Chapter 29
Approach to Hyperphosphatemia in the ICU

29.1 Introduction

Hyperphosphatemia, an elevated level of phosphate in the blood, is a common electrolyte disturbance in critically ill patients. It can result from various underlying conditions such as renal failure, tumor lysis syndrome, or rhabdomyolysis, and may lead to significant complications if not managed appropriately. Phosphate homeostasis is tightly regulated by a complex interplay of hormones, including parathyroid hormone (PTH), fibroblast growth factor 23 (FGF-23), and 1,25-dihydroxyvitamin D (calcitriol). These hormones regulate calcium and phosphate levels through feedback mechanisms involving the kidneys, bones, and intestines. Understanding these physiological mechanisms is essential for effective management of hyperphosphatemia, particularly in patients with chronic kidney disease (CKD), where FGF-23 plays a crucial role in phosphate excretion [1] [Ref: Algorithm 29.1].

1. **Assess Severity**
   - Serum Phosphate Measurement: The first step in managing hyperphosphatemia is to assess the severity of the condition by measuring serum phosphate levels. Based on the results, hyperphosphatemia can be categorized as:
   - Mild: Serum phosphate levels between 4.5 and 5.6 mg/dL.
   - Moderate: Serum phosphate levels between 5.6 and 7.8 mg/dL.
   - Severe: Serum phosphate levels greater than 7.8 mg/dL.
2. **Mild Hyperphosphatemia (4.5–5.6 mg/dL)**

   Intervention:
   - Dietary Phosphate Restriction: Advise patients to reduce their intake of phosphate-rich foods, such as dairy products, nuts, and certain meats.

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- Discontinue Phosphate-Containing Medications: Substitute medications containing phosphate with alternatives that do not contribute to the phosphate load.

Rationale:

- Controlling the intake and absorption of phosphate is often sufficient to prevent further elevation of serum phosphate levels and maintain them within the normal range.

3. **Moderate Hyperphosphatemia (5.6–7.8 mg/dL)**

Intervention:

- Phosphate Binders: Administer phosphate binders such as calcium carbonate, calcium acetate, or sevelamer to reduce serum phosphate levels by binding dietary phosphate in the gastrointestinal tract and preventing its absorption.
- Intravenous (IV) Fluids and Diuretics: Use IV fluids and diuretics to promote renal excretion of phosphate.

Rationale:

- More aggressive management is required to prevent progression to severe hyperphosphatemia, which can lead to complications like calcium-phosphate precipitation and vascular calcification.

4. **Severe Hyperphosphatemia (> 7.8 mg/dL).**

Intervention:

- Phosphate Binders: Continue the use of phosphate binders to reduce phosphate absorption.
- IV Fluids and Diuretics: Maintain IV fluids and diuretics to enhance phosphate excretion.
- Dialysis: Initiate dialysis if serum phosphate levels are critically high and unresponsive to other interventions, to rapidly reduce phosphate levels.

Rationale:

- Severe hyperphosphatemia is a medical emergency requiring prompt intervention to prevent life-threatening complications such as cardiac arrhythmias or tissue calcifications.

5. **Identify Potential Causes of Hyperphosphatemia**

After initiating treatment based on the severity of hyperphosphatemia, it is crucial to identify and address the underlying cause(s) to prevent recurrence and tailor long-term management strategies effectively. Hyperphosphatemia can result from various etiologies, including decreased renal excretion, increased intake, cellular release, and pseudohyperphosphatemia. Understanding the underlying mechanisms of each cause is vital for effective management.

A. **Decreased Renal Excretion**

Chronic Kidney Disease (CKD) and Acute Kidney Injury (AKI):

- Mechanism: The kidneys are central in maintaining phosphate homeostasis by filtering and excreting excess phosphate. In CKD and AKI, impaired renal function leads to phosphate retention.

Pathophysiology:

- FGF-23 Role: Elevated phosphate levels stimulate the secretion of FGF-23 from osteocytes. FGF-23 increases renal phosphate excretion by reducing sodium-phosphate co-transporters in the renal proximal tubules.
- PTH Interaction: PTH is also elevated in response to hyperphosphatemia and hypocalcemia, promoting phosphate excretion and calcium reabsorption.
- Vitamin D Suppression: FGF-23 suppresses 1,25-dihydroxyvitamin D synthesis, leading to decreased intestinal absorption of calcium and phosphate.
- Feedback Loops: Despite elevated FGF-23 and PTH, the declining GFR in CKD limits phosphate excretion, leading to persistent hyperphosphatemia.
- Clinical Implications: Hyperphosphatemia contributes to secondary hyperparathyroidism and vascular calcification, increasing morbidity and mortality in CKD patients.

B. **Tumor Lysis Syndrome (TLS)**

Mechanism:

Cellular Release: TLS results from the massive lysis of tumor cells, releasing intracellular phosphate into the bloodstream.

- Renal Overload: The acute phosphate load overwhelms renal excretion capacity, especially in patients with preexisting renal impairment.

C. **Rhabdomyolysis**

Mechanism:

- Muscle Breakdown: Destruction of muscle tissue releases phosphate and other intracellular ions into the circulation.
- AKI Association: The released myoglobin can cause AKI, further impairing phosphate excretion.

