The unstable overdose patient
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Associate Medical Director
California Poison Control Center, SF Division

Rob Ford - Mayor of Toronto

Objective

- Discuss clinical scenarios unique to the acutely poisoned unstable patients and representing high risk situations.
Remember

What are the most common interventions performed in acute poisoning?

Poison control center data 2011

Reminder

- Poisoned patient need really good supportive care!

Clinical Scenarios

- Aspirin overdose - Issues concerning airway
- A case of severe acidosis
- Cardiotoxicity - How is this shock different?
- Drug induced seizures
Unstable overdose case #1

- A 58 year-old male presents after ingesting an unknown quantity of aspirin in a suicide attempt. The patient appears diaphoretic and tachypneic, with a respiratory rate of 32. Lungs are clear to auscultation bilateral.
- Initial aspirin level = 110 mg/dL
- pH = 7.5, pCO2 = 17 mmHg, HCO3 = 13 mmol/L

Initial treatment should include which of the following?
- a. Intravenous fluids
- b. Bicarbonate drip
- c. Potassium supplementation
- d. Nephrology consultation
- e. All of the above

http://www.acmt.net/
Unstable overdose case #1

- Intravenous fluids - hypovolemia often not addressed
- Bicarbonate drip - enhanced elimination

Indications for dialysis:
- Rising levels
- AMS, cerebral edema, seizures
- Pulmonary edema
- Renal insufficiency
- Deteriorating clinical condition
- Profound acidemia
What about intubation?

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Unstable overdose case #1

- The treating physician is concerned that the patient is tiring and elects for rapid sequence intubation with etomidate and succinylcholine.
- Post intubation ABG
  - pH = 7.04, pCO2 55 mmHg, HCO3 = 9 mmol/L.
  - (pH = 7.5, pCO2 = 17 mmHg, HCO3 = 13 mmol/L)

The patient died 40 minutes post intubation. Think twice about intubating the aspirin poisoned patient!
Mechanical ventilation in aspirin poisoning

- Case series of 7 patients with salicylate poisoning (ASA level > 50 mg/dL) who underwent mechanical ventilation
  - post-MV pH in all patients was < 7.4
  - In 5 patients post-MV pCO2 was > 50 mmHg
  - 2/7 died post intubation (within hours)
  - One patient with severe neurologic injury

Stolbach et al. Mechanical ventilation was associated with acidemia in a case series of salicylate-poisoned patients. Acad Emer Med 2008 Sep; 15(9): 866-9

Mechanical ventilation in aspirin poisoning

- Individual case reports of hypoventilation in salicylate-poisoned patient resulting in death:
  - Deleterious effects of endotracheal intubation in salicylate poisoning Ann Emerg Med 2003; 41:583-4

Expert Opinion

- Hyperventilation is not itself an indication for intubation
- Intubation and mechanical ventilation can be associated with rapid worsening of toxicity and increased mortality.
- Maintain alkalosis through hyperventilation and intravenous sodium bicarbonate.
- Once intubated, maintain minute ventilation and low pCO2.

When is intubation indicated?

- Altered mental status
- Pulmonary edema
- Hypoventilation
- Aspiration risk

Unstable overdose case #2

- A 25 year-old female with no sig PMH suddenly collapsed while at work. Upon arrival to the emergency department she was unresponsive with a GCS of 5.
- BP is 90/p, HR 110 bpm, O2 Sat 100%, T afebrile.
- Pupils 4 mm, sluggishly reactive, lungs sounds clear, neuro exam restless, nonpurposful movements.

