Local Anesthetic Toxicity

Usually due to accidental intravascular or intrathecal injection, or due to an excessive dose.

ANESTHETIC ACTION:

- Immediate discontinuation of further local anesthetic, and call for help
- Secure airway promptly
- Ventilate with 100% O2 to normocapnia
- ACLS protocol
  - **CPR for pulseless rhythm**
  - Use epinephrine, atropine and vasopressin as established
  - No role for lidocaine or amiodarone in bupivicaine induced ventricular arrhythmias
- Intralipid 20% rapid bolus 1.5mL/kg (100mL in adults)
  - Infusion 0.25mL/kg/min for subsequent 10 min

HISTORY AND PHYSICAL EXAM

- AMPLE history
- DDx:
  - LA toxicity
  - Anaphylaxis
  - De novo seizure
- Type of local anesthetic important
- Initial presentation often lightheadedness and dizziness, then visual and auditory disturbances (poor focusing, tinnitus). On exam patients may shiver, have muscle twitches or tremors, and ultimately have generalized convulsions of a tonic-clonic nature.
- If sufficient dose or rapid injection this excitatory stage will be rapidly followed by a state of generalized depression. Seizure activity ceases and respiratory depression and arrest may follow.
- Assess for typical EKG changes of LA toxicity: increased PR interval and duration of QRS; sinus bradycardia and sinus arrest with really high concentrations of local anesthetics

MAXIMUM RECOMMENDED DOSES OF LA FOR CONDUCTION NERVE BLOCKS

Local Anesthetics	Usual Concentrations	Max Dose (mg/kg)	Max Dose + Epi (mg/kg)
Aminoesters			
Procaine	1-2	7	10
Chlorprocaine	2-3	7	10
Aminoamides			
Lidocaine	0.25-2	5 (or 400mg)	7
Mepivicaine	0.25-2	5-7 (or 400mg)	Not available
Bupivicaine	0.125-0.5	2 (or 150mg)	3 (or 200mg)
Levobupivicaine	0.125-0.5	3 (or 200mg)	4 (or 250 mg)
Ropivicaine	0.1-10	3 (or 300mg)	Not recommended

PHARMACOKINETICS

- The LA concentration is determined by:
  - **The amount injected**
  - **The rate of absorption**
    - Determined by the site of injection, dosage and volume, addition of a vasoconstrictor and the pharmacologic profile of the agent itself
    - Anesthetic drug level:
      - Intercostal nerve blockade>>caudal epidural>lumbar epidural>brachial plexus> subcutaneous tissue
    - Epinephrine decreases the rate of vascular absorption from various sites of administration and lowers the potential systemic toxicity (ie 5mcg/mL or 1:200 000)
    - Epinephrine will not decrease absorption of bupivicaine from lumbar epidural space, however will for peripheral nerve blockade
  - **The rate of tissue distribution**
    - Two compartment model: initial rapid uptake into highly perfused tissues (with rapid extraction by lungs) then slower phase of disappearance
  - **The rate of biotransformation and excretion**
    - Aminoesters are hydrolysed in the plasma by pseudocholinesterase (chlorprocaine clearance especially rapid, even in neonates)
    - Aminoadmides are degraded in the liver (95%) and excreted by the kidneys
- ½ life of lidocaine after IV administration is 80 minutes in healthy young adults, and 140 minutes in 60-70 year olds; also slower in neonates with immature hepatic enzyme systems
- Maximum infusion rate for bupivicaine
  - 0.4mg/kg/hr for children and adults
  - 0.2mg/kg/hr for neonates, probably not to exceed 48 hours
- Maximum infusion rate for lidocaine
  - 0.8mg/kg/hr for neonates—the principle metabolite *monoethylglycinexylidide* (MEGX) can cause seizures

PREGNANCY

- The 0.75% bupivicane solution is not recommended in pregnant patients
- Pregnant patients are likely more sensitive to the cardiotoxic effects of bupivicaine

PATHOPHYSIOLOGY

- CNS effects

- CNS excitation may be the result of an initial blockade of inhibitory pathways in the cerebral cortex by local anesthetic drugs, or possibly from the net stimulation of release of glutamate which is an excitatory amino acid neurotransmitter
- The CNS depression is thought to occur when a further increase in the dose of local anesthetic leads to inhibition of activity of both the inhibitory and facilitatory circuits
- Correlation exists between the potency of the local anesthetic and intravenous CNS toxicity
- Respiratory of metabolic acidosis increases the risks for CNS toxicity from local anesthetics
  - ↓ intracellular pH facilitates conversion of the base to the cationic form of LA. The cationic form does not diffuse well across the nerve membrane so ion trapping will occur
  - Hypercapnia and acidosis also ↓ plasma protein binding of local anesthetic agents
- Seizures cause hypoventilation and combined respiratory and metabolic acidosis—in this setting it is imperitive that prompt assistance of ventilation and circulatory support occurs to prevent or correct hypoxemia and hypercapnia or acidosis

- CVS toxicity
  - The primary cardiac electrophysiologic effect of LA is a decrease in the rate of depolarization in the fast conducting tissues of Purkinje fibers and ventricular muscle
  - Local anesthetics will prolong conduction time through various parts of the heart, while extremely high concentrations will depress spontaneous pacemaker activity in the sinus node—sinus brady or arrest may occur
  - All LA exert a dose dependent negative inotropic action on cardiac muscle, with bupivicaine and tetracaine more potent cardiodepressants than lidocaine
    - This depression may be related to inhibition of cardiac sarcolemmal Ca2+ currents and Na+ currents and by affecting calcium influx and triggered release from the sarcoplasmic reticulum

REFERENCES

- Miller's Anesthesia