Project: Ghana Emergency Medicine Collaborative

Document Title: Toxic Alcohols

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Ventilated Patients

Checking the “A” in ABC....
Troubleshooting the Mechanical Airway

- Try the mnemonic “DOPES”
- D = displacement
- O = obstruction
- P = pneumothorax
- E = equipment failure
- S = sedation
Toxic Alcohols
Pathophysiology and Emergency Management
What are the toxic alcohols?

- Methanol
- Ethylene Glycol
- Isopropanol
Methanol

- Where is it found?
  - Wiper fluid/de-icing products
  - Paint thinners
  - Shoe dye
  - Embalming fluid
  - “Moonshine”

- How are patients exposed?
  - Primarily ingestion
  - Possible from dermal or inhalation exposure
Methanol and metabolism

Ethanol

Methanol

Ethylene glycol

Acetaldehyde

Formaldehyde

Fomipizole/ethanol

Folinic acid

Formate

CO$_2$ + H$_2$O

Glycol aldehyde

Glycolic acid

Oxalic acid

Calcium oxalate

Aldehyde dehydrogenase

Glycolate oxidase
Methanol

- Metabolism leads to acidosis
  - Formic acid buildup
  - Lactic acidosis
- Effects of formic acid
  - Direct optic and retinal toxicity
  - Shifts cells to anaerobic metabolism by inhibiting cytochrome oxidase
Ethylene Glycol

- Where is it found?
  - Radiator anti-freeze
  - Degreasing agents
  - Metal cleaners

- How are patients exposed?
  - Primarily ingestion: no odor, no color, sweet taste
Ethylene Glycol Metabolism

- Ethylene Glycol
  - Glycoaldehyde
    - Glycolic Acid
      - Glyoxylic Acid
      - Alpha-hydro
Ethylene Glycol

- 80% hepatic metabolism
- 20% excreted unchanged in the urine
- Half-life depends on renal function
- Also causes acidosis
  - Directly from glycolic acid, glyoxylic acid, oxalic acid
  - Indirectly when NAD+ depletion leads to anaerobic metabolism → lactic acidosis
Isopropanol

- Where is it found?
  - Rubbing alcohol
  - Hand sanitizers
  - “Spirits”

- How are patients exposed?
  - Primarily ingestion

- Most common in USA
- Less toxic than other alcohols
Isopropyl Metabolism

Isopropyl → Acetone

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Methanol

- Least inebriating
- First 24hrs (direct effects of methanol)
  - CNS depression
  - Euphoria/ mild inebriation
- Later symptoms (from formic acid)
  - Visual changes
    - Blurred vision, decreased acuity, photophobia, “snowstorm” vision
    - Progresses to blindness, absent papillary response, permanent optic nerve atrophy
  - Parkinsonian symptoms
  - Abdominal pain
## Ethylene Glycol

<table>
<thead>
<tr>
<th>Stage</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>1: Neurological</td>
<td>- Initial: intoxication, euphoria</td>
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<tr>
<td>(0.5-12 hours)</td>
<td>- After 4 to 12 hours, if ingestion is severe: CNS depression, seizures,</td>
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<tr>
<td></td>
<td>meningismus, nystagmus, ataxia, ocular external muscle paralysis,</td>
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<tr>
<td></td>
<td>hyperreflexia, muscle spasms, hypocalcemia</td>
</tr>
<tr>
<td>2: Cardiopulmonary</td>
<td>- Tachycardia, mild hypertension, hyperventilation (secondary to metabolic</td>
</tr>
<tr>
<td>(12-24 hours)</td>
<td>acidosis)</td>
</tr>
<tr>
<td></td>
<td>- Acute respiratory distress syndrome, congestive heart failure, cardiac</td>
</tr>
<tr>
<td></td>
<td>dysrhythmia (secondary to hypocalcemia and QTc prolongation)</td>
</tr>
<tr>
<td>3. Renal</td>
<td>- Oliguria, flank pain, acute renal failure</td>
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<tr>
<td>(24-72 hours)</td>
<td>- Renal failure (typically reversible)</td>
</tr>
<tr>
<td></td>
<td>- Bone marrow suppression</td>
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</tbody>
</table>

Source Undetermined
Isopropanol

- Fruity odor on breath
- Gastrointestinal
  - Abdominal pain
  - Nausea/vomiting
  - Upper GI bleeds
- Neurologic
  - CNS depression (may progress to coma)
  - Nystagmus
  - Ataxia
  - Confusion
Diagnostic Evaluation

- All laboratory based – difficult to obtain promptly in Ghana
- Labs all from same sample:
  - Electrolytes
  - Osmolality
  - Ethanol level
  - Toxic alcohol levels
Evaluating Labs

Abbreviations: AG, anion gap; OG, osmolar gap.

