Pathologic Quiz Case

Repeated Positive Ethylene Glycol Levels by Gas Chromatography

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A 36-year-old white man was found unconscious following ingestion of clonazepam, alprazolam, amitriptylene, ethanol, and antifreeze in an apparent suicide attempt. Initial laboratory results included an anion gap of 23 mEq/L (reference range, 8–16), an osmolal gap of 23 mOsm/kg solution (reference range, <10), and an ethylene glycol concentration of 80.2 mg/dL (13.1 mmol/L) as measured by gas chromatography (GC) analysis on an HP 6890 OV-17 column. The patient received aggressive therapy for ethylene glycol intoxication including hemodialysis and intravenous fomepizole. Within 48 hours of admission the ethylene glycol level had fallen to 10.3 mg/dL (1.7 mmol/L). The clinical status of the patient had improved with resolution of his acidosis, correction of the anion and osmolal gaps, and regaining of consciousness. Another dialysis procedure was planned to decrease his ethylene glycol level below 10 mg/dL before psychiatric consultation and discharge. He was being treated prophylactically for delirium tremens with intravenous lorazepam injections via a central line.

The next ethylene glycol level after dialysis was elevated at 23.3 mg/dL (3.8 mmol/L) (Figure 1). His ethylene glycol levels remained elevated during the next 5 days (up to 40.6 mg/dL; 6.5 mmol/L) despite continued dialysis and intravenous fomepizole. A thorough history about continued ingestion of antifreeze while in the hospital was negative. Anion gaps were normal throughout this period, and the patient remained nonacidotic by arterial pH measurement. Given the lack of continued ingestion of antifreeze while in the hospital, the short half-life of ethylene glycol (<4 hours) during hemodialysis, and normal clinical and laboratory parameters, the elevated ethylene glycol measurements could not be explained.

What is your diagnosis?

Accepted for publication February 11, 2004.

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The authors have no relevant financial interest in the products or companies described in this article.

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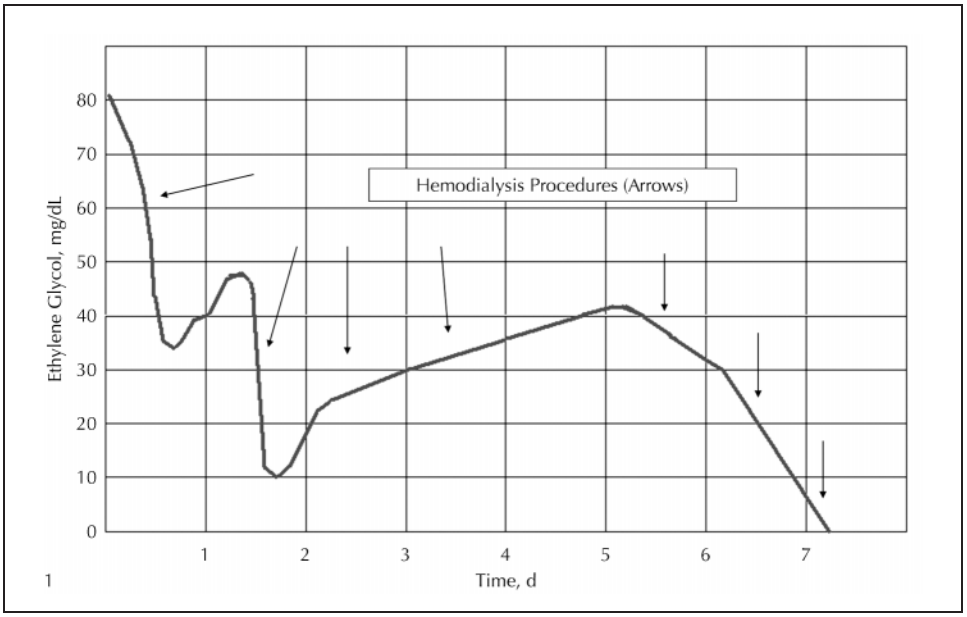
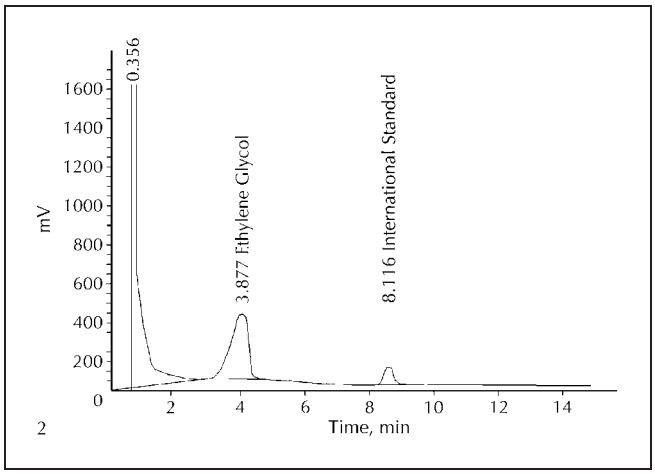


