Varying contribution of ethanol to serum osmolality in acute intoxication

Ryan Marino¹, Todd Phillips², Anthony Pizon²
¹Department of Emergency Medicine, University of Pittsburgh Medical Center, Pittsburgh, PA, USA,
²Division of Medical Toxicology, Department of Emergency Medicine, University of Pittsburgh Medical Center, Pittsburgh, PA, USA

Background
Ethanol is the most common cause of osmolal gap elevations, however, current formulas do not accurately reflect ethanol's contribution to the osmolal gap. Unexplained elevation in osmolal gap in acute ethanol intoxication presents a clinical dilemma for practitioners.

Hypothesis
Patients with acute ethanol intoxication will have varying elevations in the osmolal gap, and current formulas do not accurately reflect ethanol's contribution to the osmolal gap.

Methods
We conducted a retrospective chart review of eleven hospitals from 2010-2015. We included patients with the following laboratory testing performed concurrently: detectable serum ethanol level, serum osmolality, negative toxic alcohol panel and serum sodium, BUN, and glucose levels. Measured osmolality using freezing-point depression was compared with calculated osmolality using the standard formula (2x[Na mOsm/L] + [BUN mg/dL]/2.8 + [glucose mg/dL]/18 + [ETOH mg/dL]/4.6). Osmolal gap >10 mOsm/kg was considered abnormal. We used a linear regression to generate more precise correction factors for ethanol's contribution to osmolality at specific ethanol levels.

Results
Of 82 patients identified, 53 had an elevated osmolal gap. In a subgroup of patients with high ethanol levels (>300 mg/dL), the osmolal gap was elevated in 14 of 15 cases. We calculated a new divisor for ethanol's contribution to the osmolality formula, 3.57, which reduced the proportion of falsely elevated osmolal gaps from 64.6% to 20.7%. Furthermore, we found that the divisor for ethanol's effect on osmolality had statistically significant variability at differing ethanol levels (p=0.049). When ethanol's contribution to osmolality was stratified based on serum ethanol level and variable divisors applied at quantiles of 100 mg/dL (2.67 for 0-100, 3.27 for 100-200, 3.53 for 200-300, 3.72 for >300), the proportion of falsely elevated osmolal gaps was further reduced to 15.8%.

Discussion
Calculated osmolal gap is an important screening tool for toxic alcohol ingestions. Costly therapies are often initiated based on elevations of osmolal gap alone, which is frequently unreliable. These data show that different divisors for ethanol's contribution to osmolality are required depending on ethanol level to more accurately reflect serum osmolality and reduce unnecessary interventions.

Conclusion
Ethanol has a variable effect on the osmolal gap at different levels and most evident at severely elevated levels.