Calcium, Magnesium, and Phosphate Abnormalities in the Emergency Department

Wan-Tsu W. Chang, MD[a], Bethany Radin, DO[b], Michael T. McCurdy, MD[a,b,*]

KEYWORDS

• Hypercalcemia • Hypocalcemia • Hypermagnesemia • Hypomagnesemia
• Hyperphosphatemia • Hypophosphatemia

KEY POINTS

- Disorders of calcium, magnesium, and phosphate are relatively common clinical problems, especially among critically ill patients.
- Because of their crucial role in cellular physiology, particularly for neuromuscular function and cardiac conduction, severe derangements of these minerals can be fatal.
- Understanding the complex physiologic role of these minerals in the human body is essential to promptly identify the problem, initiate appropriate therapy, and provide an adequate disposition.

INTRODUCTION

Disorders of calcium, magnesium, and phosphate are relatively common clinical problems encountered by emergency medicine providers. Because of their crucial role in cellular physiology, particularly for neuromuscular function and cardiac conduction, severe derangements of these minerals can be fatal. Understanding the complex physiologic role of these minerals in the human body is essential to promptly identify the problem, initiate appropriate therapy, and provide an adequate disposition. This article focuses on the physiology and pathophysiology of these mineral disorders.

The authors have nothing to disclose.

[a] Department of Emergency Medicine, University of Maryland School of Medicine, 110 South Paca Street, 6th Floor, Suite 200, Baltimore, MD 21201, USA; [b] Division of Pulmonary and Critical Care Medicine, Department of Medicine, University of Maryland School of Medicine, 110 South Paca Street, 2nd Floor, Baltimore, MD 21201, USA

* Corresponding author. Division of Pulmonary and Critical Care Medicine, Department of Medicine, University of Maryland School of Medicine, 110 South Paca Street, 2nd Floor, Baltimore, MD 21201.

E-mail address: drmccurdy@gmail.com

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EPIDEMIOLOGY

Abnormalities of calcium, magnesium, and phosphate are common in hospitalized patients and are associated with increased morbidity and mortality rates.[1,2] Both acute, severe electrolyte disorders in hospitalized patients as well as chronic, mild electrolyte abnormalities in the general population are associated with adverse outcomes.[3] Risk factors for electrolyte disturbances include older age, diabetes mellitus, renal disease, diuretic use, and malnutrition.[3]

Calcium abnormalities are associated with many pathologic states, most notably malignancy. Twenty percent to 30% of patients with cancer experience hypercalcemia during the course of their disease, and malignancy accounts for more than 30% of emergency department visits for hypercalcemia.[4,5] Conversely, hypocalcemia is found in 88% of patients in intensive care units.[6]

Although approximately 75% of Americans have magnesium-deficient diets, less than 2% of the general population is actually hypomagnesemic.[7] Certain groups, such as people with coronary disease, have a relatively high incidence of this deficiency.[8] Hypomagnesemia, also common in hospitalized and critically ill patients,[9,10] is associated with longer hospitalizations and a higher mortality rate than in those with normal magnesium levels.[11]

Hypophosphatemia is found in up to 5% of hospitalized patients and is particularly prevalent among those with diabetic ketoacidosis, chronic obstructive pulmonary disease, malignancy, malnutrition, and sepsis.[12] Severe deficiency contributes to the mortality rate among these groups.[12,13] Hyperphosphatemia is a risk factor for death among patients with chronic kidney disease as well as among kidney transplant recipients.[1,14,15] The serum phosphate level is associated with cardiovascular risk even in individuals without kidney disease.[16]

NORMAL PHYSIOLOGY

Bone contains almost all of the calcium and phosphate and more than half of the magnesium in the human body. Small amounts of these ions are present in extracellular fluid and intracellular space, and they play important roles in normal physiology. Extracellular calcium is the principal substrate for bone mineralization and a cofactor for many extracellular enzymes. Calcium ions function as signaling molecules for many intracellular processes, including the contraction of cardiac, skeletal, and smooth muscles; neurotransmitter release; and various endocrine and exocrine secretions. Intracellular magnesium is an essential cofactor of enzymatic reactions and stabilizer of DNA, RNA, and ribosomes. Extracellular magnesium is crucial for normal neuromuscular excitability and nerve conduction. Organic phosphate is an integral constituent of nucleic acids; phospholipids; structural, signaling, and enzymatic phosphoproteins; and nucleotide cofactors for enzymes and proteins. Cytosolic phosphate directly regulates intracellular reactions such as those involved in glucose transport, lactate production, and ATP synthesis.

Calcium is the most abundant mineral in the human body. Ninety-nine percent of total body calcium resides in bone, of which 99% is in the mineral phase and 1% is rapidly exchangeable. Approximately half of total serum calcium is bound to proteins, mainly albumin and globulins. The normal ionized calcium concentration in serum is 1.1 to 1.4 mmol/L (4.5–5.6 mg/dL). Intracellularly, 99% of calcium exists in complexes within the mitochondrial compartment, with the cytosolic free calcium concentration being approximately 100 nmol/L. This large extracellular-to-intracellular gradient of calcium is maintained by Ca^{2+}- and H^{+}-ATPases as well as Na^{+}/Ca^{2+} exchangers.[17] Clinically, measuring the total serum calcium concentration usually suffices because it