Acid-base Calculation Difficulty, Find the Hidden Ketone, a Case Report

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INTRODUCTION

Isopropanol, or Isopropyl alcohol, is a sedative-hypnotic agent that resembles ethanol in structure and toxidrome. A higher molecular weight and lower polarity than ethanol secondary to the extra methylene group gives isopropanol better CNS penetration and a more intoxicating effect than ethanol. Central nervous system depression with an osmolar gap and normal anion gap is the classical presentation of isopropanol toxicity. Elevated anion gaps are usually associated with starvation ketoacidosis, diabetic ketoacidosis, and alcoholic ketoacidosis or ethylene glycol and methanol toxicity if considering toxic alcohol ingestion. Described here is a case report of toxic alcohol ingestion with high anion gap metabolic acidosis without an osmolar gap leading to the consideration of possible isopropanol-induced ketosis driving these metabolic derangements.

TOXICOKINETICS

The absorption of isopropanol is rapid, with nearly 80% being absorbed within 30 minutes of ingestion. About 80% of absorbed isopropanol undergoes first-order metabolism by Alcohol dehydrogenase which catalyzes the degradation primarily into acetone.[1] Isopropanol blood levels peak between 30 minutes and 3 hours post ingestion and isopropanol has a half life of 3-7 hours. Acetone can be detected in the serum approximately 3–4 h after ingestion and has a variable half-life depending on source material from 19-27 hours. Acetone is metabolized in a stepwise process, firstly by the hepatic cytochrome P450 enzymes to acetol. Acetol can undergo intrahepatic oxidation to methylglyoxal or extrahaptic reduction to 1,2-propanediol. Both methylglyoxal and 1,2-propanediol are oxidized to pyruvate which undergoes further metabolism into a variety of endogenous biochemicals.[5] Intermediary metabolism of pyruvate leads to the incorporation of carbon atoms initially introduced from acetone into carbon dioxide. [5] Case studies examining acetone elimination in severely intoxicated patients have shown that acetone elimination rate is primarily determined by expiration rather than endogenous metabolism. The majority of acetone undergoes hepatic metabolism to carbon dioxide which is subsequently expired either in its unchanged form or as carbon dioxide.[1] Acetone is an uncharged terminal ketone and does not contribute to an anion gap metabolic acidosis. However both isopropanol and acetone will raise serum osmolality.[1]

TOXICOKINETICS (CONTINUED)

The overall acid-base status can be confounded in the setting of isopropanol induced hypotension leading to hypoperfusion and a lactic acidosis; similarly, coingestants may contribute to a concomitant metabolic acidosis.[2]

TREATMENT

Unlike other toxic alcohols, treatment of isopropanol ingestion is usually supportive, consisting of IV hydration. The rapid absorption of isopropanol negates the utility of gastric emptying or activated charcoal. Co-ingestion of ethanol prolongs the half-life of isopropanol secondary to ethanol's higher affinity for alcohol dehydrogenase. Use of other alcohol dehydrogenase inhibitors like fomepizole would also prolong isopropanol intoxication. While rare, isopropanol ingestions occasionally require hemodialysis the typical indications for which are persistent hypotension or lactic acidosis and a serum isopropanol concentration >500 mg/dL. If none of these abnormalities present or persist past 6 hours, hemodialysis typically isn't required as peak absorption and metabolism usually occurs within this timeframe.[3]

CASE

This is a single patient chart review examining a 61-year-old male with a past medical history of anemia, hypertension, depression, anxiety, hepatic steatosis, alcohol abuse, and gastric ulcer, who presented to the emergency department by Emergency Medical Services after being found down by family members surrounded by multiple bottles of alcohol. On arrival, the patient was somnolent and confused, endorsing abdominal pain, nausea, non-bloody/non-bilious vomiting, headache, and dizziness over the few days prior to discovery. Reportedly, his last alcohol use prior to hospital presentation was 2-3 days prior consisting of around 6 airplane bottles of vodka; the patient's original characterization of daily alcohol consumption was 4 'drinks' per day on admission which was later amended to 8 'shots' per day. He later alluded to both inhalation and consumption of carburetor cleaner but denied consumption of other toxic alcohols. Toxicology was consulted following this revelation after initial evaluation with repeat labs revealing severe metabolic acidosis that had not corrected with fluids and glucose. Available data included: 7.28 pH/24 mm Hg pCO2/15.5 mmol/L base deficit per ABG drawn 18 hours after initial labs, 2.2 mmol/L lactic acid, 374 mOsm/kg serum osmolality, 73 mg/dL glucose, 7 mEq/L bicarbonate, 31 mEq/L anion gap, 28mg/dL BUN, 3.00 mg/dL Creatinine (baseline 0.60-0.70), 23 mL/Min/1.73m2 GFR. His volatile alcohol panel was positive for 198 mg/dL ethanol, 17 mg/dL isopropanol, and 54 mg/dL acetone with an osmolar gap of 83 (corrected to 8 when ethanol was accounted for in calculated osmolality) as well as a delta gap of 1.117. Worsening oliguria, hypotension, and pulmonary edema prompted urgent hemodialysis in consultation with nephrology. Additional interventions included normal saline, sodium bicarbonate, thiamine, folic acid, pyridoxine, magnesium, fomepizole. A beta-hydroxybutyrate level had been collected with initial labs, but hemolyzed and was not recollected. The patient had a small volume episode of urinary incontinence once after arrival however serial bladder scans revealing oliguria precluded collection of urine ketones. Bladder scan revealed urine quantity conducive to collection after 18 hours in the emergency department and receipt of 2 L of normal saline as IV fluid boluses, 50 mEq of sodium bicarbonate, continuous sodium and bicarbonate in D5W at 125 mL/h, and thiamine plus folic acid in sodium chloride at 250 mL/h. Urinalysis was positive for 1+ ketones. Given the suggested interval since ingestion as well as a volatile alcohol panel negative for ethylene glycol and methanol, we hypothesized that any consumed ethylene glycol, formic acid, or methanol had been completely metabolized to toxic metabolites such as glycolate by the time of presentation. After undergoing hemodialysis, the patient was admitted to family medicine for further evaluation and treatment.

DISCUSSION

A delta gap of 1.117 indicated a pure anion gap without alkalotic compensation, a significant deviation from expected acid-base derangement values in pure isopropanol ingestion. Carburetor cleaner has high concentrations of methanol and negligible isopropanol, prompting the decision to treat the patient based on consistency of presentation with toxic alcohol consumption, clinical decompensation, and delay in volatile gas screen results.[4]

DISCUSSION (CONTINUED)

This complex presentation illustrates the difficulty in determining causation of metabolic derangements in mixed ingestion. The patient had multiple causes of osmolar and acid base abnormalities - vomiting, alcohol withdrawal, pancreatitis, alcohol ketoacidosis, starvation ketoacidosis - that obscured an important etiology and collectively from history, exam and labs emphasizes the importance of including isopropanol ingestion in cases of unexpected ketosis.

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