

Session Title: Killer Cases in Toxicology

Session overview

In a typical emergency department, serious toxicology cases are just rare enough to present a challenge for the treating practitioner. Standard ACLS therapies are usually not effective in toxicological-induced cardiac arrest. This session will utilize a case-based approach to provide practical pearls for managing complex overdose patients with toxin-induced shock.

Objectives

- In a smoke inhalation victim, interpret laboratory results and create a treatment plan.
- Describe how calcium gluconate works as quickly as calcium chloride to raise serum calcium levels.
- Identify the role of insulin and lipid emulsion therapy for treating non-local anesthetic toxicity.
- Given a patient with toxin-induced shock, devise a treatment plan including calcium, vasopressors, insulin, and fat emulsion.

Cyanide Poisoning

Since cyanide levels are not readily available, surrogate labs must be utilized in the appropriate clinical setting to rule in/out cyanide. In an unresponsive patient with a history including the potential for cyanide exposure (eg, smoke inhalation, chemical plant), an elevated lactate and lack of oxygen utilization can be very helpful. Measure an arterial and venous blood gas and calculate the difference between the arterial and venous oxygen saturations.

Though cyanide antidote kits (amyl nitrate, sodium nitrate, sodium thiosulfate) were used for many years, hydroxocobalamin is now the standard for cyanide poisoning.

- It can be used in combination with the cyanide antidote kit or by itself.
- Hydroxocobalamin combines with cyanide to form cyanocobalamin (vitamin B12) which is then excreted in the urine. ([Gerth K, et al. Clin Toxicol 2006](#))
- Administration: Add 200 mL NS to the vial; Adults: 5 g over 15 min, Pediatrics: 70 mg/kg. May repeat dose if not improving.
- Because hydroxocobalamin is red, it interferes with certain lab values
 - Cooximetry hemoglobin measurements
 - Colorimetric laboratory tests including: Aspartate aminotransferase, Bilirubin, Creatinine, Magnesium ([Lee, Ann Emerg Med 2007](#); [Curry, Ann Emerg Med 1994](#))
- Causes red skin and urine which can last for up to a week. ([Uhl W, et al. Clin Toxicol 2006](#))

Toxin-Induced Cardiovascular Collapse

Expert consensus expert recommendations for the management of calcium channel blocker poisoning in adults were published in 2016 ([St-Onge M, et al. Crit Care Med 2016](#)).

- Majority of literature/evidence on CCB overdose is heterogenous, biased, and low-quality.
- Interventions with the strongest evidence are high-dose insulin and extracorporeal life support.
- Interventions with less evidence, but still possibly beneficial, include calcium, dopamine, norepinephrine, 4-aminopyridine (where available), and lipid emulsion therapy.
- Glucagon is no longer recommended for CCB overdose.

Treatments for Toxin-Induced Shock

1. Initial assessment and treatment should include charcoal (if indicated), atropine (if bradycardia), calcium, and crystalloid fluids. Goals: preserve organ perfusion and increase survival
2. Glucagon should be administered for BB overdoses (3-5 mg IV/IO). Beware of vomiting (ondansetron prn). If successful, glucagon infusion may be administered at a rate of 5-15 mg/hr.
 - a. Available in 1 mg vials (powder), each needs reconstitution with sterile water. This takes a few minutes to prepare, even if glucagon is stocked in your unit-based cabinets.
3. Calcium – give it, optimal dose unclear. Start with at least 1 gm CaCl₂ or 2 gm calcium gluconate.
 - a. Does calcium gluconate act slower than CaCl₂ because it needs hepatic activation? No!
 - i. Serum ionized calcium levels were measured in 15 hypocalcemic patients during the anhepatic stage of liver transplantation. Half received CaCl₂ 10 mg/kg, the other half received calcium gluconate 30 mg/kg. Equally rapid increases in calcium concentration were observed, suggesting that calcium gluconate does not require hepatic metabolism for the release of calcium in the absence of hepatic function. ([Martin, Anesthesiology 1990](#))
 - ii. A randomized prospective study in both children and dogs compared ionization of CaCl₂ and calcium gluconate ([Cote CJ, et al. Anesthesiology 1987](#)). Equal elemental calcium doses of calcium gluconate (10%) and CaCl₂ (10%):
 1. Are equivalent in their ability to raise calcium concentration
 2. The changes in calcium concentration are short-lived (minutes)
 3. The rapidity of ionization seems to exclude hepatic metabolism as an important factor in the dissociation of calcium gluconate
 - iii. In ferrets and in vitro human blood, equimolar quantities of CaCl₂ and calcium gluconate produced similar changes in plasma ionized calcium concentration. This does not support the common suggestion that CaCl₂ is preferable to calcium gluconate because of its greater ionization. ([Heining, Anaesthesia 1984](#))
4. Vasopressors should be instituted early on. Though no one vasopressor is preferred, epinephrine or norepinephrine both are good starting choices with β_1 and α_1 agonist properties.
 - a. One inpatient toxicology service reported good success with high-dose vasopressors for CCB toxicity over a 25-year period ([Levine M, et al. Ann Emerg Med 2013](#)).
 - b. Vasopressors should generally be used in conjunction with high-dose insulin therapy.
 - c. Human cases suggest that even though vasopressors are not often effective, they don't seem to be harmful (unlike in the animal data) ([Skoog CA, et al. Clin Toxicol 2017](#))
5. Insulin ([Jang, Emerg Med Clin N Am 2014](#); [Engebretsen, Clin Toxicol 2011](#))
 - a. High-dose insulin (bolus + infusion) can be safe in refractory CCB/BB overdose ([Cole, Am J Emerg Med 2018](#))
 - b. In the nonstressed state, the heart primarily catabolizes free fatty acids for its energy needs, while the stressed myocardium switches preference to carbohydrates. Insulin's positive inotropic effects seem to occur because of metabolic support of the heart during hypodynamic shock.
 - c. CCB overdose patients typically present with hyperglycemia, in part due to blocking of L-type calcium channels on the pancreas that lead to insulin secretion ([Levine, Crit Care](#))

