Local Anaesthetic Toxicity

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Local Anaesthetic

Reversibly interrupt conduction in peripheral nerves and stabilize excitable cell membrane by blocking sodium channels inhibiting depolarization.
Local Anaesthetic

- First use of LA in 1884 for eye surgery
- Procaine 1905
- Lignocaine 1948
- Bupivacaine 1963
Local Anaesthetic Toxicity

- Deleterious side-effects of a drug
  - Local
  - Systemic
Local Anaesthetic Toxicity

- **Incidence**
  - 100:10,000 (1981)
  - Seizures following interscalene 79:10,000 (1995)
  - 0-20:10,000 (2002)
Local Anaesthetic Toxicity

- Lipid solubility
  - Procaine - 50
  - Lignocaine - 150
  - Bupivacaine - 1000
# Local Anaesthetic Toxicity

<table>
<thead>
<tr>
<th>Site of Injection</th>
<th>Drug</th>
<th>Patient factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surface area</td>
<td>Potency</td>
<td>Age</td>
</tr>
<tr>
<td>Vascularity</td>
<td>Dose</td>
<td>Genetics</td>
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<td></td>
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<td>Cardiac pathology</td>
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<td>Pregnancy</td>
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<td></td>
<td>Drug interactions</td>
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<td>Acidosis</td>
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<td>Hypoxia</td>
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<td>Hypercarbia</td>
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Local Anaesthetic Toxicity

- **Patient factors:**
  - Acidosis – acidic environments $\uparrow$ ionised portion cannot escape through lipid membrane for distribution $\uparrow$ toxicity of organs where trapping occurs.
  - Pregnancy – progesterone competes with $\alpha_1$ acid glycoprotein $\uparrow$ free drug $\uparrow$ toxicity
Local Anaesthetic Toxicity

- Patient factors:
  - Disease states: cardiac / hepatic / renal failure $\downarrow$ metabolism and elimination, $\uparrow$ toxicity
  - Obesity: fat acts as reservoir for lipid soluble drug $\downarrow$ systemic toxicity
  - Electrolytes: $\uparrow$ K, $\downarrow$ Ca, hyperexcitable membrane $\uparrow$ toxicity
Cardiotoxicity

- ↑ PR, QRS intervals, refractory periods
- ↓ systemic vascular resistance, contractility
- Persistent binding to myocardial channels - VT/VF
Neurotoxicity

- blocks Na channels in CNS neurons
- biphasic effects with initial excitatory phenomenon followed by CNS depression.
Bupivacaine

- More lipid soluble (10 x lignocaine)
- Mixture of R and S isomers
- Has high affinity for cardiac Na channels, to which it binds and blocks in the inactive-open state.
Max Safe Dose

- 2.5 mg/Kg
- 0.25% - 1 ml/Kg
- 0.5% - ½ ml/Kg (0.5 ml/Kg)
- 0.75% - 1/3 ml/Kg
- 1% - ¼ ml/Kg
Max Safe Dose

- Site: ↑ blood flow to site ↑ toxicity.
  - Intrapleural > intercostal > pudendal > caudal > epidural > brachial plexus > subcutaneous
- Liver failure
# Toxicity

<table>
<thead>
<tr>
<th>Lignocaine µg/ml</th>
<th>Toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>Light headed, tinnitus, circum-oral numbness</td>
</tr>
<tr>
<td>6</td>
<td>Visual disturbances</td>
</tr>
<tr>
<td>8</td>
<td>Muscle twitching</td>
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<tr>
<td>10</td>
<td>convulsions</td>
</tr>
<tr>
<td>12</td>
<td>unconscious</td>
</tr>
<tr>
<td>15</td>
<td>coma</td>
</tr>
<tr>
<td>20</td>
<td>Respiratory arrest</td>
</tr>
<tr>
<td>26</td>
<td>Cardiovascular collapse</td>
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</tbody>
</table>
Detection of Systemic LA Toxicity

- Maintain a high degree of suspicion.
- CNS symptoms are often subtle or absent.
- Cardiovascular signs may be the first signs of local anesthetic toxicity.
Detection of Systemic LA Toxicity

- CNS excitation are typical of LA toxicity.
- Ventricular ectopy, multiform ventricular tachycardia, and ventricular fibrillation are hallmarks of cardiac toxicity of LA.
- Progressive hypotension and bradycardia, leading to asystole, are the hallmark of severe cardiovascular toxicity.
Lipid Emulsion

• In use since 1962 for TPN
Lipid Emulsion

Lipid Emulsion

- Volume distribution
- Mops LA
- ↓ plasma levels
- Direct energy source to the myocardium
- Raised triglycerides on cardiac calcium channels increase myocardial calcium concentration, hence enhancing cardiac function
Treatment of Systemic LA Toxicity

- Get help and call for 20% lipid emulsion.
- Perform airway management. Hyperventilate with 100% oxygen.
- Control the seizures
- CPR
- Adrenaline—controversial; may need higher doses than recommended in ACLS.
- Consider using vasopressin to support circulation
- Alert the nearest facility having cardiopulmonary bypass capability.
Treatment of Systemic LA Toxicity

- Perform lipid emulsion treatment (for a 70-kg adult patient):
  - Bolus 1.5 mL/kg intravenously over 1 minute \(\text{(about 100 mL)}\)
  - Continuous infusion 15 mL/kg/hr \(\text{(about 500 mL over 30 minutes)}\)
- Repeat bolus every 5 minutes x2 for persistent cardiovascular collapse.
- Double the infusion rate if cardiovascular instability persists.
- Continue infusion for a minimum of 30 minutes. Max dose 12mg/Kg