CASE REPORT

Lactate gap as a tool in identifying ethylene glycol poisoning

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SUMMARY

Ethylene glycol toxicity is a known cause of anion gap metabolic acidosis, with the presence of an osmolar gap and the right clinical context suggesting to the diagnosis. Rapid recognition and early treatment is crucial. Unfortunately, ethylene glycol levels are not readily available and must be performed at a reference laboratory. We present a case where recognising the significance of the 'lactate gap' assisted in identifying ethylene glycol poisoning.

BACKGROUND

The management of ethylene glycol poisoning requires rapid recognition to avoid end organ damage and potentially death. This may be a challenge given the non-specific signs and symptoms. Spuriously elevated levels of lactate measured using the lactate oxidase method compared with the lactate dehydrogenase method may assist in the diagnosis of ethylene glycol poisoning and can be a useful tool where ethylene glycol measurement is not readily available.

CASE PRESENTATION

A 47-year-old male grocery clerk with history of hypertension presented to the emergency department with altered mental status. Per his spouse, his symptoms started with him feeling tired, having difficulty walking, dizziness and slurring of speech. He became progressively unresponsive and incoherent. By the time he reached the emergency room he had a Glasgow Coma Scale of 3 and was intubated for airway protection. His spouse was not aware of any intentional or unintentional drug

intake. On presentation, he had a temperature of 37.5°C, a heart rate of 100 bpm, a blood pressure of 135/80 mm Hg and an oxygen saturation of 99% on the ventilator with 30% FiO₂. Exam was significant for tachycardia and there were no focal neurological deficits.

INVESTIGATIONS

Labs revealed leukocytosis (white blood cell $29.4 \times 10^9/L$), an anion gap acidosis (anion gap 21) and an osmolar gap of 45 (measured osmolality 340, calculated osmolality 285). Creatinine level was normal, and the urine analysis was unremarkable with no signs of infection or clear crystals. Urine drug screen was only positive for opiates due to an opiate home medicine that the patient was using for back pain. The ethyl alcohol, salicylate and acetaminophen levels were undetectable. Interestingly, he had a simultaneous point-of-care lactate of '>12 mmol/L' and serum lactate of 2.4 mmol/L. CT scan of the brain was negative for any acute abnormalities. His mentation did not improve despite multiple doses of naloxone.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of anion gap acidosis with an osmolar gap includes ethylene glycol, methanol poisoning as well as ethanol intoxication. Ketoacidosis and lactic acidosis would cause anion gap acidosis; however, they would only lead to a small elevation, if any, in the osmolar gap.^{1,2}

TREATMENT

Due to the concern of ingestion (ethylene glycol or methanol toxicity) based on the presence of a severe anion gap acidosis and a large osmolar gap, the patient received fomepizole and dialysis was initiated afterwards due to persistent metabolic acidosis. Following dialysis, the point-of-care lactate dropped to match that of serum lactic acid (figure 1). Both metabolic acidosis and mental status improved after dialysis.

OUTCOME AND FOLLOW-UP

The patient was extubated 48 hours later and was discharged from the hospital subsequently without permanent sequelae. The qualitative ethylene glycol test came back positive 4 days later.

DISCUSSION

The management of ethylene glycol poisoning requires rapid recognition to avoid end organ

Figure 1 Serum lactic acid and point-of-care lactic acid measurement plotted against time.

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Figure 2 Ethylene glycol metabolism.

damage and potentially death. This may be a challenge given the non-specific signs and symptoms which range from stupor, nausea and vomiting to flank pain, renal failure and death. Anion gap acidosis associated with an osmolar gap may allude to the diagnosis although this may not always be present.³ Ethylene glycol is relatively non-toxic and is the cause of the detected osmolar gap while the anion gap acidosis as well as the other signs and symptoms of toxicity (renal failure, hypocalcaemia) are due to its metabolites, namely glycolic acid and glyoxylic acid. In order to prevent the consequences of ethylene glycol poisoning, the metabolic pathway is blocked by administering drugs that inhibit alcohol dehydrogenase (fomepizole and ethanol) leading to the renal excretion of ethylene glycol (figure 2). Haemodialysis is also used to rapidly remove both the toxic metabolites as well as the parent alcohol. Emergent haemodialysis should be pursued if there is suspicion for ethylene glycol poisoning in the presence of severe anion gap acidosis and an osmolar gap. The dialysis may be repeated as needed until the ethylene glycol level is less than 20 mg/dL and the acid base disturbance is resolved.⁴

Lactic acid is generated from pyruvate during the metabolism of ethylene glycol in the presence of nicotinamide adenine dinucleotide hydride (figure 3); however, that would not explain the huge discrepancy between point-of-care lactic acid and serum lactic acid in our patient. Although a small degree of lactic acidosis may be observed with ethylene glycol poisoning, a large increase in lactic acid is typically due to interference of lactic acid measurement by the ethylene glycol metabolites, namely glycolic acid.⁵ There are two different laboratory systems used

Figure 3 Mechanism of lactic acid formation in ethylene glycol poisoning. NAD, nicotinamide adenine dinucleotide; NADH, nicotinamide adenine dinucleotide hydride.

Laboratory methods for measuring lactic acid

Figure 4 The laboratory methods for measuring lactic acid and the structural similarity between lactic acid and glycolic acid. NAD, nicotinamide adenine dinucleotide; NADH, nicotinamide adenine dinucleotide hydride.

Figure 5 Serum lactic acid measurements reflecting the true lactic acid, and the point-of-care lactic acid measurements reflecting the spuriously elevated lactic acid due to glycolic acid.

to detect lactic acid: the lactate oxidase-based system and the lactate dehydrogenase-based system. The lactate oxidase-based system measures the hydrogen peroxide generated from the metabolism of lactic acid to pyruvate via lactate oxidase. Glycolic acid is structurally similar to lactate and can use lactate oxidase and generate hydrogen peroxide, which causes a falsely elevated lactate level in machines using this method. The lactate dehydrogenase method, on the other hand, is more specific to lactic acid and is not affected by the presence of glycolic acid (figure 4). We hypothesise this is the explanation for the difference between the measured lactic acid via both methods reflecting the presence of glycolic acid in our case (figure 5). Our point-of-care instrument, namely the Premiere GEM 3500, uses the lactate oxidase system, while the lab measurement, obtained via the Roche system, uses the lactate dehydrogenase system. If you are only using one or the other of these machines, this variance could easily have been overlooked, and delayed or even negated the diagnosis. Other case reports had a similar observation,⁶⁻⁸ with one case demonstrating a linear relationship between serum glycolate and the spuriously elevated lactic acid in a case of severe ethylene glycol poisoning.⁹

Learning points

- ▶ Ethylene glycol poisoning should be in the differential diagnosis in any patient presenting with an unexplained severe anion gap acidosis.
- ▶ Depending on the timing of presentation, a high anion gap or osmolar gap may not be present.
- ▶ Spuriously elevated levels of lactate measured using the lactate oxidase method compared with the lactate dehydrogenase method may assist in the diagnosis of ethylene glycol poisoning and can be a useful tool where ethylene glycol measurement is not readily available.

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