Local Anesthetics and Adjuncts

Regional/VOS Rotation

(Slides by Randall Malchow, MD)
History

- Syringe, Needle – 1850s
- Cocaine - 1884
- Epi w/ LA - 1900
- Procaine, “Novacaine” - 1905
- Tetracaine - 1929
- Lidocaine - 1948
- Mepivacaine - 1956
- Bupivacaine - 1970
- Ropivacaine, Levobupivacaine - 1990’s
- Microspheres - ??
Factors Affecting Success of

4. Fascial planes

If nerve is invested with fascial sheath needle has to be inside. Local anesthetics will not spread through.

3. Volume Concentration Agent

The larger the volume the longer the segment of nerve affected and the easier it will be to block conduction.

2. Needle Closeness to nerve

The larger the nerve trunk the more difficult it will be for the agent to penetrate to the center. Different fibers block at different rates and concentrations.

1. Nerve Size fibers

The higher the concentration the greater the gradient for penetration of the nerve.

Lipid solubility, $pK_a$, potency will affect the readiness to block nerve impulses.
# Differences in Nerve Fibers

Increased Size and myelin directly related to Slower Onset (myelin issue is controversial)

<table>
<thead>
<tr>
<th>FIBER CLASS</th>
<th>SUBCLASS</th>
<th>MYELIN</th>
<th>DIAMETER (µ)</th>
<th>CONDUCTION VELOCITY (M/S)</th>
<th>LOCATION</th>
<th>FUNCTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>alpha</td>
<td>+</td>
<td>6–22</td>
<td>30–120</td>
<td>Afferent to and efferent from muscles and joints</td>
<td>Motor, proprioception</td>
</tr>
<tr>
<td></td>
<td>beta</td>
<td>+</td>
<td>6–22</td>
<td>30–120</td>
<td>Afferent to and efferent from muscles and joints</td>
<td>Motor, proprioception</td>
</tr>
<tr>
<td></td>
<td>gamma</td>
<td>+</td>
<td>3–6</td>
<td>15–35</td>
<td>Efferent to muscle spindles</td>
<td>Muscle tone</td>
</tr>
<tr>
<td></td>
<td>delta</td>
<td>+</td>
<td>1–4</td>
<td>5–25</td>
<td>Afferent sensory nerves</td>
<td>Pain, temperature, touch</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>&lt;3</td>
<td>3–15</td>
<td>Preganglionic sympathetic</td>
<td>Various autonomic functions</td>
</tr>
<tr>
<td>B</td>
<td>sC</td>
<td>−</td>
<td>0.3–1.3</td>
<td>0.7–1.3</td>
<td>Postganglionic sympathetic</td>
<td>Various autonomic functions</td>
</tr>
<tr>
<td></td>
<td>d gamma C</td>
<td>−</td>
<td>0.4–1.2</td>
<td>0.1–2.0</td>
<td>Afferent sensory nerves</td>
<td>Various autonomic functions; pain, temperature, touch</td>
</tr>
</tbody>
</table>
Choose the Right Local Anesthetics & Adjuncts

- Local Anesthetics
  - chloroprocaine
  - lidocaine
  - mepivacaine
  - ropivacaine
  - bupivacaine
  - mixtures

- Adjuncts
  - epinephrine
  - decadron
  - bicarbonate
  - toradol
  - hyaluronidase
  - narcotics/buprenorphine
  - clonidine
Local Anesthetics - Pharm 101

- Aromatic Ring w/ tertiary amine attached by either an amide or ester link
- Metabolism:
  - Amide l.a.'s undergo hepatic and renal met.
  - Ester l.a.'s undergo plasma esterase met.
- Mech: blockade of sodium channels, preventing influx/activation
- Isomers (R vs S):
  - S (levo)isomer: safer, longer duration
Local Anesthetics - Pharm 102

- **Protein Binding – Duration** (alpha1 acid glycoprot, albumin)
  - >p.b = > duration
  - good correlation clinically (CP 5%, Bupiv 95%)
  - binding decr w/ increasing plasma conc = toxicity

