WHAT’S NEW IN PEDIATRIC REGIONAL ANESTHESIA?

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Pediatric Regional Anesthesia

What is new?

1: From central (caudal) blocks to peripheral blocks
The use of ultrasound guidance for perioperative neuraxial and peripheral nerve blocks in children (Review)

Guay J, Suresh S, Kopp S
Implications for practice

Evidence of high quality suggests that ultrasound guidance increases the success rate and increases block duration for regional blockade in children. Although we do not have enough information to state a specific age limit, evidence indicates that improved success rate and increased block duration were more pronounced in studies including younger children. Ultrasound guidance also seems to lead to slight improvement in pain scores at one hour after surgery and decreases time to perform the block in some situations (pre-scanning before neuraxial block and out-of-plane techniques). The amplitude of the effect for these two outcomes was very small and therefore may not be clinically relevant. Ultrasound guidance also decreases the number of needle passes, but as a vast majority of blocks in children are performed with the child under deep sedation or general anaesthesia, the clinical relevance of this finding is arguable. No major complications were reported in any of the included studies. The incidence of lasting severe neurological complications is fortunately very low; therefore, it is unlikely that an optimal sample size could ever be achieved for this outcome with RCTs. No local anaesthetic toxicity was reported in the included studies, but here again, the number of participants included in our review is probably insufficient to eliminate a difference in the incidence of local anaesthetic toxicity when ultrasound guidance is used for regional blockade in children. Altogether, whether or not these differences justify the extra cost of ultrasound guidance may need to be evaluated.
Age range: 1 day to 18 years.

18279 total blocks were performed:

53.4% central blocks and 46.6% peripheral blocks.

Caudal blocks represented 82.1% of central blocks. We recorded 164 peripheral catheter placements (1.9% of all peripheral blocks):

1688 epidural catheter placements (17.3% of all central blocks): 259 thoracic and 1429 lumbar.

Complications: 12 dura punctures with 2 headache; 1 Horner’s syndrome; 2 infected catheters (0.12%).

All blocks performed under sedation/general anesthesia.
All blocks performed in spontaneous ventilation.
### Table 2. Regional blocks according to patient's age (n = 18279)

<table>
<thead>
<tr>
<th>Block</th>
<th>&lt; 1 year</th>
<th>1-3 years</th>
<th>3-8 years</th>
<th>8-12 years</th>
<th>&gt;12 years</th>
<th>Total blocks</th>
<th>%</th>
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<tbody>
<tr>
<td>Epidural</td>
<td>2092</td>
<td>3051</td>
<td>3698</td>
<td>598</td>
<td>325</td>
<td>9763</td>
<td>53.4</td>
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<tr>
<td>Peripheral</td>
<td>222</td>
<td>1144</td>
<td>2314</td>
<td>2954</td>
<td>1882</td>
<td>8516</td>
<td>46.6</td>
</tr>
<tr>
<td>Block</td>
<td>&lt;1 year</td>
<td>1-3 years</td>
<td>3-8 years</td>
<td>8-12 years</td>
<td>&gt;12 years</td>
<td>Total blocks</td>
<td>%</td>
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<tr>
<td>Central</td>
<td>2092</td>
<td>3051</td>
<td>3698</td>
<td>598</td>
<td>325</td>
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<td>53.4</td>
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<tr>
<td>Thoracic epidural</td>
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<td>Lumbar epidural</td>
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<tr>
<td>Peripheral</td>
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<td>2314</td>
<td>2954</td>
<td>1882</td>
<td>8516</td>
<td>46.6</td>
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<tr>
<td>Upper limb</td>
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<td>741</td>
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<td>2512</td>
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<tr>
<td>Interscalenic</td>
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<td>6</td>
<td>50</td>
<td>116</td>
<td>19</td>
<td>193</td>
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<tr>
<td>Supraclavicular</td>
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<td>Infraclavicular</td>
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<td>Medial</td>
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<tr>
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<td>Femoral</td>
<td>Sciatic</td>
<td>Saphenous</td>
<td>Obturator</td>
<td>Trunk, abdomen</td>
<td>Ilioinguinal-iliohypogastric</td>
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<td>405</td>
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<td>368</td>
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<td>304</td>
<td>653</td>
<td>405</td>
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<td>1696</td>
<td>222</td>
<td>222</td>
<td>2428</td>
<td>1167</td>
</tr>
<tr>
<td></td>
<td>18.3</td>
<td>7.4</td>
<td>9.3</td>
<td>0.5</td>
<td>1.2</td>
<td>13.3</td>
<td>6.4</td>
</tr>
</tbody>
</table>
International Meeting, 2013

