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Metabolic Acidosis: Got Bicarbonate?

Kendra Glassman

Acute or chronic metabolic acidosis is a condition that has serious complications. It develops from either increased acid production, increased enteric losses, or decreased renal acid secretion. Acutely, metabolic acidosis can cause serious cardiac and pulmonary complications; chronically, it can lead to alterations in protein catabolism, bone health, and hormonal changes. Correcting the metabolic acidosis is essential to minimizing these complications. Bicarbonate supplementation has been the mainstay for achieving acid-base balance; however, with ongoing medication shortages, clinicians must become creative with their treatment plan.

INTRODUCTION

The body's ability to maintain acid-base balance is critical for health. The kidneys and lungs work harmoniously along with several buffering systems to maintain homeostasis. Acidemia occurs when arterial pH falls below 7.35, which can result in a metabolic, respiratory, or mixed acid-base disorder.[1] When the concentration of hydrogen ions in the body is increased reducing the bicarbonate concentration, metabolic acidosis ensues.[2] The three primary causes of metabolic acidosis are:[3]

- Increased acid production
- Loss of enteral bicarbonate in stool from pancreatic secretions
- Decreased renal acid elimination or increased bicarbonate loss due to inability to "reclaim" filtered bicarbonate

Acute forms are most likely due to overproduction of acid; chronic forms are likely from the latter two causes.[3]

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Acute metabolic acidosis can cause decreased cardiac output and arterial dilatation resulting in hypotension, decreased oxygenation, arrhythmias, and immune compromise.[4] Chronic metabolic acidosis can lead to increased muscle degradation, increased osteoclastic activity, and alterations in endocrine function. Alterations in endocrine function include increased production of glucocorticoids and decreased production of thyroid hormones, insulin, and growth hormones.[5,6] While using bicarbonate to treat acute forms of metabolic acidosis is controversial as it has not always been shown to improve outcomes,[7] it is the mainstay for chronic metabolic acidosis to help improve cellular function and prevent long term complications.[3]

Mechanism and Classification

Identifying the cause of metabolic acidosis is essential to guiding treatment and preventing adverse events. It can be classified based on the three major mechanisms as listed above. See Table 1A and B for more in-depth mechanisms. A useful

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tool is the measurement of the anion gap.[8,9] The anion gap is a value that represents the difference between the primary positively charged cation (Na+) and negatively charged anions (Cl- and HC03-) in the blood. Calculating the anion gap can also be helpful in classifying it as either elevated anion gap acidosis or normal (hyperchloremic) anion gap.[10] Generally, excess acid production results in a high anion gap whereas excess base or decreased acid excretion by the kidneys results in hyperchloremic metabolic acidosis or normal metabolic acidosis.[8,9]

Table 1A. Causes of Metabolic Acidosis Increased Anion Gap[2,10,14]

Increased Acid Production	Ketoacidosis
	• Alcohol • Fasting • Diabetes
	Lactic Acidosis (physiologic cause)
	• Alcohol • Pulmonary Disease • Seizures • Shock
	Lactic Acidosis (toxins/medications)
	• Methanol • Ethylene Glycol • Diethylene Glycol • Propylene Glycol • Aspirin • Toluene* • Biguanides • Cyanide • Propofol
	D-Lactate
	• Bacterial Overgrowth
	Short Bowel Syndrome
Diminished Renal Acid Secretion	Renal Failure

Increased Acid Production

Increased acid accumulation that leads to metabolic acidosis can occur in a variety of clinical settings and leads to an anion gap metabolic acidosis. The main causes are due to lactic acidosis; ketoacidosis due to uncontrolled diabetes, excess alcohol or fasting; ingesting substances such as methanol, ethylene glycol, diethylene glycol, or propylene glycol; aspirin or acetaminophen poisoning, or rarely, toluene ingestion, and finally, D-lactic acidosis.[2,11]

Loss of Bicarbonate

Metabolic acidosis related to loss of base or bicarbonate occurs due to several reasons. It can be due to diarrhea, ileostomy output, enterocutaneous fistulas, or short bowel syndrome where a significant amount of bicarbonate from pancreatic secretions can be lost in the stool. The kidney compensates by reabsorbing bicarbonate and increasing acid excretion rapidly. If volume depletion occurs, the kidney will also reabsorb increased NaCl to prevent intravascular loss.[12,13] Bicarbonate reabsorption can be impaired in the setting of proximal renal tubular acidosis in diseases such as multiple myeloma.[14] Further, base can be lost if urine is exposed to the GI tract in the case of any neobladder reconstruction (ileo-conduit) and therefore urinary chloride is absorbed in the colon in exchange for bicarbonate and consequently increases bicarbonate GI losses.[14]

Decreased Renal Acid Elimination

One of the most common causes of metabolic acidosis is decreased renal acid secretion in chronic kidney disease. Usually metabolic acidosis does

Table 1B. Causes of Metabolic Acidosis Normal Anion Gap[2,10,14]