- **Lipid solubility - Potency**
  - >lip.sol. = >potency
  - poor clinical correlation (Bupiv 30; Ropiv 3)

- **pKa - Onset**
  - >pKa = slower onset
  - poor clinical correlation (CP 8.9 yet quickest)
Chloroprocaine

- New formulation truly preservative-free
  - EDTA, Sod Bisulfite (back pain, cauda equina)
  - CP interferes w/ subsequent duramorph/amide LAs
- Onset for pnb: 7-14 min
- Duration:
  - motor: 75-90 min; sensory: 90-120 min
- Lowest systemic toxicity concerns
  - t1/2 = 45 sec
- Low pH a theoretical concern
- Allergy: p-aminobenzoic acid (PABA) w/ ester LAs
Onset, Duration, Max

**Lidocaine, Mepivacaine:**
- Onset 10min
- Duration:
  - 3-4 hrs plain Lido
  - 4-6 hrs plain Mepiv
- Max:
  - Lido:
    - 500mg freq quoted
    - 600mg Brach Pl
    - 1000mg Sciatic (Cousins)

**Ropivacaine/Bupivacaine:**
- Onset – similar; 10-45min
- Duration - similar, 12-16 hours
  - Klein, ‘98: ISB w/ 0.5% ropiv, 0.5% bupiv, vs 0.75% ropiv
  - Casati, ‘01: FNB w/ 0.5% ropiv, 0.5% bupiv
- Potency- “similar”
Ropivacaine (S) vs LevoBupiv (S) vs Bupivacaine (R/S)

- All greater risk than lido/mepiv
- CNS: Convulsive doses similar (and 5X cns toxicity of lido)
- Cardiac:
  - Ropiv << cardiovasc depression/arrhythmias at equipotent doses/plasma levels
  - Ropiv > successful resuscitation after arrests, including ability to pace
### Max Dosages and Plasma Levels

**mg/kg and ug/ml**

<table>
<thead>
<tr>
<th></th>
<th>Lido</th>
<th>Mepiv</th>
<th>Ropiv</th>
<th>Bupiv</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recommended</strong></td>
<td>5-7</td>
<td>5-7</td>
<td>2-3</td>
<td>2-3</td>
</tr>
<tr>
<td><strong>Actual (PNB)</strong></td>
<td>10-20</td>
<td>10-20</td>
<td>4-5</td>
<td>4-5</td>
</tr>
<tr>
<td><strong>-Toxic</strong></td>
<td>6-10</td>
<td>6-10</td>
<td>2-4</td>
<td>2-4</td>
</tr>
<tr>
<td><strong>-Seizure (dogs)</strong></td>
<td>&gt;24</td>
<td>&gt;22</td>
<td></td>
<td>&gt;18</td>
</tr>
<tr>
<td><strong>-Card Arrest (monk)</strong></td>
<td>&gt;113</td>
<td></td>
<td>&gt;27</td>
<td>&gt;18</td>
</tr>
<tr>
<td><strong>-Card Arrest (dogs)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Max Dosage Upshot:

- Depends on route:
  - Small IV injections catastrophic (vert art)
  - Large doses low vascularity ok
    - Tracheal > Intercostal/PVB > Caudal > Epidural > PNB > SQ

- Max Dosages per kg meaningless

- Calculate Dose for Pediatric pts (<50kg)

- < Infusion doses:
  - Pregnancy, elderly, uremia, CRF, Liver Failure
Toxicity

• <<Mortality w/ early Rx of cardiac comp’s
  – Bupiv: 83% to 33% mortality (dog studies)
  – Ropiv: 17% to 0% mortality
  – Mortality: Bupiv 50%, Levo 30%, Ropiv 10%, Lido 0% (dogs)

• Upshot:
  – Treat convulsions and arrest early (due to ++ catechol’s).
  – Recall: prilocaine, benzocaine- metHgb (Methylene
Local Anesthetic Toxicity

**Prevention:**
- Avoid Bupivacaine
- Avoid Immobile needle?
- Extreme vigilance while injecting
  - IV injection poss w/ neg aspiration/neg test dose
- Aspiration after every 5cc’s
- Fractionated doses
- S&S of IV injection; epinephrine for n.stim only
- PNB/ Epid test dose (15ug)