[Med 2007](#)). This may be one way to differentiate CCB overdose from BB (may present with hypoglycemia or normoglycemia).

- d. Dose: regular insulin bolus 1 unit/kg IV, then infusion 0.5-1 unit/kg/hour
 - i. Monitor potassium
 - ii. Monitor glucose
 1. A recommended starting dose of dextrose is 0.5 g/kg/hr delivered as D₂₅W or D₅₀W (by central venous access).
 2. Insulin receptors are saturable, meaning that the hypoglycemia is limited at a certain point. You may end up needing less dextrose than you think, but still proceed with caution.
 - e. Challenges of starting high dose insulin
 - i. High dose is not familiar to physicians, nurses, and pharmacists.
 - ii. Education is required to get everyone on board (education is recommended to be recurrent and prior to your first massive CCB/BB overdose)
 - iii. Be clear with all team members (including pharmacists) what the plan is and the purpose of the high dose.
 - iv. Requires special mixing from pharmacy as normal size bags run out quickly.
6. IV Lipid Emulsion
- a. Seems to work like a shuttle to accelerate redistribution from targets to reservoir organs ([Fettiplace, et al. J Control Release 2015](#), [Fettiplace, et al. Reg Anesth Pain Med 2018](#))
 - b. Lipid effects last for 30-60 minutes. Fat emulsion undergoes lipolysis to free fatty acids which are utilized by mononuclear phagocyte system (reticuloendothelial cells).
 - c. Consider lipid emulsion for local anesthetics, CCB, BB, TCA, bupropion, chloroquine, and other lipid soluble, cardio-/neurotoxic agents ([French D, et al. Clin Toxicol 2011](#)).
 - d. Evidence-based recommendations ([Gosselin S, et al. Clin Toxicol 2016;54:899-923](#)):
 - e. 'Best' dose for oral poisonings: 20% lipid emulsion - 1.5 mL/kg bolus, 0.25 mL/kg/min X 3 min, 0.025 mL/kg/min up to 6.5 hrs ([Fettiplace MR, et al. Ann Emerg Med 2015](#))
 - f. Possible adverse effects include ALI, pancreatitis, allergic reaction, fat emboli, and DVT ([Hayes BD, et al. Clin Toxicol 2016;54:365-404](#)).
 - g. Beware of laboratory interference ([Grunbaum, Clin Toxicol 2012](#)) and incompatibility with other resuscitation medications ([Cocchio, SOJ Pharm PharmSci 2014](#)). Labs should be drawn before lipid is given, if possible, and it should be administered in its own line.
 - h. Lipid can interfere with extracorporeal treatments

Tricyclic Antidepressant Poisoning (during a sodium bicarbonate shortage)

- ASHP has a great resource center for [drug shortages](#)
- If sodium bicarbonate is not available, it may actually be the sodium that is the most important factor in reversing ECG findings from TCA poisoning, as opposed to pH manipulation. Consider administering hypertonic saline ([McKinney, Ann Emerg Med 2003](#); [Ann Emerg Med 1998](#))
- One amp/syringe (50 mL) of 8.4% sodium bicarbonate contains the same amount of sodium as 97 mL of 3% sodium chloride or 38 mL of 7.5% sodium chloride.
- A central line is recommended if giving > 3% hypertonic saline.