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Authors
Kemmerly, Thomas
Vuong, Carolyn
Kaunitz, Jonathan D

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A Novel Phosphorus Repletion Strategy in a Patient With Duodenal Perforation

Thomas Kemmerly, MD[1], **Carolyn Vuong, PharmD**[2], and **Jonathan D. Kaunitz, MD**[3,4,5]

[1]Cedars-Sinai Medical Residency Program, Los Angeles, California

[2]Departments of Medicine and Pharmacy, Greater Los Angeles Veteran Affairs Healthcare System, WLAVA Medical Center, Los Angeles, California

[3]Department of Medicine, UCLA School of Medicine, Los Angeles, California

[4]Department of Surgery, UCLA School of Medicine, Los Angeles, California

[5]Brentwood Biomedical Research Institute, Los Angeles, California, USA

Abstract

We describe a case in which a patient receiving parenteral nutrition (PN) developed hypophosphatemia. Due to lack of availability of parenteral phosphate supplements, we chose to restore phosphate using diluted hypertonic sodium phosphate enemas. Due to the recent shortages of parenteral minerals and vitamins, such an alternate means of repletion is of increasing importance. Diluted hypertonic sodium phosphate enemas are inexpensive, easy to administer, and effective since phosphate is readily absorbed across the rectal mucosa. We hope that through this type of repletion, life-threatening hypophosphatemia among patients receiving PN can be avoided.

Keywords

phosphorus; phosphates; duodenum; parenteral nutrition; drug shortage; enema; fluids-electrolytes/acid-base; nutrition; adult; life cycle; enteral access; GI access; minerals/trace elements; parenteral formulas/compounding

Background

Phosphorus is an essential element found in all living cells important for bone structure, energy storage, and gene translation. Normal serum phosphorus concentrations range from 2.5–4.5 mg/dL (0.8–1.45 mmol/L). Hypophosphatemia can be classified as moderate (serum phosphorus concentration 1–2 mg/dL) or severe (<1 mg/dL).[1] Approximately 2.4%–100% of critically ill patients are deficient in total body phosphorus for numerous reasons, including impaired absorption, increased renal excretion, or redistribution of inorganic phosphorus within the body.[1] One of the difficulties in analyzing phosphorus in the serum is that serum phosphorus concentrations often do not reflect total body stores or intracellular

Corresponding Author: Jonathan D. Kaunitz, MD, UCLA School of Medicine, Building 114, Room 217E, West Los Angeles VAMC, Los Angeles, CA 90073, USA. jake@ucla.edu.

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concentrations; therefore, clinical judgment always must be used when interpreting serum phosphorus concentrations. Yet numerous case reports report the potentially fatal complications of total-body phosphorus depletion. Several cases describe hypophosphatemic patients who developed acute respiratory failure or have difficulty weaning from ventilators.[2–4] Cardiac dysfunction in the form of arrhythmias and heart failure have also been reported.[5,6] Phosphorus depletion is also associated with central pontine myelinolysis,[7] insulin resistance,[8] neutrophil dysfunction,[9] and hemolysis.[10]

Phosphorus can be repleted via oral or intravenous (IV) administration. The oral route, being safe and well tolerated, is often used for patients with moderate phosphorus deficiency. The IV route is used for patients either with severe phosphorus deficiency or when the enteral route is contraindicated. Although the IV route is preferred for treating severe hypophosphatemia, the current national shortage of parenteral phosphate preparations has posed a health risk, particularly in critically ill patients, although an IV organophosphate solution, glycerol phosphate, has recently been imported to the U.S. market.[11]

Hypertonic sodium phosphate enemas are indicated in patients with constipation and for bowel preparation prior to flexible sigmoidoscopy.[12] Despite their effectiveness, simplicity, and low cost, these enemas can produce severe hyperphosphatemia.[13,14] The potential for these enemas to increase phosphate concentrations to toxicity indicates that phosphate is readily absorbed across the rectal mucosa and thus may serve as a useful administration route for phosphate in hypophosphatemic patients in whom the enteral route is contraindicated.

