Methanol and Ethylene Glycol Poisoning

Methanol or ethylene glycol ingestion causes serious systemic toxicity and can be fatal. Metabolism to its toxic metabolites by alcohol dehydrogenase causes anion-gap metabolic acidosis and end-organ effects. Rapid recognition and early treatment are crucial.

ANESTHETIC CONSIDERATIONS:

- CNS sedation/enubriation and possible need to secure the airway.
- If severe poisoning:
  - Coma, seizures, cerebral edema, cerebral herniation
  - Pulmonary edema, hyperpnea
  - Myocardial dysfunction, hypotension
  - Multisystem organ failure
- Methanol intoxication can cause visual changes and ultimately blindness.
- Ethylene glycol poisoning can cause renal failure and hypocalcemia.

ANESTHETIC GOALS:

- Secure airway and hyperventilate with large minute ventilation if profound metabolic acidosis.
- Provide supportive care.
- Drugs to minimize metabolic acidosis and to speed elimination of toxic metabolites.
- Consider hemodialysis in severe toxicity.

PATHOPHYSIOLOGY

- Methyl alcohol (methanol) is found in paint remover, gas-line antifreeze, windshield washing fluid, and camper fuel
- Ethylene glycol is found in antifreeze, de-icers, and industrial solvents
- The parent alcohols methanol and ethylene glycol are relatively nontoxic, and cause mainly CNS sedation
- Peak serum alcohol concentrations are reached within one to two hours of oral ingestion
- In the absence of treatment, an ingestion of approximately 1g/kg of either methanol or ethylene glycol is considered lethal, and serious toxicity has been reported following ingestions of as little as one teaspoon of methanol
- Inhalation and dermal exposures rarely cause toxicity
- Profound toxicity ensues when these parent alcohols are oxidized (primarily by alcohol dehydrogenase and aldehyde dehydrogenase)
- The methanol metabolites formaldehyde and formic acid and the ethylene glycol metabolites glycolate, glyoxylate, and oxalate accumulate following large ingestions
  - Above plasma levels of 6 mmol/L of methanol or 3 mmol/L of ethylene glycol, these metabolites can cause specific end-organ damage
  - Formate causes retinal injury with optic disc hyperemia, edema, and eventually permanent blindness, as well as ischemic or hemorrhagic injury to the basal ganglia
  - Ethylene glycol metabolites target the kidney and lead to reversible oliguric or anuric acute kidney injury (ARF) which in turn slows elimination of ethylene glycol
  - Hypocalcemia in ethylene glycol overdose results from calcium oxalate formation
- With ingestions of either parent alcohol, a profound anion gap metabolic acidosis develops, which directly correlates with the accumulation of toxic acid metabolites
  - Acidemia increases the ability of the toxic metabolites to penetrate cells, further depressing CNS function and causing a rapid downward spiral of hypoxia and acidemia

HISTORY

- Identify the original source and nature of the exposure including when the ingestion occurred and whether ethanol was also ingested
- Methanol poisoning suggested by complaints of visual blurring, central scotomata, and blindness; severe abdominal pain, possibly due to pancreatitis, that mimics a surgical emergency may occur
- Ethylene glycol is suggested by history of flank pain, hematuria, and oliguria

PHYSICAL

- Vitals, mental status, pupils
- Methanol poisoning:
  - The target organs are the retina, the optic nerve, and the central nervous system
  - Eye examination: mydriasis, retinal sheen due to retinal edema, hyperemia of optic disk, afferent papillary defect is an ominous sign of advanced poisoning
- Ethylene glycol poisoning:
  - Metabolism can lead to cranial nerve palsies and tetany (thought to result from oxalae-induced hypocalcemia)
  - Accumulation and precipitation of calcium oxalate crystals in the renal tubules can produce acute tubular necrosis and renal failure
  - Hypocalcemia due to oxalate chelation of calcium, myocardial dysfunction, pulmonary edema, and cerebral edema
- Early toxicity: CNS sedation and inebriation similar to ethanol intoxication
- Late toxicity:
  - Further decrease in mental status
  - Coma, seizures, hyperpnea (Kussmaul-Kien respirations) and hypotension suggest a substantial portion of the parent alcohol has been metabolized to its toxic byproducts
  - Cerebral herniation and multisystem organ failure in profound poisoning

INVESTIGATIONS

- ABG: Profound high anion-gap metabolic acidosis and elevated plasma osmolal gap
  - Alcohols such as ethanol, methanol, isopropyl alcohol, and ethylene glycol are osmotically active molecules that expand extracellular water; Poisonings with these agents cause a dilutional acidosis
  - The anion gap (anion gap = $[Na^+ + K^+ - (Cl^- + HCO_3^-)]$) distinguishes acidosis caused by hyperchloremia (renal tubular acidosis or excessive administration of "normal saline") from acidosis caused by "unmeasured" anions (many of which now are measurable) and dilution
  - Osmolal gap is the difference between the measured osmolality and the calculated plasma osmolality
  - Calculated Posm = (2 x plasma [Na]) + [glucose] + [urea], using mmol/L standard units
  - Plasma osmolal gap cannot distinguish among ethanol, isopropyl alcohol, methanol, or ethylene glycol