D. **Increased Intake**

- Excessive Dietary Phosphate or Phosphate-Containing Medications:
- Mechanism: High intake of phosphate through diet or medications increases serum phosphate levels, particularly dangerous in patients with reduced renal function.

E. **Cellular Release**

- Conditions like Hemolysis or Severe Infection:

- Mechanism: Breakdown of cells releases intracellular phosphate, contributing to elevated serum levels.

F. **Pseudohyperphosphatemia**

- Lab Errors and Conditions Like Hyperlipidemia or Hyperproteinemia:
- Mechanism: Interference from lipids or proteins can falsely elevate phosphate levels in laboratory assays.

6. **Long-Term Management and the Role of FGF-23**

Understanding the hormonal regulation of phosphate is essential for long-term management, especially in CKD patients.

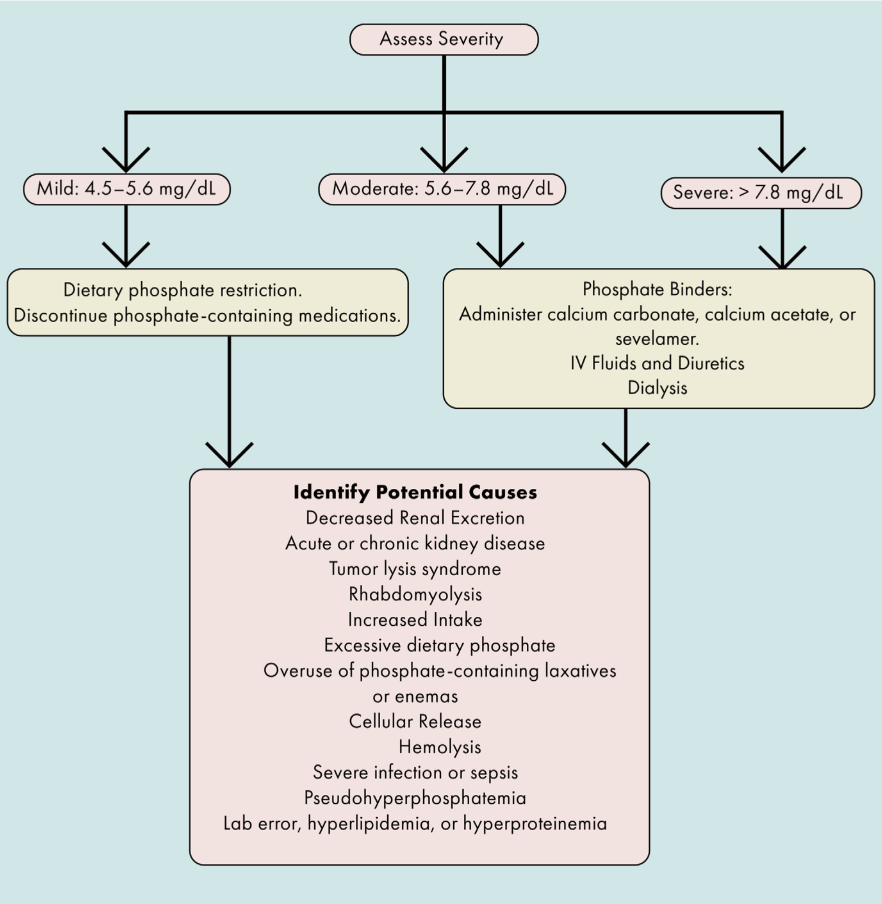
FGF-23 in Chronic Management
- Central Role: FGF-23 is crucial in regulating phosphate homeostasis by increasing renal excretion and decreasing intestinal absorption.
- CKD Implications: In CKD, elevated FGF-23 levels are a response to hyperphosphatemia but may lead to left ventricular hypertrophy and increased cardiovascular risk.
- Interplay with PTH and Vitamin D:
- PTH: Elevated phosphate and reduced calcium stimulate PTH secretion, leading to secondary hyperparathyroidism.
- Vitamin D: Suppressed 1,25-dihydroxyvitamin D levels reduce calcium absorption, exacerbating hypocalcemia.

Management Strategies
- Phosphate Binders: Long-term use helps control serum phosphate, reducing the stimulus for FGF-23 and PTH secretion.
- Vitamin D Analogues: Supplementation can suppress PTH levels and improve calcium absorption.
- Dietary Restrictions: Limiting phosphate intake reduces the burden on renal excretion mechanisms.
- Monitoring FGF-23 Levels: May provide insights into disease progression and guide therapy adjustments.

29.2 Conclusion

Effective management of hyperphosphatemia requires a comprehensive understanding of the physiological mechanisms regulating phosphate homeostasis, particularly the roles of FGF-23, PTH, and vitamin D. Assessing the severity of phosphate elevation and implementing appropriate interventions are essential steps. Addressing underlying causes, especially in CKD and AKI, is crucial for long-term management and preventing recurrence. Integrating knowledge of hormonal feedback loops and renal handling of phosphate enhances treatment strategies, ultimately improving patient outcomes.

Algorithm 29.1 Approach to hyperphosphatemia in the ICU



Bibliography

1. Murray SL, Wolf M. Calcium and phosphate disorders: core curriculum 2024. Am J Kidney Dis. 2024;83(2):241–56.