Case Presentation

The patient is a 63-year-old man who was initially evaluated for persistent abdominal pain at an outside hospital. He had been taking high doses of ibuprofen for pain control following a dental procedure that resulted in a duodenal perforation requiring emergent surgical repair. His postoperative course was complicated by a duodenal leak and a gastrointestinal (GI) hemorrhage from ulcer erosion into the gastroduodenal artery that was successfully embolized. The patient was transferred from the outside hospital to the authors' institution on postoperative day 13. The patient had received parenteral nutrition (PN) at the outside hospital, but its duration and its contents were unclear upon transfer. Due to a persistent duodenal leak and the fragility of the surrounding area, the patient was restricted to nothing by mouth and deemed too high risk for enteral nutrition (EN) via a nasogastric tube. PN was started via a dedicated peripherally inserted central catheter.

At the time of onset of PN, the patient weighed 78 kg and was 180 cm tall. This placed him at 117% of his ideal body weight. He had a history of a 14-kg weight loss compared with the previous year, although it is unclear when this weight loss began or over how long a period. He had no history of smoking or alcohol or illicit drug use. His liver function tests showed a total bilirubin of 1.2 mg/dL, alkaline phosphatase of 95 U/L, alanine aminotransferase of 42 U/L, aspartate aminotransferase of 42.4 U/L, and lactate dehydrogenase of 282.6 U/L. His lipid panel on the first day of PN showed total cholesterol of 68 mg/dL, triglycerides of 80.2 mg/dL, high-density lipoprotein (HDL) of 11 mg/dL, and low-density lipoprotein (LDL) of

41 mg/dL. He had no history of diabetes; point-of-care glucose monitoring indicated glucose concentrations ranging from 97–241 mg/dL in the 3 days prior to initiating PN, which was controlled with an insulin aspart sliding scale regimen.

PN was initiated using 20% destrose and 5% amino acid solution at 50 mL/h, which was increased to his goal rate of 100 mL/h over the course of 2 days. In total, 2 L of 20% Intravenous (IV) fat emulsion (Intralipid, Fresinius Kabi Ltd, Cheshire, UK) was administered weekly, providing 30 mmol phospholipids/wk (see the Appendix for detailed PN composition). No phosphate was added to the PN solution due to the national IV phosphorus shortage, and the patient did not receive supplementary phosphate by the enteral route.

On postoperative day 20, the patient, still PN dependent, developed progressive hypophosphatemia reaching a nadir of 2.3 mg/dL, but had been unable to receive IV phosphate due to a nationwide shortage. Blood glucose measurements during PN ranged from 108–220 mg/dL, which was controlled with additional insulin. The patient showed no evidence of alkalosis, with renal function remaining normal throughout his hospital stay.

At this point, since the provision of oral and IV phosphate replacements was not possible, there was a rising probability of hypophosphatemic complications. We chose to replenish body phosphorus rectally using dilutions of hypertonic sodium phosphate enemas, which are usually indicated for the relief of constipation. In this case, a prepackaged hypertonic phosphate enema (C. B. Fleet Company, Lynchburg, VA) was used, consisting of 19 g NaH_2PO_4/7 g Na_2HPO_4 (~208 mmol sodium phosphate) dissolved in 118 mL water. The time course of the patient's serum phosphorus concentrations and administration of diluted hypertonic phosphate enemas are illustrated in Figure 1. Initial phosphate repletion was attempted on postoperative day 21 by administering an enema dilution consisting of 12 mL of the enema solution with 108 mL of sterile water (dilution 1 or D1, ~21 mmol total/180 mM phosphate), which was hypotonic relative to plasma. The enema was ordered to be retained by the patient for 30 minutes. The patient's serum phosphorus concentration was 2.5 mg/dL just prior to enema administration and 2.3 mg/dL 10 hours later. On postoperative day 22, 24 hours after enema administration, the patient's phosphate concentration was 2.6 mg/dL. Phosphorus repletion was then attempted using 24 mL of sodium phosphate enema and 96 mL of sterile water (dilution 2 or D2, ~42 mmol total/360 mM phosphate), which was slightly hypertonic relative to plasma. Follow-up serum phosphorus level was 2.7 mg/dL on postoperative day 23 and 2.4 mg/dL on postoperative day 24. Phosphate repletion was then attempted using 36 mL of sodium phosphate enema with 84 mL of sterile water (dilution 3 or D3, ~63 mmol total/540 mM phosphate), which was roughly 2 times hypertonic relative to plasma. Serum phosphorus concentrations increased from 2.4–3 mg/dL 20 hours later. Serum phosphorus concentrations continued to increase for the following 3 days before reaching a peak of 4.1 mg/dL on postoperative day 26. Serum phosphorus concentrations steadily decreased over the course of 4 days before reaching a nadir of 2.0 mg/dL on postoperative day 30, after which another administration of D3 was given, increasing the serum phosphorus to 3.5 mg/dL the following day.

