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General principles of regional anaesthesia in children

F. Merella[1,*], N. Canchi-Murali[1] and V. Mossetti[2]

[1]Birmingham Children's Hospital, Birmingham, UK and [2]Regina Margherita Children's Hospital, Turin, Italy

*Corresponding author: federica.merella@nhs.net

Learning objectives

By reading this article, you should be able to:

- Explain the benefits of ultrasound-guided regional anaesthesia in children.
- Discuss the main physiological and anatomical differences between adults and children.
- Demonstrate knowledge of appropriate local anaesthetic agents and adjuncts, their doses in children, and measures to prevent systemic toxicity.
- Recognise the controversies in regional anaesthesia and the current recommendations.

Key points

- Regional anaesthesia in children has many well-documented benefits.
- Advances in ultrasound technology have enabled practitioners to perform regional blocks in children with greater accuracy.
- Central neuraxial blocks have been progressively replaced by peripheral nerve blocks.
- Large retrospective studies and data from a prospective registry suggest that regional anaesthesia is a viable and safe option for postoperative pain relief in children.

Regional anaesthesia (RA) in children has gained acceptance worldwide over the past few decades, and many factors have contributed to the rapid growth in its use. There is good evidence that RA provides good-quality postoperative pain relief.[1–5] In addition, advances in ultrasound (US) technology have influenced the practice of RA in paediatric practice.

The benefits of RA in children include: (i) reduced opioid consumption; (ii) reduced incidence of postoperative nausea and vomiting; (iii) reduced postoperative pain scores; and (iv) reduced incidence of respiratory complications.[6]

The prevalence of persistent postoperative pain in children after major surgery remains high.[7] RA is being increasingly used as part of multimodal analgesic regimens, and has proved to be a valid alternative to conventional opioid-based strategies.

The drive to reduce the duration of hospital stay and the increased proportion of surgery performed as day-case procedure in higher income countries, has led to an increased use and diversification of RA techniques, as these techniques improve postoperative pain relief and enable early discharge after surgery.

Single-shot or catheter techniques, such as paravertebral, transversus abdominis plane, and ilioinguinal and iliohypogastric blocks, are increasingly being offered as part of multimodal analgesic regimens for thoracic and abdominal procedures, although they are still under-utilised.[8–10]

Safety of RA in children

Serious adverse events after RA in children are rare. The first and second French-Language Society of Paediatric Anaesthesiologists audits (Association des Anesthésistes Réanimateurs Pédiatriques d'Expression Française

Federica Merella MD EDAIC is a consultant paediatric anaesthetist at Birmingham Children's Hospital, who has a special interest in paediatric regional anaesthesia.

Naveen Canchi Murali MD FRCA is a consultant paediatric anaesthetist at Birmingham Children's Hospital, who has a special interest in paediatric regional anaesthesia.

Valeria Mossetti MD is a consultant paediatric anaesthetist at Reginal Margherita Children's Hospital in Turin, Italy, who has expertise in regional anaesthesia for children. She has published several articles on the subject and is a member of the faculty of the European Society of Regional Anaesthesia & Pain Therapy (ESRA) Italia faculty. She has also been an invited speaker at previous ESRA and European Society of Paediatric Anaesthesiology (ESPA) conferences.

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[ADARPEF]) reported a rate of complications at 0.12% (95% confidence interval [CI]: 0.09–0.17).[11,12]

Subsequent data from the Pediatric Regional Anesthesia Network (PRAN) registry of more than 100,000 nerve blocks confirmed similar findings.[13] Transient neurological deficit was recorded in only 25 cases (2.4 in 10,000 [95% CI: 1.6–3.6 in 10,000]), but none resulted in permanent sequelae. The most common adverse events were catheter malfunctions, such as displacement, occlusion, and disconnection, which occurred in 4% of cases.

