

POINTS TO REMEMBER

- Anion gap is an estimate of unmeasured anions, including organic acids and proteins, which maintain electric neutrality in the blood; one formula to determine anion gap is

$$\text{Anion gap (mmol/L)} = [\text{Na}^+] - ([\text{Cl}^-] + [\text{HCO}_3^-])$$

- The main contributors to serum osmolality are sodium, chloride, glucose, and urea; osmolal gap represents the difference between a predicted osmolality based on these solutes and the measured osmolality, where:

$$\text{Predicted osmolality (mOsm/kg H}_2\text{O)} = 1.86 \times$$

$$\text{Na}^+ \text{ (mmol/L)} + \text{Glucose (mg/dL)/18} +$$

$$\text{Blood urea nitrogen (mg/dL)/2.8} + 9$$

- High anion gap metabolic acidosis is associated with several causes, which can be remembered by the mnemonics MUDPILES and GOLDMARK.
- Methanol toxicity manifests on routine laboratory testing first as an increased osmolal gap followed by an increasing anion gap with metabolic acidosis.
- The toxic effects of methanol are mediated by formic acid, which impairs oxidative phosphorylation, particularly in the central nervous system and optic nerves, causing central nervous system depression, visual disturbances, and, in severe cases, coma, seizures, and death.
- Timing of specimen collection and coingestion of ethanol can prevent detection of increased anion and osmolal gaps in methanol toxicity.

mended threshold to initiate hemodialysis is a serum methanol concentration of >50 mg/dL, poor patient outcome better correlates with the severity of acidemia (blood pH), the development of seizures, and cerebral edema (7).

Commentary

James H. Nichols*

This case of methanol ingestion highlights several aspects of the laboratory management of toxic alcohols. Primary alcohols—ethanol, methanol, and ethylene glycol—are oxidized by alcohol dehydrogenase to form aldehydes and further metabolized to acids that contribute to the anion gap as

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unknown ingestion. Ethanol and fomepizole are both effective antidotes (1), as they bind to alcohol dehydrogenase with higher affinity, preventing metabolism while the toxic alcohol is eliminated. Fomepizole has been added to the WHO Model List of Essential Medicines (2) (the minimum medicine needed for a basic healthcare system) most likely because the sale and distribution of ethanol is banned in several areas of the world. Epidemics of methanol poisoning have occurred recently in the Czech Republic (2012), Russia (2016), Turkey (2015), and arise almost yearly in India (latest in 2017). Bootlegging is common in areas without access to ethanol. Although legitimate manufacturers separate the toxic alcohols during distillation, home stills may create contaminated products that are distributed during local festivals and added to or even sold as legitimate liquor because methanol is less expensive.

In this case, the patient had a history of alcoholism and ingested solvents in his workshop. Our hospital has encountered homeless patients who drink toxic alcohols intentionally to be admitted for a warm bed and access to legitimate ethanol. Ethanol as an antidote raises concern over promotion of further alcohol addiction and its consequences. For that reason, fomepizole may represent a better treatment choice.

Commentary

Leon D. Sanchez*

Gau and Scott's case report is an excellent review of how the frontline physician needs to approach the workup for an anion gap metabolic acidosis and the substantially rarer and more difficult to identify osmolal gap. The toxic alcohols are the classic substances responsible for combined anion and osmolal gap acidosis. Diagnosis of toxic alcohol ingestion absent a clear history requires an astute clinician who can recognize the metabolic derangements and expand the diagnostic workup sufficiently to identify and manage the likely culprit.

Although the current ease of obtaining access to information about management of rare conditions is much greater than in the past, it is difficult to begin treatment if there is any difficulty in recognizing the problem. As the case demonstrates, the use of laboratory data to help expand a

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differential diagnosis and revisit information from the history can help the clinician arrive at the correct diagnosis.

Case reports are a way for providers to be exposed to unusual clinical presentations to enable recognition of similar presentations in future practice. The review of how to calculate anion and osmolal gaps, together with Table 2 outlining the causes of anion gap metabolic acidosis, will be valuable to practitioners. It is important to note that diagnosing the presence of toxic alcohols by calculating anion and osmolal gaps may miss some toxic alcohol poisonings, especially when ethanol is coingested, as it may affect the timing of methanol metabolism (1).

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