- Do caudals
- Pay attention to peripheral blocks, they can be dangerous!
The European Society of Regional Anesthesia and Pain Therapy and the American Society of Regional Anesthesia and Pain Medicine Joint Committee Practice Advisory on Controversial Topics in Pediatric Regional Anesthesia

Giorgio Ivani, MD,* Santhanam Suresh, MD,† Claude E. Coffey, MD,‡ Adrian Bosenberg, MB, ChB, FFA(SA),§ Per-Anne Lonnqvist, MD,|| Elliot Krane, MD, FAAP,** Francis Veyckemans, MD,†† David M. Polaner, MD, FAAP,‡‡ Marc Van de Velde, MD,§§ and Joseph M. Neal, MD|||
Therapy (PRA). Experts from both societies discussed important and controversial topics in PRA and provide guidance, wherever possible, from an evidence-based perspective and on the basis of expert opinion when conclusive evidence is lacking in the literature. Four topics were selected by participant consensus according to the current main areas of PRA controversy: 1) the performance of regional nerve blocks under deep sedation (DS) or GA, 2) the value of a test dose, 3) the use of air versus normal saline for loss of resistance (LOR) for epidural space detection, and 4) regional anesthesia and the risk of obscuring compartment syndromes.
90’s

- **New Local Anesthetics**
  1. Ropivacaine
  2. Levobupivacaine

- **New Adjuvants**
  1. Clonidine
  2. Ketamine

- **first studies in children**
C Berde.

Convulsions associated with pediatric regional anesthesia

the only guidelines for 25 years

but

only about bupivacaine

no Ropivacaine, Levobupivacaine, Clonidine, Ketamine etc
Caudal block

- Bupivacaine n=12,075, Ropivacaine n=6,358
- 25% of patients undergoing a caudal block received a local anesthetic dose with the potential to cause local anesthetic toxicity.
The effectiveness of ambulatory continuous peripheral nerve blocks for postoperative pain management in children and adolescents

Visoiu M et al

They reported 93.1% ambulatory efficacy of CPNBs (339 catheters)
Ambulatory continuous peripheral nerve blocks in children and adolescents: a longitudinal 8-year single center study

Gurnaney H et al.


Evidence B3

This audit of 1285 children shows ambulatory CPNBs can provide postoperative analgesia and may reduce the need for inpatient parenteral opioid therapy.
Peripheral nerve catheters in children: an analysis of safety and practice patterns from the pediatric regional anesthesia network (PRAN).

Walker BJ et al
Sevoflurane or Propofol?


General anesthesia with sevoflurane decreases the time to onset of surgical anesthesia relative to propofol anesthesia.

Differential Bindings to receptors in the spinal cord that mediate immobility in response to surgical stimuli.
Pediatric Regional Anesthesia

What is new?