Another analysis of neuraxial techniques, which included 18,650 caudal blocks, showed an incidence of complications of 1.9% (95% CI: 1.7–2.1), with a peak in children younger than 6 months.[14]

Similar findings were reported from the UK National Paediatric Epidural Audit, which showed only a few serious adverse events, including two epidural abscesses, one case of meningism, one post-dural puncture headache, and five cases of severe neuropathy/radiculopathy, which resolved over a period of 4–10 months.[15] A single case of cauda equina syndrome in a 4-month-old child was the only persistent neurological deficit reported in 10,633 neuraxial blocks. In a more recent single-centre prospective study, Vicchio and colleagues found similar results.[16] Although neuraxial complications can be potentially devastating, their incidence is extremely low; some cases are potentially preventable, whilst in others the aetiology is unclear.[17,18]

In addition, the risk of infection from continuous epidural infusion is low, and its main risk factor is the duration of catheter placement.[18]

Regional anaesthesia has a protective effect in reducing surgical stress and the minimum alveolar concentration of volatile anaesthetic agents.[6] Another potential advantage is the option that certain surgical procedures may be performed using neuraxial anaesthesia in neonates and infants breathing spontaneously with minimal airway instrumentation. When appropriate, peripheral nerve blocks (PNBs) should be offered as an alternative to neuraxial anaesthesia.[12,13]

US imaging in RA

Kapral and colleagues published the first report of the use of US imaging in RA in 1994.[19] A few years later, its first application in RA practice in children was reported.[20] Since then, the use of US in the performance of RA in children has increased rapidly.

US as a diagnostic tool

Ultrasonography is a valuable aid in visualising anatomical structures, such as sacral dimples or hairy birthmarks in young children. Such features could arouse suspicions of underlying spinal dysraphism or bony defects, both of which are deemed contraindications to neuraxial techniques. US has also enabled anaesthetists to assess the degree of angulation of the spinal processes for epidural anaesthesia, guiding clinicians in optimising the angle of insertion of the Tuohy needle.

Advantages of US compared with other techniques

Historically, high volumes of local anaesthetic (LA) have been used to compensate for imprecise needle placement during landmark-based regional blocks, potentially exposing children to the risk of LA toxicity. US imaging permits a careful evaluation of anatomical targets, visualisation of anatomical variations and of vital structures surrounding the nerves, and distribution of LA around the nerve or plexus. Advances in US technology have improved accuracy and clarity in identifying structures and fascial planes, allowing newer techniques to be developed (*transversus abdominis* plane, quadratus lumborum, pectoralis, and serratus anterior blocks).

In children with skeletal or connective tissue disorders, such as epidermolysis bullosa and syndactyly, the responses to a peripheral nerve stimulator (PNS) can be unreliable and the muscle contractions elicited by these stimuli could be harmful to the fragile tissues. US-guided nerve blocks in such cases prevent the need for the use of a PNS and reduce the potential for tissue damage.[20]

Studies in adults and children demonstrate that US-guided regional block increases precision and success rate, enables a faster onset of block, and reduces the amount of LA injected.[9,21]

Technical considerations

On a transverse-axis view, peripheral nerves can appear as small circles of a few millimetres in diameter, with little interposing adipose tissue or muscle septa. The appearance of nerves can vary from hypo- to hyperechoic, depending on their diameter and the frequency and angle of the US beam.

Whilst it is important to stress that every nerve has its own particular US appearance, as a general rule, more central, compact structures like plexuses tend to generate hypoechoic pictures, whilst moving peripherally towards their terminal branches, nerves often appear hyperechoic, because of the presence of large subepineural and interfascicular connective tissues.

As nerves and plexuses are often located close to vital structures, such as the spinal cord, pleura (Fig. 1A), major blood vessels, and peritoneum, high-frequency US probes (10–15 MHz) are recommended in children, with an active transducer surface length between 25 and 30 mm.

The in-plane (IP) technique, maintaining the needle path along the transducer long axis, Fig. 1(B), is the technique of choice in children, as it permits continuous visualisation of needle tip and its entire length during performance of the block.

Lack of training in US-guided RA is believed to be one of the factors limiting its uptake in paediatric practice. Adequate integrated training in US imaging and needling techniques is vital for the safe performance and increased appropriate use of RA in children.[21]

Local anaesthetics

Local anaesthetics are weak bases classified as amide or ester, depending on the intermediate chain between their hydrophobic and hydrophilic domains. Free fractions of both ester and amide LAs bind to the voltage-dependent Na^+ channel, preventing depolarisation of the cell membrane, which ultimately blocks the nerve conduction for afferent pain signals and efferent motor transmission.

