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CASE REPORT

Massive hyperphosphatemia in a patient with neuronal intestinal dysplasia after bowel preparation with oral sodium phosphate

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Abstract

Oral sodium phosphate-based laxatives are frequently used for bowel preparation or relief of constipation in some countries. However, these agents are not without risk. Small and clinical insignificant increments on serum phosphorus levels are observed in almost all individuals after use of oral sodium phosphate. Some patients are prone to severe hyperphosphatemia such as elders, those with chronic or acute renal disease and those with poor bowel motility. Severe hyperphosphatemia accompanied with hypocalcemia may be life-threatening in these patients. We present an 18-year-old woman with neuronal intestinal dysplasia who developed symptomatic and severe hyperphosphatemia after bowel preparation with oral sodium phosphate enema. Urgent hemodialysis was performed two times for severe hyperphosphatemia.

Keywords

Extreme hyperphosphatemia, neuronal intestinal dysplasia, sodium phosphate

History

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Introduction

Colonoscopy has become the principle method to diagnose intestinal pathologies and oral sodium phosphate based enemas are widely used for adequate pre-procedural bowel cleansing. Sodium phosphate-based enemas can cause some electrolyte disorders, which usually resolve within 24 h. They are associated with metabolic derangements such as hyperphosphatemia, hypocalcemia, hyponatremia or mild hypernatremia, hypokalemia and anion-gap metabolic acidosis.[1–4] Some individuals are prone to severe and symptomatic hyperphosphatemia which could be associated with high morbidity and mortality.

Case report

An 18-year-old woman patient with abdominal discomfort was admitted to our gastroenterology clinic. She had been evaluated for nausea, vomiting and abdominal pain three years ago. Laparoscopy revealed mild ischemia and thickness of a jejunal segment (measuring 15 cm) at this time. About three months later, laparoscopy was performed again because of clinical and imaging findings of ileus. Extensive ischemia was noticed on a jejunal segment (measuring 10 cm) and this segment was removed. Gross and microscopic examination of the resected intestine was found to be consistent with intestinal neuronal dysplasia type B.

At admission, the physical examination was unremarkable except mild abdominal tenderness without rebound or guarding. Her BMI was 18.7 kg/cm^2. The laboratory data revealed that BUN 12 mg/dL, Creatinine 0.41 mg/dL, eGFR (MDRD equation): 215 mL/min/1.73 m^2, eGFR (Cockcroft–Gault formula): 147.5 mL/min, Sodium 135 mEq/L, Potassium 5.3 mEq/L, Total Calcium 8.8 mg/dL, Phosphorus 4.2 mg/dL, Albumin: 4.2 g/dL. A colonoscopy was performed after bowel preparation with oral phosphate solution (Fleet Phosphosoda®) with standard regimen. Diffuse muscle weakness, carpopedal spasm, tetany and confusion become observable 6 h after the last dose of aqueous Fleet Phosphosoda®. Blood pressure was 102/53 mmHg, heart and respiratory rate were within normal range. Renal function and electrolyte data were Glucose: 89 mg/dL, BUN 14 mg/dL, Creatinine 0.87 mg/dL, eGFR (MDRD equation): 90 mL/min/1.73 m^2, eGFR (Cockcroft–Gault formula): 69.5 mL/min, Sodium 137 mEq/L, Potassium 3.2 mEq/L, Total Calcium 4.9 mg/dL, Phosphorus 19.6 mg/dL, Magnesium: 1.4 mg/dL, Albumin: 3.8 g/dL, Uric acid: 4.1 mg/dL, LDH: 332 U/L. Emergent hemodialysis (HD) was prescribed on Day 0 and Day 1. The patient received HD through a femoral catheter, using polysulphone high flux dialyzer (F-80 dialyzer, surface area 1.8 m^2, Fresenius 2000S machine) and dialysate (K 3 mEq/L, Ca 3.5 mmol/L, HCO_3 30 mEq/L). Her blood flow rate was 300 mL/min and duration of HD was 4 h for each dialysis session. Calcium and phosphorus levels returned

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Table 1. Main laboratory data of the patient with hyperphosphatemia and acute kidney injury.

