Quick Reference on Metabolic Alkalosis

Rodrigo Cardoso Rabelo, DVM, PhD[a,*],
Helio Autran de Morais, DVM, PhD[b]

KEYWORDS

• Metabolic alkalosis • Bicarbonate • Hypochloremia • Base deficit
• Acid-base disorders • Hypoalbuminemia

KEY POINTS

- *Metabolic alkalosis is underdiagnosed in small animal practice*. It is characterized by an increase in bicarbonate (HCO_3^-) concentration, elevated base excess (BE), and compensatory hypoventilation (increased P_{CO_2}).
- *Hypochloremic alkalosis is the most common form of metabolic alkalosis, typically resulting from gastrointestinal losses or diuretic therapy*. Hypoalbuminemia can also lead to metabolic alkalosis.
- *Management of metabolic alkalosis focuses on correcting volume depletion, restoring chloride and potassium concentrations, and addressing the underlying cause.*

INTRODUCTION

- Metabolic alkalosis is a process leading to increase in pH and is characterized by an increase in *serum bicarbonate (HCO_3^-) concentration* and *base excess (BE)* with a compensatory *elevation of arterial carbon dioxide tension ($Paco_2$)* (**Fig. 1**).
- There is a compensatory hypoventilation that increases P_{CO_2} and minimizes the change in pH:
  - In dogs, for each 1 mEq/L increase in HCO_3^-, P_{CO_2} increases by 0.7 mm Hg.
  - Respiratory compensation for metabolic alkalosis is similar in cats.
- In *small animal practice*, metabolic alkalosis is commonly associated with:
  - Hypochloremia
    - Decrease in chloride in relation to sodium in patients with vomiting of stomach content or receiving loop diuretics.

[a] Department of Emergency and Critical Care, Intensivet Veterinary Consulting; [b] Department of Clinical Sciences, Oregon State University, Carlson College of Veterinary Medicine, Corvallis, OR, USA
* Corresponding author. Intesivet, SHIS QI 23, Comércio Local, Ed. Fashion Loja 7, Lago Sul, Brasília, DF 71660-800, Brazil.
E-mail address: rodrigo.rabelo@intensivet.com.br

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Abbreviations	
BE	base excess
SID	strong ion difference

- Recently, hypochloremic metabolic alkalosis has been identified on a subset of cats with chronic kidney disease.[1,2]
  - Retention of more sodium than chloride in patients with increased mineralocorticoid activity. This type of hypochloremic alkalosis cannot be corrected with chloride administration (so-called chloride-resistant metabolic alkalosis).
- Hypoalbuminemia
  - Hypoalbuminemia can cause metabolic alkalosis because albumin is a weak acid.
  - In vitro, a 1 g/dL decrease in albumin concentration is associated with an increase in pH of 0.093 in cats and 0.047 in dogs.[3–6]
  - Treatment for hypoalbuminemic alkalosis should be directed at the underlying disease leading to hypoalbuminemia and restoring colloid oncotic pressure.

ANALYSIS

- Indications: Measurement of BE and HCO_3^- concentration is useful in severely ill pets at risk of developing alkalosis (eg, vomiting) or in animals that have a condition known to be associated with metabolic alkalosis or an increase in total carbon dioxide (total CO_2) concentration.
  - A blood gas analysis is necessary to determine if the high total CO_2 is caused by a metabolic alkalosis or a compensation for respiratory acidosis.

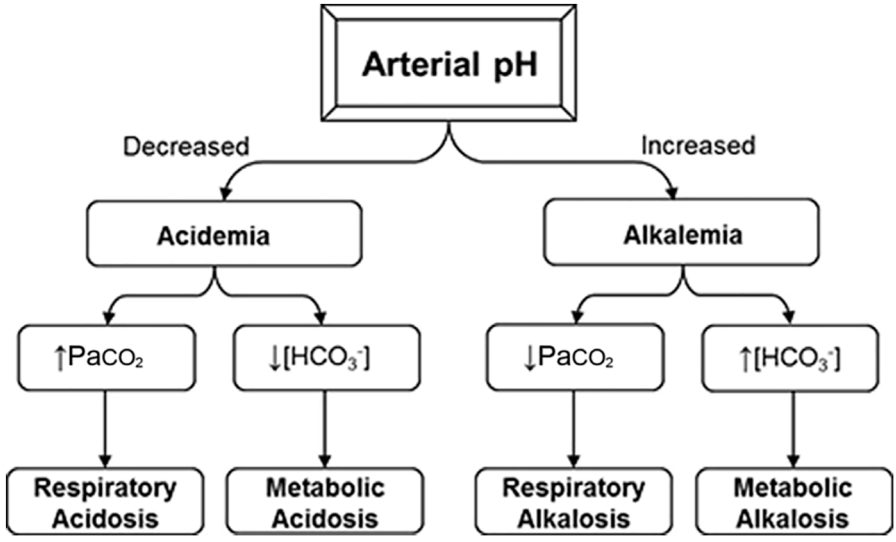


Fig. 1. Algorithm for evaluation of patients with acid-base disorders. *From*[7] Foy DS, de Morais HA. A quick reference on metabolic alkalosis. Vet Clin North Am Small Anim Pract 2017;47(2):198.