Esters are rapidly metabolised by plasma pseudocholinesterase in adults and young children (including neonates), whilst amides require hepatic biotransformation by cytochrome P450 enzymes, whose function is still immature at birth. Compared to esters, amide LAs produce a lower

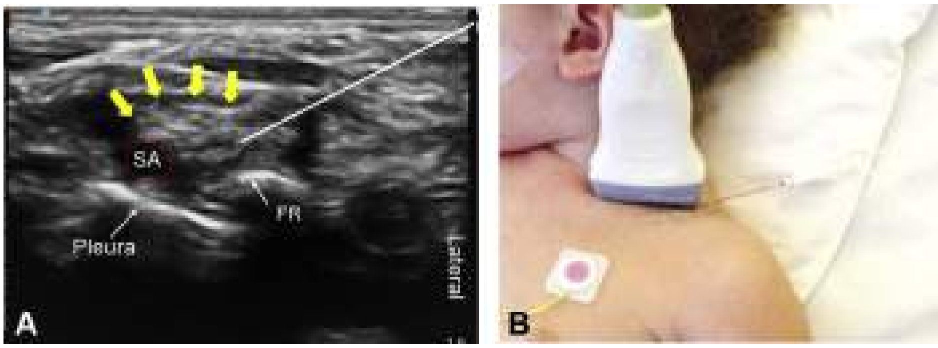

Fig 1 (A) US image of the right supraclavicular area in a young child. The yellow arrows indicate the brachial plexus sitting on top of the first rib. FR, first rib; SA, subclavian artery. The fine white line indicates the needle path and trajectory. (B) Patient positioning for a supraclavicular brachial plexus block. Linear US transducer positioned along the plexus short-axis view using an IP needle approach.

incidence of allergic reactions, greater lipid solubility and potency, prolonged duration of action, and a greater stability to hydrolysis. Hence, in current paediatric practice, the only ester LA used in practice is tetracaine, which is indicated for spinal anaesthesia in neonates, infants, and young children.

Lidocaine is the oldest, safest, and most popular amide LA, but has a short duration of action. The newer S-enantiomers, levobupivacaine and ropivacaine, introduced in the early 2000s, are considered the drugs of choice for RA in children. Both drugs have a prolonged action with better cardiac and neurotoxicity profiles compared with the respective racemic preparations. In addition, ropivacaine has differential neural block properties, with an increased motor-sparing effect.

In 2018, the European Society of Regional Anaesthesia & Pain Therapy (ESRA) and the American Society of Regional Anesthesia and Pain Medicine (ASRA) joint committee published evidence-based recommendations, harmonising the choice, dosage of LA, and adjuvant use for RA in children (Table 1).[22]

Key differences between adults and children

Neonates and infants differ from older children and adults in anatomical, physiological, and pharmacokinetic characteristics. Whilst appreciation of smaller and more superficial structures is a critical step, anatomical differences in the spine must also be considered before performing neuraxial blocks (Table 2).

Infants have an increased cardiac output and immature hepatic function (in both synthetic and clearance pathways), which can result in increased systemic absorption and accumulation of LA. The accumulation of LA potentially increases the risk of LA systemic toxicity (LAST), especially with repeated bolus doses or a continuous infusion (Table 2).

LA systemic toxicity

Local anaesthetic systemic toxicity is a very rare, but potentially fatal event in children, with an estimated incidence of 0.76–1.6:10,000; the majority of cases occur in infants.[12,13,23]

In the second ADARPEF study, LAST resulted in one case of convulsions, whilst the UK epidural audit reported only two respiratory arrests and one seizure.[12]

The current PRAN registry reported seven events, five of which in infants (0.76 in 10,000 [95% CI: 0.3–1.6 in 10,000]).[13] Only three cases (two cardiac arrests and one seizure) required rescue treatment with an intra-lipid. Measures suggested to minimise the risk of LAST include a high level of vigilance; continuous monitoring of vital signs (including ECG); strict compliance with recommended LA doses; and gentle aspiration followed by slow and fractionated injection of LA, avoiding excessive pressure. Conditions that could enhance toxicity, such as hypoxaemia, acidaemia, and hypercarbia, should also be avoided. The maximum safe doses for ropivacaine and levobupivacaine should follow those doses suggested for bupivacaine (Table 1).

