JOP – Journal of the Pancreas 2000; 1(4): 204-207

Severe Hypophosphatemia in a Patient with Acute Pancreatitis

Evagelos Rizos, George Alexandrides, Moses S Elisaf

Department of Internal Medicine, Medical School, University of Ioannina. Ioannina, Greece

ABSTRACT

Context: We describe a patient with alcohol-induced pancreatitis who developed severe life-threatening hypophosphatemia of multifactorial origin during hospitalization.

Case Report: Decreased phosphate levels along with urine phosphate wasting were already noticed on the patient's admission due to underlying chronic alcoholism. However, a further deterioration of hypophosphatemia appeared on the second day of hospitalization presumably resulting from an increased transfer of phosphate from extracellular to intracellular fluid.

Conclusions Phosphate deficiency is often overlooked in patients with acute pancreatitis. Our case emphasizes that serum phosphate levels should be checked along with serum calcium levels in patients with acute pancreatitis, especially in alcoholic patients.

INTRODUCTION

Acute pancreatitis is not reported as a potential cause of severe hypophosphatemia [1, 2]. We herein describe a patient with alcoholic pancreatitis who developed marked life-threatening hypophosphatemia during hospitalization. This severe phosphate depletion was due to chronic alcoholism-induced inappropriate phosphaturia but also to the movement of phosphate into cells resulting from pancreatitis-induced catecholamine release as well as from glucose infusion.

CASE REPORT

A 32 year old male patient was admitted to our clinic with severe mid-epigastric pain radiating to the back, nausea and vomiting. He was a heavy drinker and had consumed more than 600 g of ethanol weekly for more than 5 years. He suffered from hypertension in the past few years without being on any medication. There were no signs or symptoms of malabsorption (weight loss, abnormal stools, bone pain, etc.), which would point to the diagnosis of chronic pancreatitis. No evidence of any other chronic disease was noticed, while laboratory investigation (including renal function tests and serum electrolytes) performed 3 months before admission was reported to be normal. On admission, the temperature was 37.8 °C, blood pressure 120/80 mmHg, heart rate 100 beats/min, and respiration rate 18 cycle/min. Physical examination revealed a mild systolic murmur on the left sternal border and diffuse tenderness all over the epigastrium. The bowel sounds were diminished. An electrocardiogram showed normal findings except for sinus tachycardia. Ultrasound of the abdomen showed ascitic fluid and an enlarged edematous pancreas. Computed tomography of the abdomen disclosed scattered areas of pancreatic necrosis but no pancreatic calcifications. Laboratory investigation on admission revealed leukocytosis, hyperamylasemia, mild hyperglycemia hypocalcemia and hypomagnesemia, but marked hypophosphatemia associated with inappropriate phosphaturia (fractional excretion of phosphate ($FEPO_4^{3-}$) >20%) and a renal threshold for phosphate excretion

($TmPO_4^{3-}$/GFR) <0.80 mmol/L (Table 1). The diagnosis of severe acute pancreatitis was established according to the Ranson criteria. The patient received 3 L of normal saline and 1 L of 5% glucose solution along with potassium chloride (27 mmol/L potassium) and magnesium sulfate (4.2 mmol/L magnesium). However, on the second day, a further deterioration of serum phosphate levels was noticed and phosphate solutions were added in the intravenously administered fluids for 3 days (5 mmol/L potassium phosphate of administered fluids; total amount of potassium phosphate 40 mmol) resulting in a progressive improvement of serum phosphate levels. The patient was discharged on the 8th day of hospitalization with serum phosphorus levels and the other laboratory values within normal limits (Table 1). Subsequent laboratory evaluation performed 3 and 6 months after the patient's discharge did not disclose any abnormalities, while the patient was reported to have restricted alcohol consumption considerably.

