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Severe hyperphosphatemia and symptomatic hypocalcemia after bowel cleansing with oral sodium phosphate solution in a patient with postoperative hypoparathyroidism

Case Report

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Abstract: Oral sodium phosphate (NaP) is increasingly being used for bowel preparation. There are several reports of significant serum electrolyte changes after the administration of oral NaP solution in renal failure. We report a case of postoperative hypoparathyroidism who developed severe hyperphosphatemia and associated hypocalcemia after bowel preparation with oral NaP. A 39-year old woman was admitted to the hospital because of multiple bone fractures. The diagnosis of primary hyperparathyroidism was confirmed. Further assays suggested Cushing's disease and MRI disclosed a pituitary microadenoma. Considering the diagnostic suspect of multiple endocrine neoplasia type 1, computed tomography of abdomen was performed, showing a mass in the right adrenal. The patient underwent transsphenoidal surgery and then total parathyroidectomy. Despite total removal of the microadenoma by transsphenoidal surgery, there was no suppression in serum cortisol levels. So, an operation was scheduled for the adrenal tumor. The patient was administered 45 mL oral NaP solution for bowel cleansing before the surgery. Although her calcium and phosphorus levels were normal before NaP administration, four hours later she developed respiratory distress and tetany. Laboratory studies revealed severe hyperphosphatemia and hypocalcemia. We conclude that the use of NaP for bowel preparation should be avoided in patients with hypoparathyroidism.

Keywords: *Sodium phosphate • Hyperphosphatemia • Hypocalcemia • Bowel preparation • Hypoparathyroidism*

1. Introduction

Oral sodium phosphate (Fleet®) is a low-volume, hyperosmotic agent used as part of a colorectal-cleansing preparation for elective abdominal and gynecological surgery, colonoscopic examination or other colorectal-related procedures [1].

In several studies, it has been demonstrated that the efficacy and tolerability of oral sodium phosphate solution was generally similar to, or significantly better than, that of polyethylene glycol (PEG) or other colorectal cleansing regimens [2,3].

We know that symptomatic and sometimes even life-threatening electrolyte disturbances such as hyperphosphatemia and hypocalcemia occur by using oral NaP solution in patients who have risks, such as renal failure [4].

In a case report it is shown that asymptomatic hypoparathyroidism is a new risk factor for electrolyte disturbance after colon cleansing with NaP [5].

We present a patient with postoperative hypoparathyroidism who developed severe hyperphosphatemia and symptomatic hypocalcemia after bowel cleansing with oral NaP solution although she did not have renal impairment.

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Table 1. Biochemical parameters on admission.

Variable	Normal Range	On Admission
Glucose (mg/dl)	70-115	87
Sodium (mmol/L)	135-145	135
Potassium (mmol/L)	3,5-5,5	2.7
Urea (mg/dl)	10-50	16
Creatinine (mg/dl)	0,6-1,3	0.4
Calcium (mg/dl)	8,4-10,6	11.8
Ionized calcium (mg/dl)	4.2-5.2	5.72
Phosphorus (mg/dl)	2.5-5.0	1.4
Magnesium (mg/dl)	1.6-3.0	1.6
Albumin (g/dl)	3,5-5,4	3.6
Alkaline phosphatase (U/L)	40-150	124

2. Case Report

A 39-year-old woman was admitted to the hospital because of multiple fractures after fall. Her physical and radiographic examinations revealed bone fractures of right humerus, neck of left femur, and L4 vertebrae.

History revealed an 8-year period of surgery due to nephrolithiasis. Amenorrhea has been present for 5 years. Endocrinologic family history was uneventful. Her vital signs on admission were as follows: respiratory rate 24 breaths/min, oxygen saturation 96%, heart rate 80 beats/min, blood pressure 130/70 mm Hg, and temperature 37°C. Otherwise, physical examination was normal except painful joint movement. The patient's chest radiography and electrocardiogram (ECG) were normal.

Laboratory tests on admission showed hypercalcemia (total calcium: 11.8 mg/dl; normal range, 8.8-10.6 mg/dL, and ionized calcium: 5.72 mg/dL; normal range, 4.2-5.2 mg/dL), markedly increased levels of intact parathyroid hormone analyzed by IRMA (76.9 pmol/L; normal range, 1.6-6.9 pmol/L) and hypophosphatemia (1.4 mg/dl; normal range, 2.5-4.5 mg/dl). The results of other laboratory tests are shown in Table 1.