2: The need of LA and Adjuvants guidelines
ESRA/ASRA Recommendations on Local Anesthetics and Adjuvants in Pediatric Regional Anesthesia

S Suresh, C Ecoffey, PA Lonnqvist, A Bosenberg, G Oliveira, J De Andres, O De Leon Casasola, G Ivani
# LAs in children:
## Onset, duration of action, potency

<table>
<thead>
<tr>
<th>Drug</th>
<th>Onset of action</th>
<th>Duration of action</th>
<th>Potency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chloroprocaine</td>
<td>Short</td>
<td>1h30min–2h</td>
<td>1</td>
</tr>
<tr>
<td>Lidocaine</td>
<td>Short</td>
<td>1h30min–2h</td>
<td>1</td>
</tr>
<tr>
<td>Bupivacaine</td>
<td>Intermediate</td>
<td>3h–3h30min</td>
<td>4</td>
</tr>
<tr>
<td>Levobupivacaine</td>
<td>Intermediate</td>
<td>3h–3h30min</td>
<td>3.9</td>
</tr>
<tr>
<td>Ropivacaine</td>
<td>Intermediate</td>
<td>2h30min–3h</td>
<td>3.3</td>
</tr>
</tbody>
</table>
Caudal Block: Evidence-Based Conclusions and Clinical Advice

- Ropivacaine 0.2% (2 mg/ml) or levobupivacaine/bupivacaine 0.25% (2.5 mg/ml) is recommended for the performance of caudal blocks in children and should not exceed 2 mg/kg ropivacaine or 2.5 mg/kg bupivacaine or levobupivacaine.
The use of local anesthetics for lumbar or thoracic epidural in children should not exceed a dosage of 1.7 mg /kg of ropivacaïne, bupivacaïne or levobupivacaïne.
Continuous epidural infusions: Evidence-Based Conclusions and Clinical Advice

• In children less than 1 year, the risk of systemic toxicity is enhanced by higher free plasma concentrations of LAs associated with consistently low serum proteins.

• This risk is even greater before the age of six months when the liver is immature, and especially when continuous infusions or repeated bolus doses are used.

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Bupivacaine/Levobupivacaine</th>
<th>Ropivacaine</th>
<th>Chloroprocaine</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 3 month old</td>
<td>0.0625%-0.125%, 0.2 mg/kg/h</td>
<td>0.1%-0.2%, 0.2 mg/kg/h</td>
<td>1.5%, 0.2 mg/kg/h</td>
</tr>
<tr>
<td>&lt; 1 year old</td>
<td>0.125%, 0.3 mg/kg/h</td>
<td>0.1-0.2% 0.3 mg/kg/h</td>
<td>1.5%, 0.3 mg/kg/h</td>
</tr>
<tr>
<td>&gt; 1 year old</td>
<td>0.125%, 0.4 mg/kg/h</td>
<td>0.1%-0.2% 0.4 mg/kg/h</td>
<td>1.5%, 0.5 mg/kg/h</td>
</tr>
</tbody>
</table>
Single Injection Local Anesthetic Dosage for Peripheral Nerve and Fascial Plane Blocks

The introduction of ultrasound-guided regional anesthesia has increased the use of peripheral nerve blocks in children during recent years. Nonetheless few publications have addressed the pharmacodynamics of local anesthetics in children. In addition, pharmacokinetics properties of local anesthetics significantly differ between different types of blocks. Many studies have examined dose responses of single peripheral nerve blocks in pediatrics. Nonetheless, dosage have been examined in very few block types by more than one study, and this limits the reliability of the findings. Intercostal nerve blocks are known to have the greatest rate of reabsorption and therefore the highest potential risks for local anesthetic systemic toxicity. Conversely, higher local anesthetic dosages (2.5mg/kg) used for intercostal nerve blocks have resulted in plasma levels below potential toxic levels.
The performance of ultrasound guided upper extremity peripheral nerve blocks (e.g., axillary, infraclavicular, interscalene, supraclavicular) in children can be performed successfully and safely using:

- A recommended local anesthetic dose of bupivacaine, levobupivacaine or ropivacaine of 0.5-1.5 mg/kg (Evidence B2).
Evidence –Based Conclusions and Clinical Advice

