Chapter 26
Approach to Hypocalcemia in the ICU

26.1 Introduction

Hypocalcemia, defined as an abnormally low level of calcium in the blood, is a critical condition that can have serious consequences if not managed promptly and effectively. Calcium plays a vital role in various physiological processes, including muscle contraction, nerve function, blood clotting, and cardiac rhythm regulation. The management of hypocalcemia in an intensive care setting requires a systematic approach, beginning with the confirmation of the condition and continuing through appropriate treatment based on the severity of symptoms and laboratory findings [1] [Ref: Algorithm 26.1].

1. **Initial Assessment**

   - **Confirm True Hypocalcemia**

     Begin by confirming hypocalcemia through laboratory tests. Total serum calcium levels can be affected by albumin levels and blood pH, so it is essential to adjust the calcium level for serum albumin and consider the effects of acid-base status on calcium binding.

   - Correcting for Albumin: Calcium binds to albumin; thus, hypoalbuminemia can lead to a falsely low total calcium level while ionized calcium remains normal. The corrected calcium can be calculated using the formula:

     $$\text{Corrected Calcium}\left(\text{mg/dL}\right) = \text{Measured Total Calcium} + \left[0.8 \times \left(4.0 - \text{Serum Albumin}\left(\text{g/dL}\right)\right)\right]$$

   - Effects of Blood pH: Alkalemia increases calcium binding to albumin, decreasing ionized calcium levels, while acidemia decreases binding, increasing ionized calcium levels. In ICU patients with frequent acid-base

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disturbances, these shifts can significantly impact ionized calcium levels, which is the biologically active form.

- **Measure Ionized Calcium**

  If available, measure ionized calcium directly, as it is the most accurate marker of biologically active calcium, especially in critically ill patients where albumin levels and pH can be significantly altered. Ionized calcium measurement is superior to total calcium in assessing true calcium status under these conditions [2].

2. **Clinical Manifestations**

After confirming hypocalcemia, assess the severity based on clinical manifestations and the measured calcium level.

A. **Mild Hypocalcemia (Calcium Level 7.5–8.5 mg/dL)**

- Symptoms: Patients may be asymptomatic or present with mild symptoms, such as:
- Paresthesias, particularly tingling around the mouth, hands, and feet.
- Muscle cramps or mild muscle stiffness.
- Fatigue, anxiety, or mild prolongation of the QT interval on an EKG.
- Management:
- Oral Calcium and Vitamin D Supplementation: First-line treatments to correct calcium levels.
- Correct Magnesium Levels: Magnesium deficiency can impair PTH secretion and calcium absorption; correct if deficient.
- Monitor Cardiac Rhythm: Even in mild cases, monitor for changes in cardiac rhythm due to potential QT prolongation.

B. **Moderate Hypocalcemia (Calcium Level 6.0–7.5 mg/dL)**

- Symptoms: More pronounced symptoms, including:
- Intensified paresthesias.
- Muscle spasms, particularly in the hands and feet (carpopedal spasm).
- Positive Trousseau's sign (hand spasm induced by inflating a blood pressure cuff).
- Positive Chvostek's sign (twitching of facial muscles when tapped).
- More noticeable QT interval prolongation on EKG.
- Psychological symptoms like irritability, confusion, or mood changes.
- Management:
- Higher Doses of Oral Calcium and Vitamin D: May be required to restore calcium levels.
- Ensure Adequate Magnesium Levels: Correct any deficiencies.
- Cardiac Monitoring: Monitor EKG for arrhythmias due to QT prolongation.

C. **Severe Hypocalcemia (Calcium Level <6.0 mg/dL or Ionized Calcium <1.0 mmol/L)**

- Symptoms: Severe hypocalcemia is a medical emergency characterized by:
- Neuromuscular: Tetany (severe, involuntary muscle contractions), seizures, laryngospasm leading to respiratory distress.
- Cardiac: Significant prolongation of the QT interval, potentially leading to life-threatening arrhythmias like Torsades de Pointes, heart failure, or hypotension.
- Neuropsychiatric: Severe irritability, psychosis, or altered mental status.
- Management:
- IV Calcium Administration:
- Calcium Gluconate: Preferred for peripheral IV administration due to lower risk of tissue necrosis if extravasation occurs. Administer 1–2 g (10–20 mL of 10% solution) over 10–20 min.
- Calcium Chloride: Contains three times more elemental calcium than calcium gluconate but poses a higher risk of tissue injury with extravasation. Reserved for central line administration in severe cases.
- Continuous Infusion: May be necessary for persistent symptoms or critically low calcium levels. Prepare an infusion of calcium gluconate diluted in 1000 mL of D5W, administered at a rate adjusted based on serial ionized calcium measurements.
- Correct Magnesium Levels: Essential to correct any concurrent magnesium deficiency to ensure effective treatment.
- Continuous Cardiac Monitoring: Due to the risk of arrhythmias, patients require close cardiac monitoring in an ICU setting.

