Case Report

ISSN 1738-5997 (Print) · ISSN 2092-9935 (Online)
Electrolyte Blood Press 2021;19:51-55
https://doi.org/10.5049/EBP.2021.19.2.51

A Case Report of Very Severe Hyperphosphatemia (19.3 mg/dL) in a Uremic Patient Taking Honey and Persimmon Vinegar

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Received: November 19, 2021
Revised: November 26, 2021
Accepted: November 27, 2021
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We report a case of severe hyperphosphatemia in advanced CKD with poor compliance. A 55-year-old male patient with underlying type 2 diabetes mellitus, hypertension, and chronic kidney disease presented emergently with general weakness and altered mental status. The creatinine level was 14 mg/dL (normal range: 0.5-1.3 mg/dL) 2 months prior to consultation, and he was advised initiation of hemodialysis, which he refused. Subsequently, the patient stopped taking all prescribed medications and self-medicated with honey and persimmon vinegar with the false belief it was detoxifying. At the time of admission, he was delirious, and his laboratory results showed blood urea nitrogen level of 183.4 mg/dL (8-23 mg/dL), serum creatinine level of 26.61 mg/dL (0.5-1.3 mg/dL), serum phosphate level of 19.3 mg/dL (2.5-5.5 mg/dL), total calcium level of 4.3 mg/dL (8.4-10.2 mg/dL), vitamin D (25(OH)D) level of 5.71 ng/mL (30-100 ng/mL) and parathyroid hormone level of 401 pg/ml (9-55 pg/mL). Brain computed tomography revealed non-traumatic spontaneous subdural hemorrhage, presumably due to uremic bleeding. Emergent hemodialysis was initiated, and hyperphosphatemia and hypocalcemia were rectified; calcium acetate and cholecalciferol were administered. The patient's general condition and laboratory results improved following dialysis. Strict dietary restrictions with patient education were implemented. Multifaceted interventions, including dietary counseling, administration of phosphate-lowering drugs, and lifestyle modifications, should be implemented when encountering patients with CKD, considering the extent of the patient's adherence.

Key Words: Hyperphosphatemia, Chronic kidney disease, Dietary counseling, Case report

INTRODUCTION

Chronic kidney disease (CKD) is a major public health burden, with rising global prevalence and many complications[1]. The risk of CKD-mineral and bone disorder (MBD) is increased in patients with CKD[2]. CKD-MBD syndrome includes anomalous laboratory test results, bone fragility, and vascular calcification and is associated with increased risks of morbidity and mortality[3].

Hyperphosphatemia, in particular, has been associated with increased mortality risk in CKD-MBD patients[4,5]. Hyperphosphatemia occurs late in the course of CKD, as adaptive responses fail to maintain mineral homeostasis[6]. Renal phosphate excretion in CKD is maintained by increased levels of parathyroid hormone (PTH) and fibroblast growth factor 23 (FGF23), up to a certain extent. However, as CKD progresses and the glomerular filtration rate (GFR) decreases,

phosphate retention occurs, and mineral homeostasis eventually fails[6,7]. Excessive retention of phosphate can cause adverse events such as vascular calcification, parathyroid gland hyperplasia, uremic bone disorders, and cardiovascular events[8]. Therefore, phosphate control is essential in CKD patients. It is recommended to limit dietary phosphate intake among patients who have CKD stage 3 and above[2,9]. Phosphate levels can be further managed through renal replacement therapy (through hemodialysis) and the use of phosphate-binding drugs, calcitriol, and active vitamin D analogs.

Herein, we report a case of severe hyperphosphatemia in a patient with advanced CKD with poor compliance and poor dietary control.

CASE REPORT

A 55-year-old male patient was transferred to the emergency department with general weakness and a change in mental status. The patient had been taking medication for type 2 diabetes mellitus (DM) and hypertension (HTN) for 10 years. The patient was also treated at a local clinic for CKD. The creatinine level (normal range: 0.5-1.3 mg/dL) was 6.14 mg/dL 10 months ago and had risen to 14 mg/dL 2 months ago. He was advised to start hemodialysis, which he refused at that time. Subsequently, the patient stopped taking all his medications and self-medicated with honey and persimmon vinegar for 3 weeks, assuming this was a detoxifying regimen. The day before transfer, he suffered from loss of consciousness and was admitted at a local clinic.