- Typical reference range: Normal HCO_3^- concentration is approximately 19 to 23 mEq/L in dogs and 17 to 21 mEq/L in cats.
  - Normal BE is approximately 0 to -5 in dogs and cats; these values may vary among laboratories and analyzers.
  - Total CO_2 is almost synonymous with HCO_3^- in samples handled anaerobically.
- Danger values: pH greater than 7.6 indicates a severe metabolic alkalosis.
- Artifacts: HCO_3^- concentration is calculated in blood gas machines based on pH and P_{CO_2}.
  - Artifacts that interfere with P_{CO_2} or pH affect the estimation of HCO_3^- concentration because HCO_3^- is not measured in most machines. It is calculated based on the measured pH and HCO_3^- concentration.
- Drug effects: Sodium bicarbonate, potassium acetate, citrate or gluconate, and loop diuretics can cause metabolic alkalosis.

METABOLIC ALKALOSIS

- Metabolic alkalosis can result from increase in the strong ion difference (SID) or decrease in nonvolatile weak acids, mainly albumin. SID is the difference between all strong cations and strong anions in blood, usually simplified as SID = $[Na^+] + [K^+] - [Cl^-]$.
- Causes: Metabolic alkalosis can result from the following (**Box 1**):
  - Increase in SID

Box 1
Principal causes of metabolic alkalosis

SID alkalosis

Concentration alkalosis (recognized by # $[Na^+]$)
- Pure water loss
  - Water deprivation
- Hypotonic fluid loss
  - Vomiting
  - Diarrhea

Hypochloremic alkalosis (recognized by ↑ corrected $[CL^-]$)
- Vomiting of stomach content[a]
- Diuretic administration (loop diuretics and thiazides)[a]
- $NaHCO_3$ administration
- Chronic kidney failure in cats

Chloride-resistant hypochloremic alkalosis
- Hyperadrenocorticism
- Hyperaldosteronism

Miscellaneous
- Marked potassium deficiency

Nonvolatile ion buffer alkalosis
- Hypoalbuminemic alkalosis
  - Liver failure
  - Protein-losing nephropathy
  - Protein-losing enteropathy

[a]Most important causes in small animal practice.

Modified from[7] Foy DS, de Morais HA. A quick reference on metabolic alkalosis. Vet Clin North Am Small Anim Pract 2017;47(2):198.

- Concentration alkalosis:
  - Decrease in free water, recognized by an increase in sodium and chloride concentration with corrected chloride within reference range.
- Hypochloremic alkalosis:
  - Decrease in corrected chloride concentration.
  - Most common mechanism for metabolic alkalosis in dogs and cats.
  - Usually caused by vomiting of stomach contents or diuretic administration. In cats, it can also occur in patients with chronic kidney disease without vomiting.
- Chloride-resistant alkalosis is a particular kind of SID alkalosis that does not respond to chloride administration.
  - It is secondary to increased mineralocorticoid activity.
  - Metabolic alkalosis is usually mild, and SID is increased because of a mild increase in sodium associated with a mild decrease in chloride concentrations.
  - Rare in dogs and cats.

○ Decrease in nonvolatile weak acids
- Hypoalbuminemic alkalosis
  - Albumin is the only weak acid in a concentration high enough that can raise blood pH when its concentration is decreased.
  - Hypoalbuminemia is an often-overlooked cause of metabolic alkalosis.

- Signs
  - ○ Mild cases are usually asymptomatic or have signs associated with the underlying disease.
  - ○ Patients with *severe alkalemia (pH >7.60) may have muscle twitching or show neurologic signs (altered mentation, seizures). Cardiac arrhythmias can also occur, especially in patients with hypokalemia.*
- *Electrolyte changes*
  - ○ Hypokalemia
    - Alkalosis drives K^+ into cells and increases renal K^+ loss via aldosterone.
    - Hypokalemia can perpetuate alkalosis by enhancing renal ammoniagenesis and H^+ excretion.
  - ○ Hypochloremia
    - Primary decrease in chloride is the hallmark of *hypochloremic alkalosis.* Low Cl^- impairs bicarbonate excretion, sustaining the alkalosis.
  - ○ Hypophosphatemia
    - Alkalosis promotes renal phosphate loss and intracellular shifting, lowering serum phosphate concentration.
  - ○ Ionized hypocalcemia
    - Alkalosis increases calcium binding to albumin, reducing ionized calcium despite normal total calcium concentration.
- Stepwise approach: An algorithm for the differential diagnosis of metabolic alkalosis is presented in **Fig. 2**.

MANAGEMENT OF METABOLIC ALKALOSIS

- The primary treatment for metabolic alkalosis involves identifying and addressing the underlying cause, correcting fluid and electrolyte imbalances, and restoring acid-base homeostasis.
- A stepwise approach for treatment is presented in **Box 2**.
- Management should be tailored based on whether the alkalosis is chloride-responsive or chloride-resistant.

