

Severe Hypophosphatemia in Respiratory Alkalosis

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ABSTRACT

Hypophosphatemia is a potentially life-threatening condition that can occur in many clinical situations. Respiratory alkalosis induced by hyperventilation causes a low serum phosphate level but not true phosphate depletion. Although the measured serum phosphate can be profoundly decreased, phosphate supplementation is typically not necessary. A 36-year-old Caucasian woman presented to the university hospital with tachypnea and hypophosphatemia. She had a tracheal transplant 9 months previously, with several subsequent presentations for symptoms of recurrent tracheal stenosis. Bronchoscopy revealed no recurrent tracheal stenosis. The patient was supported and reassured, and the tachypnea relented. A sodium phosphate intravenous infusion was initiated but was discontinued when the patient's serum phosphate concentration rapidly corrected. Hypophosphatemia from respiratory alkalosis can be attributed to an intracellular shift of phosphate stores. The hypophosphatemia rapidly improves without need for supplementation when hyperventilation resolves. An understanding of the pathophysiology guides treatment.

(*Adv Stud Med.* 2003;3(6):345-348)

CASE REPORT

A 36-year-old Caucasian woman with a history of a cadaveric tracheal transplant 9 months prior to admission, followed by multiple stents for tracheal stenosis, presented with acute shortness of breath and inability to clear secretions. She had generalized weakness, paresthesias in her extremities, and arthralgias in her wrists and hands.

HISTORY

The patient had a major depressive episode and a drug overdose approximately 19 months prior to admission. She was intubated for 7 days and subsequently developed tracheal stenosis. She had an emergency tracheostomy followed by a

cadaveric tracheal transplant 10 months later. Postoperatively, she required multiple stents within the transplanted trachea. She subsequently suffered with anxiety and fear of restenosis.

PHYSICAL EXAMINATION AND LABORATORY STUDIES

At this presentation, the patient was anxious and tachypneic, with a respiratory rate of 32 breaths per minute. All of her other vital signs were normal. Her room air oxygen saturation was 98%. Her breath sounds were clear. She had no stridor. An emergency bronchoscopy revealed only minimally occlusive concretions with no stenosis (Figures 1 and 2).

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Drs O'Brien and Coberly have reported they have no financial or advisory relationships with corporate organizations related to this activity.

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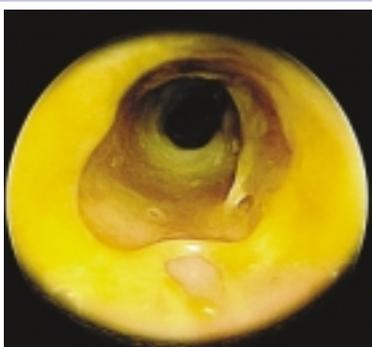
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Figure 1. Photograph Taken During Bronchoscopy



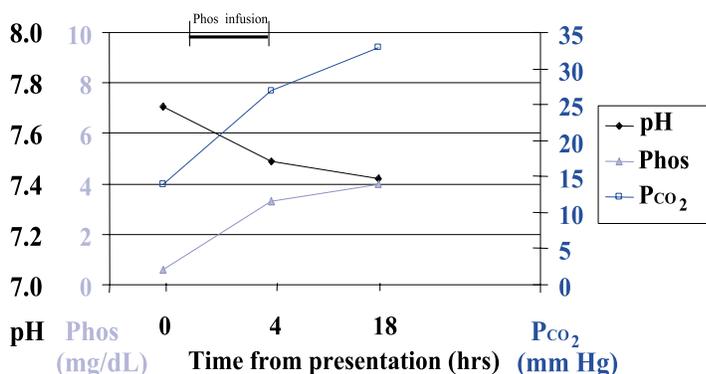
The photograph shows the inside of the endothelialized tracheal stent, which is free of obstruction with only minimal secretions at the proximal edge (yellow).

Figure 2. Photograph Taken During a Previous Bronchoscopy in the Same Patient



The photograph shows both secretions (bright yellow) and a partially obstructed lumen with a crescent of concretions (inferiorly) at the distal aspect of the stent.

Figure 3. pH, P_{CO}₂, and Phosphate 0–18 Hours from Patient Presentation



P_{CO}₂ = partial pressure of carbon dioxide; phos = phosphate.