Table 1. Patient's laboratory data

Parameters	On admission	Second day	Third day	Fifth day	After 1 week	Reference values
Total leukocytes (L^{-1})	$16.5x10^9$	$18x10^9$	$14x10^9$	$11x10^9$	$8x10^9$	($4-10x10^9$)
Serum urea (mmol/L)	19.0	10.3	9.3	8.6	7.5	(8-20)
Serum creatinine (ì mol/L)	115	70.2	70.2	70.2	70.2	(53-106)
Serum glucose (mmol/L)	8.85	7.60	7.20	6.80	6.38	(3.58-6.87)
Serum albumin (g/L)	41	36	ND	37	39	(38-50)
Serum amylase (IU/L)	890	668	368	ND	75	(<90)
AST (IU/L)	75	250	190	ND	55	(10-37)
ALT (IU/L)	60	190	150	ND	48	(10-37)
LDH (IU/L)	570	1145	2500	ND	520	(270-450)
Serum potassium (mmol/L)	4.5	3.9	4.0	4.3	4.2	(3.5-5.3)
Serum sodium (mmol/L)	142	138	140	141	136	(136-145)
Serum chloride (mmol/L)	103	107	ND	105	104	(98-110)
Serum calcium (mmol/L)	1.92	1.85	1.90	1.95	2.05	(2.025-2.6)
Serum phosphate (mmol/L)	0.55	0.35	0.70	0.80	1.03	(0.84-1.45)
Serum magnesium (mmol/L)	0.55	1.00	0.90	0.85	0.70	(0.65-1.20)
Serum PTH (pg/ml)	ND	78	ND	ND	12	(11-54)
FEK^+ (%)	9	8	ND	7	3	(<13)
$FEMg^{++}$ (%)	18	12	ND	10	9	(<4)
$FEPO_4^{3-}$ (%)	39	34	32	25	18	(<20)
$TmPO_4^{3-}$/GFR (mmol/L)	0.65	0.67	0.75	0.81	0.90	(>0.80)
Arterial pH	7.39	ND	ND	ND	ND	(7.36-7.45)
Arterial PCO_2 (mmHg)	35	ND	ND	ND	ND	(36-44)
Arterial PO_2 (mmHg)	79	78	ND	85	90	(80-105)
Serum bicarbonate (mmol/L)	21	ND	ND	ND	ND	(22-26)

FE: fractional excretion; $TmPO_4^{3-}$/GFR renal threshold for phosphate excretion

DISCUSSION

In our case, the severe hypophosphatemia, already noticed on the patient's admission, further deteriorated during hospitalization.
Hypophosphatemia was due to a combination of factors, as happens in the vast majority of hospitalized patients with severe phosphate depletion [1, 2, 3]. The underlying chronic alcoholism could have played a prominent role in the pathogenesis of the severe hypophosphatemia which was evident on the patient's admission [4]. This decrease in serum phosphate levels was mainly attributed to inappropriate phosphate loss, which, in turn, can be ascribed to an alcohol-induced

reversible tubular defect in phosphate conservation [4, 5] as well as to coexistent alcohol-induced hypomagnesemia which is the most common electrolyte abnormality encountered in such patients [6, 7]. In fact, it has been shown that phosphaturia is common in experimental magnesium depletion and is corrected with magnesium repletion. This phosphaturia is probably due to a proximal tubular defect in phosphate transport [8]. However, in our case, inappropriate phosphaturia persisted during hospitalization, even when the magnesium balance was restored. Phosphate wasting was then progressively decreased, an improvement possibly related to a transient alcohol-induced proximal tubular abnormality, which is known to improve after alcohol abstinence [5].

Even though the role of the alcohol-induced renal phosphate wasting is of paramount importance, the marked hypophosphatemia observed on the second day of hospitalization could be the result of the increased transfer of phosphate from the extracellular to the intracellular fluid. This shift could be related to the increased sympathoadrenergic activity following acute pancreatitis which can stimulate cellular phosphate intake [9] as well as to the glucose solutions given, since even small amounts of glucose have been reported to cause significant decreases in serum phosphate concentrations [10]. In this setting, it should be mentioned that hypophosphatemia is common in acutely ill patients and occurs in the acute phase response secondary to hyperglycemia and to the shifts of extracellular phosphate into cells [11]. Interestingly, high inflammatory cytokines, which have been shown to play a pivotal role in severe acute pancreatitis [12], were recently demonstrated to be well correlated with serum phosphate levels in patients with sepsis [13]. The hypocalcemia-induced increased parathyroid hormones (PTH) levels could also have played a minor role in the phosphate wasting observed [14]. Finally, increased gastrointestinal phosphate losses may also have contributed to the significant deterioration of the serum phosphate levels.

