Chapter 19
Approach to Metabolic Alkalosis in the ICU

19.1 Introduction

Metabolic alkalosis is a condition characterized by an increase in blood pH due to an excess of bicarbonate (HCO_3^-) or a loss of hydrogen ions (H^+). It involves two phases: the generation phase, where the initial disturbance occurs, and the maintenance phase, where the alkalosis is sustained. The generation phase often results from a loss of acid via gastrointestinal (GI) or renal routes or an excessive gain of bicarbonate, while the maintenance phase is typically due to impaired renal excretion of bicarbonate.

Sustained metabolic alkalosis usually requires both a generating factor and a maintenance factor. The kidneys play a crucial role in excreting excess bicarbonate; thus, impaired renal function or factors that reduce bicarbonate excretion are essential in maintaining alkalosis. Severe metabolic alkalosis is associated with significant mortality risks. Studies have shown that mortality increases markedly when the arterial pH exceeds 7.55, reaching as high as 80% with pH levels above 7.65. This underscores the critical nature of timely diagnosis and intervention [1] [Ref: Algorithm 19.1].

19.2 Pathophysiology

19.2.1 Generation Phase

- Loss of Acid: Common causes include vomiting or nasogastric suction, leading to the loss of gastric hydrochloric acid (HCl). Renal losses can occur due to diuretic use, which increases the excretion of sodium and chloride, indirectly causing bicarbonate retention.

S. B. Mishra et al., *Mastering ICU Care*,
https://doi.org/10.1007/978-981-95-0179-3_19

- Gain of Bicarbonate: Excessive ingestion of bicarbonate or antacids, often seen in conditions like milk-alkali syndrome, can elevate serum bicarbonate levels [2].

19.2.2 Maintenance Phase

- Impaired Bicarbonate Excretion: The kidneys are central to maintaining acid-base balance. Under normal circumstances, the kidneys can excrete excess bicarbonate to correct alkalosis. However, factors such as volume depletion, hypokalemia, and decreased chloride availability impair the kidney's ability to excrete bicarbonate, thus maintaining the alkalosis.

19.2.3 Role of Chloride Depletion

Chloride depletion plays a pivotal role in driving metabolic alkalosis, often referred to as "chloride depletion alkalosis." In conditions like vomiting, diuretic use, or Bartter and Gitelman syndromes, there is a significant loss of chloride. Chloride is essential for bicarbonate excretion in the distal nephron; its depletion impairs the kidney's ability to excrete bicarbonate, thereby maintaining alkalosis [3].

19.2.4 Role of Potassium Depletion

Potassium depletion exacerbates metabolic alkalosis by several mechanisms:

- Increased Hydrogen Ion Secretion: Hypokalemia stimulates the renal secretion of hydrogen ions to conserve potassium, leading to increased bicarbonate reabsorption.
- Enhanced Ammonia (NH_3) Generation: Hypokalemia increases renal ammonia production, which combines with secreted hydrogen ions to form ammonium (NH_4^+), facilitating further acid loss.

19.3 Renal Mechanisms in Acid-Base Regulation

- Proximal Tubule: The Na^+-H^+ exchanger plays a significant role in bicarbonate reabsorption. Hydrogen ions are secreted in exchange for sodium, facilitating the reabsorption of filtered bicarbonate.

- Collecting Ducts: In the distal nephron, specifically the alpha-intercalated cells, hydrogen ions are secreted via H^+-ATPase and H^+-K^+-ATPase pumps. This secretion is vital for acid excretion and bicarbonate reabsorption.
- Distal Nephron Segments: Both bicarbonate reabsorption and secretion occur here, and their regulation is crucial in the maintenance phase of metabolic alkalosis [4].