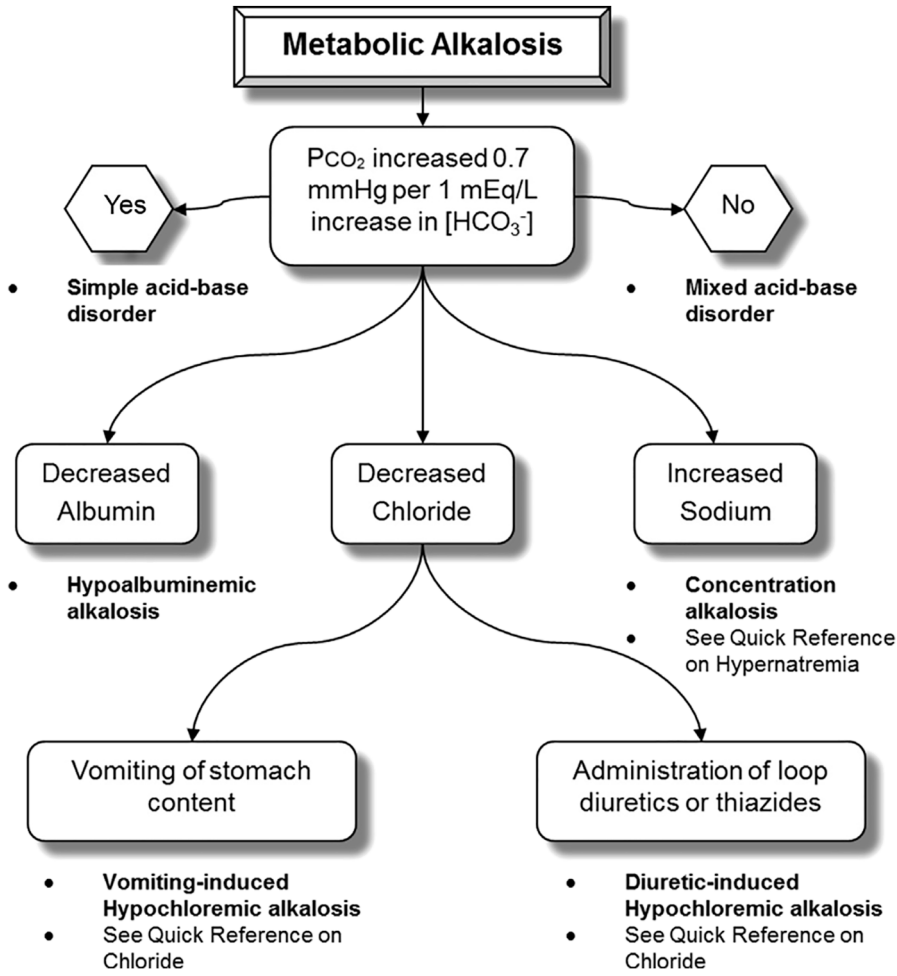


Fig. 2. Algorithm for evaluation of patients with metabolic alkalosis. *From*[7] Foy DS, de Morais HA. A quick reference on metabolic alkalosis. Vet Clin North Am Small Anim Pract 2017;47(2):199.

Box 2
Therapeutic approach for patients with metabolic alkalosis

1. Confirm metabolic alkalosis via blood gas analysis (↑ pH, ↑ HCO_3^-, compensatory ↑ $Paco_2$).
2. Determine if chloride-responsive or chloride-resistant:
   - Chloride-responsive: Treat with 0.9% NaCl + KCl as needed
   - Chloride-resistant: Adress the underlying disease
3. Correct abnormalities in potassium and ionized calcium concentration
4. Identify and treat the underlying cause (eg, vomiting, diuretics, endocrine disorders, renal disease)
5. Monitor response and adjust treatment accordingly

- Therapeutic strategies involve:
  - Fluid therapy for volume expansion.
  - Correction of electrolyte abnormalities (chloride, potassium, calcium).
  - Treatment of the underlying problems.
  - Targeted pharmacologic interventions for severe or refractory cases:
    - Acetazolamide
      - Mechanism: Promotes bicarbonate excretion in urine by inhibiting renal carbonic anhydrase.
      - Indication: Chloride-resistant alkalosis in volume overloaded patients.
    - Spironolactone
      - Mechanism: Blocks the renal mineralocorticoid receptor decreasing distal aldosterone-mediated sodium reabsorption and renal hydrogen loss.
      - Indication: Metabolic alkalosis secondary to hyperaldosteronism.
- Monitoring Therapy and Supportive Care.

KEY TAKEAWAYS FOR TREATMENT

- Fluid therapy is the first-line treatment, with 0.9% NaCl the preferred fluid for chloride-responsive hypochloremic alkalosis.
- Hypoalbuminemic alkalosis is usually mild and treatment is directed at the underlying disease leading to hypoalbuminemia and restoring colloid oncotic pressure.
- Correction of hypokalemia, hypochloremia, and ionized hypocalcemia are crucial to restoring acid-base homeostasis and preventing complications.
- Acetazolamide and spironolactone can be used in resistant cases but require careful monitoring.

DISCLOSURE

The authors have nothing to disclose.

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