Early recognition of toxicity is paramount. However, as the majority of children are either anaesthetised or heavily sedated, the detection of CNS symptoms can be challenging. Cardiovascular toxicity can occur without any preceding CNS symptoms.

Table 1 ASRA/ESRA recommendations for a single-injection LA dose for neuraxial nerve block and PNB in children

Nerve block	Drug and concentration	Dose (ml kg^{-1})
Spinal anaesthesia	Tetracaine 0.5%	0.5–1
	(Child <5 kg) hyper-isobaric bupivacaine 0.5%	1
	(Child 5–15 kg) hyper-isobaric bupivacaine 0.5%	0.4
	(Child >15 kg) hyper-isobaric bupivacaine 0.5%	0.3
Caudal	Ropivacaine 0.2% or levobupivacaine 0.25%	0.5–1.2
Upper limb	Bupivacaine, levobupivacaine 0.25%, or ropivacaine 0.2%	0.5–1.5
Lower limb	Bupivacaine, levobupivacaine 0.25%, or ropivacaine 0.2%	0.5–1.5
Fascial plane blocks	Bupivacaine 25% or ropivacaine 0.2%	0.2–0.75

Table 2 Key anatomical and physiological differences between adults and young children

Characteristics		Clinical implications
Anatomical	Nerves, vessels, and tendons are smaller; very superficial; with less adipose tissues; and lie close together	Potential risk of injury to nerve and structures around nerves; US imaging improves accuracy of needle placement
	The endoneurium has less connective tissue Nerves have shorter diameter with incomplete myelin sheath. Complete myelination may take several years	Early onset of both sensory and motor blocks with a risk of prolonged motor block, even with lower concentrations of LA
	Neonates: The dural sac ends at S3–S4 (S2 in adults)	Caution must be taken whilst advancing needle during caudal anaesthesia to avoid dural puncture
	The intercristal line is at L5-S1 (L4–L5 in older children and adults) Spinal cord terminates at L3 (L1 in adults)	Spinal anaesthesia should be performed below L4
Physiological	Results of high cardiac output: (i) Increased systemic absorption of LA (ii) Relatively high proportion of cardiac sodium gated channels are in an open state, with a high affinity to LA	Increased risk of cardiac toxicity
	Hepatic metabolism of LA is not fully functional until 9 months of age. There is reduced concentration of α_1-acid glycoprotein until 1 yr of age	Risk of drug accumulation after repeated doses of LA or during continuous infusion
	Lumbar ortho-sympathetic component is poorly represented in children	Children are less prone to hypotension after neuraxial block

Lipid resuscitation therapy (LRT) in the form of intralipid 20% has shown encouraging results both in animal models and human studies. The latest research results suggest that LRT could work through a multimodal mechanism, which comprises the ability to remove drugs from the brain and myocardium, and redistribute them to muscle and liver, enhancing detoxification. Lipid rescue also improves myocardial performance through its lipid substrates.[24] Ten of the eleven documented cases of LAST in children have been successfully treated with LRT.[25] The Society for Pediatric Anesthesia (SPA) and the ESRA/ASRA joint committee have recently proposed a management guideline for LAST in paediatrics, adapted from the latest adult ASRA guidelines, limiting the maximum cumulative amount of LRT to 10 ml kg^{-1} (Box 1).[25,26]

Adjuncts in paediatric RA

The analgesic effect of a single-shot PNB does not generally extend over 12 h, requiring a plan for supplemental analgesia in the extended postoperative period. The use of adjuncts has been advocated for PNB in children and can provide the following advantages: (i) early onset of block; (ii) enables the use of diluted LA, especially in neonates and young infants, reducing the total dose of LA; (iii) potential reduction in the incidence of LAST; (iv) prolonged duration of block (at least a 50% increase over LA alone); and (v) reduced use of opioids, with concomitant reduction in adverse effects.