Initial laboratory test results were normal except for the following: phosphate concentration, 0.6 mg/dL (normal, 2.0–4.0 mg/dL); potassium concentration, 3.3 mEq/L (normal, 3.5–5.0 mEq/L); and bicarbonate concentration, 16 mEq/L (normal, 22–26 mEq/L) with an anion gap of 18. Serum calcium and magnesium were 9.3 mg/dL (normal, 9.0–10.3 mg/dL) and 1.2 mEq/L (normal, 1.5–2.5 meq/L), respectively. Her initial arterial blood gas revealed the following: pH, 7.71 (normal, 7.36–7.44); partial pressure of carbon dioxide (P_{CO}₂), 14 mm Hg (normal, 32–48 mm Hg); partial pressure of oxygen (P_O₂), 204 mm Hg (normal, 83–108 mm Hg); and oxygen saturation, 98% on 40% FiO₂.

TREATMENT

After the procedure, treatment of the patient focused on her hyperventilation. She was supplemented with potassium, magnesium, and intravenous phosphate. Four hours later, her arterial blood gas improved as follows: pH, 7.49; P_{CO}₂, 27 mm Hg; and P_O₂, 116 mm Hg. Her serum phosphate concentration rose to 3.3 mg/dL. The sodium phosphate infusion was stopped. Eighteen hours after presentation, the patient had a pH of 7.42, P_{CO}₂ of 33 mm Hg, and a P_O₂ of 89 mm Hg. Her serum phosphate concentration further increased to 4.0 mg/dL (Figure 3).

DISCUSSION

The average adult body contains 11 to 14 g phosphorus per kg of fat-free tissue: approximately 85% in bone, 5% in muscle, and 10% divided elsewhere. Phosphorus circulates through intracellular and extracellular spaces as phosphate ion. The average American adult consumes 1000 to 1500 mg dietary phosphorus daily, exceeding the recommended daily allowance of 700 mg. Excess is eliminated in both urine and stool.

Hypophosphatemia is defined as serum phosphate concentration less than 2.5 mg/dL (mild), less than 2.0 mg/dL (moderate), or less than 1.5 mg/dL (severe).¹ Hypophosphatemia occurs in 0.22% to 2.15% of adult hospital admissions, and up to 50% of admissions to Veterans Affairs hospitals in the United States.² Hypophosphatemia can occur in many clinical situations. The most common causes are alcoholism, dietary deficiency, and, as in this case, respiratory alkalosis. Causes of hypophosphatemia fall into 4 categories: (1) impaired dietary intake and/or absorption of phosphorus; (2) redistribution; (3) increased urinary losses of phosphorus; and (4) disease states with combined losses (Table 1).

The clinical manifestations of hypophosphatemia span the spectrum of body systems (Table 2) and can be life threatening.³ Repletion of phosphate is crucial in many situations; however, the serum phosphate concentration responds unpredictably to intravenous infusion. Iatrogenic hyperphosphatemia can result in metastatic calcification, hypotension, and impaired renal function.⁴ With respiratory alkalosis, it is important to understand that severe hypophosphatemia will normalize with treatment of the underlying acid-base disturbance, making phosphate supplementation unnecessary.^{5,6}

In respiratory alkalosis (Figure 4), as carbon dioxide (CO₂) decreases, intracellular CO₂, which is readily diffusible across the cell membrane, moves into plasma. The loss of CO₂ from the cell causes the intracellular pH to rise. This rise in pH stimulates glycolysis, which requires phosphate ions to make adenosine triphosphate.⁷ This phosphate is obtained from circulating inorganic phosphate stores, which are readily diffusible across the cell membrane. The serum phosphate concentration falls as a result of the intracellular phosphate shift.

In contrast, in metabolic alkalosis (Figure 5), the intracellular pH does not rise because bicarbonate is poorly diffusible across the cell membrane. There is no increase in intracellular glycolysis, no need for influx of phosphate, and

Table 1. Causes of Hypophosphatemia

DECREASED INTAKE OR MALABSORPTION

- Dietary deficiency
- Hyperalimentation
- Chronic alcoholism
- Vomiting and diarrhea
- Malabsorption syndromes
- Vitamin D deficiency
- Phosphate binders

REDISTRIBUTION OF BODY STORES

- Hyperventilation
 - Sepsis
 - Salicylate poisoning
 - Hepatic encephalopathy
 - Panic attacks
 - Diabetic ketoacidosis
 - Neuroleptic malignant syndrome
 - Gout
- Hormonal effects
 - Insulin or glucagon infusion
 - Epinephrine administration
 - Androgens
 - Anovulatory hormones
 - Steroids

INCREASED URINARY EXCRETION

- Hyperparathyroidism
- Aldosteronism
- Renal tubule defects
 - Fanconi syndrome
 - Neurofibromatosis
 - Kidney transplant
 - Rickets

- Volume expansion
- Licorice ingestion
- SIADH
- Medications
 - Diuretics
 - Xanthine derivatives

DISEASE STATES

- Acute renal failure
- Thermal injury
 - Recovery from hypothermia
 - Hyperthermia
 - Burns
- Trauma
- Leukemias and lymphomas
- Hungry bone syndrome

SIADH = syndrome of inappropriate antidiuretic hormone secretion.

