An Overview of Diagnosis and Management

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SAMANTHA BREAZ, PHARMD
DANBURY HOSPITAL

Disclosure Statement

- In accordance with ACPE standards, all relevant financial relationships with ineligible companies have been identified and mitigated. The faculty has no other conflicts of interest to disclose.

Off-Label Discussion

- This activity may include discussion of unlabeled or unapproved uses of medications. All content is evidence-based and presented in a balanced, unbiased manner, drawing on established clinical guidelines and peer-reviewed data. Learners are encouraged to consult the official prescribing information for each product to review approved indications, contraindications, and warnings.

Learning Objectives

At the conclusion of this CPE activity, participants should be able to:

1. Recognize the pathophysiology of methanol, isopropyl alcohol, and ethylene glycol poisoning
2. Review treatment options in patients presenting with a toxic alcohol ingestion
3. Calculate the serum osmolar gap and anion gap in a patient presenting with a toxic alcohol ingestion.

Abbreviations used:

- CNS: Central nervous system
- N/V: Nausea/vomiting
- AG: anion gap
- AMS: altered mental status
- GI: gastrointestinal
- AACT: American Academy of Clinical Toxicology
- ADH: alcohol dehydrogenase
- ALDH: aldehyde dehydrogenase
- PPI: Proton pump inhibitor
- OG: osmolar gap
- AG: anion gap

Background

https://poisoncenters.org/national-poison-data-system

- In the 2023 annual National Poison Data System report, 2.7% of total cases were exposed to alcohols
- Miscellaneous alcohols contributed to 7.6% of total exposures associated with fatalities
- Methanol, ethylene glycol, and isopropyl alcohol (isopropanol) are the most common toxic alcohols that are readily available and cheaper than alcohol
  - The toxicity lies in their metabolites rather than the parent compound

Diagnosis of Toxic Alcohol Ingestion

- Concentrations are measured by gas chromatography
  - Not readily available in hospitals
  - Only clinically useful within 2 hours of lab drawn
- Urine microscopy to detect calcium oxalate crystals (for ethylene glycol poisoning)
- Lab abnormalities (ABG, Chem7, osmolality, anion gap)
- Signs and symptoms

Diagnosis (cont)

- In the absence of DKA or alcoholic ketoacidosis, the osmol and anion gap suggest methanol or ethylene glycol poisoning
  - Visual changes = Methanol
- Signs suggesting ethylene glycol toxicity
  - Inebriation without ethanol smell
  - Metabolic acidosis with large anion gap
  - Altered mental status
  - Osmolar gap
  - Calcium oxalate crystals with hypocalcemia
  - Renal injury

Anion Gap(AG)

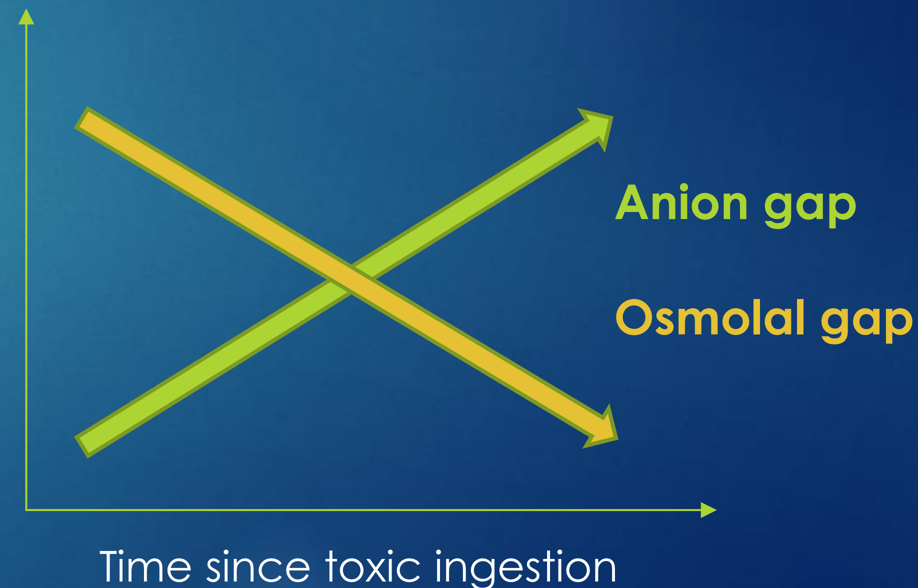
- **Anion Gap (mEq/L) = Na – (Cl + HCO_3)**
  - Normal = 8-12 mEq/L
- Correct for hypoalbuminemia
- Albumin corrected AG (mEq/L) = anion gap + [2.5 × (4 – albumin (g/dL))]
- Elevated suggests metabolic acidosis

- Interpret in relation to time of ingestion! Early after ingestion, anion gap may be normal

Osmolarity? Osmolality?

