

Ethylene Glycol and the Lactate Gap

A 51-year-old female presents to the emergency department via emergency medical services after being found unarousable by family. Physical exam is unrevealing. She is protecting her airway and has normal vital signs (BP, 138/85 mmHg; HR, 77 beats/min; RR, 15 breaths/min; T, 36.9 C). Routine laboratory tests (CBC, BMP, VBG) show a pH of 7.4, serum bicarbonate of 22 mmol/L, and lactate >17 mmol/L (panic value). Repeat laboratory testing 2 hours later using a different analyzer shows a minor decrease in serum bicarbonate to 20 mmol/L, but a lactate of 1.6 mmol/L. Ethylene glycol ingestion is suspected.

Diagnosis of toxic alcohol ingestion and toxicity is fairly cut and dry, if you work at one of the few hospitals in the U.S. that can measure serum concentrations. For the rest of us, history, clinical gestalt, and several surrogate markers of toxin concentration are what we rely upon. The most frequently used surrogate marker is the osmolar gap, which looks at the difference between the measured and unmeasured osmotically active molecules in the blood (*N Engl J Med* 2018;378:270-280). Another possible marker for ethylene glycol overdose is the "lactate gap."

Ethylene glycol, while inebriating, is not our major concern for end-organ toxicity. Ethylene glycol is metabolized to glycolate/glycolic acid, glyoxylic acid, and oxalic acid, all of which result in end-organ toxicity. Glycolate is structurally similar to L-lactate, the main enantiomer of lactate present in humans (*Annals Clin Biochem* 2013;50:70-72). Measurement of lactate is either through use of tests that use the enzymes lactate oxidase or lactate dehydrogenase and subsequent measurement of hydrogen peroxide or NADH, respectively. As it turns out, lactate oxidase will metabolize glycolate and glyoxylic acid in a similar manner to L-lactate. This can result in astronomical falsely elevated lactate concentrations that do not fit the clinical picture (e.g., not acidemic, no signs of global hypoperfusion, not hypotensive). In one multicenter study, the problem was more common among point-of-care lactate tests (*Annals Clin Biochem* 2013;50:70-72). Significant interference was described in 10/19 analyzers. These results are consistent with clinical practice, case reports, and smaller studies (*CMAJ* 2007;176:1097-1099; *Clin Toxicol* 2009;47:236-238).

Serum lactate concentrations that are greater than the upper limit of detection are infrequent. If you have a patient with that reading, first you should make sure they are not actively dying or seizing. Next, call the lab to see how the sample was analyzed. If lactate oxidase was used, identify if they have a lactate dehydrogenase method. If the lactate comes back low with the lactate dehydrogenase test, obtain a serum osmolality, and call the poison center to discuss the case; it's possible that you have a patient with an ethylene glycol ingestion.

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Did you know?

Since rapid measurement of serum toxic alcohol concentrations is often difficult to obtain, multiple surrogate markers have been proposed in addition to the osmolar gap

Some authors have proposed urine fluorescence as a tool for evaluating antifreeze (ethylene glycol) ingestion. Antifreeze has fluorescein as a component to aid mechanics in identifying leaks. This might fluoresce in the urine of a patient who has recently ingested antifreeze. Unfortunately, there are multiple limitations to the sensitivity and specificity of this test and we do not recommend its use. Another option is to look for calcium oxalate crystals (dihydrate and monohydrate) in the urine. This can identify a possible ethylene glycol ingestion because crystal formation is the underlying cause of renal injury in patients after ethylene glycol ingestion.



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