At the time of transfer, his blood pressure was 160/80 mmHg, heart rate was 70 beats/min, respiratory rate was 20 breaths/min, body temperature was 36.5°C, and oxygen saturation was at 100% with oxygen supplementation at 2 L/min via nasal cannula. Physical examination revealed dry mouth, dry skin, decreased skin turgor, and tremors of the upper extremities. On the day of admission, his laboratory results were as follows: white blood cell count, 4,700/μL (4,000-8,000/μL); hemoglobin level, 5.5 g/dL (12-18 g/dL); blood urea nitrogen level, 183.4 mg/dL (8-23 mg/dL); serum creatinine level, 26.61 mg/dL (0.5-1.3 mg/dL); serum sodium level, 136 mEq/L (136-146 mEq/L); serum osmolality, 349 mOsm/kg (280-295 mOsm/Kg); serum potassium level, 5.7 mEq/L (3.5-5.1 mEq/L); chloride concentration, 95 mEq/L (98-110 mEq/L); total calcium 4.3 mg/dL (8.4-10.2 mg/dL); serum albumin level, 3.0 g/dL (3.5-5.2 g/dL); vitamin D (25(OH)D) level, 5.71 ng/mL (30-100 ng/mL); and parathyroid hormone level 401 pg/ml (9-55 pg/mL). Very severe hyperphosphatemia was documented at 19.3 mg/dL (2.5-5.5 mg/dL). The prothrombin time was 13.5 seconds (10-13.6 seconds), activated partial thromboplastin time (aPTT) was 33.2 seconds (22.5-34.5 seconds), fibrinogen level was 408.0 mg/dL (100-400 mg/dL), fibrinogen degeneration product level was 28 μg/mL (0-5 μg/mL), and D-dimer level was 16.77 mg/L fibrinogen-equivalent units (FEU) (0-0.55 mg/L FEU). Arterial blood gas analysis showed pH 7.27 (7.35-7.45), HCO_3^- 12.6 mmol/L (21-28 mmol/L), and P_{CO2} 21 mmHg (35-48 mmHg) indicating metabolic acidosis. Urinalysis showed nephrotic range proteinuria based on albumin-to-creatinine ratio, 7777.8 mg/g Cr (0-30 mg/g Cr) and protein-to-creatinine ratio 20.540 g/g Cr (0-0.2 g/g Cr). Serum and urine protein electrophoresis revealed proteinuria of nephrotic origin. Kidney sonography showed hyperechoic kidneys with size of 7-8 cm, which suggested for CKD.

A Foley catheter was inserted, yielding a small amount of urine. A temporary femoral catheter was immediately inserted, and hemodialysis was initiated. He became alert following hemodialysis, and the arm tremors improved with correction of hypocalcemia.

Brain computed tomography (CT) was performed to evaluate loss of consciousness and revealed acute subdural hemorrhage (SDH) in the right cerebral convexity (Fig. 1). Since he had never undergone any traumatic injuries prior, the bleeding was deemed a non-traumatic spontaneous SDH, presumably due to uremic bleeding. Conservative management was maintained since there were no changes

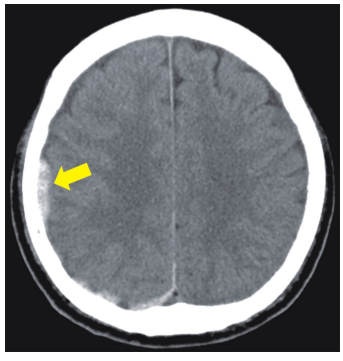

Fig. 1. A brain CT scan reveals acute subdural hemorrhage in right cerebral convexity (yellow arrow).
Abbreviations: CT, computed tomography.

Table 1. Laboratory results of the patient before and after 3 times dialysis

Variables (Normal range)	Before dialysis	After dialysis
BUN (8-23 mg/dL)	183.4 mg/dL	40.6 mg/dL
Serum creatinine (0.5-1.3 mg/dL)	26.61 mg/dL	8.64 mg/dL
Serum phosphate (2.5-5.5 mg/dL)	19.3 mg/dL	4.3 mg/dL
Serum total calcium (8.4-10.2 mg/dL)	4.3 mg/dL	6.8 mg/dL
WBC (4,000-8,000/μL)	4,700/μL	7,900/μL
Hemoglobin (12-18 g/dL)	5.5 g/dL	8.1 g/dL
Na (136-146 mEq/L)	136 mEq/L	137 mEq/L
Serum osmolality (280-295 mOsm/Kg)	349 mOsm/Kg	285 mOsm/Kg
Cl (98-110 mEq/L)	95 mEq/L	99 mEq/L
pH (7.35-7.45)	7.27	7.391
$HCO3^-$ (21-28 mmol/L)	12.6 mmol/L	23.4 mmol/L

Abbreviations: BUN, blood urea nitrogen; WBC, white blood cell; Na, sodium; Cl, chloride.

in the course of SDH.

On day 3 after admission, the femoral catheter was discontinued and a tunneled dialysis catheter was inserted via the right jugular vein for maintenance of hemodialysis. Two tablets of calcium acetate (710 mg) were administered three times a day for treatment of hyperphosphatemia and hypocalcemia, with combined calcium and cholecalciferol (100 mg/1,000 IU) twice daily for treatment of hypocalcemia and vitamin D deficiency. Olmesartan, amlodipine, and hydrochlorothiazide (40 mg/10 mg/12.5 mg) were also initiated as combination therapy, along with carvedilol, at 32 mg, all administered once daily for blood pressure control. Supplements of vitamin B and C were provided once a day, and ferrous sulfate (80 mg as iron), two tablets per day, was also administered.