Severe hypophosphatemia may be associated with serious clinical manifestations, which occur when serum phosphate levels fall below 1 mg/dL and include muscular abnormalities (weakness, rhabdomyolysis, impaired diaphragmatic function, respiratory failure, and heart failure), neurologic abnormalities (paresthesias, dysarthria, confusion, stupor, seizures and coma) hemolysis, platelet and leukocyte dysfunction, and metabolic acidosis [1, 2].

Even though severe hypophosphatemia is extremely dangerous, phosphate deficiency is often overlooked in this clinical setting and phosphate determination is not generally included in the routine laboratory investigation of a patient with acute pancreatitis. Thus, we suggest that serum phosphate levels should be carefully monitored along with serum calcium levels in patients with acute pancreatitis and in particular in alcoholic patients who exhibit a wide array of metabolic abnormalities.

Key words Hypophosphatemia; Pancreatitis; Phosphorus Metabolism Disorders; Water-Electrolyte Imbalance

Correspondence
Moses Elisaf
Department of Internal Medicine
University of Ioannina
Medical School
GR-451 10 Ioannina
Greece
Phone: +30-651.97500
Fax: +30-651.45944
E.mail address: melisaf@cc.uoi.gr

References

1. Crook M, Swaminathan R. Disorders of plasma phosphate and indications for its measurement. Ann Clin Biochem 1996; 33:376-96.

2. Weisinger JR, Bellorin-Font E. Magnesium and phosphorus. Lancet 1998; 352:391-6. [98382044]

3. Camp MA, Alon M. Severe hypophosphataemia in hospitalized patients. Miner Electrolyte Metab 1990; 16:365-8.

[91211659]

4. Elisaf MS, Siamopoulos KC. Mechanisms of hypophosphataemia in alcoholic patients. Int J Clin Pract 1997; 51:501-3. [98197668]

5. DeMarchi S, Cecchin E, Basile A, Bertotti A, Nardini R, Bartoli E. Renal tubular dysfunction in alcohol abuse-Effects of abstinence. N Engl J Med 1993; 329 1927-34. [94067239]

6. Elisaf M, Merkouropoulos M, Tsianos EV, Siamopoulos KC. Pathogenetic mechanisms of hypomagnesemia in alcoholic patients. J Trace Elem Med Biol 1995; 9:210-4. [96403914]

7. Elisaf M, Merkouropoulos M, Tsianos EV, Siamopoulos KC. Acid-base and electrolyte abnormalities in alcoholic patients. Miner Electrolyte Metab 1994; 20:274-81. [95214601]

8. Ginn HE, Shanbour LL. Phosphaturia in magnesium deficient rats. Am J Physiol 1967; 212:1347-50.

9. Body JJ, Cryer PE, Offord KP, Heath H. Epinephrine is a hypophosphatemic hormone in man. Physiological effects of circulating epinephrine on plasma calcium, magnesium, phosphorus, parathyroid hormone, and calcitonin. J Clin Invest 1983; 71:572-8.

10. Thompson JS, Hodges RE. Preventing hypophosphatemia during total parenteral nutrition. JPEN J Parenter Enteral Nutr 1984; 8:137-9. [84188768]

11. da Cunha DF, dos Santos VM, Monterio JP, de Carvalho da Cunha SF. Hypophosphatemia in acute-phase response syndrome patients. Preliminary data. Miner Electrolyte Metab 1998; 24:337-40. [98371197]

12. Brady M, Christmas S, Sutton R, Neoptolemos J, Slavin J. Cytokines and acute pancreatitis. Bailliére's Clinical Gastroenterology 1999; 13:265-89.

13. Barak V, Schwartz A, Kalickman I, Nisman B, Gurman G, Shoenfeld Y. Prevalence of hypophosphatemia in sepsis and infection: the role of cytokines. Am J Med 1998; 104:40-7. [98187567]

14. Wesson LG. Homeostasis of phosphate revisited. Nephron 1997; 77:249-66.