- Osmolarity: total number of particles in 1 L of solution (mOsm/L)
- Osmolality: total number of particles per kg (mOsm/kg)

- Osmolar and Osmolal are used interchangeably
  - The specific gravity of human serum= 1.01
  - 1 L of serum ≈ 1 kg
- Normal Serum Osm= 275-295 mmol/kg



Osmolar Gap (OG)

- The osmolar gap(mOsm/L) is the difference between measured osmolality and calculated osmolarity

Calculated serum osmolarity (mOsm/L)=2*Na + (BUN/ 2.8) + (glucose/18) + (ethanol/4.6)

Na measured in mEq/L; BUN, glucose, and ethanol in mg/dL

- Osmolar gap < 15-20 mOsm/L= ketoacidosis, lactic acidosis, renal failure
- Osmolar gap > 20 mOsm/L= suspicion for toxic alcohol poisoning
- OG doesn’t reflect severity of poisoning, especially late in poisoning and absence of an OG doesn’t exclude poisoning.

Approach to the Osmolar Gap

1. **Serum osmolarity (mOsm/L)**= 2*Na + (BUN/ 2.8) + (glucose/18) + (ethanol/4.6)
2. Calculate the osmol gap (OG):**OG= measured Osm – calculated Osm**
3. You can then estimate toxic alcohol concentration with the osmolar gap:
4. **Toxic alcohol concentration = conversion factor * OG**

Estimated alcohol concentration (mg/dL)	Conversion factor
Ethanol	4.6
Methanol	3.2
Ethylene glycol	6.2
Isopropyl alcohol	6.0

METHANOL

ETHYLENE GLYCOL

ISOPROPANOL

Methanol (Methyl Alcohol)

- Colorless, volatile liquid with a faint sweet odor
- Commonly found in
  - Windshield-wiper fluid
  - Several types of antifreeze
  - Contaminated moonshine
  - Industrial solvents
- Least inebriating of the 3 alcohols

- First 24 hours: mild CNS depression, inebriation, visual disturbances
- Next 6-30 hours(Latent period): N/V, GI bleed, pancreatitis, abdominal pain, CNS depression, AMS, metabolic acidosis(delayed)
- Severe intoxication: tremors, muscle rigidity, basal ganglia hemorrhage

Treatment of Methanol Poisoning

- Treatment
  - Prevent metabolism
    - Ethanol and fomepizole
  - Promote elimination
    - Hemodialysis
    - Folinic or folic acid (off-label use per FDA) until acidosis resolves
  - Supportive management
    - Treat acidosis with sodium bicarbonate at pH <7.3

Treatment of Methanol Poisoning

- American Academy of Clinical Toxicology recommends fomepizole or ethanol to be given based on:
  - Plasma methanol concentration >20 mg/dL, or
  - Recent history of ingestion of methanol with serum osmol gap >10 mOsm/L, or
  - Strong clinical suspicion of poisoning with AT LEAST 2:
    1. Arterial pH <7.3
    2. Serum HCO_3 <20 mEq/L
    3. Osmol gap >20 mOsm/L

Fomepizole (4-methylpyrazole, 4-MP)

- Competitive inhibitor of alcohol dehydrogenase (ADH)
- Preferred treatment for methanol AND ethylene glycol poisoning
- Does not cause CNS depression or hypoglycemia unlike ethanol
  - **Dose**: 15 mg/kg loading dose followed by 4 doses of 10mg/kg every 12 hours. After 48 hours: 15mg/kg every 12 hours.

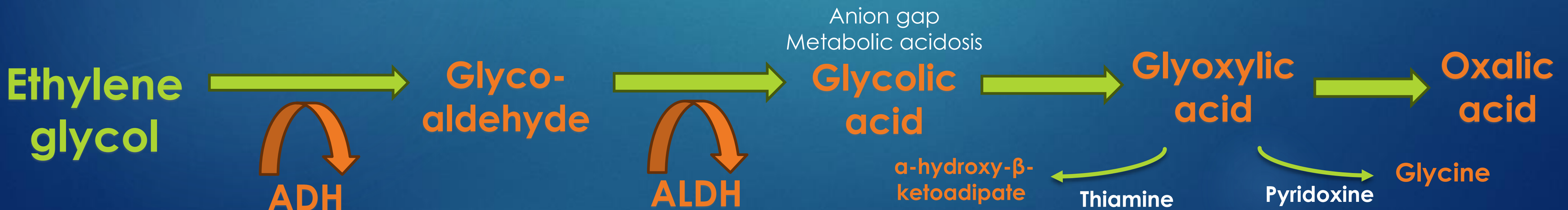
- **Eliminated the need for dialysis in patients who don't have profound acidosis and no signs of optic or renal injury**

