ToxTalks:
A Bulletin for Healthcare Professionals Who Manage Poisoned Patients

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Toxic Alcohols

Overview
Alcohols are hydrocarbons with a hydroxyl (-OH) group, and while most are technically toxic, only some are commonly included under the term "toxic alcohol." These alcohols are not intended for ingestion and typically include methanol, ethylene glycol, and isopropanol (isopropyl alcohol). Ingestion of methanol or ethylene glycol classically results in an anion gap metabolic acidosis and may cause significant harm or death if untreated.

Pharmacology
Toxic alcohols are rapidly absorbed after ingestion. They are metabolized via alcohol dehydrogenase (ADH) followed by aldehyde dehydrogenase (ALDH) which occurs at a rate of 10 mg/dL/h resulting in accumulation of organic acid metabolites which are responsible for toxicity. The intoxicating and CNS depressant effects of toxic alcohols are assumed to be secondary to GABAA agonism and glutaminergic NMDA antagonism, similar to ethanol. Methanol and ethylene glycol are also eliminated unchanged, with half-lives of 52 and 17 hours respectively. This route of elimination is utilized when ADH is inhibited, such as when fomepizole has been administered. The half-life of ethylene glycol may be significantly increased with renal dysfunction.

Available Forms
Methanol is commonly found in windshield washer fluid, camp stove or chafing dish fuel, carburetor cleaner, gas-line antifreeze, de-icing agents, and solvents. It may also be a by-product in the production of moonshine but is typically discarded. The most common source of ethylene glycol is antifreeze, but others include de-icing agents, hydraulic brake fluid, fountain pen ink, paints, and solvents. Isopropanol is most commonly available as rubbing alcohol.

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Clinical Effects

All alcohols are intoxicating to varying degrees and may result in CNS depression. Any may lead to complications of significant intoxication such as aspiration or other complications from prolonged down time such as rhabdomyolysis, dehydration, etc. Anion gap metabolic acidosis is typical with ethylene glycol and methanol, but occasionally isopropyl alcohol toxicity will produce a non-anion gap acidosis. Additional end-organ dysfunction may occur and depends on the toxic alcohol ingested. Methanol can cause basal ganglia infarcts or hemorrhages, and visual impairment classically described as "snowfield vision" which may lead to permanent damage or blindness. Ethylene glycol causes acute kidney injury by precipitation of calcium oxalate monohydrate crystals in rental tubules which may lead to renal failure. Less often, it may result in CNS injury thought to be caused by deposition of oxalate crystals in the brain. This can produce a variety of clinical manifestations including altered mental status, cerebral edema, cranial nerve palsies, and peripheral neuropathy. Isopropanol may cause hemorrhagic gastritis.

Diagnostic Evaluation

When toxic alcohol poisoning is suspected, laboratory studies at a minimum should include a comprehensive metabolic panel, lactate, blood gas, and ethanol. In addition, toxic alcohols should be considered in all cases of an unexplained anion gap acidosis. Serum osmolality may be useful to calculate an osmol gap which is the difference between the measured serum osmolality and calculated osmolarity.

When calculating the osmol gap, the serum osmolality and metabolic panel should be sent from the same sample. Classically, there will be an anion gap metabolic acidosis and osmolar gap on laboratory evaluation. It is important to note that the osmolar gap will be highest immediately after absorption and decrease as the alcohol is metabolized. The anion gap displays the opposite trend and increases as the alcohol is metabolized. A normal osmol gap is less than 10, but concern for toxic alcohols is typically at levels higher than 20. Depending on when the patient presents and when labs are performed, the "classic" pattern may be absent. Quantitative levels for methanol and ethylene glycol concentrations should be sent when there is high suspicion for ingestion. These are typically diagnostics that will be performed at a lab outside of the clinician's hospital and may not result for >24 hours. Levels greater than 25 mg/dL have potential for significant toxicity and require treatment. Treatment should not be delayed while awaiting these studies. With ethylene glycol

ingestion urinalysis may display calcium oxalate crystals and urine may fluoresce under woods lamp, but neither are sensitive or specific. CT or MRI of the brain may be required for patients with coma, altered mental status, or focal deficits. In general, other causes of anion gap metabolic acidosis should be considered and appropriate evaluations performed. Unlike other toxic alcohols, isopropyl alcohol will cause ketosis without acidosis. An ethanol level greater than 100 mg/dL is protective against toxic alcohols as it is preferentially metabolized by ADH. There are other toxic alcohols such as diethylene glycol which do not currently have available testing and can still result in significant harm or death.

Management

Initial management should consist of standard assessment and resuscitative measures. The regional poison center or medical toxicology should be involved if there is any concern for toxic alcohol ingestion. Based upon clinical suspicion and/or initial labs, fomepizole should be administered to inhibit ADH and the conversion of parent alcohols to their toxic metabolites. If fomepizole is unavailable, IV or PO ethanol may be used with a target concentration of >100 mg/dL. Administration of thiamine, folate, and pyridoxine may help shunt metabolization to nontoxic pathways. Serum alkalinization with sodium bicarbonate may be considered in cases of methanol toxicity. Extra-corporeal methods of removal, chiefly intermittent hemodialysis (IHD), are effective and indicated if the patient meets certain criteria which are complex and should be discussed with nephrology and toxicology. CRRT is less effective but may be required if the patient cannot tolerate IHD. Fomepizole administration should continue during and after dialysis and will require dosing adjustments as it is dialyzable as well. Treatment should continue until the toxic alcohol level is less than 20 mg/dL.

Summary

Toxic alcohol ingestion requires complex management and may result in significant harm or death. Fomepizole and IHD are the major treatments. For significant suspicion, treatment should not be delayed for quantitative results. Any concern for toxic alcohol ingestion should be discussed with a poison center or medical toxicologist. Healthcare providers are encouraged to contact the Blue Ridge Poison Center at 1-800-222-1222, or call the dedicated HCP line: 1-800-451-1428.