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Local Anesthesia Toxicity

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Introduction

- Local anesthesia (LA) provides a way to relieve temporary pain in a small part of the body and has been used for over 100 years (Fencl, 2015).
- LA prevents the passage of surgical stimuli into the central nervous system (CNS) making a surgical procedure less painful for the patient (Noble, 2015).
- According to Noble, "altering the passage of stimuli from smaller diameter neurons in a confined area with lower drug dosages is called LA, such as the injection of LA around a surgical incision" (Noble, 2015, p.325).
- When performing LA administration one must be aware of the risk of local anesthetic systemic toxicity (LAST) (Fencl, 2015).
- It is a very serious and sometimes fatal complication to administration. It can result from the patient's risk factors, current medications or inadvertent injection directly into the vascular system- resulting in immediate absorption of the anesthetic agent into an exceptionally vascular area (Fencl, 2015).
- According to Stannard (2015), 20 out of 10,000 peripheral nerve blocks (PNBs) and 4 per 10,000 epidurals result in LAST.
- PNBs improve short-term pain control, lowers pain scores from0-72 hours post procedure and reduces hospital length of stay (Joshi, Gandhi, Shah, Gadsden, & Corman, 2016).
- Early response at the first sign of toxicity is pertinent and improves chances of successful treatment. Once the reaction is noticed, immediate supportive care needs to be initiated due to the chance of severe cardiac depression. Advanced Cardiac Life Support (ACLS) should be started immediately and is considered the first-line treatment for this complication (Noble, 2015).

Signs and symptoms

- The classic description is progressive "biphasic" effect on the CNS then to the CVS
- CNS excitation progresses to seizure or CNS depression. This is followed by CVS excitation (tachycardia or ventricular arrhythmia) then depression (bradycardia or asystole) (Ciechanowicz & Patil, 2012).
- Cardiovascular system toxicity is classically three phases
- Initial phase: hypertension and tachycardia
- Intermediate: myocardial depression and hypotension
- Terminal: peripheral vasodilation, severe hypotension and arrhythmias (bradycardia, conduction blocks or asystole) (Christie, Picard & Weinberg, 2015).
- Early: metallic taste, auditory changes, visual disturbance (mainly focusing), lightheadedness, apprehension, drowsiness and numbness of tongue and lips; Restlessness, agitation, myoclonus, nystagmus and slurred speech occur at high doses
- The early signs are caused by blocking inhibitory pathways in cerebral cortex- which allows for disinhibition of facilitator neurons resulting in excitatory cell dominance causing dizziness or lightheadedness (*Dewaele & Santos, 2013).*
- Tachycardia and hypertension can occur after injection without epinephrine (Weinburg, 2002).
- Cardiovascular manifestations: Dysrhythmias and conduction delays (from prolonger PR interval to asystole), chest pain, shortness of breath, palpitations, lightheadedness, diaphoresis, hypotension, and syncope

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Pathophysiology

- Systemic toxicity from local anesthetic (LA) occurs due to accidental intravascular injection, absorption from the tissues or repeated doses without balanced elimination
- The pathophysiology of LAs are thought to be an extension of their uses.
- Blocking cardiac voltage-gated sodium channels, prevention myocyte depolarization, blocking repolarization via potassium channels and blocking sarcoplasmic reticulum voltage-dependent calcium channels to limit the increase of calcium available for contraction (Ciechanowicz & Patil, 2012).
- Myocyte ATP is reduced which limits energy available for connecting actin-myosin cycle and ion channel involvement is extensive (Ciechanowicz & Patil, 2012).
- Bupivacaine, Levobupivacaine and Ropivacaine are long acting amide-based LA most commonly used in clinical practice (Ciechanowicz & Patil, 2012).
- LAs rapidly cross cell membranes and toxicity can act in many sites including ionotropic and metabotropic.
- In the brain, LA affects inhibitory and excitatory pathways
- In the heart, LAs can cause conduction blocks through sodium, potassium and calcium channels- resulting in dysrhythmias and reduced contractility (Christie, Picard & Weinberg, 2015).
- LA can disrupt intracellular signal originating at metabotropic receptors- leading to reduced monophosphate concentrations and decreased contractility.
- In addition, the heart has preference for fats and ketone bodies. To be oxidized, the fats must be carried across the mitochondrial membranes by a translocase system which is inhibited by concentrations of LA leading to enhanced potency (Christie, Picard & Weinberg, 2015).
- LAST can be fatal if it is not recognized early enough!