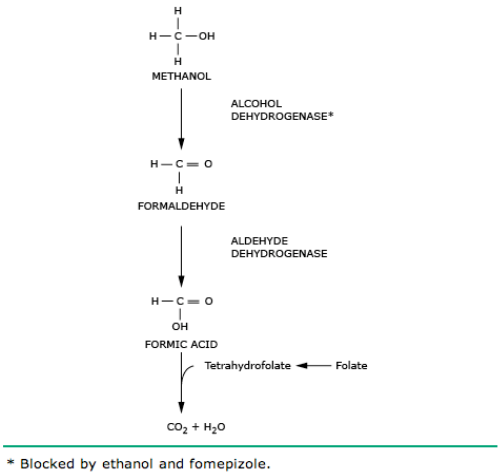
- Only the parent alcohols and not their toxic metabolites are detected by an elevated plasma osmolal gap
- Serum bicarb can be less than 8 mmol/L
- Basic electrolytes with anion gap determination, serum calcium (hypocalcemia with ethylene glycol), glucose to rule our hypoglycemia as cause of any altered mental status, serum osmolality
- BUN and Cr (renal failure with ethylene glycol)
- Serum ethanol, methanol, ethylene glycol, and isopropyl alcohol concentrations
- Urine for oxalate crystals (ethylene glycol)
- Acetaminophen and salicylate levels (common coingestions)
- ECG to rule out conduction system poisoning (ethylene glycol can prolong the QTc interval via its effects on serum calcium)
- Lactate may be elevated in ethylene glycol poisoning

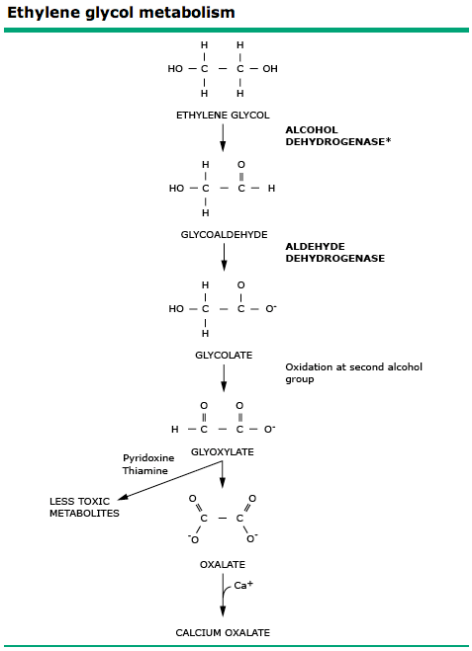
EMERGENT MANAGEMENT

- Secure the patient's airway in severely intoxicated patients as necessary and provide supportive care
  - Hyperventilate with large minute ventilations if a significant metabolic acidosis exists
- Treat hypotension with iv crystalloid, followed by standard vasopressors as necessary
- Activated charcoal does not absorb alcohols
- Inhibit the enzyme alcohol dehydrogenase with either fomepizole (15 mg/kg iv loading dose, followed by 10 mg/kg q12h x 4 doses), or ethanol if fomepizole is not available (8 mL/kg of a 10% ethanol solution, followed by 1 ml/kg of 10% ethanol solution infused per hour; titrate to serum ethanol concentration of 100 mg/dL)
- Administer sodium bicarbonate (1-2 meq/kg bolus, followed by infusion of 132 meq NaHCO3 in 1L D5W to run at 200-250 cc/h for patients with a pH below 7.3) to correct systemic acidosis (limits the pentration of toxic acids eg. formic acid into end-organ tissues by converting them to the anion which cannot diffuse across the cell membrane)
- Treat with cofactors (folic acid, thiamine, and pyridoxine) to optimize nontoxic metabolic pathways for the elimination of the parent alcohol or its metabolites
  - Folic acid 50 mg iv q6h
  - Thiamine 100 mg iv
  - Pyridoxine 50 mg iv
- Treat hypocalcemia if ethylene glycol poisoning
- Hemodialysis is the best method to rapidly remove both toxic acid metabolites and parent alcohols, and is indicated in severe toxicity:
  - High anion gap metabolic acidosis, regardless of drug level
  - Elevated serum toxic alcohol levels (more than 50 mg/dL) unless arterial pH is above 7.3
  - Evidence of end-organ damage (eg. visual changes, renal failure)

COMPLICATIONS

- Severely poisoned patients who present in coma may not survive despite maximum intensive therapy





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