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Metabolic Acidosis – Not Always the Medication to Blame

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ABSTRACT

Background: Metabolic acidosis is a clinical disturbance characterized by an increase in acidity of plasma. Metabolic acidosis is considered a sign of an underlying disease. Identification of this underlying condition is the cornerstone to initiate appropriate management. Metabolic acidosis is typically classified as having a normal anion gap (AG) (i.e. non-AG) or a high AG. An increase in the AG can result from either a decrease in unmeasured cations (e.g. hypokalemia, hypocalcemia, hypomagnesemia) or an increase in unmeasured anions (e.g. hyperphosphatemia, high albumin levels).

Case: A 46-year-old male with a history of type 2 diabetes mellitus, recently started on liraglutide. He was presented to the emergency department with 4 days of nausea, vomiting, and diarrhea and one day of lethargy. He appeared to be dyspneic upon presentation, and he was initially placed on noninvasive positive pressure ventilation. The arterial blood gases (ABG), however, showed metabolic acidosis. After admission and resolution of diabetic ketoacidosis, his bicarbonate was still low, and a sodium bicarbonate drip was begun. Correction only had occurred after stopping liraglutide.

Conclusion: Vehicle solvent such as propylene glycol should be considered in the differential diagnosis of high anion gap metabolic acidosis, and its level should be measured in intractable cases.

INTRODUCTION

Metabolic acidosis is a clinical disturbance that is characterized by an increase in acidity of plasma. Metabolic acidosis is considered a sign of an underlying disease. Identification of this underlying condition is the cornerstone to initiate appropriate management. Plasma, like any other body fluid compartment, is neutral; total anions match total cations [(1)].

Metabolic acidosis is typically classified as having a normal AG (i.e. non-AG) or a high AG. Non-AG metabolic acidosis is also characterized by hyperchloremia and is sometimes referred to as hyperchloremic acidosis. Calculation of the AG is thus helpful in the differential diagnosis of metabolic acidosis [(2)].

An increase in the AG can result from either a decrease in unmeasured cations (e.g. hypokalemia, hypocalcemia, hypomagnesemia) or an increase in unmeasured anions (e.g. hyperphosphatemia, high albumin levels). In certain forms of metabolic acidosis, other anions accumulate; by recognizing the increasing AG, the clinician can formulate a differential diagnosis for the cause of that acidosis [(1)].

The clinical history in metabolic acidosis is helpful in establishing the etiology when symptoms relate to the underlying disorder. The age of onset and a family history of acidosis may point to inherited disorders, which usually start during childhood. Important points in the history include the following:

- Diarrhea - GI losses of HCO^{-3}
- History of diabetes mellitus, alcoholism, or prolonged starvation - Accumulation of ketoacids
- Polyuria, increased thirst, epigastric pain, vomiting -Diabetic ketoacidosis (DKA)
- Nocturia, polyuria, pruritus, and anorexia - Renal failure [(3)]
- Ingestion of drugs or toxins - Salicylates, acetazolamide, cyclosporine, ethylene glycol, methanol, metformin, topiramate
- Visual symptoms, including dimming, photophobia, scotomata - Methanol ingestion
- Renal stones – Renal tubular acidosis (RTA) or chronic diarrhea
- Tinnitus, blurred vision, and vertigo - Salicylate overdose[(1)].

CASE

A 46-year-old male with a history of type 2 diabetes mellitus, recently started on liraglutide, was presented to the emergency department with 4 days of nausea, vomiting, and diarrhea and one day of lethargy. He appeared to be dyspneic upon presentation, and he was initially placed on noninvasive positive pressure ventilation. The ABG, however showed metabolic acidosis with a pH of 7.08 and bicarbonate of 10 mEq/L. The blood glucose was 740 mg/dL with diabetic ketoacidosis. He was admitted to the intensive care and was started on an insulin drip and aggressive fluid resuscitation. Although the diabetic ketoacidosis resolved, his bicarbonate was still low, and a sodium bicarbonate drip was begun. After 3 days of a

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continuous infusion, the bicarbonate level finally started to improve. The patient therefore had a high anion gap metabolic acidosis secondary to DKA plus an unknown cause. Methanol, ethylene glycol and propylene glycol levels were checked, and propylene glycol was detectable at 0.20 mg/ml. He was successfully extubated and sodium bicarbonate tablets were continued. He was recommended to continue the liraglutide injections after discharge, but the patient readmitted again to ICU with similar symptoms of nausea, vomiting and abdominal pain. He was seen by a nephrologist and stoppage of the liraglutide was recommended, followed by resolution of symptoms and improvement of the general condition

DISCUSSION

Propylene glycol is a common vehicle solvent for some intravenous medications, including lorazepam, propofol and liraglutide. It has been shown that serum concentrations of propylene glycol greater than 0.18 mg/ml may cause high anion gap metabolic acidosis, hemolysis, central nervous system depression, seizures, arrhythmias, acute renal tubular necrosis, and renal failure [4- 8]. In that case with diabetes and metabolic acidosis after correction of ketoacidosis using fluid and insulin according to our local guild lines, the general condition of the patient didn't improve and he was readmitted to the hospital. After investigation and measuring level of propylene glycol, we found high level that was causing this acidosis and thus was corrected after stopping it.

The patient's high anion gap metabolic acidosis is likely secondary to being started on liraglutide. Common side effects of liraglutide are gastrointestinal side effects like nausea and vomiting that the patient had, but the solvent, propylene glycol is notorious to cause high anion gap metabolic acidosis. Other causes of high anion gap metabolic acidosis are diabetic ketoacidosis, toxic alcohols like methanol, ethylene glycol, and isopropyl alcohol, medications like aspirin and solvents like propylene glycol.

CONCLUSION

Vehicle solvent such as propylene glycol should be considered in the differential diagnosis of high anion gap metabolic acidosis, and its level should be measured in intractable cases.

Conflict of Interest: None declared.

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