Bicarbonate Use in the Critically Ill Patient
Guest Faculty: Dr. Gabriel Wardi and Dr. Kit Tainter

Key Article
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Definition and Epidemiology
A metabolic acidosis is a process caused by an increase in weak acids (serum proteins, albumin, and inorganic phosphate) or a decrease in strong ion difference (Na+, K+, Mag2+, Ca2+, Cl-). This approach is referred to as the Stewart model and clinical applications are still debated and it is of uncertain benefit in the ED. More practically, the base excess can be used to easily identify a metabolic component of an acidosis in clinical practice (B.E. < -2 mEq/L signifies the presence of a metabolic acidosis). The Henderson–Hasselbalch method defines metabolic acidosis by the presence of an acid–base imbalance associated with a plasma bicarbonate concentration below 20 mmol/L. Metabolic acidosis is broken into acute (within a few days) or chronic (weeks to years).

Many providers in the ED further classify metabolic acidosis based on presence or absence of anion gap. A non-gap acidosis can be identified by either the presence of an anion gap of < 12 and bicarbonate < 20 mEq/L OR the presence of an anion gap where the change in bicarbonate is greater than the change in anion gap (i.e., an anion gap and non-gap acidosis). A gap acidosis is defined by the presence of an anion gap > 12 and bicarbonate < 20 mEq/L, which may also be identified in presence of a non-gap acidosis (as above) or metabolic alkalosis.

Acute metabolic acidosis is well-recognized in the ED and ICU however epidemiological data are sparse. Various definitions make this difficult as well: previously defined in some large retrospective observational studies as *severe metabolic acidosis* as pH < 7.20, pCO2 < 45 and HCO3 < 20 (up to 48.3% in-hospital mortality), *moderate metabolic acidosis* defined as pH < 7.3, base excess < -4 mmol/L, PCO2 < 45 (up to 21.5% in hospital mortality). Mortality of patients with moderate or severe metabolic acidosis is higher than patients with sepsis.

Type of Metabolic Acidosis
- Diabetic ketoacidosis: medical emergency in patients with DM as a result of insulin deficiency. Hepatic metabolism of fatty acids produces beta-hydroxybutyrate and acetoacetate, both strong anions in the body
- Lactic acidosis: strong anion in the body as more than 99% is present as lactate, another strong anion. Seen in patients with sepsis, heart failure, cardiogenic, hypovolemic shock, among others

- Hyperchloremic (or non-gap) acidosis: broad group of conditions characterized by an imbalance of chloride and bicarbonate, through any number of mechanisms (diarrhea, fistula, renal tubular acidosis, normal saline administration, carbonic anhydrase inhibitors, among others). Balanced crystalloids contain some buffer - acetate, lactate, gluconate - that replaces chloride and are metabolized by the liver faster than renal chloride excretion.
- Classic mnemonic is FUSED-CARS: fistula (pancreatic, biliary), uretero-gastric conduit, saline administration, endocrine (hyper-PTH), diarrhea, carbonic anhydrase inhibitor (acetazolamide), ammonium chloride, renal tubular acidosis, spironolactone.

Physiologic Effects of Metabolic Acidosis

Animal and experimental data showing any of the following may be present, although we lack strong evidence in humans showing a causal relationship:

1. Decreased catecholamine reactivity
2. Increased nitric oxide production, resulting in hypotension
3. Fatal dysrhythmias

Role of Bicarbonate in Management of Metabolic Acidosis

Rationale for bicarbonate therapy is that intravenous administration of a "push" sodium bicarbonate (typically given as 50 mEq/L sodium, 50 mEq/L bicarbonate), would increase the strong ion difference, and thus the pH and improve cardiac function. More recently, there is enthusiasm about using isotonic bicarbonate solutions for resuscitation (150 mEq/L Na, 150 mEq/L bicarbonate in either 1 L sterile water or D5) to improve outcomes in patients with metabolic acidosis and renal insufficiency.

Systematic review published in 2019 found that pH, serum bicarbonate, base excess, serum sodium and pCO2 increased after IV administration of bicarbonate; serum anion gap and potassium decreased. Although these did not assess for intracellular acidosis due to back-diffusion of CO2 and decreased ionized calcium, no evidence showed any decrease in ionized calcium or decreased cardiac output.

However, this is a paucity of randomized trials to guide actual practice, with only 2 RCTs published.

1. Hoste et al. (2005) compared use of sodium bicarbonate to tris(hydroxymethyl)aminomethane in 18 patients with mild metabolic acidosis - and found no clinically important change in outcome.
2. Jaber et al. (2018) published the BICAR-ICU in 26 French ICUs for patients with severe acidemia, notably excluding those with DKA or CKD to receive either 4.2% sodium bicarbonate or usual care. No difference in primary outcome (composite of death or at least one organ failure at 7 days) between groups although there was a reduced need for RRT in the sodium bicarbonate group. Patients with acute kidney injury that received bicarbonate were noted to have increased survival and decreased need for RRT.

Bicarbonate for DKA

Rationale: reverses acidotic state, but also may reverse effect acidosis has on insulin resistance.

Evidence: Few retrospective studies, but none show any difference in time to resolution of DKA, length of stay in hospital, acidosis, ketosis, or glycemic control. Also noted was high incidence of hypokalemia that required correction in patients receiving bicarbonate.
Importantly, we lack RCTs to help guide therapy in this area. It is not recommended for pH > 6.9 and may not provide benefit in pH < 6.9.

Bicarbonate for Lactic Acidosis
Rationale: May transiently improve pH to improve outcomes, counteracting the effect of hyperlactatemia and accompanying acidosis.
Evidence: 2 small, randomized, cross-over, single center trials have been completed. Both showed no change in blood pressure, cardiac output, but increase in pH. Prior reviews have also been written about this detailing lack of benefit.

Bicarbonate for Cardiac Arrest
Rationale: May counteract the effects of profound metabolic acidosis that occur during cardiac arrest. Had previously been recommended as a first-line medication in cardiac arrest.
Evidence: Small observational studies have shown increased rates of ROSC for out-of-hospital cardiac arrest, however one study showed lower survival rates and worse neurologic outcomes. A small RCT showed no benefit in rates of ROSC, mortality, or neurologic outcomes.

AHA 2020 Guidelines: Routine use of sodium bicarbonate is not recommended for cardiac arrest. Patients with arrest from agents that cause sodium-channel blockade and hyperkalemia may benefit from this.

Bicarbonate for NAG-MA
Rationale: Patients who lose bicarbonate though any number of mechanisms (e.g., GI tract through diarrhea or urine through renal tubular acidosis) benefit from bicarbonate supplementation