Unstable overdose case #2

- Blood glucose = 158 mg/dL
- ABG: pH 7.01, pCO2 = 21 mmHg HCO3 = 8 mmol/L
Unstable overdose case #2

- Blood glucose = 158 mg/dL
- ABG: pH 7.01, pCO2 = 21 mmHg HCO3 = 8 mmol/L

Call poison control! 1-800-222-1222!
Unstable overdose case #2

- Initial treatment includes the following:
  - Intubation
  - IV fluids
  - Additional laboratory studies
  - STAT head CT negative

- Additional laboratory studies:
  - Tylenol, aspirin, ethanol levels negative
  - WBC 19K
  - Na 142, K 4.3, Cl 101, HCO3 9, BUN 8, Cr 1.5, Glucose 155
  - Anion gap 22
  - Serum ketones negative
  - Lactate 10 mmol/L

Clinical clues to the diagnosis

- Sudden collapse
- Severe acidosis
- Elevated anion gap
- Elevated lactate
- No ketones
Selected drugs and toxins causing lactic acidosis

- Acetaminophen
- Antiretroviral drugs
- Beta-agonists
- Caffeine
- Carbon Monoxide
- Cyanide
- Hydrogen sulfide
- Iron
- Isoniazid
- Metformin
- Propofol
- Salicylates
- Seizures; shock, hypoxia
- Sodium azide
- Theophylline

Unstable overdose case #2

- Additional history
- Works in a laboratory with access to chemicals
- Has access to potassium cyanide
- Co-oximetry reveals no evidence of CO

Cyanide: Pathophysiology
Electron Transport Chain

NADH → e⁻ → H⁺ → ATP
Electron Transport Chain

- NADH
- ADP
- ATP
- cytochrome aa3
- CN

Treatment of CN Poisoning

- Removal from source
- 100% oxygen by tight-fitting mask/ET tube
- Cyanide antidote kit?
- Hydroxocobalamin?
Nitrites

Sodium thiosulfate

Hydroxocobalamin

• Combines with CN to form Vitamin B12.
• Appears to be effective and safe
• Preferred drug for CN due to smoke inhalation (safer than nitrites)
Hydroxocobalamin

• Side effects:
  – Red Skin, secretions 2-7 days
  – Nausea, vomiting
  – Occasional HTN and muscle twitching

Unstable overdose case #3

• A 45 year-old female with a history of depression presents 1 hour after a large ingestion of her antihypertensive medications. On arrival she is somnolent but arousable and has a GCS of 14.
• Vital signs: BP 83/50, HR 65, RR 18, O2 sat 98% RA
• Finger stick glucose = 235
• Venous lactate = 5 mmol/L

Unstable overdose case #3

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• Finger stick glucose = 235
• Venous lactate = 5 mmol/L
• **rr**

Calcium Channel Blockers
Beta Blocker
Digoxin
Clonidine
Hyperkalemia
Unstable overdose case #3

• Further history reveals that the patient took verapamil

Calcium Antagonist Toxicity

Deceased Automaticity & Conduction

Negative Inotropic Effects

Dilated Vascular Smooth Muscle

HR
AV Block

CO

SVR

SHOCK

Therapeutic approaches to shock

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Vasopressors

- 48 patients with verapamil or diltiazem overdose:
  - IV fluids and vasopressors used almost exclusively
  - Only 1 death
  - Doses of vasopressors higher than usual (NE 100 ug/min, DA 100 ug/kg/min)
  - Many patients required more than one pressor and some up to 5
  - Conclusion: fluids and aggressive use of vasopressors is treatment of choice

Unstable overdose case #3

- How does shock in the context of poisoning differ than shock from other causes?
  - May need higher doses of vasopressors
  - May need multiple different vasopressors

High dose insulin therapy

- Proposed mechanisms:
  - Increased ionotropy
  - Improved uptake of carbohydrates in myocytes
    - Vasodilation of peripheral vascular beds
  - Strong animal evidence of efficacy
  - Human evidence primarily case reports and case series
Evidence - animal

- Experimental studies:
  - Kline et al. Verapamil dog model
    - Kline JA, Tomaszewski CA, Schroeder JD, Raymond RM. Insulin is a superior antidote for cardiovascular toxicity induced by verapamil in the anesthetized canine. J Pharmacol Exp Ther 1993; 267:744–750.

