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Opinion

The Urinary Anion and Osmolal Gaps in Metabolic Acidosis

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Abstract

Relevant physiology and use of the urinary anion and osmolal gaps in the assessment of metabolic acidosis are reviewed and discussed.

Human beings produce a daily load of 50-100 MEq of non-volatile acids, primarily related to the metabolism of dietary protein. To maintain acid-base balance, the kidneys respond by excreting ammonium (NH_4+) and reabsorbing filtered bicarbonate. For that reason, the normal response of the kidney to metabolic acidosis is to promote NH_4+ excretion and reabsorption of filtered bicarbonate.

Measurement of the Urinary Anion Gap (UAG) is useful in evaluating patients with a non-anion (i.e hyperchloremic) metabolic acidosis by providing an estimate of the excreted NH_4+. As opposed to plasma electrolytes and other solutes, urinary components may vary widely in both health and disease, affected by diet, hydration, kidney disease, medications and many other factors. NH_4+ is usually excreted with the Cl- ion, but may also be excreted with ketoacids, bicarbonate, hippurate and other anions. Normally, the gastrointestinal absorption of Na+ and K+ exceeds the absorption of Cl-, leaving the remaining Cl- to complex with NH_4+ for excretion.

The urinary anion gap may be calculated as ({Na+ plus K+} minus Cl-). Note that this formula is different than in the calculation of the plasma anion gap, but similarly represents the quantity of unmeasured anions minus the unmeasured cations in the urine. In normal individuals, the urinary anion gap is usually positive (20-90 MEq/L) due to the excretion of Na+ and K+ and the relatively lower excretion of Cl- .

In patients with a non-anion gap (hyperchloremic) acidosis, however, the normal response of the kidneys is to increase NH_4+ excretion and reabsorb bicarbonate. Since NH_4+ is generally excreted with Cl-, this will lead to a negative urinary anion gap (-20 to -50 MEq/L).

Patients with distal (Type I) renal tubular acidosis (RTA) have a deficit in the ability to excrete Hydrogen ions in the form of NH_4+. Since the measurement of the urinary electrolytes in this situation would not account for the expected rise in NH_4+ and accompanying Cl-, the urinary anion gap is likely to be positive (i.e normal). Conversely, patients suffering from hyperchloremic acidosis related to diarrhea are likely to have lost significant amounts of Na+ and K+ in the stool and in the presence of normal renal tubular function will reabsorb Na+ and K+ and excrete NH_4+ complexed with Cl-, leading to a negative urinary anion gap.

The following case may be illustrative

A 39 year-old woman with Sjögren's syndrome is seen with a history of recent diarrhea, abdominal cramping and generalized weakness. Among her laboratory work are: Na+ 136 K+ 2.6 Cl- 112 CO2 16 BUN 19 Cr 1.0. Sjögren's syndrome is associated with a distal RTA (type I) and this patient's hypokalemia and hyperchloremic acidosis could be related to that. The patient's urinary electrolytes, however, showed Na+ 28, K+ 39, and Cl- 101, giving a highly negative anion gap of 34, indicating normal renal tubular excretion of NH_4+ and Cl- and implicating the patient's diarrhea as the cause of her acid-base-electrolyte disturbance.

The usefulness of the urinary anion gap is dependent on the relationship between the UAG and NH_4+ excretion. Patients with excretion of large amounts of unmeasured anions may lose this association and render the use of the UAG less helpful. Examples of these unmeasured urinary anions would include beta-hydroxybutyrate and acetoacetate in diabetic ketoacidosis, exogenous bicarbonate therapy, D-lactate and hippurate related to toluene inhalation. In those situations, use of the urinary osmolal gap is helpful. The urinary osmolality gap is calculated as:

Measured urinary osmolality minus (2 X (Na+ plus K+) + (urea (mg/dl)/2.8) + (glucose (mg/dl)/18) or in scientific units:
Measured urinary osmolality minus (2 X (Na+ plus K+) + urea +glucose)

The normal range of the osmolal gap is 10-100 mosmol/kg of which about half is usually related to NH_4+; in cases of acidosis related to diarrhea the osmolal gap may be therefore very high.

The urinary osmolal gap is less useful in the presence of methanol, ethyl alcohol, ethylene glycol or mannitol ingestion or in the recovery phase of diabetic ketoacidosis due to the presence of small, osmotically active but uncharged particles in the urine.

Conclusion

The understanding of the relevant physiology and use of the urinary anion and/or osmolal gaps are helpful in the assessment of metabolic acidosis.

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