Hemodialysis in Methanol Poisoning

- Extracorporeal treatments in poisonings workgroup (EXTRIP) developed recommendations for use of hemodialysis in severe methanol poisoning:
  1. Coma, seizures, new vision deficits
  2. Severe metabolic acidosis (pH <7.15)
  3. Persistent metabolic acidosis despite adequate supportive measures/antidotes
  4. Anion gap > 24 mmol/L
  5. Serum methanol concentration > 50 mg/dL
  6. Renal failure
- **Endpoint**: undetected methanol concentration OR <25 mg/dL with normal acid-base balance

Ethylene Glycol

- Colorless, sweet tasting fluid found in antifreeze
- 3 stages to poisoning:
  - <u>30 min-12hr after ingestion</u>: anion gap metabolic acidosis, hematuria, neurological symptoms
  - <u>12-36 hrs</u>: cardiopulmonary effects
  - <u>2-3 days</u>: renal insufficiency/kidney failure
- Highest mortality in patients with severe acidosis (pH < 7.1) and longest time from exposure to treatment (>10 hr)



Treatment of Ethylene Glycol Poisoning

- Similar to methanol poisoning
  - Blocking metabolism to its toxic byproducts
  - Ethanol or fomepizole
- AACT recommendations for treatment:

1. EG level > 20 mg/dl or documented ingestion of toxic amounts
2. Serum osmol gap > 10 mOsm/L
3. OR clinical suspicion of EG poisoning and AT LEAST 2:
   - pH <7.3
   - bicarbonate concentration < 20 mE/L
   - presence of oxalate crystals in urine

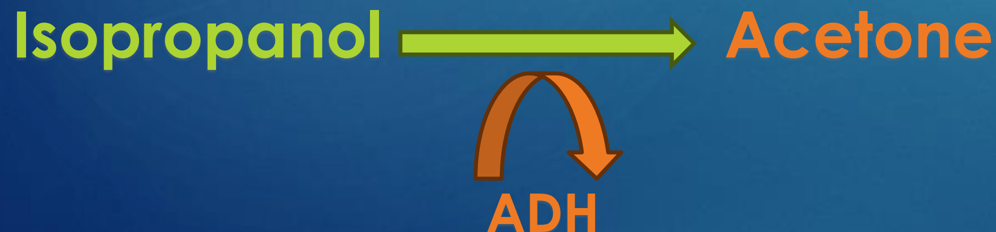
Treatment of Ethylene Glycol Poisoning

- Cofactor administration: pyridoxine and thiamine
- Hemodialysis
- Per AACT when any of the clinical factors are present:
  - Persistent metabolic acidosis < 7.25 pH despite therapy
  - Renal failure
  - EG levels > 50 mg/dL
  - Glycolic acid levels 8-10 mmol/L

Endpoint for dialysis: Ethylene glycol levels < 20 mg/dL and resolution of acid-balance

Isopropyl Alcohol (Isopropanol)

- Primarily found in rubbing alcohol
- Symptoms similar to ethanol intoxication
  - GI, neurologic effects, pseudo-renal failure
  - Conversion to acetone gives off a fruity odor
  - Osmolar gap without acidosis
    - Normal acid-base status, hyper osmolality, and high acetone levels suggest poisoning
    - **Serum Acetone = (measured SCr – baseline Cr)*100**



Treatment of Isopropanol Poisoning

- Airway management, IV hydration, and proton-pump inhibitors for GI bleed control
- Consider dialysis when:
  - Levels > 200 mg/dL and significant symptoms such as coma and/or hemodynamic instability
- Fomepizole is not indicated!
  - Inhibiting ADH prolongs isopropanol's half-life and symptoms

Putting them all together..

Alcohol	Methanol	Ethylene glycol	Isopropanol
Symptoms	Blurry vision GI, tremors/ CNS	CNS, cardiac, AKI/renal failure	GI, headache, coma
Lab abnormalities	↓ HCO_3	↓Ca, ↓HCO_3	Falsely ↑ SCr (normal BUN)
Osmolar gap	+ (early)	+ (early)	+ (early)
Anion gap	+ (late)	+ (late)	-
Serum acetone	-	-	+
Urine ketones	-	-	+
Urine oxalate crystals	-	+	-
Treatment	Ethanol, fomepizole, dialysis, folinic/folic acid	Ethanol, fomepizole, dialysis, pyridoxine, thiamine	Supportive, dialysis PPIs for GI bleed