Laboratuary parameters	At admission	Day 0	Day 1	Day 2	Day 3	Day 4
Serum BUN (mg/dL)	12	14	5	6	12	10
Serum creatinine (mg/dL)	0.41	0.87	0.85	1.01	1.08	0.60
eGFR (MDRD equation), (mL/min/1.73m^2)	215	90	93	76	70	138
eGFR (Cockcroft–Gault formula) (mL/min)	147.5	69.5	71.2	59.9	56	100.8
Serum sodium (mEq/L)	135	137	148	143	137	135
Serum potassium (mEq/L)	*5.3*	3.2	3.5	3.4	3.6	4.8
Serum total calcium (mg/dL)	8.8	4.9	8.0	7.5	7.3	7.9
Serum phosphorus (mg/dL)	4.2	19.6	3.4	2.8	2.3	1.7

eGFR, estimated glomerular filtration rate. At admission, Fleet Phosphosoda® was given for bowel preparation. On Day 1, colonoscopy was performed. The patient received hemodialysis on Day 0 and Day 1. After hemodialysis on Day 0, hyperphosphatemia normalized and clinical symptoms of hypocalcemia ameliorated.
Renal function started to improve on Day 4.

to normal levels on Day 1, whereas eGFR started to return to the baseline level on Day 4 (Table 1).

Discussion

Aqueous (Fleet®PhosphoSoda®, C.B. Fleet Company, Lynchburg, VA) solution contains 48 g of monobasic and 18 g of dibasic sodium phosphate per 100 mL. Each 45 mL of liquid preparation contains 29.7 g of sodium phosphate and providing the equivalent of 5.8 g of elemental phosphorus and 5 g of sodium.[5] Standard regimen for bowel preparation is that two 45 mL doses taken the night before and morning of colonoscopy along with 1 L of water.

Increases in serum phosphorus levels after use of oral sodium phosphate was reported in all individuals[6] even in subjects with normal kidney function. Mean increase of serum phosphate levels are reported as 1.1–4.1 mg/dL.[6] Hypocalcemia is also frequent accompanied with hyperphosphatemia and the average decrease in serum calcium level is 0.32–0.6 mg/dL.[6] In our patient, serum phosphorus level increased from 4.2 to 19.6 mg/dL and serum calcium level decreased from 8.8 to 4.9 mg/dL after preparation with Fleet Phosphosoda® with standard dose. Initially, renal function was normal as well. Acute kidney injury is a miserable and rare complication of severe hyperphosphatemia after the use of oral sodium phosphate which is termed as Acute Phosphate Nephropathy.[7] Two clinical patterns of oral sodium phosphate-induced nephropathy could be observed. In acute form, there is acute kidney injury and severe hyperphosphatemia and hypocalcemia accompanied with clinical symptoms such as cardiovascular collapse, tetany and changes of mental status, usually in hours after oral sodium phosphate intake. In second form, there is a more insidious course of irreversible renal dysfunction with days to months. Serum calcium and phosphorus levels are not abnormal except the first three days of oral sodium phosphate intake if they are measured. Clinical and laboratory findings of our patient are consistent with acute form of oral sodium phosphate induced nephropathy.

The main underlining mechanism of kidney injury is that a tubular injury develops secondary to hypovolemia-induced increased proximal salt and water reabsorption, high amount of phosphate delivery in distal nephron, which results calcium phosphate deposition.[8] Precipitation of calcium phosphate in the kidneys due to high phosphate load lead to nephrocalcinosis.[9] Classical renal biopsy findings are marked tubular and interstitial calcium phosphate deposits with acute and chronic tubular injury.[8] Advanced age, excessive or repeated doses, chronic kidney disease, poor water intake or dehydration, female gender, pre-existing electrolyte disturbances, heart failure, ascites, diuretics, non-steroidal anti-inflammatory drugs and renin–angiotensin system blockage are suggested as risk factors for developing acute phosphate nephropathy.[5,7,10–13] Recently, severe hyperphosphatemia (5.3–45 mg/dL) and hypocalcemia (2–8.7 mg/dL) were reported in 11 elderly patients received high amount of Fleet enemas for constipation. Most of these patients presented with hypovolemia and hypotension within 24 h. Hypokalemia and hypernatremia were frequent electrolyte abnormalities. All patients had acute kidney injury and 50% of patients died.[10]