- The performance of ultrasound guided lower extremity peripheral nerve blocks (e.g., femoral, sciatic, popliteal, adductor canal) can be performed successfully and safely using:
  - a recommended local anesthetic dose of **bupivacaine or ropivacaine of 0.5-1.5 mg/kg** (Evidence B2)
Evidence – Based Conclusions and Clinical Advice

The performance of ultrasound guided fascial plane blocks (e.g., rectus sheath, transversus abdominis plane block, fascia iliaca) can be performed successfully and safely using a recommended local anesthetic dose of: bupivacaine or ropivacaine of 0.25-0.75 mg/kg (Evidence B1)
Continuous Infusion Local Anesthetic Dosage for Peripheral Nerve and Fascial Plane Blocks

Very limited data is available regarding plasma levels associated with continuous infusions through peripheral nerve block catheters in children. Safety data regarding both short-term and long-term use of continuous infusions have been published, using different LAs and infusions rates, including the use of ambulatory infusions following hospital discharge. No incidence of LAST was observed during these infusions and no neurologic complications were noted. Nonetheless, dose ranging studies addressing efficacy of continuous local anesthetic infusions in children are rarely available.
Continuous infusion of local anesthetic for peripheral nerve and fascial plane blocks can be safely and successfully performed with **0.1% ropivacaine or bupivacaine using an infusion dose of 0.1-0.3 mg/kg/hr** (Evidence B3)
List of published adjuvants used in association with neuraxial blocks in children

- Preservative-free morphine
- Synthetic opioids (fentanyl, sufentanil, buprenorphine, diamorphine)
- Alpha-2 adrenoceptor agonists (clonidine, dexmedetomidine)
- Racemic ketamine and S-ketamine
- Corticosteroids (dexamethasone)
- Midazolam
- Neostigmine
- Magnesium
Fundamental requirements of adjuvant drugs

Not only does there need to be published evidence for an enhanced effect compared to control (plain local anesthetics):

- **Preferably meta-analysis data** should verify the beneficial effect of the adjuvant in order to recommend routine use outside clinical trials
- There should be sufficient insight into the mechanism of action of the adjuvant
- **The side effect profile** should be tolerable in comparison with the use of plain local anesthetics
- The adjuvant must be available as a **preservative-free preparation**
- Overall safety issues must be acceptable
Rationale for the use of Adjuvants

• To enhance and prolong the analgesic effect of a single injection of local anesthetics

• The vast majority of pediatric surgical procedures do not merit the use of catheter techniques
Some do not qualify

- midazolam, neostigmine, buprenorphine
  - side effects outweigh the benefits

- dexamethasone, fentanyl:
  - little or no added benefit over intravenously administered route of the same agent
• Therapeutic ratio
  – Toxic (apoptotic) dose/Analgesic dose
• Morphine > 300
• Clonidine > 300
• Ketamine < 1 !!!

Neuraxial Analgesia in Neonates and Infants: A Review of Clinical and Preclinical Strategies for the Development of Safety and Efficacy Data

Suellen M. Walker, MBBS, PhD, FANZCA, FFPMANZCA,* and Tony L. Yaksh, PhD†

Neuraxial drugs provide robust pain control, have the potential to improve outcomes, and are an important component of the perioperative care of children. Opioids or clonidine improves analgesia when added to perioperative epidural infusions; analgesia is significantly prolonged by the addition of clonidine, ketamine, neostigmine, or tramadol to single-shot caudal injections of local anesthetic; and neuraxial intrathecal anesthesia/analgesia is increasing in some centers. However, it is difficult to determine the relative risk-benefit of different techniques and drugs without detailed and sensitive data related to analgesia requirements, side effects, and follow-up. Current data related to benefits and complications in neonates and infants are summarized, but variability in current neuraxial drug use reflects the relative lack of high-quality evidence. Recent preclinical reports of adverse effects of general anesthetics on the developing brain have increased awareness of the potential benefit of neuraxial anesthesia/analgesia to avoid or reduce general anesthetic dose requirements. However, the developing spinal cord is also vulnerable to drug-related toxicity, and although there are well-established preclinical models and criteria for assessing spinal cord toxicity in adult animals, until recently there had been no systematic evaluation during early life. Therefore, in the second half of this review, we present preclinical data evaluating age-dependent changes in the pharmacodynamic response to different spinal analgesics, and recent studies evaluating spinal toxicity in specific developmental models. Finally, we advocate use of neuraxial drugs with the widest demonstrable safety margin and suggest minimum standards for preclinical evaluation before adoption of new analgesics or preparations into routine clinical practice. (Anesth Analg 2012;115:638–62).
Safety and efficiency of dexmedetomidine as adjuvant to local anesthetics