**Treatment:**
- Rx Seizures ASAP
- Airway, CPR as necessary
- Acidosis, anemia, hypoxia, hypercarbia, and hyperkalemia all increase risk
- Amiodarone (vs lido), vasopressin (vs epi)
- Defibrillation
- Intralipid immediately available
Intralipid: Only Significant Rx for Cardiac

- **Weinberg, Reg Anes and PM, ’03:**
  - 12 dogs, Bupiv 10mg/kg IV. 10min int cardiac massage
  - 6 dogs saline; 6 dogs 20% IL
  - 100% survival IL grp (0 survival in control)

- **Rosenblatt, M. Anes, ’06:**
  - 1st Case Rpt of successful resusc in pt w/ Bupiv toxicity (using IL)
Intralipid- cont

- **Recommended Dosage:**
  - 1ml/kg over 1min, repeat up to 3ml/kg over 10min
  - After return of NSR, 0.25ml/kg/min until norm hemodynamics

- **Comments:**
  - Propofol: useful for Sz treatment only (not cardiac arrest)
  - Inexpensive, long shelf-life, stable room temp
  - Should be part of any block area
LA Mixtures

- Amide Mixtures - additive toxicity
- Amide + Ester - less than additive
  - avoid cp/bupiv; lido/tetracaine 0.2% common
- Duration of combination: = duration of shortest local (ie little benefit to combination)
- Supplementation of blocks:
  - 40cc x 0.5%bup ISB + 40cc x 1.5% mepiv w/ epi in 148 patients - no problem
Epinephrine

- **vascular marker**
- improves quality of block and < onset time?
- prolong duration
  - 70% increase for lido
  - 30% increase for bup/ropiv
- reverse vasodilation of LA’s
- Moore: max epi dose 0.25mg

- 30-50% decrease in plasma concentration of LA’s
- always add fresh epinephrine (epi unstable in basic soln’s)
- **Use of Epinephrine**
  - Lido w/ epi 1:200k < Neural blood Flow (to 20% of baseline, Partridge, Anes, 1991)
  - Min evidence that epi 1:400k < Neural blood flow (Neal, RAPM, 2003)
  - Growing trend in US to omit epi during USG blocks for fear of < NBF (or use min concentration 1:400k)
Decadron

- Minimal studies of steroids for PNBs; extensive epidural use
- Appears safe, although limited data
- Appears to > duration by 6 hrs
- 4 mg in block currently
- Communicate with in-Room Provider (no intraop decadron); “Decadron” sticker on qtt chamber
Clonidine and Bicarbonate

- **Clonidine:**
  - Blocks: pnb, spinal, epidural, ivra
  - Dose: up to 1ug/kg for PNB; 15-30ug for spinal
  - Side effects: min
  - increases duration 3hrs (YaDeau)

- **Bicarbonate:**
  - increases nonionized form for transport
  - lidocaine/mepivicaine only (1meq/10cc)
  - avoid it w/ bup/ropiv (0.1meq/10cc)
  - Advantages:
    - decreases onset
    - increases quality of block/higher success rate
    - denser motor block
    - decreases burning of local anesthetics
Other Adjuncts:

- **Toradol**
  - mixed results in pnb’s
  - effective in ivra, inguinal field blocks, and intraarticular

- **Narcotics**
  - generally not helpful
  - Intraarticular may be effective
  - **Buprenorphine 300mcg** shown to be effective

- **Hyaluronidase**
  - RBBB - routine
  - 150 units standard
  - increases spread & uptake (less duration)
Upshot of Adjuncts

- **Clonidine**: safe, but min effect, expensive
- **Epi**: ? Effect on NBF, best vascular marker
- **Bicarbonate**: precipitates for ropiv/bupiv
- **Dexamethasone**: minimal information in literature (appears to significantly prolong PNB)
- **Avoid all adjuncts if not necessary** (soft tissue surgery, minor surgery, etc)
- **Consider > use of CPNB for longer duration?**