landmarks influence the level of needle insertion.
Curvatures of the spine	Single spinal curvature, with high degree of flexibility	Cervical curvature appears at 3-6 mo; lumbar curvature at 8-9 mo	Thoracic kyphosis, lumbar lordosis present	• In adolescents and adults, a steeper needle insertion angle is required when performing an epidural compared to neonates. • In infants and neonates, there is increased cephalad spread of LA due to lack of lumbar lordosis compared with adolescents and adults.
Vertebrae	Cartilaginous bones	Delayed ossification	Bones are ossified	• In neonates and infants, sharp needles may traverse into bone, damaging ossification nuclei and increasing the risk of intraosseous LA injection. • Short-bevel, blunt-tip needles can decrease this risk. • In neonates and infants, there is better US visualisation of anatomy within the spinal canal (eg, spinal cord, nerve roots, dura).
Sacral vertebrae	Incomplete fusion	Fusion begins by 8 y of age	Sacral bone fusion completes by 25 y of age	• Sacral hiatus serves as portal of caudal injection until 6-8 y of age when fusion typically begins. • Sacral epidural approaches are possible until fusion complete.

Structure	Neonate	12-mo-old	Adult	Clinical Implication
Epidural fat/fascia/sheath/ aponeurosis	Increased fluidity of epidural fat and loosely attached fascia and sheaths	Increased fluidity of fat up to 6-8 y of age; loose attachment of fascia, sheath and aponeurosis	Paucity of epidural fat, increased fibrous tissue; firmly attached fascia, sheaths and aponeuroses	• In neonates and infants, is it easier to thread epidural catheters several centimetres along the epidural space without resistance, allowing thoracic-level epidural catheters to be threaded from a caudal or lumbar level entry point. • In neonates and infants, there is leakage of LA around the nerve roots. • In neonates and infants, a relatively large volume of LA is required to achieve a high-quality epidural block. • In neonates and infants, there is better US visualization of anatomy within the spinal canal in neonates and infants.
Ligament	Less dense	Less dense	Dense	• In neonates and infants, loss of resistance is subtle as compared with adults
Meninges				
Pia mater	Highly vascular	Highly vascular	Less vascular	• In children, systemic LA absorption is faster.
CSF volume	10 mL/kg	Infants 4 mL/kg Child 3 mL/kg	Adult 2 mL/kg	• In neonates and infants, a relatively larger dose of LA is required when performing spinal anaesthesia compared with adults. • In neonates and infants, SAB has a shorter duration of action compared with adults.
CSF volume in spinal canal relative to intracranial space	50%	50%	25% in spinal canal	• In neonates and infants, a relatively larger dose of LA is required when performing SAB.
Autonomic nervous system	Immature sympathetic nervous system, parasympathetic dominance, reduced autonomic compliance of the heart, smaller vascular bed in the lower limbs	Immature sympathetic nervous system, parasympathetic dominance, reduced autonomic compliance of the heart, smaller vascular bed in the lower limbs	Mature	• In children, peripheral vasodilation and hypotension are less common when performing central neuraxial blocks compared with adults.

Table 1. Differences in the Central Neuraxial Space Between Neonates, Infants, Children and Adults. CSF indicates cerebrospinal fluid; LA, local anaesthetic; SAB, subarachnoid block; US, ultrasound

Structure	Neonate	Child	Adult	Clinical Implication in Children
Myelination	Very immature	Myelination completed by 12 y of age	Complete myelination	• LA rapidly penetrates the nerves, producing fast-onset block. • A low concentration of LA can achieve a high-quality dense block.*
Endoneurium	Loose endoneurium	Loose endoneurium	Relatively firm	• Greater spread of LA produces a fast onset and high-quality block. • LA is absorbed quickly away from the nerves, producing a shorter-duration block.*
Vasculature surrounding nerves	Rich vasculature	Rich vasculature	Less vascular	• LA is absorbed quickly away from the nerves, resulting in a shorter duration of block.*