Peter Marhofer* and Chad M. Brummett**

KEY POINTS

- Dexmedetomidine has demonstrated efficacy in preclinical and clinical studies.

- A dose-dependent effect has been demonstrated. Present data suggest that 100 μg may be the ideal dose for peripheral nerve blocks.

- Preclinical and clinical studies suggest that the combination with local anesthetic is well tolerated without evidence of neurotoxicity.

- The effect of dexmedetomidine in peripheral nerve blocks is not because of central nervous system effects or vasoconstriction. Instead, it acts at the nerve level by maintaining a hyperpolarized state.

- Dexmedetomidine causes lower heart rate and an increased incidence of bradycardia. Although avoidance is warranted for those in whom bradycardia would be detrimental, major adverse events have not been reported.
Conclusions
• Neuroaxial blocks
  – Caudal blocks: Meta-analysis data show that adjuvant use of clonidine is associated with improved postoperative analgesia compared to plain local anesthetics. 1-2 mcg/kg

Preservative-free ketamine is also effective in this setting but animal toxicity data suggest that ketamine should be avoided in newborns and infants due to a potential risk of increased neuronal apoptosis within the spinal cord. 0.5 mg/kg

– Epidural blocks: Adjuvant use of preservative-free morphine and clonidine improve the quality of postoperative analgesia.
– Intrathecal blocks: Adjuvant use of preservative-free morphine, synthetic opioids and clonidine improve the quality and duration of intrathecal blocks
Conclusions

• Peripheral nerve blocks
  – Meta-analysis data show that adjuvant use of preservative-free clonidine is associated with improved postoperative analgesia compare to plain local anesthetics.
  – No other adjuvants have been shown to improve postoperative analgesia in the context of peripheral nerve blocks in children.
Management of Local Anesthetic Systemic Toxicity (LAST)
In the event of cardiovascular collapse as a result of LAST basic life support should be instituted and includes
1. Stop administration of local anesthetic and call for help
2. Immediate hyperventilation with 100% oxygen
3. Suppression of seizures if present (midazolam thiopentone, propofol)
4. External cardiac massage and
5. Epinephrine 1mcg.kg or 1:1000 0.1ml.kg
6. Administration of 20% Intralipid 1.5 mL/kg i.v. over 1 minute Follow immediately with an infusion at a rate of 0.25 mL/kg/min, Lipid emulsion in propofol should not be used in lieu of intralipid.
   a. Continue chest compressions (lipid must circulate)
   b. Repeat bolus every 3-5 minutes up to 3 mL/kg total dose until circulation is restored
   c. Continue infusion until hemodynamic stability is restored.
   d. Increase the rate to 0.5 mL/kg/min if BP declines
   e. A maximum total dose of 10mL/kg in first 30mins is recommended
7. If no response consider ECMO if available
There a number of theories as to the mechanism of action of the lipid emulsion works: These include “(i) lipid sink” i.e. a distinct lipid compartment in the blood stream trapping lipophilic (ii) at the mitochondrial level (interrupt fatty acids transport into cardiac mitochondria) and Intralipid supplies new energy (iii) activation calcium channels increasing intracellular calcium
To date there have been in the order of 10 case reports of intralipid use for LAST in children of which 9 were successful
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