Bicarbonate Losses	• Diarrhea • GI Losses (ostomy, fistula) • RTA (type 2) • Carbonic anhydrase inhibitors • Urologic Causes (ileal loop, ileal conduit) • Magnesium Sulfate
Diminished Renal Acid Secretion	• Renal Tubular Acidosis (RTA) (Type 2,4)

not ensue until patients have progressed to stage 4 chronic kidney disease (CKD) where acids from the metabolism of protein are not excreted, resulting in metabolic acidosis.[16,17] There are 2 mechanisms that responsible for the 3 types of renal tubular acidosis (RTA) that can cause metabolic acidosis:

1. Defects in secreting or transporting H+ ions from the distal convoluted tubules cause distal RTAs and low renin/low aldosterone level induced RTAs.
2. Increased bicarbonate losses from impaired reabsorption of bicarbonate causes, discussed earlier, results in a proximal RTA.[15]

Typical distal RTAs may cause severe acidosis, whereas low renin/low aldosterone secretion

Table 2. Sources of Bicarbonate Replacement

Medication	Bicarbonate Content
INTRAVENOUS	
Sodium Bicarbonate ($NaHCO_3$)	
• 4.2% Solution	• 42mg/mL (0.5mEq/mL bicarbonate & sodium)
• 7.5% Solution	• 75mg/mL (0.9mEq/mL bicarbonate & sodium)
• 8.4% Solution	• 84mg/mL (1mEq/mL bicarbonate & sodium)
Lactated Ringer's Solution	• 1 mEq lactate = 1mEq bicarbonate
Acetate (TPN additive)	• 1 mEq acetate generates 1mEq bicarbonate
ORAL/ENTERAL	
Sodium Containing Products	
Sodium Bicarbonate Tablets (Neut)	
• 325mg	• 325mg = 3.85mEq of bicarbonate and Na
• 650mg	• 650mg =7.7mEq of bicarbonate and Na
Sodium Bicarbonate Powder	
• (All grams: 1, 120, 454, 500, 1000, 2500, 10000, 12000, 25000, 45000)	• 7.7mEq each of bicarbonate and sodium per 650mg
Baking Soda (from your kitchen)	
• 1/2 teaspoon	• 26.8mEq bicarbonate and sodium
Sodium Citrate (Bicitra)	
• Cytra-2 (Na Citrate 500mg; Citric Acid 334mg/5mL)	• Each 1mL contains 1mEq each of bicarbonate and sodium
• Oracit (Na Citrate 490mg; Citric Acid 640 mg/5mL)	
• Shohl's Solution (Na Citrate 500mg; Citric Acid 300mg/5mL)	
• Generic (Na Citrate 500mg; Citric Acid 334mg/5mL)	
Potassium Containing Products	
Potassium Citrate (Urocit-K)	
• Urocit-K 5 or Generic 5	• 5mEq (540mg) bicarbonate & potassium
• Urocit-K 10 or Generic 10	• 10mEq (1080mg) bicarbonate & potassium
• Urocit-K 15 or Generic 15	• 15mEq (1620mg) bicarbonate & potassium
Potassium Citrate (Cytra-K)	
• Powder (K citrate 3300mg; Citric Acid 1002mg/packet)	• 30mEq bicarbonate and potassium per packet
• Solution (K citrate 1100mg; Citric Acid 334mg/5 mL)	• 2mEq/mL bicarbonate and potassium; 10mEq each per 5mL
Lemon Juice*	
• Lemon Juice Concentrate (2 Tablespoons)	• ~1.67 mEq bicarbonate and 0.9 mEq potassium
Sodium and Potassium Containing Products	
Sodium & Potassium Citrate, Citric Acid (Polycitra)	
• Cytra-3 (Na Citrate 500mg, K Citrate 550mg, Citric Acid 334mg/5mL)	• 1 mL contains: 1mEq K, 1mEq sodium, 2mEq bicarbonate
• Generic (Na Citrate 500mg, K Citrate 550mg, Citric Acid 334 mg/5mL)	

*Other juices contain bicarbonate also[32]

Table 3. Strategies to Manage Parenteral Nutrition Shortages

1. Be judicious on the use of parenteral nutrition and try to provide nutrition via the oral or enteral route when able.
   a. Switch to oral medications if the patient is able to take small amounts of medications and foods orally or enterally.
   b. Use intravenous or parenteral supplementation for patients who require parenteral nutrition or intravenous supplementation.
2. Reconsider the use of automatic electrolyte replacement protocols and reserve replacement for symptomatic patients or critical levels.
3. Consider the use of premixed parenteral nutrition solutions or electrolyte admixtures.
4. Report product shortages to U.S. FDA Drug Shortage Program (DSP) and adverse patient events to the shortages to ISMP Medication Errors Reporting Program (MERP).