Table 2. Age-Related Differences in Peripheral Nervous System Between Children and Adults. LA indicates local anaesthetic. *The rapidity of onset and density of blocks as well as absorption of LA in and out of the nerves are inversely proportionate to age

LOCAL ANAESTHETIC CHOICE

Amide local anaesthetics (LAs) are frequently used in PRA. Ropivacaine and levobupivacaine are considered less cardiotoxic than bupivacaine.[6] Ester LAs, such as chloroprocaine, are metabolized efficiently by plasma cholinesterases and are considered safer than amide LAs.[6,7] Important differences in the pharmacokinetics in children are outlined in Table 3.[3,8,9]

Weight-based calculation of the maximum LA dose is essential in avoiding life-threatening local anaesthetic systemic toxicity (LAST).[10] Recommended doses are outlined in Table 4.[2]

ADDITIVES

Currently, there is no strong evidence for the routine use of additives in PRA. However, clonidine (1-2 μg/kg) or dexmedetomidine (1 μg/kg) are popular additives and may prolong analgesia.[11] Clonidine can be safely used in central neuraxial blocks. Both clonidine and dexmedetomidine are systemically absorbed and will contribute to postoperative sedation. Clonidine and dexmedetomidine are usually avoided in preterm babies and in infants less than 6 months old due to systemic absorption and prolonged sedation. Adrenaline is not recommended due to the risk of spinal cord ischaemia.[12]

PERIPHERAL NERVE CATHETERS

Peripheral nerve catheters (PNCs) allow continuous analgesia and should be considered for any child who has (or is anticipated to have) significant acute pain, such as postoperative pain, ischemic pain or amputation pain.[2] PNCs reduce opioid requirements and subsequently minimize the risk of opioid-related adverse effects, such as nausea, vomiting, constipation and respiratory depression.

Compared with a single injection regional block, continuous catheter techniques allow the following:

- Prolonged duration of analgesia
- Reduced opioid requirement and opioid-associated adverse effects
- Earlier ambulation[2]
- Shorter hospital stay[2]

A PNC can be left in situ for up to 7 days; however, each additional day beyond the fourth day increases the risk of catheter-related infection.[13] When deciding upon the duration of catheter use, the analgesic benefits should be weighed against the risk of infection.

Complications specifically related to PNC include the following:

- Catheter equipment failure, including dislodgement, migration, blockage, leakage, disconnection
- Skin reactions resulting from dressings
- Risks associated with single injection techniques (eg, nerve injury, failed block, LAST)

	Pharmacokinetic Consideration in Children	Clinical Implication in Children
Absorption	• Higher cardiac output and lower tissue binding, resulting in higher rate of systemic absorption.	• Shorter duration of LA action • Increased risk of LAST
Distribution	• Neonates have higher extracellular fluid volume and higher volume of distribution. • Low plasma concentration of α1-acid glycoprotein (0.2–0.3 g/L at birth), reaching adult levels (0.7–1.0 g/L) by 1 year of age. This results in an increased unbound fraction of LA in the plasma.	• Higher dose requirement in neonates after a single injection of LA, but LA accumulates with repeated doses • Higher unbound free fraction of LA in plasma, increasing risk of LAST
Metabolism	• Lignocaine and bupivacaine are initially metabolized by CYP3A7. By 9 mo of age, they are metabolised by CYP3A4. • Ropivacaine and levobupivacaine are metabolised by CYP1A2 which is relatively immature until 3 y, with full development by 8 y	• Half-life of amide LA in neonates 3-8 times longer than adults; hence, have increased risk of systemic toxicity when used as an infusion
Clearance for LA bolus injection	• Up to 2 y: Cm and clearance of amide LA decreased after bolus injection, and elimination half-life prolonged • > 2 y: clearance and elimination half-life increase progressively and exceed that of adults before returning to adult levels during adolescence	Free fraction of LAs ↑ in infants
Clearance for continuous infusion	• AAG ↑ on POD 1 and 2 protects against LAST • AAG ↓on POD 3 resulting in ↑ free fraction • Thus, it is advised to stop LA infusion in infants after 48 h • Lignocaine: continuous infusion results in substantial decrease in intrinsic clearance, since lignocaine metabolism is impaired by its own metabolites • Clearance is rate limited for both bupivacaine and ropivacaine and primarily dependent on protein binding • Bupivacaine: clearance decreases by more than 40%, and risk of accumulation exists • Ropivacaine: clearance remains unchanged	• Lignocaine is unsuitable for continuous infusion • Chloroprocaine and ropivacaine are considered to be safer choices