Pathologic Diagnosis: Central Venous Line Contamination of Blood Samples by Propylene Glycol from Intravenous Lorazepam Injections

The patient had been receiving intravenous lorazepam injections for prophylaxis of delirium tremens via his central line, which had also been used for sample collections. Intravenous lorazepam is a viscous solution containing suspended lorazepam at a concentration of 4 mg/mL (10 mmol/L) and preservatives, which include, by volume, 80% propylene glycol, 18% polyethylene glycol-400 (PEG-400), and 2% benzyl alcohol. Injection of an aliquot of lorazepam solution into our GC resulted in a false ethylene glycol peak (ie, elution at the same time as ethylene glycol; Figure 2). Pure samples of each of the preservatives were obtained and injected into the GC, showing that the false ethylene glycol peak was due to propylene glycol as seen with injection of the lorazepam mixture. A peripherally collected blood sample did not show a peak on the GC matching that of ethylene glycol, proving that the central venous line was contaminated and was the source of interference.

Ethylene glycol is a polyalcohol used to depress freezing points in many commercial products such as antifreeze and windshield deicing fluid. Because of this ready availability, ethylene glycol ingestion is a relatively common cause of poisoning in the United States. In 2001, 4938 exposures involving ethylene glycol were reported to the American Association of Poison Control Centers.[1] Although the majority of these were unintentional ingestions, ethylene glycol intoxication is also seen following suicide attempts and in severe alcoholics who use it as an alcohol substitute when they cannot obtain ethanol. Mortality from ethylene glycol poisoning is low (<1% in 2001), mainly because of early diagnosis and treatment. Following ingestion, ethylene glycol is converted into a number of toxic metabolites, such as glycoaldehyde, glycolic acid, and oxalic acid, by the liver enzyme aldehyde dehydrogenase. Accumulation of these anionic metabolites leads to an elevated anion gap in metabolic acidosis. The most toxic of these metabolites is oxalic acid, which precipitates with calcium in the urine, producing calcium oxalate crystalluria. Calcium oxalate crystals are directly toxic to the kidney tubules and glomeruli (producing rapid renal shutdown if not treated) and to end organs (heart and liver) wherein deposition produces parenchymal necrosis.

In addition, as long as significant levels of ethylene glycol remain in circulation, the uncharged parenteral ethylene glycol molecule will cause an elevated osmolal gap. Although this picture of metabolic acidosis with elevated anion and osmolal gaps is the classic presentation of ethylene glycol intoxication, these findings may vary depending on how long after ingestion the test is performed.[2] In addition, elevated anion or osmolal gaps may be present in other settings, such as methanol poisoning. Therefore, the best way to identify ethylene glycol in the blood is by direct confirmation with GC. Interference with other glycols is known to occur with GC, and awareness of such



interferences helps to avoid false positive results and improper management.

Propylene glycol is a common preservative found in many intravenous medications. Toxicity is rare, but severe acidosis has been reported in patients who receive large cumulative doses of medications containing this substance as a preservative.[3,4] Although propylene glycol can interfere with ethylene glycol analysis by GC,[5] such interference is rare because circulating levels of propylene glycol are usually extremely low. In contrast, venous line contamination with propylene glycol is more likely to cause false positive ethylene glycol readings. Diagnostic samples are often drawn from indwelling lines for convenience, a practice that has been shown to interfere with laboratory tests for many analytes.[6,7] Such interference can influence clinical decision making, as seen in this case where the patient had received repeated dialysis and fomepizole therapy based on persistent false positive ''ethylene glycol'' elevation. The potential for laboratory interference, even with ''gold standard'' measurements, occurs when one laboratory measurement (ethylene glycol level) is not correlated with other laboratory parameters (anion and osmolal gap) and, more importantly, clinical symptoms.

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