

**Guidelines
For the Management of
Metabolic Acidosis**

By

**Dr. Sinan Butrus
F.I.C.M.S**

2009 AD

2709 K

Clinical Standards & Guidelines

**Kurdistan Board
For Medical Specialties**

Bordê Kurdistan Bo Psporayati Pzisti

Setting Clinical and Professional Excellence

Metabolic acidosis is a clinical disturbance characterized by an increase in plasma acidity and should be considered a sign of an underlying disease process.

Bicarbonate is produced in the kidney while acid is produced from endogenous or exogenous sources

Bicarbonate (HCO_3^-) is in equilibrium with the metabolic components while carbonic acid (H_2CO_3) is in equilibrium with the respiratory component

Metabolic acidosis can be caused by:

- Increase in the generation of H^+ from endogenous sources as in ketoacidosis (due to diabetes, alcoholism and starvation) and lactic acidosis (due to circulatory failure, drugs, toxins or hereditary causes)
- Increase in the generation of H^+ from exogenous sources (ingestion of metformin , iron, salicylate, isoniazid, ethylene glycol, methanol , paraldehyde, ammonium chloride, and hyperalimentation fluids)
- Inability of the kidneys to excrete the hydrogen from dietary protein intake (renal failure, type I & type IV renal tubular acidosis RTA)
- The loss of bicarbonate (HCO_3^-) due to wasting through the kidney (type II renal tubular acidosis) or the gastrointestinal tract (diarrhea, intestinal fistula, uretero-sigmoidostomy)
- Rapid volume expansion with normal saline resulting in increase in the chloride load that exceeds the renal capacity to generate equal amounts of HCO_3^- .
- The kidneys response to a respiratory alkalosis

Clinical Presentation:

Subjective dyspnea from the patient's observation of hyperventilation

Nausea and vomiting , abdominal pain, diarrhea, polyphagia, bone pain and generalized muscle weakness

Palpitations, chest pain, headache, visual changes, mental confusion

Tinnitus, blurred vision and vertigo can occur with salicylate poisoning.

Visual disturbances, dimming, photophobia, scotomata, and frank blindness can be seen in methanol intoxication.

Physical:

Patients with acute metabolic acidosis demonstrate tachypnea and hyperpnea as prominent physical signs; Kussmaul respiration (an increase in tidal volume rather than respiratory rate and is appreciated as deliberate, slow, deep breathing.).

Chronic metabolic acidosis (as in uremia & renal tubular acidosis RTA) is associated with substantial bone disease from bone buffering of calcium carbonate.

Long bone malformations, stunted growth & vitamin D resistant rickets in pediatric & fractures in adult patients are noted.

Sever cases ($\text{pH} < 7.10$) may cause fatal ventricular arrhythmias, reduced cardiac contractility and reduced inotropic response to catecholamines, resulting in hypotension and congestive heart failure with stupor & coma particularly when it is associated with a toxic ingestion.

Cranial nerve palsies may occur with ethylene glycol intoxication.

Retinal edema may be seen in methanol ingestions.

Work up

- A low HCO_3^- level
- Measure pH and PCO_2 by arterial blood gas ABG in a patient with a low HCO_3^- level to differentiate a metabolic compensation of a respiratory alkalosis (pH > 7.45) from a primary metabolic acidosis (pH < 7.35). However, $[\text{HCO}_3^-]$ level of < 15 mEq/L, almost always is due, at least in part, to metabolic acidosis.

ABG will also judge the appropriateness of respiratory compensation of a metabolic acidosis, and to detect respiratory acidosis, which is signified by an elevated PCO_2 level as the normal respiratory response (Kussmaul breathing) to a metabolic acidosis is a decrease in pCO_2 (A quick rule of thumb: The PCO_2 should approximate the last two digits of pH, i.e. if the pH is 7.25 then PCO_2 should be close to 25 mm Hg.)

Failure to have an appropriate respiratory response to metabolic acidosis represents a failure of airway and/or breathing, which must be addressed before any other workup commences.