There is some evidence that retention of oral sodium phosphate due to poor bowel motility or colitis can be risk factor for severe hyperphosphatemia induced kidney injury.[5] Delayed bowel transit is accepted as relative contraindications to the use of oral sodium phosphate.[14] In a case series of the children exhibiting symptomatic hyperphosphatemia and hypocalcemia after sodium phosphate-containing laxatives, 18 of 28 children have pre-existing gastrointestinal comorbidity or other major systemic disease.[15] NID type B was diagnosed in our patient before. NID is classified into two clinically and histologically distinct subtypes.[16] NID Type A constitutes about 5% of the patients with NID and there is congenital aplasia or dysplasia of the sympathetic innervations. Acute onset of clinical symptoms such as episodes of intestinal obstruction, diarrhea and bloody stool in neonatal period is characteristic in NID Type A. NID Type B is a disease of the submucous plexus of intestine. The presence of hyperganglionosis, giant glia and ectopic ganglia cells in the involved intestinal segment is characteristic histological features.[17] The findings of acute or chronic intestinal obstructions of the low type are frequent clinical picture of NID Type B, but fatal intestinal ischemia was described in an adult patient.[18] A weak intestinal propulsive motility, which can delay intestinal transit is principal functional abnormality and could be responsible for severe hyperphosphatemia in our patient. Increased transit time of the phosphate including enema in the intestine could be resulted in increased amount of the intestinal absorption of phosphorus.

The majority of clinical findings of hyperphosphatemia, particularly the neuromuscular and neurological symptoms such as muscle cramps, carpopedal spasm, laryngeal spasm,

convulsion, confusion, seizure and coma are related to hypocalcemia. Some of these symptoms are present in our patient. Hyperphosphatemia secondary to massive acute phosphate load induced hypocalcemia is mainly due to calcium-phosphate precipitation in the tissues.

Acute severe hyperphosphatemia and related hypocalcemia can be life-threatening. If renal function is normal, phosphate load excreted by kidneys within 6–12 h. HD is mandatory in severe and symptomatic hyperphosphatemia, particularly in patients with renal dysfunction. In our patient, there was severe and symptomatic hyperphosphatemia, but renal dysfunction was not prominent. We initiated urgent HD to treat hyperphosphatemia effectively and rapidly aiming to resolve clinical findings and also to prevent acute kidney injury due to severe hyperphosphatemia.

Although the effects of different dialysis modalities or prescriptions on phosphate removal were well studied in patients with end-stage renal failure (ESRD), there are sparse information in adult patients with acute severe hyperphosphatemia due to oral sodium phosphate enemas. In general, multiple intermittent HD sessions or continuous hemofiltration were required or used in patients with severe renal failure or hemodynamically unstable patients accompanied with acute hyperphosphatemia.[19,20] Rebound hyperphosphatemia which is well known entity in patients with ESRD or tumor lysis syndrome was not reported in acute hyperphosphatemia due to oral sodium phosphate enema if there was no severe renal impairment. Resistant hyperphosphatemia after a single HD therapy is observed in a patient with severe renal dysfunction.[19] If urine output and renal function are preserved, a single HD therapy may be sufficient to treat hyperphosphatemia.

In ESRD patients, most of phosphate is found intracellularly and a small percentage is distributed in the extracellular space. Consequently, only small amount of plasma phosphate are directly available for dialytic removal and large rebound of phosphate are observed after HD. The PO_4 removal is between 20 and 40 mmol per HD session in ESRD patients. However, dialytic removal of phosphate is mainly due to plasma phosphorus concentration[21] and the PO_4 removal could be much more in single HD session. In our patient, plasma phosphate level dramatically reduced to normal values after the first HD and we did not observe rebound hyperphosphatemia. Urinary excretion of phosphate could elicit additional continuous phosphate clearance,[22] because urine output is not compromised in our patient. We performed second HD session aiming to prevent rebound hyperphosphatemia. It seems that second HD session might be unnecessary in our patient.

Calcium replacement therapy is dilemma in patients with severe hyperphosphatemic patients who are already high CaxP product. In our patient, CaxP product was already high ($96.04\ mg^2/dL^2$) before the first HD session. After the intake of two calcium gluconate ampules, only partially improvement of muscle weakness and confusion were observed. We had to use dialysate containing high Ca (1.75 mmol/L) during HD therapy despite further increase risk of metastatic calcification for couple of hours because she had life-threatening findings due to hypocalcemia. In spite of potential metastatic calcification risk, calcium replacement therapy was used in these patients.[19,22]

In conclusion, sodium phosphate enemas, even in standard doses, may lead to severe metabolic disorders associated with a high mortality and morbidity. Fleet phosphosoda® was withdrawn from US market in 2008.[9] A detailed consensus guidelines for the safe prescription and administration of oral bowel-cleansing agents is reported recently.[23] In Turkey, oral sodium phosphate enemas are widely in use. Their use should be avoided at least high-risk patients. In general practice, the specific attention is given mostly pre-existing kidney disease. However, the potential adverse effects of oral sodium phosphate enemas might be overlooked in patients who have other risk factors.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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