In neuraxial block, the ESRA/ASRA joint committee has suggested that the use of either preservative-free morphine (10–20 $\mu g\ kg^{-1}$) or clonidine (1–2 $\mu g\ kg^{-1}$) through intrathecal injection improves the quality analgesia and the duration of blocks.

The intrathecal injection of racemic ketamine is not recommended in neonates and infants because of concerns over potential neurotoxic effects. It should be used with caution and only in older children at a dose not exceeding 0.5 $\mu g\ kg^{-1}$. Dexamethasone is not recommended in the absence of any evidence from paediatric studies to support its use.

In the context of PNBs, findings from a recent meta-analysis on α_2-adrenoceptor agonists, clonidine and dexmedetomidine, showed an improvement in postoperative analgesia compared with plain LA.[27] In absence of more data on toxicity, the minimum effective dose is generally recommended.

Currently, there is no evidence to recommend other additives (such as midazolam, neostigmine, magnesium, buprenorphine, and tramadol), and their use in children should be considered only in the context of clinical trials.

Controversies in paediatric RA

Several aspects of paediatric RA have generated debate amongst experts. Recent recommendations released by the ESRA/ASRA joint committee on some of these critical topics aim to provide clarification and guidance on safe practice in children.[28]

The following sections provide a summary of recommendations on asleep compared with awake analgesia, compartment syndrome, the value of a test dose, and saline compared with loss-of-resistance techniques.

Awake *vs* asleep

RA has been successfully described in awake children for short duration of surgery. Potential advantages of awake RA include early detection of symptoms of LAST, reduced risk of intra-neural injection, permanent nerve damage and of complications associated with general anaesthesia (GA), including opioid-related adverse effects. However, in paediatric patients, awake RA may not always be practical and may be associated with an increased risk of failure or potential harm. Causative factors include high levels of patient anxiety, uncontrolled movements during the performance of a block,

Box 1

Management of local anaesthetic toxicity in children: SPA guidelines.

- Stop injecting the local anaesthetic and call for help.
- Confirm or establish adequate IV access.
- Maintain the airway and give 100% oxygen. Consider tracheal intubation and optimize lung ventilation.
- If seizures occur give a benzodiazepine, such as midazolam 0.05–0.1 mg kg^{-1} min^{-1} i.v., while assessing cardiovascular status throughout.
- Treat hypotension with small epinephrine dose (max 1 mcg kg^{-1}).
- Avoid propofol, vasopressin, calcium channel blockers and beta blockers.
- Administer intravenous intralipid as an initial bolus injection of 20% lipid emulsion 1.5 ml kg^{-1} over a min.
- Start an infusion of 20% lipid emulsion at 0.25 ml kg^{-1} min^{-1}.
- Increase the infusion to 0.5 ml kg^{-1} min^{-1} if cardiovascular stability is not restored.
- Repeat bolus every 3–5 min up to 4.5 ml kg^{-1} as total dose until circulation is restored.
- The total dose should not exceed 10ml kg^{-1}.
- Recognize arrhythmias and or cardiac arrest: cardiopulmonary resuscitation (CPR)/pediatric advanced life support (PALS)/advanced paediatric life support (APLS) guidelines.
- Continue chest compressions (lipid must circulate). May need prolonged compressions.
- Consider alerting nearest cardiopulmonary bypass/ECMO centre and ICU if no return to spontaneous circulation after 6 min.
- Monitor and correct acidosis, hypercarbia and hyperkalemia.

and difficulty in assessing the intensity of painful stimuli reported by young patients.

The late ADARPEF study reported an incidence of postoperative neurological symptoms of 0.17% in 29,870 blocks performed under GA. LAST occurred in only one awake patient.[12] In The current PRAN study, the risk of neurological complications or severe LAST was 2.2 in 10,000 (95% CI: 1.5–3.4) for nerve blocks performed under GA, and 15.2 in 10,000 (95% CI: 7.8–28.4) for blocks placed in sedated or awake patients.[13] Such risk remained higher (odds ratio: 2.93; 95% CI: 1.34–5.52; $p<0.01$), even when adjusted for age and validated findings from a previous analysis.[29] Nerve injuries in both studies recovered without sequelae.