Source: Undetermined
Evaluating Labs

- Calculate serum osmolality
  \[ \text{Osmc} = [2 \times (\text{sodium})] + (\text{BUN}/2.8) + (\text{glucose}/18) + (\text{ethanol}/4.6) \]
- Measure serum osmolality
- Calculate osmolar gap
- Calculate anion gap
- Check urine for calcium oxalate crystals
- Definitive: toxic alcohol concentration
Evaluating Labs

- Ethylene glycol:
  - Hypocalcemia
  - Renal failure
  - Low bicarbonate

- Methanol:
  - Low bicarbonate

- Isopropanol
  - No anion gap
  - Falsely elevated creatinine
Treatment Algorithm

One or more of the following criteria:
- anion gap >12
- osmolar gap >10
- ethylene glycol >20 mg/dL
- methanol > 20 mg/dL
- Evidence of metabolic acidosis
- Evidence of renal failure

Administer fomepizole 15 mg/kg (Class II)

Ethylene glycol
Methanol

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Treatment Algorithm

**Ethylene Glycol**
1. Administer thiamine 100 mg IV AND administer pyridoxine 100 mg IV (Class III)
2. Order renal consult if:
   - presentation is delayed
   - patient is acidemic
   - there are signs of renal insufficiency
3. Admit to ICU

**Methanol**
1. Administer folic acid (leucovorin) 50 mg IV OR administer folic acid 50 mg IV (Class III)
2. Order ophthalmologic consult
3. Consider renal consult for potential hemodialysis if:
   - ingestions is large
   - presentation is delayed
   - there are visual disturbances
3. Admit to ICU

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Toxic Alcohol Metabolism

- Methanol
  - Fomepizole/ethanol
- Ethanol
- Ethylene glycol
- Alcohol dehydrogenase
  - Formaldehyde
  - Acetaldehyde
  - Formate
  - CO$_2$ + H$_2$O
- Glycol aldehyde
  - Aldehyde dehydrogenase
- Glycolic acid
  - Oxalic acid
  - Calcium oxalate
  - 10-formyltetrahydrofolate synthetase
- Folinic acid
Treatment

- Airway, Breathing, Circulation
- Consider gastric aspiration
  - Only for LARGE ingestions
  - Only if VERY recent (<1 hour)
- Activated charcoal for coingestions
- Antidote
  - Fomepizole: $1,000 per vial; 15 mg/kg dose
  - Alcohol: used since 1940s with success
Treating with Alcohol

- Higher affinity for ADH
  - 68x greater than ethylene glycol
  - 15x greater than methanol
- IV or PO formulations available
- Goal: blood alcohol between 100 and 150mg/dL
Treating with Alcohol

- IV: 10% ethanol in D5W
  - 60-80 mg/kg loading dose
  - 80-130 mg/kg/hr maintenance
- PO: 20% ethanol
  - Mix with orange juice
  - 80 mg/kg loading dose
  - 80 mg/kg/hr maintenance
  - Chronic Alcoholics: 150mg/kg/hr
Treating with Alcohol

- Side effects
  - Hypoglycemia (90% of patients)
  - CNS depression
  - Intoxication
  - Thrombophlebitis
  - Hypotension
- Frequently require modifications in infusion rate to maintain 100mg/dL blood level
- Should be admitted to ICU
Pediatric Considerations

Children who ingest more than a taste of ethylene glycol or any amount of methanol are referred by poison control centers to the ED for evaluation. In children 18 months to 4.5 years of age, a mouthful is between 5 and 10 mL and could potentially result in concentrations that exceed 20 mg/dL of either toxic alcohol.

No guidelines are currently available from the AACT or the AAPCC for treating children with toxic alcohol ingestion. In addition, the FDA has not officially approved fomepizole for use in children. Several case studies and case series report the administration of fomepizole to pediatric patients. Fomepizole is preferred over ethanol in children, since they are at risk for hypoglycemia (secondary to poor glycogen stores), hypothermia, and CNS depression.
Treating Isopropanol Ingestions

- VERY DIFFERENT from other toxic alcohols
- Inhibiting ADH will make the patient worse!

- ABCs
- Administer PPI (hemorrhagic gastritis)
- Supportive care
- Consider co-ingestions
Conclusions

- Consider treatment if pt symptomatic (inebriated) or witnessed significant ingestion
- Don’t forget cofactors!
- Consider dialysis (only needed acutely)
- If treating with alcohol, monitor carefully for hypoglycemia
- Remember: osmolar gap first, anion gap second