Table 3. Differences in Paediatric and Adult Pharmacokinetics. AAG indicates α1-acid glycoprotein; Cm, peak plasma concentration; CYP, cytochrome P450; LAST, local anaesthetic systemic toxicity; POD, postoperative day

EQUIPMENT

Age-appropriate equipment should be used to maximize the likelihood of block success and minimize the risk of inadvertent vascular or organ injury. Note also the following:

- Use ultrasound (US) guidance to allow accurate catheter placement and reduce the risk of inadvertent vascular or organ injury.[14] This is particularly important in children because their nerves are more superficial and adjacent major organ and vascular structures are in close proximity.

		Maximum Hourly Infusion Rate, by Age, mg/kg/h		
	Maximum Bolus Dose, mg/kg	4 mo to 1 y	1 to 4 y	>4 y
Ropivacaine	3	0.25	0.35	0.4
Bupivacaine	2	0.25	0.35	0.4
Levobupivacaine	3	0.25	0.35	0.4
Lidocaine	5 (10 with adrenaline)	Not recommended		
2-Chloroprocaine	7 (10 with adrenaline)	10 (without adrenaline)		
Procaine	7 (10 with adrenaline)	Not recommended		

Table 4. Local Anaesthetic Dose Recommendations

- When selecting an appropriate needle, consider the depth of the intended block to be performed and the size of the patient. Consider using a smaller gauge to minimize local tissue trauma. A shorter needle length will maximize needle control during block placement.
- Use a short bevel or Touhy needle; it is associated with less risk of direct nerve injury compared with a sharp, long-bevelled needle.
- To minimize the risk of catheter dislodgement, secure the catheter carefully and consider tunnelling it.

CONTROVERSIES

Awake Versus General Anaesthesia

In adult patients, regional anaesthesia performed awake or under light sedation allows early detection of LAST and reduced risk of intraneural injection. However, in children, performing a regional block awake or with minimal sedation may result in child distress and movement during block placement. Furthermore, a frightened child is unlikely to report symptoms of LAST. The American and European Societies of Regional Anaesthesia Joint Committee Statement recommends that PRA performed under general anaesthesia or deep sedation has an acceptable safety profile and is considered to be the standard of care.[15]

Compartment Syndrome

Compartment syndrome (CS) is caused by increased pressure inside a fascial compartment resulting in impaired blood flow and, if unrecognized, may result in muscle ischaemia and myonecrosis. One of the early symptoms of CS is pain, and there is concern that PRA could mask this pain. While there is no current evidence that the use of regional analgesia increases the risk of CS or delays its diagnosis,[15] caution should be exercised, and we recommend the following for patients at risk of CS:

- Maintain a high index of suspicion and careful monitoring. If CS is suspected, compartment pressures should be urgently assessed.
- Use dilute LA solutions (eg, 0.1% ropivacaine) because they are less likely to mask ischaemic pain and less likely to produce a motor block.
- Avoid the use of additives because they will increase the density of the sensory and motor block.[15]

Saline Versus Air

The most common techniques for performing an epidural block are loss of resistance (LOR) to saline, LOR to air or a combination of these techniques.