ABGs also measure base excess/base deficit (BE/BD) which is measured by gauging the amount of acid or base that is required to titrate the patient's blood sample to a pH of 7.40.

- Oxygenation does not affect the acid-base status of a patient and generally should not be part of the discussion unless severe hypoxia is leading to ischemia. In that case, measurement of PO_2 can identify severe hypoxia as a precipitant of lactic acidosis.
- Serum electrolytes, albumin, glucose, urea & creatinine.

To differentiate between the causes of metabolic acidosis, electrolytes and bicarbonate levels are used in the calculation of serum anion gap (AG) which is corresponding to the presence of unmeasured anions as standard electrolyte panels do not measure all the anions present in the serum.

$$\text{AG} = [(\text{Na}^+) + (\text{K}^+)] - [(\text{Cl}^-) + (\text{HCO}_3^-)] \quad \text{Normal range is 12-20 mEq/L}$$

It is important to note that the anion gap decreases by 2.5 mEq for every 1g/dL decrease in serum albumin.

Metabolic acidosis with a normal AG i.e. AG is $\leq 10-12$ mEq/L which is associated with the loss of HCO_3^- from the kidney or GI tract, or the failure of the kidney to excrete H^+ .

A urinalysis should be performed and a urine pH should be obtained. A urine AG is calculated from the measurement of urine Na^+ , K^+ , and Cl^- to differentiate between GI and renal losses of HCO_3^- in non-AG metabolic acidosis.

Metabolic acidosis with a high AG (AG is > 10-12 mEq/L) which is associated with the addition of endogenously or exogenously generated acids.

Measure the delta anion gap (Δ anion gap) / delta HCO_3^- (ΔHCO_3^-) and also measure the osmolar gap (calculated by subtracting the calculated serum osmolality from the measured serum osmolality)

The concept behind delta/delta is based on the assumption that for every increase in anion gap of 1 mmol/L above normal, serum HCO_3^- will drop by an equal amount below normal

The change in anion gap AG (or delta AG) detects the presence of a second acid-base disorder in patients with an high anion gap metabolic acidosis (elevated AG) & is calculated by the following equation: $(\text{AG}-10) / (24-\text{HCO}_3^-)$

* If the result of the ratio is > 2; it is usually because the bicarbonate level was higher than usual to start with which occurs in combined high anion gap metabolic acidosis with either respiratory acidosis (chronic lung disease such as COPD) or with concurrent metabolic

alkalosis; mathematically reflected in a high anion gap as in both the bicarbonate was high to begin with, it will appear to fall only a small amount so the numerator is large, the denominator is small, and the result is (> 2).

* If there is a pure high anion gap metabolic acidosis, the problem is due to an unmeasured anion. The Anion Gap rises more than the HCO_3^- falls, since the anions are unable to diffuse out of the bloodstream, while bicarbonate and hydrogen ions diffuse with ease [as H_2CO_3] so usually the delta ratio will give a result of (1-2).

* If the ratio is between (0.4-1) then it is usually indicating that the drop in serum HCO_3^- is not accompanied by a corresponding increase in the AG. This suggests that a portion of the H^+ load is not accompanied by an unmeasured anion and indicates a concomitant normal anion gap acidosis must exist alongside high anion gap acidosis(e.g. patient with severe diarrhea/cholera who have a normal anion gap acidosis due to the diarrhea, and become dehydrated and develop a lactic acidosis from shock so develop a high anion gap metabolic acidosis or in cases of congenital renal tubular acidosis with diabetic ketoacidosis DKA.

* If the anion gap is normal, and all of the change has occurred in the chloride / bicarbonate proportions, then the numerator will be low and the denominator will be high so a normal anion gap acidosis produces a delta ratio (< 0.4). The classic is a hyperchloremic metabolic acidosis from over enthusiastic saline administration.

- CBC count: high WBC count is a nonspecific finding, but it should prompt consideration of septicemia, which causes lactic acidosis. Severe anemia with compromised O_2 delivery may cause lactic acidosis

- Ketone level elevations indicate diabetic, alcoholic and starvation ketoacidosis.