The patient expressed minimal discomfort and never experienced the cathartic effects of enema administration during any of the 4 administrations.

Discussion

The most common electrolyte disturbances from the use of sodium phosphate enemas are hyperphosphatemia and hypercalcemia.[14] Inorganic phosphate is passively absorbed by the colon down its concentration gradient.[15] Since the sodium phosphate solution used for enemas is highly concentrated (~1.75 M),[1] a ~6-fold lumen to plasma concentration gradient is created when phosphate enemas are administered, facilitating rapid phosphate entry into the plasma. In patients with normal renal function, phosphate concentrations rise, on average, to 3.1–4.0 mg/dL.[16] In our patient, administration of D3 increased serum phosphorus concentrations 0.6 mg/dL after the first administration and 1.5 mg/dL after the second. Although the IV fat emulsion that the patient received contains phospholipids, doubt has been raised with regard to the effectiveness of phosphorus in this form for phosphorus repletion.[17]

Considerations must be taken as phosphate repletion needs to occur more carefully in patients with renal dysfunction, who may have potentially fatal hyperphosphatemia. Other potential contraindications include patients with increased intestinal permeability, those with cirrhosis, and patients with fistulizing rectal disease since they may all have variable rates of absorption. Phosphate repletion using sodium phosphate enemas can be risky in healthy patients as well. Dilute phosphate enemas were used for phosphate repletion with careful and frequent monitoring and escalating dilutions to reduce the risk of potentially fatal hyperphosphatemia. It is recommended that care be taken when attempting repletion of body phosphate stores by any means.

As the nationwide shortage of IV phosphate solutions continues, novel methods of phosphate repletion may be necessary in patients who cannot tolerate phosphate repletion administered by the oral route or by feeding tubes. This case is an example of an inexpensive, seemingly safe, and well-tolerated means for phosphate repletion in such patients when parenteral phosphate preparations are unavailable. Additional benefits may arise from freeing an IV catheter in critically ill patients, which may otherwise be occupied for several hours when administering IV phosphate. This case also illustrates that repletion need not be done every day since the effects of phosphate repletion via the rectal route may last for several days.

Appendix

Composition of the PN solution:

The base solution contains dextrose (D) 20% and amino acids (aa) 5% only.

PN electrolytes content:

Na^+ 60 mEq/L	Cl^- 50 mEq/L
K^+ 30 mEq/L	Acetate 102 mEq/L
Ca^{++} 0 mEq/L	Multivitamins (MVI)[a] 10 mL/2-L bag
Mg^{++} 12 mEq/L	Trace element (MTE-4)[b] 1 mL/2-L bag
Phosphorus 0 mmol/L	Regular insulin 10 units/2-L bag

[a] MVI 10 mL contains 100 mg vitamin C, 1 mg vitamin A, 5 mcg vitamin D, 6 mg vitamin B_1, 3.6 mg vitamin B_2, 6 mg vitamin B_6, 40 mg niacinamide, 15 mg dexpanthenol, 10 mg vitamin E, 60 mcg biotin, 600 mcg folic acid, 5 mcg vitamin B_{12}, and 150 mcg vitamin K.

[b] MTE-4 1 mL contains 5 mg zinc, 1 mg copper, 0.5 mg manganese, and 10 mcg chromium.

PN daily prescription at goal rate (100 mL/h): 1950 mL 20% dextrose/5% amino acids + 20% IV fat emulsion 1 L 2×/wk provides 2002 kcal (~25 kcal/kg/d), 97.5 g protein (~1.2 g/kg/d), 17% kcal from fat, and 5.17 mg carbohydrate (CHO)/kg/min (total CHO per day = 390 g, total protein per day = 97.5 g).