19.4 Diagnostic Approach

1. **Confirm Compensation**
   - Arterial Blood Gases (ABG): Review ABG to assess respiratory compensation. In metabolic alkalosis, the body hypoventilates to retain CO_2, which combines with water to form carbonic acid, partially offsetting the alkalosis. Assessing compensation ensures that concurrent acid-base disorders are not overlooked [5].
2. **Evaluate Clinical History**
   - Vomiting or Nasogastric Suction: Indicates loss of gastric acid.
   - Diuretic Use: Loop and thiazide diuretics cause loss of sodium and chloride.
   - Recent Surgery: May cause fluid shifts and electrolyte imbalances.
   - Mineralocorticoid Excess: Conditions like hyperaldosteronism increase sodium retention and potassium loss.
3. **Serum Calcium Assessment**
   - Serum Calcium >14 mg/dL (3.5 mmol/L): Suggests milk-alkali syndrome or hypercalcemia of malignancy, both of which can contribute to metabolic alkalosis.
4. **Assess Chloride Responsiveness via Urine Chloride**
   - Urine Chloride <10 mmol/L: Indicates chloride-responsive metabolic alkalosis, commonly due to volume depletion from vomiting or diuretic use. The low urine chloride reflects the kidneys' attempt to conserve chloride.
   - Management: Administration of isotonic saline replenishes chloride and volume, allowing the kidneys to excrete excess bicarbonate.
   - Urine Chloride >30 mmol/L: Suggests chloride-resistant metabolic alkalosis, often due to mineralocorticoid excess or severe potassium depletion.
5. **Assess Potassium Status**
   - Hypokalemia: Further exacerbates alkalosis and is common in both chloride-responsive and resistant forms. Measurement of serum and urine potassium can help in identifying the cause.

6. **Blood Pressure Measurement**

- Low or Normal Blood Pressure:
  - Bartter Syndrome: Characterized by hypokalemia, metabolic alkalosis, normal to low blood pressure, and high urinary calcium excretion.
  - Gitelman Syndrome: Similar to Bartter syndrome but with low urinary calcium excretion.
- High Blood Pressure:
  - Mineralocorticoid Excess: Conditions like primary hyperaldosteronism cause sodium retention (leading to hypertension), potassium loss, and metabolic alkalosis.

19.5 Mortality Risks

Severe metabolic alkalosis is associated with increased mortality rates. An arterial pH greater than 7.55 significantly elevates the risk of cardiac arrhythmias, neuromuscular instability, and decreased cerebral blood flow. Mortality rates can reach up to 80% when pH exceeds 7.65, emphasizing the urgency of prompt diagnosis and management [6].

19.6 Treatment Modalities

Address Underlying Causes
- Vomiting: Use antiemetics to control nausea and vomiting.
- Diuretic Use: Discontinue or adjust dosage under medical supervision.
- Mineralocorticoid Excess: Treat underlying endocrine disorders.

Chloride Repletion
- Intravenous Saline Infusion: Restores volume and chloride levels in chloride-responsive alkalosis, promoting renal bicarbonate excretion.

Potassium Repletion
- Oral or Intravenous Potassium Chloride: Corrects hypokalemia, reduces renal hydrogen ion secretion, and aids in correcting alkalosis.