Table 2. Manifestations of Hypophosphatemia

MUSCULOSKELETAL

Tetany, arthralgias, myalgias, muscle edema, generalized weakness, fasciculations, rhabdomyolysis, osteomalacia

RESPIRATORY

Acute respiratory failure, depressed diaphragmatic contractility

CARDIOVASCULAR

Arrhythmias, hypotension, cardiomyopathy, depressed myocardial contractility

NEUROLOGIC

Paresthesias, altered mental status, seizures, dysarthria, peripheral neuropathy, intention tremors

ENDOCRINE

Insulin resistance, hyperparathyroidism

HEMATOLOGIC

Leukocyte dysfunction, platelet dysfunction, hemolysis, erythrocyte dysfunction with decreased levels of 2,3-diphosphoglyceride and adenosine triphosphate

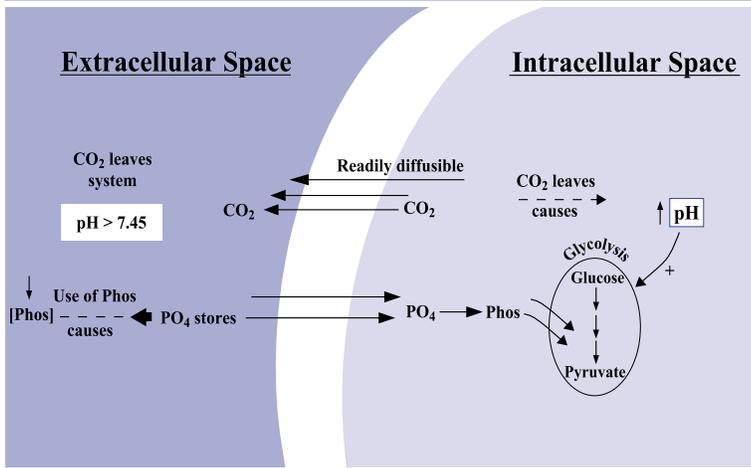
RENAL

Acute tubular necrosis, metabolic acidosis, hypercalcemia

PSYCHIATRIC

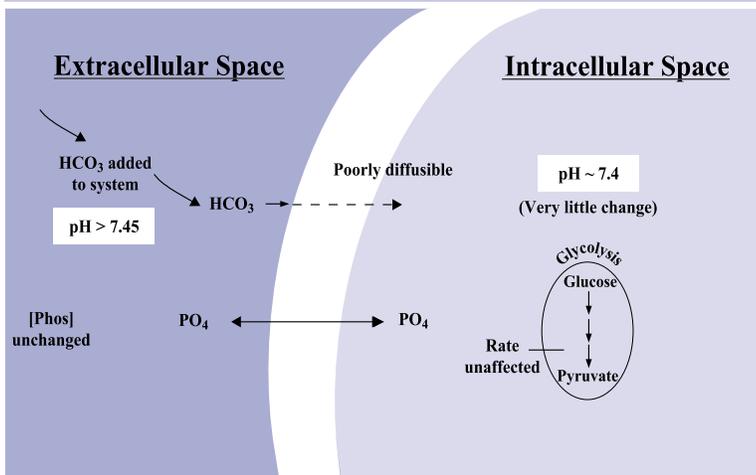
Depression, paranoid delusions, hallucinations, extreme anxiety

Figure 4. Schematic Representation of Respiratory Alkalosis



The diagram depicts the efflux of carbon dioxide (CO_2) from cells and the influx of phosphate from the extracellular space into the cell for use in glycolysis.

Figure 5. Schematic Representation of Metabolic Alkalosis



The diagram depicts the poor diffusion of excess extracellular bicarbonate (HCO_3^-) across the cell membrane and the preservation of both intracellular pH and extracellular phosphate concentration.

the extracellular space maintains its phosphate concentration.⁸

In the case presented, respiratory alkalosis best explains the severe hypophosphatemia. The patient had no other contributing factors that would account for the phosphate abnormality. Treatment of the patient's hyperventilation allowed for resolution of the respiratory alkalosis and contributed to normalization of the hypophosphatemia. Though the effect of the abbreviated phosphate infusion on the serum phosphate concentration is difficult to ascertain, the rapid correction in the face of profound hypophosphatemia points to phosphate redistribution as a major mechanism.

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