LOR to air may be associated with a risk of air embolism, incomplete analgesia due to air trapping, nerve root compression, subcutaneous emphysema and pneumocephalus. These risks are heightened in infants and neonates because their epidural space is smaller and the same volume of air would cause more disturbance. The total volume of injected air should not exceed 0.5-1 mL in infants and neonates.

LOR to saline overcomes many of the issues associated with the LOR to air technique; however, the volume of saline injected should still be minimised because this can dilute the LA injected, and a large volume of injectate may cause a transient reduction in cerebral blood flow in smaller infants and neonates.[16] Furthermore, it may be more difficult to identify a dural puncture using the LOR saline technique because of the inability to easily differentiate between saline and cerebrospinal fluid.

A combination of air and saline allows for an obvious LOR while minimising the risk of injecting air and minimising the volume of saline injected.[15] This technique is also associated with a lower risk of dural puncture than when either saline or air is used alone. There is currently no clear evidence regarding which technique is superior, and any of the above techniques are acceptable provided the injected volume is kept to a minimum.[15]

Patients With Preexisting Neurologic Conditions

In patients with preexisting neurologic conditions affecting cardiac and respiratory function, PRA may be beneficial in optimising analgesia, minimising opioid-related ventilatory impairment and minimising haemodynamic disturbances related to pain after surgery. However, there is concern that PRA may create new or worsened neurologic deficits, due to the dose-dependent neurotoxicity of LAs.[17] Preexisting neurologic disease is not an absolute contraindication to PRA. If PRA is planned, a thorough neurological examination should be documented prior to the procedure. A conservative approach is recommended, and the individual patient's risks versus benefits should be carefully considered.[17]