The final clinical diagnosis was end-stage renal disease (ESRD) with severe hyperphosphatemia, with SDH secondary to uremic bleeding. The patient's general condition and laboratory results improved following dialysis, including creatinine, phosphate, and calcium levels (Table 1). Strict dietary restriction was implemented, and patient education

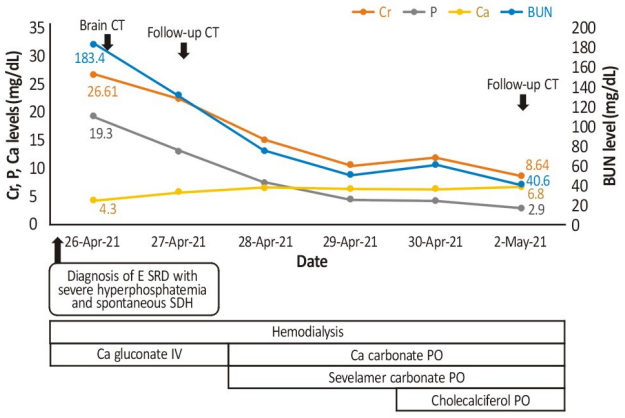

Fig. 2. Changes of blood chemistry with in-hospital treatment. Abbreviations: Cr, creatinine; P, phosphate; Ca, calcium; BUN, blood urea nitrogen; CT, computed tomography; ESRD, end-stage renal disease; SDH, subdural hemorrhage; IV, intravenous; PO, per oral.

was provided to the patient to prevent hyperphosphatemia and hyperkalemia. The timeline of the patient's clinical course is shown in Figure 2.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this manuscript and any accompanying images.

DISCUSSION

We presented a case of severe hyperphosphatemia in a patient with advanced CKD with poor clinical and lifestyle adherence. The patient should have started dialysis several months ago, but refused therapy and self-medicated with honey and persimmon vinegar for 3 weeks under the false impression of its detoxifying effects. One hundred grams of persimmon contains 17 mg phosphorus, while both honey and vinegar are also rich in phosphorus[10]. It is recommended to limit dietary phosphate intake in those with CKD stages 3 to 5 and to initiate dietary counseling at these stage[2,9]. In addition, in patients with advanced CKD, complex treatment using drugs that include phosphate binders, calcitriol, and active vitamin D analogs is important. In previous papers, hyperphosphatemia (16.5 mg/dL) was reported

in hemodialysis patient undergoing hemicolectomy surgery and not taking phosphate binder[11]. In another paper, hyperphosphatemia (17.9 mg/dL) caused by sodium phosphate enema in patient with CKD and liver cirrhosis was reported[12]. To our knowledge, this report is the highest level with hyperphosphatemia in patients with CKD.

Maintaining phosphate balance is critical for CKD patients. Phosphate is required for cell metabolism, bone structure, and protein synthesis[6,13]. About 60-80% of the dietary phosphate is absorbed by the intestine. Approximately 85% of phosphate is in the bone in the form of crystalline calcium phosphate. Bone is an important regulator of phosphate homeostasis and can either release or absorb phosphate[14]. FGF23, a phosphatonin produced by osteocytes and osteoblasts, promotes urine phosphate excretion and decreases the synthesis of 1,25-dihydroxyvitamin D ($1,25(OH)_2D$)[15]. Decreased $1,25(OH)_2D$ levels, in turn, stimulate PTH secretion. The stimulation of FGF23 secretion appears to arise from increased serum $1,25(OH)_2D$ levels and increased dietary phosphate intake. As CKD progresses, phosphate retention occurs, and phosphate homeostasis is maintained by FGF23 by increasing urinary phosphate excretion and decreasing gut phosphorus absorption. PTH also inhibits phosphate reabsorption in the renal proximal tubule. PTH and $1,25(OH)_2D$ enhance the liberation of phosphate from bone.

In advanced CKD, mineral homeostasis fails due to an imbalance in phosphate intake and renal excretory capacity[6,7]. Phosphate retention induces PTH secretion, and PTH levels are markedly increased. PTH, in turn, enhances bone resorption by releasing more phosphate. The resulting hyperphosphatemia contributes to the development of vascular calcification, and hyperphosphatemia is an independent risk factor for cardiovascular disease[8,16]. Hyperphosphatemia also contributes to exacerbation of CKD[17].

Therefore, phosphate control is essential in CKD patients. Phosphate control not only prevents disease progression but also improves the patient's quality of life. A multifaceted intervention, including dietary counseling, phosphate-lowering drugs, and lifestyle modification, should be provided to patients with CKD considering the extent of patients' adherence to treatment goals. Our patient had poor adherence and had false beliefs in folk remedies, and eventually developed severe hyperphosphatemia with a serum phosphate level of 19.3 mg/dL. The patient improved with medication and dialysis.

In conclusion, phosphate control is essential for CKD patients at stages 3 to 5 of the disease. We suggest for advanced CKD patients to be provided multifaceted interventions, to prevent complications and slow disease progression. Adequate phosphate control can improve patient prognosis.

Acknowledgements

This work was supported by a grant (BCRI20076, BCRI21025, BCRI21046) from the Chonnam National University Hospital Biomedical Research Institute.

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