During the 6-month period, the patient developed symptoms consistent with Cushing's syndrome such as proximal muscle weakness and emotional lability. Multiple bone fractures and patient's history led us to also consider Cushing's syndrome. Further laboratory examination revealed normal plasma ACTH (36.09pg/ml; normal range, 5-77 pg/ml) and elevated serum cortisol (27.3 ug/dl; normal range, 5-25 ug/dl at 8 a.m.) with a lack of diurnal rhythm. Other pituitary hormone levels and results of 2 mg and 8 mg dexamethasone suppression tests are shown in Table 2.

Table 2. Results of endocrine tests.

Variable	Normal ranges	On admission
TSH (μIU/ml)	0.35-4.94	2.3
FT3 (pg/ml)	1.7-3.7	2.63
FT4 (ng/dl)	0.7-1.48	1.08
FSH (mIU/ml)	1.3-13.6	14.3
LH (mIU/ml)	1.2-10	4.0
Estradiol (pg/ml)	21-251	40.0
GH (ng/ml)	0-10	0.2
IGF-1 (ng/ml)	94-284	195
Prolactine (ng/ml)	1.2-30.0	20.3
PTH (pmol/L)	1.6-6.9	76.9
Cortisol (μg/dl) morning	5-23	27.3
ACTH (pg/ml) morning	5-77	63.4
24-hr urinary cortisol (μg/24 hr)	20-90	281.4
Cortisol (2 mg DST) (μg/dl)	<1.8	15.4
Cortisol (8 mg DST) (μg/dl)	50% decrease from baseline	10.0

ACTH: corticotropin; DST: dexamethasone suppression test; FT3: free triiodothyronine; FT4: free thyroxin; FSH: folicle-stimulating hormone; GH: growth hormone; LH: luteinizing hormone; PTH: parathormone; TSH: thyrotropin

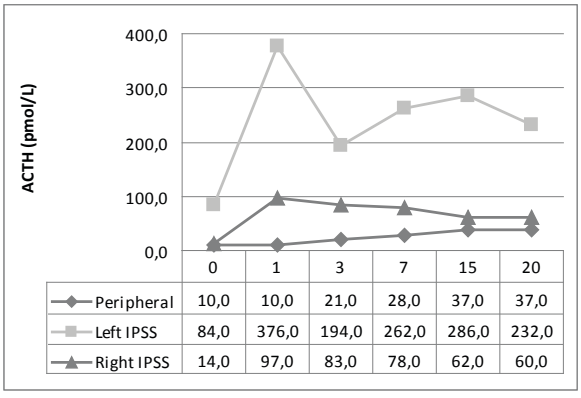
Bone mineral density (BMD) results, measured by dual energy x-ray absorptiometry (DXA), revealed severe osteoporosis. Neck ultrasonography revealed a parathyroid adenoma at the inferior of left thyroid lobe. Magnetic resonance imaging of pituitary gland revealed 4x3 mm microadenoma. Considering the diagnostic suspect of multiple endocrine neoplasia (MEN) type 1, computed tomography of abdomen was performed for possible enteropancreatic endocrine tumors, showing a mass of 51x46x43 mm in the right adrenal.

Figure 1 shows the results of bilateral inferior petrosal sinus (IPS) ACTH sampling before and after intravenous administration of 100 μg CRH. The basal IPS/peripheral (P) ACTH ratio was 1.4 for the right and 8.4 for the left IPS, resulting in a right-to-left ACTH gradient of 6.0. Following CRH stimulation, the left IPS / P ACTH ratio was 37.6 after 1 min, 9.24 after 5 min, 9.36 after 7 min i.e. which was high supporting the presence of a functional adenoma secreting ACTH in the left pituitary side.

Cushing's disease was thought to be primarily responsible for the patient's clinical course. So, pituitary microadenoma was removed with transsphenoidal surgery at first. After that, total parathyroidectomy was performed and oral supplementation of calcium (1500 mg/day) and calcitriol (1 μg/day) was started.

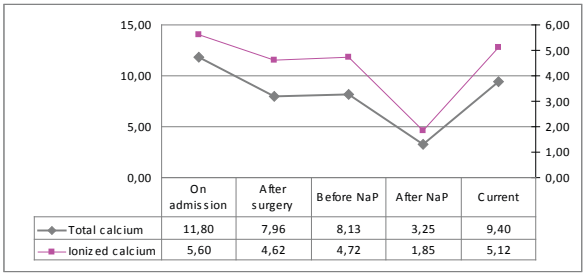
Twenty-four-hour urine cortisol level was still high after pituitary adenomectomy; so 2 mg and 8 mg dexamethasone suppression tests were repeated, but

Figure 1. Inferior petrosal sinus sampling results before pituitary surgery.