3. **Diagnostic Evaluation**

After initial management, identify the underlying cause of hypocalcemia to guide long-term treatment.

1. **Measure Serum Parathyroid Hormone (PTH)**

A. **Low Parathyroid Hormone Levels (Hypoparathyroidism)**
Hypoparathyroidism occurs when there is insufficient production or action of PTH, leading to impaired regulation of calcium levels.

- Parathyroid Agenesis:
- Isolated: Congenital absence of parathyroid glands.
- DiGeorge's Syndrome: Genetic disorder with thymic aplasia/hypoplasia and absent or underdeveloped parathyroid glands.
- Parathyroid Destruction:
- Surgical: Accidental removal or damage during thyroid or neck surgeries.
- Radiation: Damage from neck radiation therapy.

- Infiltration: Metastases or systemic diseases like sarcoidosis infiltrating the glands.
- Autoimmune: Autoimmune destruction of parathyroid tissue.
- Reduced Parathyroid Function:
- Hypomagnesemia: Low magnesium impairs PTH secretion and action.
- Autosomal Dominant Hypocalcemia: Activating mutations in the calcium-sensing receptor suppress PTH secretion despite low calcium levels.

B. **High Parathyroid Hormone Levels (Secondary Hyperparathyroidism)**
Elevated PTH in response to low calcium levels, often due to impaired calcium absorption or metabolism.

- Vitamin D Deficiency or Impaired Production/Action:
- Nutritional Deficiency: Poor intake or limited sunlight exposure.
- Renal Insufficiency: Impaired conversion to active 1,25-dihydroxyvitamin D.
- Vitamin D Resistance: Genetic defects in the vitamin D receptor.
- Parathyroid Hormone Resistance Syndromes:
- PTH Receptor Mutations: Resistance to PTH action.
- Pseudohypoparathyroidism: Genetic defect in the PTH signaling pathway.
- Drugs:
- Calcium Chelators: Citrate (in blood transfusions), EDTA.
- Inhibitors of Bone Resorption: Bisphosphonates, plicamycin.
- Altered Vitamin D Metabolism: Phenytoin, ketoconazole.
- Miscellaneous Causes:
- Acute Pancreatitis: Saponification binds calcium.
- Acute Rhabdomyolysis: Phosphate release precipitates calcium.
- Hungry Bone Syndrome: Post-parathyroidectomy increased bone uptake.
- Osteoblastic Metastases: Increased bone formation traps calcium.

2. **Measure Serum Phosphate**

- Role: Phosphate levels are closely linked to calcium metabolism, regulated by PTH and vitamin D.
- Interpretation:
- Elevated Phosphate Levels: Suggest hypoparathyroidism or renal failure.
- Low Phosphate Levels: May indicate vitamin D deficiency or impaired absorption.

3. **Measure Serum Vitamin D**

- Role: Essential for calcium absorption in the intestines.
- Interpretation:
- Low 25-Hydroxyvitamin D Levels: Indicate vitamin D deficiency.
- Low 1,25-Dihydroxyvitamin D Levels: Seen in renal insufficiency or vitamin D resistance.

4. **Calcium Reabsorption Mechanisms in the Kidneys**
   Understanding renal calcium handling helps contextualize why renal conditions can exacerbate hypocalcemia.

   - Proximal Tubules: Approximately 65% of filtered calcium is reabsorbed passively via paracellular transport, driven by sodium and water reabsorption.
   - Thick Ascending Limb: About 20% is reabsorbed here, also via paracellular pathways influenced by the lumen-positive voltage gradient.
   - Distal Convoluted Tubules: Fine-tuning of calcium reabsorption occurs here (~10%), regulated by PTH and vitamin D. Active transcellular transport mechanisms are involved [3].

   Renal conditions affecting these processes, such as acute kidney injury or chronic kidney disease, can impair calcium reabsorption, contributing to hypocalcemia.
5. **Detailed Guidelines on IV Calcium Administration**
   Indications for IV Calcium
   - Severe symptomatic hypocalcemia (e.g., tetany, seizures).
   - Critically low ionized calcium levels.
   - Presence of cardiac arrhythmias due to hypocalcemia.
   - In situations where rapid correction is necessary.

   Calcium Preparations

   - Calcium Gluconate:
   - Concentration: 10% solution contains 90 mg elemental calcium per 10 mL.
   - Advantages: Safer for peripheral administration, less irritating to veins.
   - Administration: 1–2 g (10–20 mL) diluted in 50–100 mL of 5% dextrose or normal saline, infused over 10–20 min.
   - Calcium Chloride:
   - Concentration: 10% solution contains 270 mg elemental calcium per 10 mL.
   - Advantages: Higher bioavailability of elemental calcium.
   - Disadvantages: Risk of severe tissue injury with extravasation; should be administered via central line.
   - Administration: 500–1000 mg (5–10 mL) administered cautiously over 10–20 min.

