

Session Title: What's New in Emergency 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 patient with anticholinergic poisoning, determine when it is appropriate to administer physostigmine.
- 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.

Physostigmine

Physostigmine gets a bad rap, in my opinion. ([PharmERToxGuy blog 2017](#), [Pharm EM Pearl 2019](#))

Use in TCA Overdose

Physostigmine was part of the 'coma cocktail,' until 2 patients developed asystole in the setting of TCA overdose ([Pentel 1980](#)). TCA overdose pathophysiology is complex, with more than just anticholinergic effects contributing. We overreacted and stopped using physostigmine regularly even when true anticholinergic poisoning was staring at us. The safety of physostigmine for seizures or cardiotoxicity in the setting of TCA toxicity is difficult to predict; risks/benefits should be weighed ([Suchard 2003](#)).

Use in Anticholinergic Poisoning

Clearly beneficial:

- Physostigmine controlled agitation and reversed delirium in 96% and 87% of patients, respectively. ([Burns 2000](#)) Benzodiazepines controlled agitation in 24% of patients but were ineffective in reversing delirium.
- One group published 10-years of poison center experience with physostigmine and concluded that it had a good safety profile and often improved or resolved anticholinergic delirium when administered in doses less than 2 mg. ([Arens 2018](#))
- Another poison center group confirmed that physostigmine reversed delirium in four out of 5 patients compared to non-antidotal therapy (36%) without increased reports of adverse events. ([Boley 2018](#))

Indications

Presence of peripheral or central antimuscarinic effects without significant QRS or QT prolongation

- Peripheral: dry mucosa, dry skin, flushed face, mydriasis, hyperthermia, decreased bowel sounds, urinary retention, and tachycardia
- Central: agitation, delirium, hallucinations, seizures, and coma

Adverse Effects

Have atropine available at the bedside in case you overshoot or an alternative diagnosis is underlying.

Contraindications (package insert)

Reactive airway disease, peripheral vascular disease, intestinal or bladder obstruction, intraventricular conduction defects, AV block, and in patients receiving choline esters and succinylcholine.

Dose

- 1 to 2 mg in adults and 0.02 mg/kg (max, 0.5 mg in children) IV infused over at least 5 minutes
- Onset is within minutes ([Holzgrafe 1973](#)); can be repeated after 10 to 15 minutes

My Algorithm

1. Lorazepam 2 mg IV for agitation, can be repeated
2. Physostigmine 1 mg IV over 5 minutes (mixed in 50 mL NS), can be repeated

Stock it in your ED.

Toxin-Induced Cardiovascular Collapse

Expert consensus recommendations for management of calcium channel blocker poisoning in adults ([St-Onge 2017](#))

- 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 1990](#))
- ii. A randomized prospective study in both children and dogs compared ionization of CaCl_2 and calcium gluconate ([Cote 1987](#)). Equal elemental calcium doses of calcium gluconate (10%) and CaCl_2 (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 CaCl_2 and calcium gluconate produced similar changes in plasma ionized calcium concentration. This does not support the common suggestion that CaCl_2 is preferable to calcium gluconate because of its greater ionization. ([Heining 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 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 2017](#))
5. Insulin ([Jang 2014](#); [Engebretsen 2011](#))
- a. High-dose insulin (bolus + infusion) safe in refractory CCB/BB overdose ([Cole 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 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 D_{25}W or D_{50}W (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 ([Schult 2022](#))
 - 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 2015](#), [Fettiplace 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 2011](#)).
 - d. Evidence-based recommendations: [Gosselin 2016](#)
 - 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 2015](#))
 - f. Possible adverse effects include ALL, pancreatitis, allergic reaction, fat emboli, and DVT ([Hayes 2016](#)).
 - g. Beware of laboratory interference ([Grunbaum 2016](#), [Petersen 2018](#)) and incompatibility with other resuscitation medications ([Cocchio 2014](#)). Labs should be drawn before lipid is given, if possible, and it should be administered in its own line.
 - h. Lipid may 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 2003](#); [McCabe 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.