Nursing Implication

- A checklist was developed by the American Society of Regional Anesthesia and Pain Medicine (ASRA) for the management of LAST (Neal et al., 2012).
- Stage 1: Get help
- Stage 2: Initial Focus
  - Airway management: ventilate with 100% oxygen
  - Seizure management: benzodiazepines preferred. AVOID Propofol in patients with cardiovascular instability
- Stage 3: Cardiac Arrhythmia Management
  - Initiate ACLS if needed
  - *Avoid* vasopressin, calcium channel blockers, beta blockers or LA
  - *Reduce* epinephrine does to < 1mcg/kg
- Stage 4: Lipid Emulsion Management
  - *Bolus* 1.5 ml/kg IV over 2 minutes
  - *Continuous* infusion
  - May repeat bolus
- The lipid emulsion creates a lipid phase that extracts the lipid soluble molecules from the plasma phase decreasing toxicity and potentially reversing LAST (Nicholas & Thornton, 2016).
- Stage 5: Stabilization
- ASRA concludes:
  - Be prepared
  - Risk reduction
  - Detection
  - Treatment (Neal et al., 2012).
- See Table 1

AMERICAN SOCIETY OF REGIONAL ANESTHESIA AND PAIN MEDICINE

Checklist for Treatment of Local Anesthetic Systemic Toxicity

The Pharmacologic Treatment of Local Anesthetic Systemic Toxicity (LAST) is Different from Other Cardiac Arrest Scenarios

- ❑ **Get Help**
- ❑ **Initial Focus**
  - ❑ **Airway management:** ventilate with 100% oxygen
  - ❑ **Seizure suppression:** benzodiazepines are preferred; AVOID propofol in patients having signs of cardiovascular instability
  - ❑ **Alert the nearest facility having cardiopulmonary bypass capability**
- ❑ **Management of Cardiac Arrhythmias**
  - ❑ **Basic and Advanced Cardiac Life Support (ACLS) will require** adjustment of medications and perhaps prolonged effort
  - ❑ **AVOID vasopressin, calcium channel blockers, beta blockers, or local anesthetic**
  - ❑ **REDUCE individual epinephrine doses to <1 mcg/kg**
- ❑ **Lipid Emulsion (20%) Therapy** (values in parenthesis are for 70kg patient)
  - ❑ **Bolus 1.5 mL/kg** (lean body mass) intravenously over 1 minute (~100mL)
  - ❑ **Continuous infusion 0.25 mL/kg/min** (~18 mL/min; adjust by roller clamp)
  - ❑ Repeat bolus once or twice for persistent cardiovascular collapse
  - ❑ Double the infusion rate to 0.5 mL/kg/min if blood pressure remains low
  - ❑ **Continue infusion** for at least 10 minutes after attaining circulatory stability
  - ❑ Recommended upper limit: Approximately 10 mL/kg lipid emulsion over the first 30 minutes
- ❑ **Post LAST events at www.lipidrescue.org and report use of lipid to www.lipidregistry.org**

Table 1. Checklist created by ASRA. Image provided by Neal, Mulroy & Weinberg, 2012.

Conclusion

- When the effectiveness of the checklist was researched by Neal et al. (2012), results showed improved outcomes and excellent medical management of LAST.
- Prevention measures (in a checklist form) have been put in place to help reduce the risk of LAST by The American Society of Regional Anesthesia and Pain Management (ASRA)
- This is a helpful tool utilized by anesthesia staff to help focus on the immediate needs of the patient and manage cardiac events for someone diagnosed with LAST.
- By educating all staff, effective management of this emergent situation will help influence a positive patient outcome.
- Comprehensive training on LAST guidelines and treatment, along with best practice measures for patients receiving LA are essential for optimistic patient outcomes.

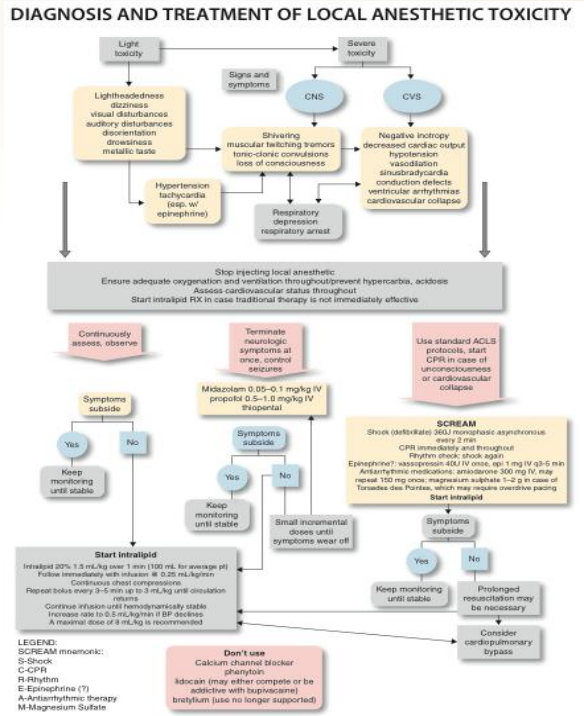

Table 2. Image retrieved from http://www.nysora.com/regional-anesthesia/foundations-of-ra/3075-toxicity-of-local-anesthetics.html

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