The nitroprusside test is used to detect the presence of ketoacids in the blood and the urine. This test only measures acetoacetate and acetone; therefore, it may underestimate the degree of ketonemia and ketonuria because it will not detect the presence of beta-hydroxybutyrate (BOH). This limitation of the test can be especially problematic in patients with ketoacidosis who cannot convert BOH to acetoacetate because of severe shock or liver failure.

If assay for BOH is unavailable, an indirect method to circumvent this problem is to add a few drops of hydrogen peroxide to a urine specimen; this enzymatically will convert BOH into acetoacetate, which will be detected by the nitroprusside test.

- Serum lactate normal level is 0.5-1.5 mEq/L. Lactic acidosis is considered present if the plasma lactate level exceeds 4-5 mEq/L in an acidemic patient.

- Salicylate levels: therapeutic levels range up to 20-35 mg/dL. Plasma levels >40 -50 mg/dL are in the toxic range.

- Iron levels as toxicity ≥ 300 mg/dL is associated with lactic acidosis.

- Urinalysis: A urine pH is normally acidic at < 5.0 . In acidemia, the urine normally becomes more acidic. If the urine pH is ≥ 5.5 in the face of acidemia, this finding is consistent with a type I-distal renal tubular acidosis RTA and in salicylate poisoning.

Ethylene glycol toxicity may present with calcium oxalate crystals, which appear needle shaped, in the urine.

Measuring the urine AG is helpful in cases of non-AG metabolic acidosis.

Urine AG = $([\text{Na}^+] + [\text{K}^+]) - [\text{Cl}^-]$

In the face of metabolic acidosis, the kidneys increase the amount of NH_3 synthesized to

buffer the excess H^+ and NH_4^+ excretion increases. The increased unmeasured NH_4^+ thus increases the measured anion Cl^- in the urine, and the net effect is a negative AG, which is a normal response to systemic acidification. The finding of a positive urine AG in the face of non-AG metabolic acidosis points toward a renal acidification defect (e.g., RTA).

- Electrocardiography may be used to detect electrolyte imbalances (e.g., hyperkalemia)
- Imaging Studies: if iron ingestion is suspected, perform imaging studies on the abdominal area, including the kidneys, ureters, and bladder

High AG warrants the following:

Lactic acidosis - Lactate, D-lactate

Ketoacidosis - Beta-hydroxybutyrate, acetoacetate.

Renal failure - Sulfate, phosphate, urate.

Ingestions - Salicylate, iron, methanol or formaldehyde, ethylene glycol (glycolate, oxalate), paraldehyde (organic anions), sulfur (SO_4^{2-}), phenformin/metformin

Massive rhabdomyolysis (release of H^+ and organic anions from damaged muscle)

Several mnemonics are used to prompt recall of the differential diagnosis of high anion gap acidosis. Two, neither of which is completely comprehensive, are as follows:

MUDPILES:

M-methanol; U-uremia; D-DKA, AKA; P-paraldehyde, phenformin; I-iron, isoniazid;

L-lactic (ie, CO, cyanide); E-ethylene glycol; S-salicylates

DR. MAPLES:

D-DKA; R-renal; M-methanol; A-alcoholic ketoacidosis; P-paraldehyde, phenformin;

L-lactic (ie, CO, HCN); E-ethylene glycol; S-salicylates

GOLD MARK:

G-Glycols (ethylene and propylene), O-Oxoproline, L-lactate, D-lactate, M-Methanol, A-Aspirin, R-Renal failure, and K-Ketoacidosis

Normal AG (i.e., hyperchloremic acidosis) warrants the following:

GI loss of HCO_3^- : diarrhea, pancreatic fistula

Renal HCO_3^- loss - Type 2 (proximal) RTA, renal dysfunction

Hypoaldosteronism (ie, type 4 RTA)

Hyperventilation

Ingestions - Ammonium chloride, acetazolamide, hyperalimentation fluids, some cases of ketoacidosis particularly during treatment with fluid and insulin

The AG can rise because of

increases in unmeasured anions

decreases in unmeasured cations (e.g., hypocalcemia, hypomagnesemia)

secondary to an increase in albumin

increase in negative charges on albumin, which is caused by alkalosis.

