Osmolal Gap without Anion Gap in a 43-Year-Old Man

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CASE DESCRIPTION

A 43-year-old man presented to the emergency department (ED) 2 h after ingesting 10 oz of antifreeze mixed with Gatorade in a suicide attempt. The antifreeze was green, of an unknown brand, and purchased at a local gas station. He subsequently confessed to his wife, who brought him to a community hospital ED. He denied abdominal pain, nausea, vomiting, urinary symptoms, or visual changes. Initial laboratory tests (Table 1) were clinically relevant for the following: arterial whole-blood pH, 7.34; P_{CO_2}, 33 mmHg (4.4 kPa); serum bicarbonate, 18 mmol/L; serum ethanol, 10 mg/dL (2.17 mmol/L); and serum anion gap, 18 mmol/L. The serum osmolal gap (75 mOsm/kg) was calculated as follows: Osmolal gap = freezing-point depression osmometer value -(2 × [Na^+] + [glucose]/18 + [blood urea nitrogen]/2.8 + [ethanol]/4.6), where the Na^+ concentration is in millimoles per liter and the glucose, blood urea nitrogen, and ethanol concentrations are in milligrams per deciliter.

With the advice of the local Poison Control Center, the patient was given 15 mg/kg fomepizole intravenously. He was placed on suicide precautions and transferred to a tertiary care center for further evaluation and treatment. On arrival at the tertiary care ED 8 h after ingestion and 3 h after fomepizole administration, the patient had a normal mental status and normal vital signs. Thiamine (100 mg), folic acid (50 mg), and pyridoxine (50 mg) were administered intravenously as cofactors for secondary metabolic pathways. At that time, laboratory test results (Table 1) were clinically relevant for the following: arterial whole-blood pH, 7.39; P_{CO_2}, 28 mmHg (3.7 kPa); serum bicarbonate, 18 mmol/L; creatinine, 1.1 mg/dL (97.2 μmol/L); lactate, 5.3 mmol/L; anion gap, 14 mmol/L; and osmolal gap, 72 mOsm/kg. No crystals were visible in the urine.

CASE FOLLOW-UP

Given the improving anion gap and the lack of clinically relevant acidemia, there was debate about whether this patient had actually ingested ethylene glycol (EG) or had instead ingested propylene glycol (found in "safer" antifreezes) or isopropyl alcohol. Therefore, a test for the serum concentration of EG was ordered for confirmation. The sample for measurement of EG by gas chromatography had to be sent by courier to the closest clinical laboratory offering the test, with the results expected in 4–8 h. While the sample was en route for testing by gas chromatography, the hospital pathologist performed a modified version of a commercially available veterinary enzymatic assay.

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This test had been validated by our laboratory, and the results of these studies have been published (*1*). The serum concentration of EG (Table 1) measured by enzymatic assay was 308 mg/dL (49.6 mmol/L). On the basis of this information, the patient was continued on fomepizole, and plans were made for hemodialysis. Ten hours after admission, the gas chromatography result indicated an EG concentration of 315 mg/dL (50.9 mmol/L), in close agreement with the results of the enzymatic assay (the gas chromatography results were negative for methanol and isopropyl alcohol). After hemodialysis was performed, the patient's postdialysis serum showed an osmolal gap of 6 mOsm/kg and an EG concentration of 50 mg/dL (8.2 mmol/L). After a second hemodialysis course, the EG concentration according to the enzymatic assay was 1.4 mg/dL (0.2 mmol/L); the fomepizole treatment was then discontinued. The patient's renal function remained normal, and he recovered completely. He was discharged from the hospital to a psychiatric treatment facility.

1. Juenke JM, Hardy L, McMillin GA, Horowitz GL. Rapid and specific quantification of ethylene glycol levels: adaptation of a commercial enzymatic assay to automated chemistry analyzers. Am J Clin Pathol 2011;136:318 –24.

Questions to Consider
• What are the major ingredients found in antifreeze that can contribute to toxicity after ingestion?
• In a patient with an increased osmolal gap and normal anion gap, can EG poisoning be ruled out?
• What are some factors that may cause a normal anion gap in EG poisoning?
• Can a normal osmolal gap be used to determine when fomepizole therapy should be discontinued?

Table 1. The patient's laboratory results on presentation, after transfer to the tertiary care center, and on hospital day 2 after hemodialysis.[a]

	Initial presentation	Tertiary ED (3 h later)	Actual, day 2 (after hemodialysis)	Expected, day 2 (if untreated)	Reference interval
Sodium, mmol/L	140	138	141	Normal	137–145
Potassium, mmol/L	4.0	4.2	3.6	Normal	3.6–5.0
Cloride, mmol/L	104	106	103	Normal	98–107
Bicarbonate, mmol/L	18	18	32	Low	22–30
BUN,[b] mg/dL	11	10	3	High	9–20
Creatinine, mg/dL	1.13	1.1	0.6	High	0.5–1.2
Glucose, mg/dL	106	107	138	Normal	75–110
Anion gap, mmol/L	18	14	6	High	8–20
pH	7.34	7.39	7.46	Low	7.35–7.45
Lactate, mmol/L	Unavailable	5.3	1.7	High	0.5–2.0
Serum osmoles, mOsm	367	358	296	Normal to high	275–295
Osmolal gap, mOsm/kg	75	72	6	Normal to high	0–10
EG (gas chromatography), mg/dL	Unavailable	315	Unavailable	High	Nondetectable
EG (enzymatic assay), mg/dL	Unavailable	308	50	High	Nondetectable

[a] For conversion to the SI unit of measure: blood urea nitrogen, 1 mg/dL = 0.36 mmol/L; creatinine, 1 mg/dL = 88.4 μmol/L; lactate, 1 mg/dL = 0.11 mmol/L; EG, 1 mg/dL = 0.16 mmol/L.
[b] BUN, blood urea nitrogen.

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Final Publication and Comments

The final published version with discussion and comments from the experts will appear in the March 2014 issue of *Clinical Chemistry*. To view the case and comments online, go to http://www.clinchem.org/content/vol60/issue3 and follow the link to the Clinical Case Study and Commentaries.

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