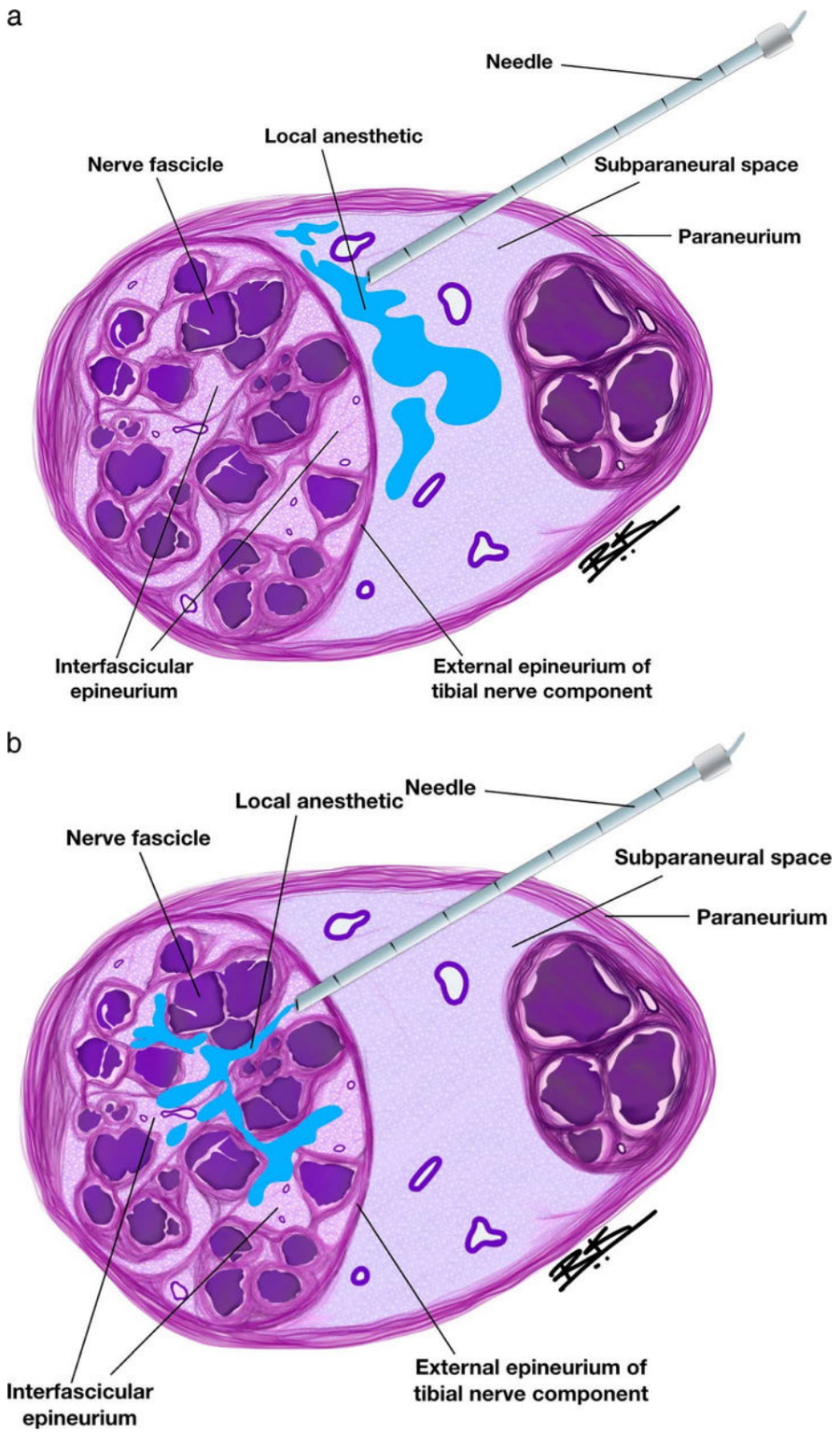

Figure. (a) Subparaneural injection. (b) Interfascicular injection. (c) Intrafascicular injection. Illustration by Dr Rammurthy Kulkarni Affiliation: Dr. Rammurthy, Consultant Anesthesiologist, Axon Anesthesia Associates, Sathya Sai Orthopedic and Multispeciality Hospital, Bangalore.

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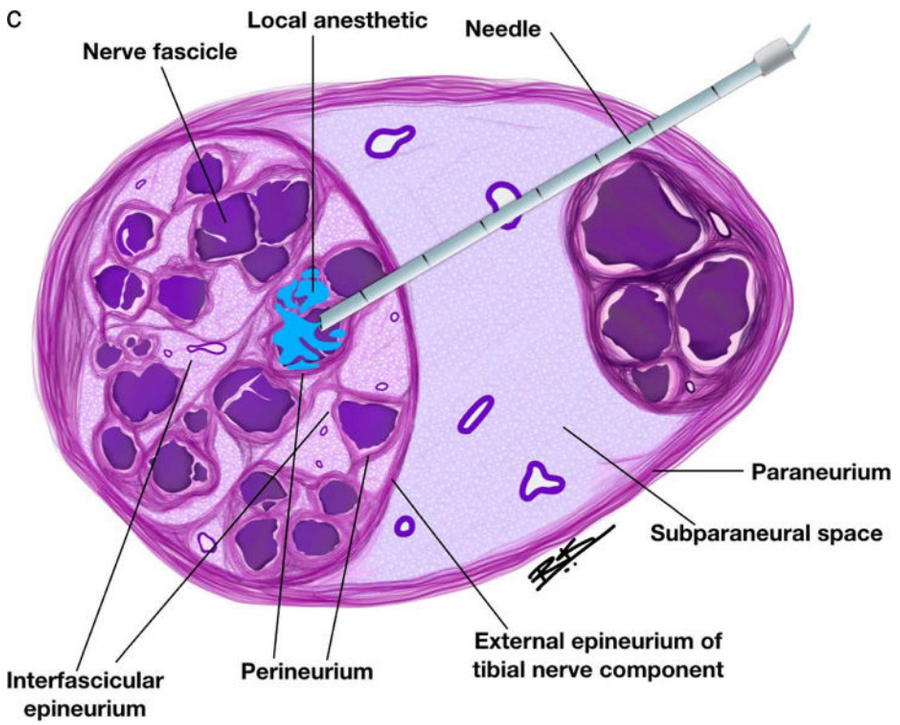

Figure. Continued.