The ASRA/ESRA committee advises that, given the acceptable safety record (risk of complications: 0.66%; risk of paralysis: 0–0.004%), paediatric RA performed under GA or deep sedation should be considered the standard technique in children.

Careful patient selection is the key to identifying the few highly motivated children where awake RA could be a viable option.

Acute compartment syndrome

A sudden increased pressure within a fascial compartment can cause an acute compartment syndrome (ACS), for example after a fracture, trauma or an ischaemic vascular event. Expansion of soft tissues within a non-compliant space can cause ischaemia with initial signs of motor and sensory dysfunction, which, if unrecognised or misinterpreted, can lead to necrotic injury of nerves and muscles. A compartment pressure >30 mmHg is considered critical and should prompt immediate intervention. Continuous epidural or perineural catheter LA, and single-shot LA, have all been blamed for masking early signs of ACS.

However, only a few case reports of ACS in paediatrics have been published, and none of them showed a convincing link between RA and delayed diagnosis of ACS, which suggests that sudden pain in previously comfortable patients treated with RA should raise suspicion of ACS.

The ESRA/ASRA committee reported that common symptoms of ACS of both upper and lower limbs were (i) increasing pain with increasing analgesic requirement, and (ii) swelling. Conversely, (i) pain remote from the site of surgery, (ii) paraesthesia not ascribed to the analgesic technique, and (iii) pain on passive movement of the limb were more-reliable signs of impending lower-limb ischaemia.

The board concluded that there is no convincing evidence that RA complicates the diagnosis of ACS, provided patients are adequately monitored and assessed in the perioperative period. The current best practice guidelines are suggested as follows:

(i) Concentration of LA for a single shot in peripheral and neuraxial blocks: bupivacaine, levobupivacaine, or ropivacaine 0.1–0.25%; these are less likely to mask ischaemic pain or to produce muscle weakness.
(ii) Dose for continuous infusion: bupivacaine, levobupivacaine, or ropivacaine 0.1% as the maximum permitted concentration.
(iii) For high-risk surgery for ACS, when a sciatic nerve catheter is indicated, a restriction in LA volume and concentration is advisable.
(iv) Cautious use of LA adjuvants is recommended, as they could enhance the duration and density of the block.
(v) High-risk patients should be adequately reviewed by the acute pain services to allow the detection of potential, early ACS signs and symptoms.
(vi) If ACS is suspected, measurement of compartment pressure should be performed urgently.

Test dose and intravascular injection

Adding adrenaline (epinephrine) (2–5 μg kg^{-1}) to LA to detect accidental intravascular injection in children is controversial. GA and deep sedation are both confounding factors for a correct interpretation of an increase in HR. In addition, false-negative results might be caused by incomplete i.v. administration of the test dose and, although the absence of T-wave changes might be reassuring, it does not entirely exclude intravascular injection.

Given the intrinsic challenge in interpreting a negative response, the use of a test dose should remain discretionary. If a test dose is used, the LA solution should be injected slowly, in fractioned boluses (0.1–0.2 ml kg^{-1}), with intermittent aspiration and under ECG monitoring.

Finally, a test dose should be interpreted as positive, if T wave or HR modification happens within 30–90 s after its injection.

Air or saline for loss-of-resistance technique

Given the paucity of studies supporting either technique, when used appropriately and when also minimising the injected volume, both techniques have an acceptable level of safety in both infants and children, but in neonates and infants, the cumulative volume of injected air should be limited to 1 ml.

Conclusions

A growing body of literature has dispelled concerns about the safety of RA under GA or deep sedation in paediatric practice. Training in the acquisition of US imaging and needling skills, knowledge of paediatric anatomy and physiology, and familiarity with the latest guidelines are key elements to the successful and safe practice of RA in children.

Declaration of interest

The authors declare that they have no conflicts of interest.

MCQs

The associated MCQs (to support CME/CPD activity) will be accessible at www.bjaed.org/cme/home by subscribers to *BJA Education*.

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