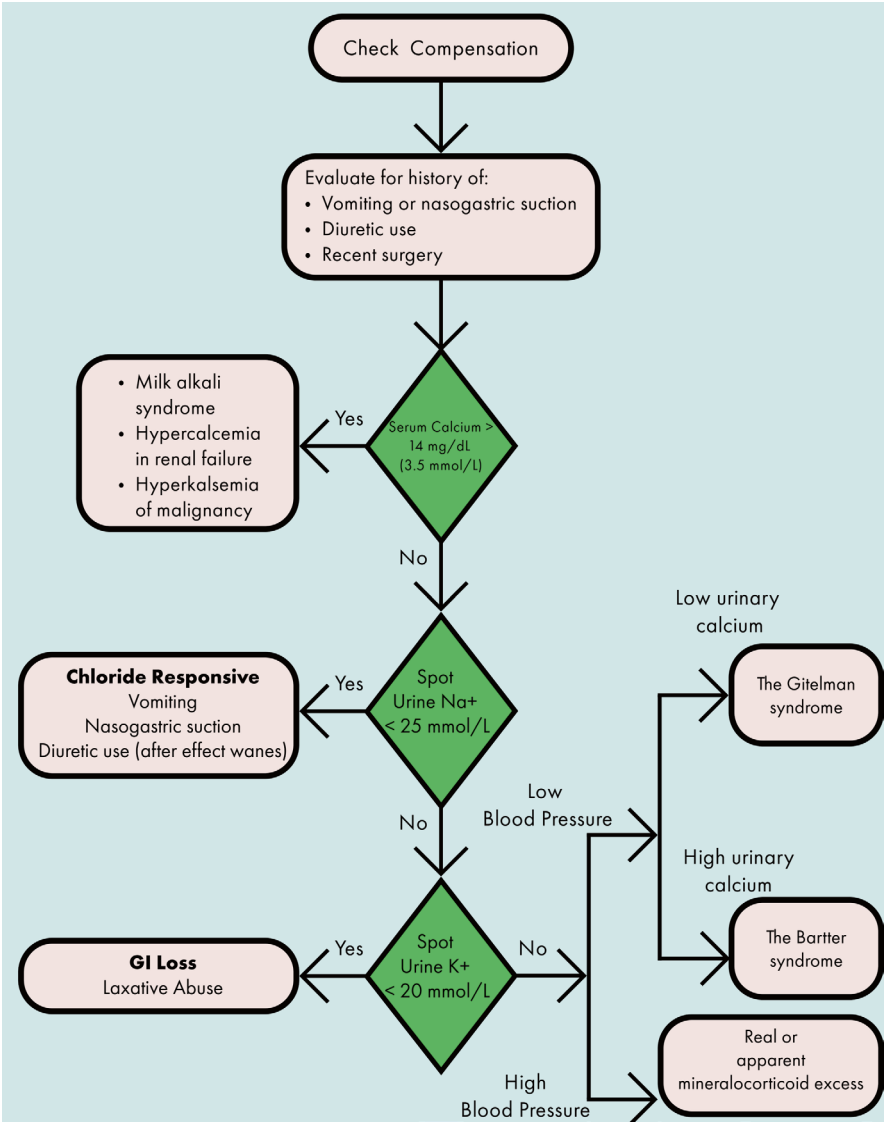
Acetazolamide
- Carbonic Anhydrase Inhibitor: Promotes renal bicarbonate excretion by inhibiting bicarbonate reabsorption in the proximal tubule. Useful in patients who cannot tolerate volume repletion.

Supportive Care
- Monitor Electrolytes and ABGs: Regular monitoring to guide therapy.
- Dialysis: In severe cases or when conservative measures fail, especially in patients with renal failure.

19.7 Conclusion

Effective management of metabolic alkalosis requires a systematic approach that includes understanding the pathophysiological mechanisms, accurately diagnosing the underlying cause, and implementing appropriate treatment strategies. Recognizing the roles of chloride and potassium depletion, renal function, and hormonal imbalances is crucial. Prompt intervention not only corrects the biochemical abnormalities but also reduces the associated mortality risks.

Algorithm 19.1: Approach to metabolic alkalosis in the ICU



Bibliography

1. Do C, Vasquez PC, Soleimani M. Metabolic alkalosis pathogenesis, diagnosis, and treatment: core curriculum 2022. Am J Kidney Dis. 2022;80(4):536–51.
2. Emmett M. Metabolic alkalosis: a brief pathophysiologic review. Clin J Am Soc Nephrol. 2020;15(12):1848–56.
3. Gennari FJ. Pathophysiology of metabolic alkalosis: a new classification based on the centrality of stimulated collecting duct ion transport. Am J Kidney Dis. 2011;58(4):626–36.
4. Pahari DK, Kazmi W, Raman G, Biswas S. Diagnosis and management of metabolic alkalosis. J Indian Med Assoc. 2006;104(11):630–4, 6.
5. Tinawi M. Pathophysiology, evaluation, and management of metabolic alkalosis. Cureus. 2021;13(1):e12841.
6. Soifer JT, Kim HT. Approach to metabolic alkalosis. Emerg Med Clin North Am. 2014;32(2):453–63.