Liposomal Bupivacaine in RA

Studies have revealed no superiority of liposomal bupivacaine over nonliposomal bupivacaine in peripheral nerve blocks. Currently, there is no role for liposomal bupivacaine in paediatric regional analgesia, and more evidence is required to support its use.[18]

SAFETY

US and Peripheral Nerve Stimulation

US allows visualisation of the needle tip and spread of injected LA, and it minimises the risk of inadvertent injury to nearby vascular or organ structures. Furthermore, the use of US results in faster onset, increases the duration, increases the block density and reduces the LA volume required. There are fewer needle insertions and better user appreciation of the underlying anatomy.[2] In children, linear high-frequency probes can be used for most blocks.

Peripheral nerve stimulation is a useful adjunct when combined with US guidance. The needle position is judged to be adequate when muscle contraction in the desired nerve distribution occurs at 0.5-0.8 mA. If muscle contractions continue to occur at $<$0.5 mA, the needle should be withdrawn slightly to avoid nerve damage or intraneural injection (Figure a-c). This technique is useful to improve reliability when teaching trainees, for deeper blocks when perfect nerve visualisation may not be possible (such as the lumbar plexus block, anterior sciatic block) and in low-resource settings where US equipment may not be available.[2]

Test Dosing

A test dose containing LA, adrenaline or both, may be administered to identify inadvertent intravascular needle placement.[19] The paediatric test dose is 0.5 μg/kg of adrenaline (or 0.1 mL/kg of LA containing 5 μg/mL adrenalin). Some institutions use 1.5% lidocaine with 1:200 000 adrenaline. A positive test dose is defined as an increase in heart rate ($>$10 beats per minute), increase in systolic blood pressure ($>$15 mm Hg) or 25% change in T-wave amplitude or ST segment size. However, test doses have a high false-negative rate.[19] Other methods of detecting intravascular needle placement include aspiration for blood and observing the LA spread during injection on US. However, there is no absolutely reliable method to detect intravascular needle placement; therefore, we recommend that any injection of LA is performed slowly with intermittent aspiration while observing the electrocardiographic morphology.[19]

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Aseptic Precautions

Regional blocks must be performed under aseptic conditions to minimize the risk of infection. For children younger than 2 months, chlorhexidine (2% or 1%) can cause chemical burns, so alcohol is preferred.[20] In older children, 2% chlorhexidine with 70% alcohol is recommended.

Local Anaesthetic Systemic Toxicity

When PRA is performed under general anaesthesia or deep sedation, the earliest signs of LAST are cardiovascular including peaked T waves and dysrhythmias. Infants $<$6 months old are at highest risk of LAST due to unrecognized intravascular injection, rapid absorption, distribution of LA and decreased levels of α1-acid glycoprotein.[2] All providers must be familiar with current LAST management guidelines, and weight-based dosing must be followed.

ENHANCED RECOVERY AFTER SURGERY

Enhanced recovery after surgery (ERAS) protocols are multidisciplinary, multimodal, evidence-based pathways designed to optimize perioperative medical care and facilitate early recovery.[2] Regional anaesthesia is an important element of ERAS because it allows optimal analgesia, reduces opioid requirements and facilitates earlier return of bowel function and ambulation.[2]

SUMMARY

PRA is an essential element of perioperative care and should be considered in children undergoing surgery. It has a high safety profile and can be performed under GA or deep sedation. Safety precautions, such as US guidance (when available) and careful LA dose calculation, should always be taken when performing PRA.

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