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Acid-Base and Electrolyte Teaching Case

Approach to the Treatment of Methanol Intoxication

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Methanol intoxication is an uncommon but serious poisoning. Its adverse effects are due primarily to the impact of its major metabolite formic acid and lactic acid resulting from cellular hypoxia. Symptoms including abdominal pain and loss of vision can appear a few hours to a few days after exposure, reflecting the time necessary for accumulation of the toxic byproducts. In addition to a history of exposure, increases in serum osmolal and anion gaps can be clues to its presence. However, increments in both parameters can be absent depending on the nature of the toxic alcohol, time of exposure, and coingestion of ethanol. Definitive diagnosis requires measurement with gas or liquid chromatography, which are laborious and expensive procedures. Tests under study to detect methanol or its metabolite formate might facilitate the diagnosis of this poisoning. Treatment can include administration of ethanol or fomepizole, both inhibitors of the enzyme alcohol dehydrogenase to prevent formation of its metabolites, and hemodialysis to remove methanol and formate. In this Acid-Base and Electrolyte Teaching Case, a patient with methanol intoxication due to ingestion of model airplane fuel is described, and the value and limitations of current and new diagnostic and treatment measures are discussed.

INDEX WORDS: Toxic alcohols; serum osmolal gap; serum anion gap; fomepizole; methanol; methanol intoxication; ethanol; hemodialysis.

Note from the editors: This article is part of a series of invited case discussions highlighting either the diagnosis or treatment of acid-base and electrolyte disorders.

INTRODUCTION

Methanol intoxication can cause severe cellular dysfunction and death,[1] primarily due to the accumulation of organic acids and their anions produced by its metabolism.[2-4] Effective methods of treatment that include administering inhibitors of the enzyme alcohol dehydrogenase to prevent its metabolism[5] and hemodialysis[6] to remove it and its toxic metabolites from the body are readily available. However, recognition of the intoxication is often hampered by the lack of specific signs and symptoms and the limitation of present diagnostic modalities.[7] Although mortality is low if treatment is initiated promptly,[8] a delay can cause it to increase to as high as 44%.[9,10]

In this Acid-Base and Electrolyte Teaching Case, a case of methanol intoxication is presented, which was previously reported by Rastogi et al,[11] and current methods of diagnosis and treatment are discussed.

CASE REPORT

Clinical History and Initial Laboratory Data

A 22-year-old woman presented to the emergency department 30 hours after ingesting 16 ounces of model airplane fuel. She reported no abdominal pain, nausea, vomiting, visual disturbances, or headache. On physical examination, temperature was 37.2°C; pulse rate, 100 beats/min; blood pressure, 132/50 mm Hg in the sitting position; and respirations, 16 breaths/min. Lungs were clear to auscultation, and cardiac, abdominal, and neurologic examination findings were normal. No ophthalmic changes were reported. Laboratory studies performed during the hospitalization are shown in Table 1 and revealed a low serum bicarbonate level, elevated serum osmolality and osmolal gap, and increased serum creatinine level. The latter was shown to be due to laboratory error caused by interference of nitromethane in the airplane fuel with serum creatinine measurement as performed by the usual Jaffé method.[11]

Additional Investigations

Urinalysis showed no cells or crystals. Serum acetaminophen, ethyl alcohol, acetone, and isopropyl alcohol results were negative. Methanol concentration obtained on admission reported 2 days later was 71 mg/dL.

Diagnosis

Acute methanol intoxication.

Clinical Follow-up

The patient initially was given fomepizole and dialyzed for 4 hours. Additional doses of fomepizole were given and dialysis was

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Table 1. Laboratory Studies During Hospitalization

Test	Admission	17 h After Admission	Day 2	Day 3
Sodium, mEq/L	141	140	143	142
Potassium, mEq/L	3.5	3.2	3.8	3.6
Chloride, mEq/L	111	104	109	112
Total carbon dioxide, mEq/L	18	28	25	25
SUN, mg/dL	14	5	7	4
Serum creatinine, mg/dL[a]	23.7[b]	10[b]	8.4[b]	6.0
eGFR,[c] mL/min/1.73 m^2	2	5	6	9
Anion gap, mEq/L	11	8	9	5
Serum osmolality, mOsm/kg/H_2O	357	303	303	303
Osmolal gap, mOsm/kg/H_2O	70	—	—	—
Methanol, mg/dL	71	26	—	—
Serum albumin, g/dL	4	—	—	—

Note: Conversion factors for units: serum creatinine in mg/dL to μmol/L, ×88.4; SUN in mg/dL to mmol/L, ×0.357.