Table 4. Helpful Websites

1. **Reporting Drug Shortages:** U.S. FDA Drug Shortage Program (DSP)
   https://www.fda.gov/drugs/drug-shortages/how-report-shortage-or-supply-issue
2. **Reporting Adverse Events to Shortages:** ISMP Medication Errors Reporting Program (MERP)
   https://www.ismp.org/
3. **Drug Shortage Lists**
   a. American Society of Health-System Pharmacists (ASHP), Drug Shortages Resource Center
      https://www.ashp.org/shortages?
   b. U.S. FDA Drug Shortages
      https://www.fda.gov/drugs/drug-safety-and-availability/drug-shortages
   c. A.S.P.E.N. Latest News and A.S.P.E.N. Product Shortage Latest News
      https://www.nutritioncare.org/ProductShortages/

induced RTAs are often milder with hyperkalemia as the hallmark sign.[18]

Consequences

Bicarbonate is essential for health. Without it, serious consequences can result if untreated. Management of metabolic acidosis varies depending on acute or chronic status. In acute metabolic acidosis, symptoms usually do not develop unless pH falls to < 7.10, where patients can develop nausea, emesis, and an overall sense of malaise. In order to compensate, breathing often becomes more laborious resulting in longer, deeper breaths. Severe forms can have cardiac manifestations along with hypotension and shock, arrhythmias, and in the most extreme case, coma.[4-6]

Treatment has only been demonstrated to be beneficial in non-anion gap acidosis and continues to be controversial in high anion gap metabolic acidosis.[7] There are risks associated with treatment in the latter case as it can lead to hypernatremia and volume overload in addition to hypotension, decreased cardiac output, and an increase in mortality.[19] Many studies have not associated treatment with decreased mortality; yet most sources continue to recommend administering bicarbonate in severe acidemia (pH <7.10) to

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correct the acidosis with the intention of reversing organ failure.[7,20]

Correction of chronic metabolic acidosis is essential. Symptomatically, patients experience less dyspnea due to decreased hypercapnic breathing.[21] Metabolic acidosis can also lead to decreased muscle function, decreased bone mineral density, and influence hormone levels.[5,22,23] In children, correction of the acidosis can result in improved skeletal growth.[24] Patients with RTA can experience calcium containing kidney stones, which can be reversed with bicarbonate replacement.[25] Progression to chronic kidney disease can be slowed down the when the acidosis is corrected.[26]

Treatment

Correcting metabolic acidosis depends on many factors including the degree and chronicity of acidosis, ongoing acid production or bicarbonate losses, renal function, and whether oral/enteral vs. parenteral sources are needed. Once these factors have been evaluated and the level of bicarbonate has been determined, calculating the bicarbonate deficit can be helpful in estimating the amount of bicarbonate needed. The following formula can be used:

Bicarbonate deficit= (0.6 x body weight [kg]) x (desired bicarbonate - actual bicarbonate)

While this provides a rough estimate of the bicarbonate needed it should not replace serial measurements of HC03 (CO_2 on a basic metabolic panel) and pH in order to determine if further supplementation is required. The clinician must also be mindful of the serum potassium as it can become depleted with ongoing GI losses, but often appears normal in the setting of acidosis. Once the acidosis is resolved, potassium levels should be monitored and replete as needed.

Methods of Supplementation

Bicarbonate can be administered in several ways including orally/enterally, intravenously, and via dialysate during hemodialysis. Administering sodium bicarbonate is the most common and fastest method to correct metabolic acidosis,[7] however, other sources are available. If administered as another anion such as citrate or acetate, the liver will convert it to bicarbonate. In the acute care setting, tromethamine (THAM), had previously been used, which is a non-sodium-based buffer to correct the acidosis, however it has been discontinued by the manufacturer and is no longer available in the United States.[25] Acetate or citrate can also be given via sodium or potassium salts depending on the type of deficiency and supplementation needed. Of note, the typical Western diet, which is high in animal protein, can contribute to acid production. Recommending a diet rich in fruits and vegetables can lead to an increase in base load and may help with minimizing chronic acidosis.[28] With the ever-increasing medication shortages, clinicians have become creative, using everyday sources of base such as baking soda as an alternative. Table 2 provides sources of bicarbonate supplementation.[29-31]

Parenteral Nutrition Shortages

With patients on parenteral nutrition (PN) support, maximizing acetate, which is converted to bicarbonate in the body, will help restore metabolic balance. This has been difficult given recent PN shortages.[32] Most recently, potassium and sodium acetate have been on the TPN shortage list making replacing bicarbonate difficult. When possible, replacing losses via the enteral route during shortages is recommended, however, some patients are unable to tolerate any source of enteral replacement. Other options might be to use premade PN mixtures and reserving custom PN for patients in which it is needed. Table 3 and 4 lists helpful websites and tips to help manage parenteral shortages.

CONCLUSION

Metabolic acidosis can occur due to several mechanisms. The first step is to identify the cause and determine if this is an acute or ongoing process. If left untreated, either in the acute or chronic setting it can have deleterious effects. Treatment traditionally has been with sodium bicarbonate drips or acetate in parenteral nutrition solutions. Given the recent shortages, clinicians must become creative in finding alternate ways to maintain acid-base balance. ■

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