Evidence Clinical

- 12 patients treated with a standardized protocol
- Primary toxin was: BB (5 patients), CCB (2 patients), Combined BB and CCB (2 patients), Polydrug (3 patients)
- 7 pts on pre-existing vasopressors, all tapered off
- 2 pts PEA arrest subsequently improved and survived after HIEET
**High dose insulin euglycemia therapy (HIET)**

- **Bolus**: 1 unit / kg
- **Drip**: 1-10 unit / kg / hour
- **Start dextrose infusion (D10)**
- **Measure glucose q 10 min**

**Unstable overdose case #3**

- How does shock in the context of poisoning differ than shock from other causes?
  - May need higher doses of vasopressors
  - May need multiple different vasopressors
  - May consider unusual antidotes
  - High dose insulin

**Other Antidotes?**

- What is the mechanism?
- Animal evidence in verapamil models
- No good human data

**Intravenous Lipid Emulsion as Antidote Beyond Local Anesthetic Toxicity: A Systematic Review**

- [lipidrescue.org](http://lipidrescue.org)

**Other Antidotes?**

*TOXICOLOGY/CASE REPORT*

**Methylene Blue in the Treatment of Refractory Shock From an Amlodipine Overdose**

David H. Jiang, MD, Lewis S. Nelson, MD, Robert S. Hofmann, MD

Methylen blue administered at 2 mg/kg followed by infusion of 1 mg/kg/hr rapidly improved blood pressure and allowed for weaning of all pressors in a patient with severe amlodipine overdose.
Other Antidotes?

Methylene Blue in the Treatment of Refractory Shock From an Amlodipine Overdose

Mechanism is through decreased nitric oxide release.

Unstable overdose case #3

- How does shock in the context of poisoning differ than shock from other causes?
  - May need higher doses of vasopressors
  - May need multiple different vasopressors
  - May consider unusual antidotes
    - High dose insulin
    - Intravenous lipid emulsion
    - Methylene blue

Unstable overdose case #4

- A 26 year-old female presents to the emergency department brought in by medics after a witnessed generalized tonic clonic seizure. She was given 2 mg of Ativan in the field which initially stopped the seizure, however upon arrival in the emergency department she begins seizing again. Additional doses of ativan result in transient cessation of seizure activity followed by recurrent seizures activity.
Unstable overdose case #4

Most acute idiopathic seizures are treated with:
- Benzodiazepines
- Phenytoin
- Barbiturates
- Propofol

Should drug induced seizures be treated the same way?

What causes drug induced seizures?

- Impaired inhibition
- Enhanced excitation
- Disorders of conduction
- Metabolic failure

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<td>Theophylline</td>
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Why not phenytoin for drug induced seizures?

Because it doesn’t work!
Why not phenytoin for drug induced seizures?

- 90 patients with alcohol related seizures
- Random assignment to phenytoin (1gm) or placebo
- End points
- Seizure recurrence
- 12 hour seizure free period
- Phenytoin group had no benefit

Unstable overdose case #4

- A 26 year-old female presents to the emergency department brought in by medics after a witnessed generalized tonic clonic seizure. She was given 2 mg of Ativan in the field which initially stopped the seizure, however upon arrival in the emergency department she begins seizing again. Additional doses of ativan result in transient cessation of seizure activity followed by recurrent seizures activity.
- Further history reveals that the patient overdosed on isoniazid

Pyridoxine (B6) and GABA

- Glutamine
- Glutamic Acid (brain)
- GABA
- Pyridoxal 5’ Phosphate
- GAD
- Pyridoxine
- INH
Treatment of INH seizures

- Benzos, Benzos, Benzos
- No role for phenytoin
- Give pyridoxine (5 grams empiric dose)
- Intubation and paralysis may be necessary

General approach to drug induced seizures

- Try to define the etiology
- Always start with a benzodiazepine
- Avoid phenytoin
- Think about antidotes
- Add barbiturates for synergy

In summary

- Case #1 - Aspirin
  - Intubation can be tricky and can lead to rapid deterioration
  - Do not intubate simply for tachypnea
- Case #2 - Cyanide
  - Think of CN in patients with severe lactic acidosis
  - Use hydroxocobalamin or cyanide antidote kit

In summary

- Case #3 - Verapamil overdose
  - High dose vasopressors
  - High dose insulin
  - Think about intralipid and methylene blue
- Case #4 - Isoniazid
  - Benzo first line in drug induced sz
  - Think about antidotes (pyridoxine)