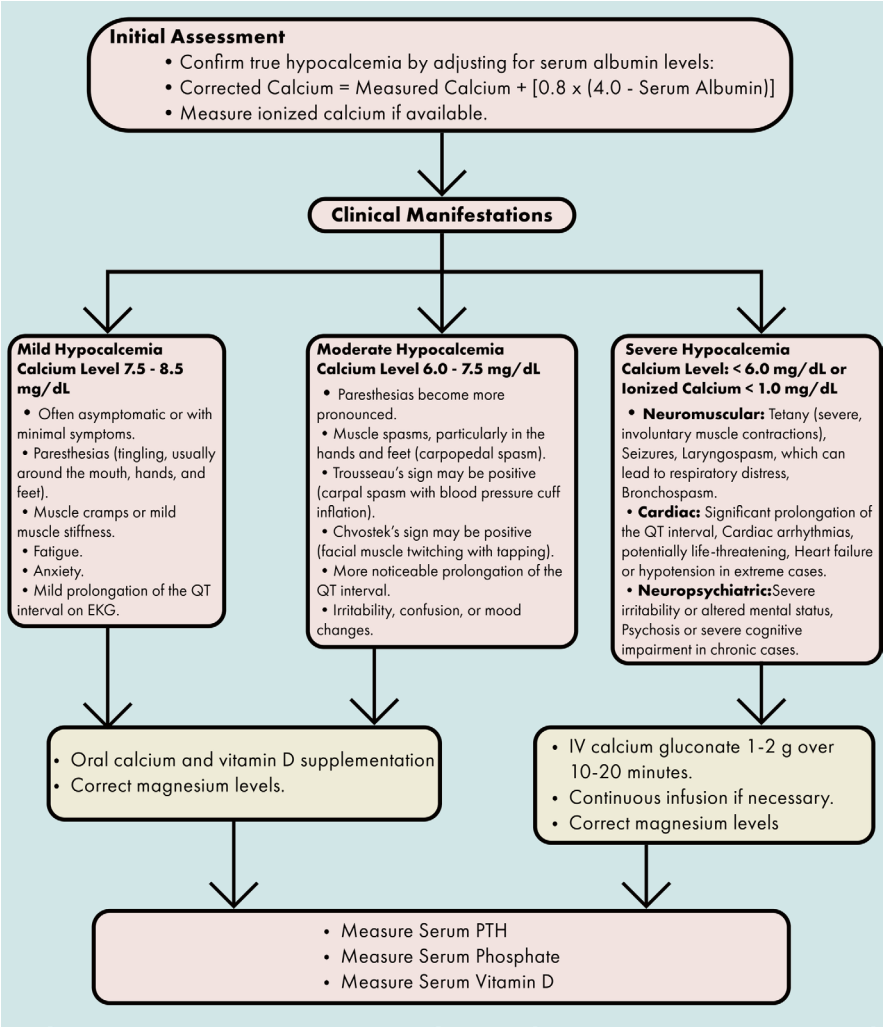
Administration Guidelines
- Monitoring:
- Cardiac Monitoring: Continuous EKG monitoring during administration due to the risk of arrhythmias.
- Serial Calcium Measurements: Check ionized calcium levels every 4–6 h to guide therapy.
- Infusion Rates:
- Bolus Dose: Provides immediate correction; effects last 1–2 h.

- Continuous Infusion: May follow bolus dose; typically 0.5–1.5 mg/kg/h of elemental calcium.
- Precautions:
- Avoid Rapid Administration: Can cause cardiac arrhythmias or vasodilation leading to hypotension.
- Extravasation Risk: Ensure secure IV access to prevent tissue necrosis.
- Drug Interactions: Do not mix with bicarbonate or phosphate-containing solutions to prevent precipitation.

26.2 Conclusion

Managing hypocalcemia in the ICU requires careful assessment and prompt treatment to prevent serious complications. A systematic approach includes confirming true hypocalcemia, understanding the patient's acid-base status, and recognizing the significance of ionized calcium levels. Clinical manifestations guide the urgency and aggressiveness of treatment, with severe cases necessitating immediate IV calcium administration and continuous cardiac monitoring due to the risk of life-threatening arrhythmias. Understanding the underlying mechanisms, including calcium reabsorption in the kidneys and the roles of PTH and vitamin D, is essential for identifying the cause and preventing recurrence. By following this comprehensive approach, healthcare providers can ensure that patients with hypocalcemia receive timely and effective care, optimizing outcomes in the ICU setting.

Algorithm 26.1: Approach to hypocalcemia in the ICU



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