AG can be decreased by

increase in unmeasured cations (e.g., hypercalcemia, hypermagnesemia, lithium intoxication, high immunoglobulin G IgG levels)

decrease in unmeasured anions (e.g., hypoalbuminemia).

Laboratory errors can also affect the AG

Hyperproteinemia, hyperlipidemia, and hyperglycemia resulting in underestimation of serum sodium level can falsely depress AG.

Bromide intoxication can be mistaken for Cl^- , which can result in an inappropriate depression of the AG.

The osmolal gap is the measured plasma osmolality minus calculated osmolality.

The serum osmolality is composed of all osmotically active substances including ionic and nonionic substances such as serum ions, glucose, BUN besides; alcohols, excess serum lipids and proteins, and delivered substances such as mannitol

The calculated osmolality is $P_{\text{osm}} = [2 \times \text{Na}^+] + [\text{glucose in mg/dL}]/18 + [\text{BUN in mg/dL}]/2.8$

Normal osmolal gap is 10-15.

Metabolic acidosis with elevated osmolal gap (>15) indicates poisoning with methanol, ethylene glycol, isopropanol, acetone and propylene glycol (found as a diluent for some intravenous medications such as lorazepam).

Management

The initial therapeutic goal is to raise the systemic pH $\geq 7.1-7.2$ at which dysrhythmias become less likely and cardiac contractility and responsiveness to catecholamines will be restored.

Metabolic acidosis can be reversed by treating the underlying condition or by replacing the bicarbonate. The decision to give bicarbonate should be based upon the pathophysiology of the specific acidosis, the clinical state of the patient, and the degree of acidosis.

Treating the underlying conditions in high AG states usually is sufficient in reversing the acidosis. Treatment with bicarbonate is unnecessary, except in extreme cases of acidosis when the pH is $<7.1-7.2$.

For all cases of diabetic ketoacidosis, the role of bicarbonate is controversial, regardless of the pH or bicarbonate level.

In hyperchloremic acidosis, the central problem is with the reabsorption or regeneration of bicarbonate. In these conditions, therapy with bicarbonate makes physiologic sense and is prudent in patients with severe acidosis.

Sodium bicarbonate 1mEq/mL (8.4 %) solution use is limited to severe cases of acidosis (pH $< 7.1-7.2$)

50 mEq IV over 5 minutes or 2-5 mEq/kg IV infusion over 4-8 hr according to the severity or emergency

Bicarbonate therapy may have potential complications:

including volume overload, hypokalemia, hypercapnia, CNS acidosis, overshoot alkalosis, tissue hypoxia (leftward shift of hemoglobin-oxygen dissociation curve)

Dialysis therapy is indicated in cases of significant metabolic acidosis in the setting of renal failure & toxicity ingestions (e.g., salicylate, methanol, and ethylene glycol)

References:

1. Antonia Quinn Metabolic Acidosis in Emergency Medicine Clinical Presentation May 30, 2014
<http://emedicine.medscape.com/article/768268>.
2. Christie P Thomas Metabolic Acidosis Workup. Dec 8, 2014.
<http://emedicine.medscape.com/article/242975>.
3. Naveen R. Difference Between Metabolic and Respiratory Acidosis May 23, 2013.
www.differencebetween.com/difference-between-metabolic-and-vs-respiratory-acidosis/
4. Acidosis Apr 23, 2015.
www.nlm.nih.gov/medlineplus/ency/article/001181.htm
5. Keith Wrenn The delta (Δ) gap: An approach to mixed acid-base disorders.
Annals of Emergency Medicine. Volume 19, Issue 11, November 1990, Pages 1310–1313
www.sciencedirect.com/science/article/pii/S0196064405822929
6. Prashant Kumar. Arterial Blood Gas Interpretation.
www.pt.slideshare.net/homeprashant/ab-ginterpretation-prashant
7. Kraut J, Madias N. Metabolic acidosis: pathophysiology diagnosis and management.
Nat Rev Nephrol 2010; 6: 274-85.