ToxTidbits

Maryland Poison Center
UNIVERSITY OF MARYLAND SCHOOL OF PHARMACY

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The Maryland Poison Center's Monthly Update: News, Advances, Information

Blame it on the Booze: Osmol Gaps and Toxic Alcohols

Toxic alcohol (TA) such as methanol or ethylene glycol can have devastating effects if left untreated. Methanol metabolizes to formaldehyde by alcohol dehydrogenase (ADH) into formic acid by aldehyde dehydrogenase (ALDH) which causes oculotoxicity ("snowfield vision") and neurotoxicity. Ethylene glycol metabolizes to glycolaldehyde by ADH to glycolic acid and oxalic acid by ALDH which causes nephrotoxicity (formation of calcium oxalate crystals). The final metabolites of these TAs produce a profound anion gap metabolic acidosis that causes significant morbidity and death. The National Academy of Clinical Biochemistry recommends that clinical laboratories provide direct measurements of methanol and ethylene glycol (*Clin Chem. 2003 Mar;49(3):357-79*). Despite this recommendation, many hospitals struggle to obtain the results of TA levels within a clinically relevant timeframe. As a workaround, the osmol gap (OG) has been the go-to diagnostic tool for identifying TA ingestions and trended until the gap minimizes.

The OG refers to the difference between measured and calculated osmoles. Serum osmolality is the concentration of osmotically active solutes in the blood. To calculate the OG, subtract the calculated osmolarity using the primary solutes (sodium, glucose, urea) from the measured osmolality. A high OG indicates that there are more unaccounted osmotically active solutes in the blood, such as TAs. Caution should be taken when interpreting an OG as other factors such as ketoacidosis, ethanol, renal failure, lactate, and pseudohyponatremia can contribute to an OG. Fortunately, ethanol can be easily factored into calculating the OG. It is essential that the glucose, sodium, blood urea nitrogen, and ethanol levels are drawn from the same sample to get an accurate calculation of the OG.

A = **Measured osmolality** = All osmotically active solutes in blood

B = **Calculated osmolarity** = Expected osmotically active solutes in blood

$$Calculated\ Osmolarity\ \left(\frac{mOsm}{L}\right) = 2Na + \frac{Gluc}{18} + \frac{BUN}{2.8} + \frac{Ethanol}{4.6}$$

Use CHEM7 and serum ethanol; Units: Na⁺ (mmol/L); Gluc, BUN, and ethanol (mg/dL)

A-B = **Osmol gap**: Unmeasured ("unknown") remaining solute in blood

$$Plasma\ osmolal\ gap = \left[\begin{matrix}measured\\ osmolality\end{matrix}\right] - \left[\begin{matrix}calculated\\ osmolarity\end{matrix}\right]$$

A and B must be from same sample

A common challenge clinicians face is differentiating between alcoholic ketoacidosis (AKA) and TA ingestion as both can elevate the OG. Cohen and colleagues found that older age, a high ethanol concentration, and a high anion gap were associated with diagnosing AKA (*Clin Toxicol (Phila). 2021 Aug;59(8):715-720*). The positive predictive value of a positive ethanol level for diagnosing AKA was 88.3% as opposed to 11.7% for diagnosing TAs from the same study. When describing the OG in patients with AKA, it was found that the median OG was 27, with 82% having an OG >10, 69% had a OG >20, 44% had a OG >30, and 20% had a OG >40 (*Clin Toxicol (Phila). 2024 Oct;62(10):609-614*). It is important to note that the high OG is present early in a TA exposure as only the parent compounds are osmotically active, not the metabolites. When ruling out toxic alcohol exposures, it is important to take into account the exposure history, ethanol level, presence of ketones, and clinical manifestations as well, not just the OG alone.

If you have questions on interpreting an osmol gap or suspicion of toxic alcohols, please contact your local poison center at 1-800-222-1222.

Did you know?

During the COVID-19 pandemic, the FDA found 84% of the sampled hand sanitizer imported from Mexico tested positive for methanol contamination in 2020.

Populations most at risk for methanol poisoning are children and people who ingest these products as an alcohol substitute. Hand sanitizer that was purchased in 2020 can be checked on the FDA website if it was recalled for methanol contamination. (Source)

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