The unstable overdose patient
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California Poison Control Center, SF Division

Objectives

• Discuss clinical scenarios unique to the acutely poisoned patient and representing high risk situations. These cases require the clinician to think differently than they otherwise would in managing other critically ill patients.

Outline

• Aspirin overdose - Issues concerning airway
• Cyanide toxicity - Blood agents
• 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
Unstable overdose case #1

• Initial treatment includes the following:
  • Intravenous fluids
  • Bicarbonate gtt
  • Potassium supplementation
  • Nephrology consultation

Question

• Who would intubate this patient?

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, pCO\textsubscript{2} 55 mmHg, HCO\textsubscript{3} = 9 mmol/L.

Unstable overdose case #1

• The patient died 40 minutes post intubation.
Salicylate Toxicity

- Key Points
  - Cellular toxicity results in elevated anion gap metabolic acidosis
  - Stimulates respiratory center of brain produces respiratory alkalosis (overcompensation)
  - Acidosis results in worsening toxicity and should be avoided at all costs.

When is intubation indicated?

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

Mechanical ventilation in aspirin poisoning

- Case series of 7 patients with salicylate poisoning (asa level > 50mg/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.

American College of Medical Toxicology (ACMT) Guidance Document:
Management Priorities in Salicylate Toxicity
http://www.acmt.net
accessed 1/2014

Expert Opinion

- Coingestion or therapeutic administration of CNS/respiratory depressant drugs may also precipitate clinical deterioration
  - Alcohol
  - Opiates
  - Benzodiazepines
  - Antihistamines

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Unstable overdose case #2

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

Blood glucose = 158 mg/dL
- ABG: pH 7.01, pCO2 = 21 mmHg HCO3 = 8 mmol/L
Unstable overdose case #1

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

Unstable overdose case #2

- 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

Unstable overdose case #2

- Clues to the diagnosis
  - Sudden collapse
  - Severe metabolic acidosis
  - Elevated anion gap
  - Elevated lactate
  - Absence of ketones

Cyanide: Pathophysiology
Electron Transport Chain

- NADH
- ADP
- cytochrome aa3
- CN

Sodium thiosulfate

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

Nitrites

- 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
Mechanism of shock in drug overdose

<table>
<thead>
<tr>
<th>Drug Overdose</th>
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<tbody>
<tr>
<td>• Fluid Loss</td>
<td>• NL to high cardiac output</td>
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<tr>
<td>• Blood Loss</td>
<td>• Low SVR</td>
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<tr>
<td>• Hypovolemic Shock</td>
<td>• Low cardiac output</td>
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<td>• BB</td>
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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
- Further history reveals that the patient took verapamil

Mechanism of shock in drug overdose

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Treatments

- Intravenous Fluids
- Atropine
- Vasopressors
- Cardiac Pacing
- Calcium
- High does insulin
- Other treatments?

Vasopressors

- Of 48 patients with verapamil or diltiazem overdose:
  - IV fluids and vasopressors used almost exclusively
  - Only 1 death
  - Doses of vasopressors high than usual (NE 100 ug/min, DA 100 ug/kg/min
  - Many patients required more that one pressor and some up to 5
  - Conclusion: fluids and aggressive us of vasopressors as treatment of choice (Not HIET or calcium)

Critical Care Management of Verapamil and Diltiazem Overdose With a Focus on Vasopressors: A 25-Year Experience at a Single Center

Michael Levine, MD; Steven E. Gurney, MD; Angela PatalasJones, RN; ErnestoRatziu, MD

Study objective: Transient or sustained hypotension can cause serious morbidity and death, and there exist limited human data describing management and outcome of a large number of such patients. This article describes the management and outcome of patients with verapamil/diltiazem overdose, with an emphasis on vasopressor dosing, at a single center.

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

High dose insulin therapy

- Strong animal evidence of efficacy
- Human evidence primarily case reports and case series

Evidence - animal

- Experimental studies:
  - Kline et al. Verapamil dog model

Kline et al. Insulin a superior antidote for cardiovascular toxicity induced by verapamil in the canine.
Evidence Clinical

High-dose insulin: A consecutive case series in toxin-induced cardiogenic shock

Joel S. Bolger, Samuel J. Stellpflug, John R. Cole, Carolyn R. Harris, and Kristin M. Ungerbraten
Department of Emergency Medicine, Regions Hospital, St. Paul, MN, USA

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 HiET

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
  - Intravenous lipid emulsion
  - Methylene blue
Other Antidotes?

**PROGRESSIVE CLINICAL PRACTICE**

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

Grant Cave, MBChB, FCEM, and Marlyn Harvey, MBChB, FCEM

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

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.
Unstable overdose case #4

• Why not phenytoin for drug induced seizures?