Abbreviations: eGFR, estimated glomerular filtration rate; SUN, serum urea nitrogen.

[a]Values obtained using the Jaffé reaction.

[b]Values proved to be inaccurate due to interference of nitromethane in ingested airplane fuel with measurement of serum creatinine.

[c]As calculated by the Chronic Kidney Disease Epidemiology Collaboration creatinine equation.

Adapted from Rastogi et al[11] with permission of the National Kidney Foundation.

repeated during the hospitalization. With treatment, acid-base parameters and serum osmolality (Table 1) returned to normal and the patient was discharged.

DISCUSSION

This patient had a history of exposure to methanol, a markedly increased serum osmolal gap, and metabolic acidosis. These features are suggestive of methanol intoxication.[7,12] Methanol intoxication is a relatively uncommon but important poisoning: approximately 5,000 cases are reported to the US Poison Control each year.[2,8,13] Methanol is present in several household cleaning solutions and dyes, model airplane fuel, windshield washer fluid, gas line antifreeze, and illegally produced alcoholic beverages. Intoxication is most commonly due to ingestion, but can also result from inhalation or absorption through the skin.[13] Symptoms can include dyspnea, nausea, vomiting, abdominal pain, impaired sensorium, and impaired vision.[14] Ophthalmologic examination can reveal optic papillitis (found in 10% of cases). Muscle rigidity and masked facies can be observed when the putamen is damaged.[15] The majority of the clinical abnormalities are due to the effects of formic acid, the major metabolite of methanol (Fig 1). Interference with cytochrome oxidase by formate causes tissue

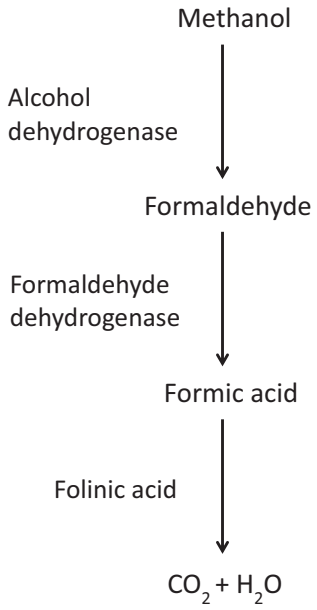

Figure 1. Metabolism of methanol. Methanol undergoes serial oxidation: methanol is catalyzed by the enzyme alcohol dehydrogenase to formaldehyde and then formaldehyde is catalyzed by the enzyme formaldehyde dehydrogenase to formic acid. Folinic acid given to a patient will accelerate the conversion to carbon dioxide (CO_2) and water (H_2O). Adapted from Rastogi et al[11] with permission of the National Kidney Foundation.

hypoxia and lactic acidosis.[13] Clinical abnormalities can be delayed as long as 96 hours if ethanol or certain antiviral medication, such as abacavir, are coingested because both inhibit the enzyme that catalyzes the metabolism of methanol, alcohol dehydrogenase.[3,16-19] Both the nonspecificity of the clinical abnormalities and the delay between exposure and their appearance can hinder establishing the diagnosis, thus resulting in high mortality.[10] An increase in the serum osmolal gap (caused by accumulation of methanol in the blood) and anion gap (caused by accumulation of formate and sometimes lactate in the blood) can also serve as clues to the presence of methanol intoxication.[16,20] The marked increase in serum osmolal gap in the present case (70 mOsm/kg/H_2O) reflects in part a high methanol concentration and is indicative of toxic alcohol ingestion because an osmolal gap greater than 15 to 20 mOsm/kg/H_2O is rarely observed with other causes of increased osmolal gap.[2,13] However, the osmolal gap exceeds the level predicted based on the measured methanol concentration (71 mg/dL; osmolality, 23 mOsm/kg/H_2O). The explanation for this disparity is not clear, but possibly could reflect accumulation of osmotically active substances such as nitromethane and/or polyalkylene glycol found in the airplane fuel.

Although the osmolal gap and anion gap were increased in this case, individuals can have methanol