	0	1	3	7	15	20
Peripheral	10,0	10,0	21,0	28,0	37,0	37,0
Left IPSS	84,0	376,0	194,0	262,0	286,0	232,0
Right IPSS	14,0	97,0	83,0	78,0	62,0	60,0

Figure 2. Calcium levels during clinical course.



	On admission	After surgery	Before NaP	After NaP	Current
Total calcium	11,80	7,96	8,13	3,25	9,40
Ionized calcium	5,60	4,62	4,72	1,85	5,12

revealed no suppression in serum cortisol levels. An operation was scheduled as the size of tumor in right surrenal gland was greater than 4 cm which was deemed as possibly functional (it was thought as a probable neuroendocrine tumor secreting CRH). The patient was administered 45 mL oral sodium phosphate (Fleet®) for bowel cleansing the night before the surgery.

Although her electrolyte levels were normal before the NaP administration, four hours later she developed confusion, severe respiratory distress, and tetany. Blood samples were obtained immediately. Serum phosphorus level was 12.9 mg/dl, serum total and ionized calcium levels were 3.03 mg/dl and 1.72 mg/dl, respectively (Figure 2). Serum magnesium level was 0.82 mg/dl (normal range, 1.8-2.6 mg/dl). In arterial blood gas analysis pH was 7.33, pO_2 59.1 and pCO_2 38.3, and oxygen saturation was 87.8%. The QT interval was not prolonged in the ECG.

The patient was placed in intensive care unit and given intravenous calcium gluconate and oral calcitriol dosage enhancing 2 µg/day. Oral calcium acetate was also added to the treatment to decrease gastrointestinal absorption of phosphorus. Twenty four hours after the event, the patient was completely asymptomatic and the electrolyte profile returned to normal ranges. Maintenance treatment for hypocalcemia was continued with oral calcium and calcitriol treatment by same doses before NaP administration. After that, right adrenal gland was removed with surgery. Pathological examination revealed adrenocortical neoplasia. Immunohistochemical staining for surgical specimen could not be performed due to technical inadequacy. Serum cortisol level following 2 mg dexamethasone suppression test was 1.6 µg/dL, showing suppression. The patient was accepted as cured for Cushing's syndrome.

3. Discussion

Oral NaP, a low volume hyperosmotic agent containing monobasic and dibasic sodium phosphate, is increasingly being used for colorectal cleansing since it is equally effective and less costly than other agents. Several studies and reports have demonstrated significant serum electrolyte disturbances associated with oral NaP administration including hyperphosphatemia and hypocalcemia [5-11]. In patients without comorbid conditions, these electrolyte changes are usually transient and clinically insignificant. There are multiple reports of clinically significant even fatal hyperphosphatemia and hypocalcemia after NaP administration in patients with renal impairment. Fine and et al found 12 cases of severe hyperphosphatemia after oral or rectal NaP administration in the literature [12]. All had some degree of abnormal renal function and four of them died because of the complications associated with hyperphosphatemia and hypocalcemia. Dipalma et al investigated the serum and urine biochemical changes after administration of oral NaP for bowel cleansing in 7 healthy volunteers [13]. They found a significant rise in serum phosphate level and falls in serum calcium levels but there were no significant clinical adverse effects as in Liberman et al. [6]. Our patient, who had acquired hypoparathyroidism, had normal serum creatinine, calcium, and phosphate levels before bowel cleansing. Although she was receiving adequate supplementation of calcium and calcitriol, she developed severe hyperphosphatemia, hypocalcemia and respiratory distress after a single dose of 45 mL oral phosphosoda. We assume that she had a tendency toward hyperphosphatemia after phosphosoda since she had hypoparathyroidism, because hypoparathyroid patients may not be able to excrete the exogenous phosphate load. The serum phosphate level is determined by the rate of renal tubular reabsorption of the filtered load and PTH is the major known hormonal regulator of renal phosphate excretion [14,15]. PTH inhibits the phosphate transport by reducing the apical expression of Na/PO_4 co-transporter (NaPi-2) [14]. Since intestinal phosphate absorption

is highly efficient, rapid administration of exogenous phosphate (oral or rectal NaP) normally increases the renal excretion but the presence of hypoparathyroidism may lead to hyperphosphatemia because of reduced phosphate excretion via increased expression of NaPi-2 co-transporters in the proximal tubule.

Our case showed that administration of a single dose of 45 mL of oral phosphosoda may result in severe and clinically significant hyperphosphatemia and associated hypocalcemia in a hypoparathyroid patient without renal impairment or decreased intestinal motility. We recommend the use of alternative agents such as PEG for bowel cleansing in patients with hypoparathyroidism as in those with renal impairment or poor intestinal motility.

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