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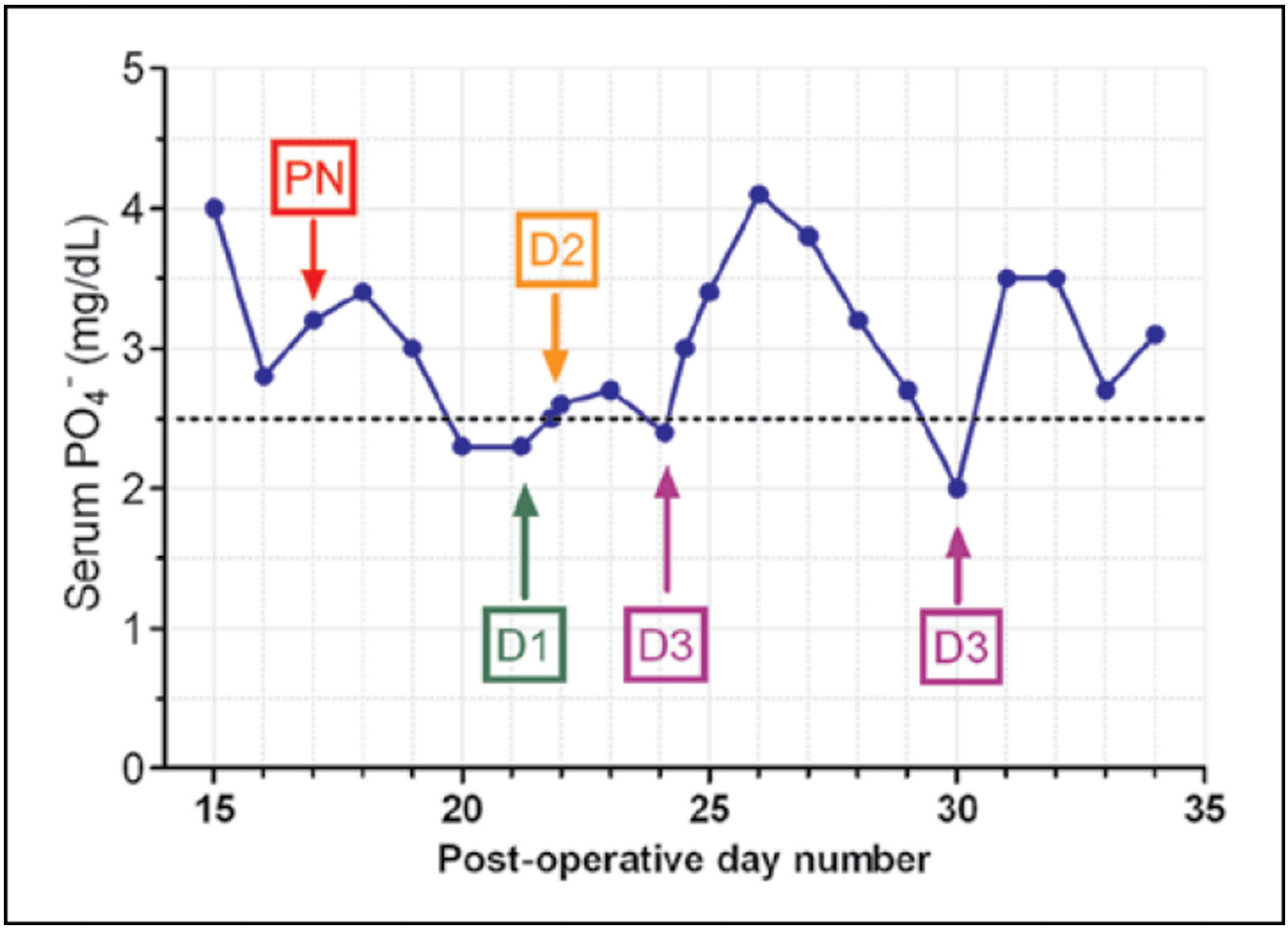

Figure 1.

Time course of serum phosphorus concentrations. Parenteral nutrition (PN) and diluted sodium phosphate enemas, denoted as D1, D2, and D3, were given as indicated by the arrows. Please see the text for their composition: D1 = 21 mmol/180 mM, D2 = 42 mmol/360 mM, and D3 = 63 mmol/540 mM sodium phosphate, total volume of each = 120 mL. The dotted line denotes the lower limit of normal of serum phosphorus concentration as defined by the clinical laboratory.