AJKD
AMERICAN JOURNAL OF KIDNEY DISEASES

An Unusual Case of Metabolic Alkalosis in a Patient With CKD

CLINICAL PRESENTATION

An 83-year-old woman presented with 4 days of right-sided chest pain and 2 weeks of progressive dyspnea, weight gain, and peripheral edema. She was treated with azithromycin for a cough 2 weeks prior, with resolution of symptoms. Her history was significant for chronic kidney disease (CKD) G3A3 (estimated glomerular filtration rate, 36 mL/min/1.73 m^2, as calculated by the CKD Epidemiology Collaboration equation[1]; urine protein-creatinine ratio, 400 mg/g) secondary to hypertension and prior use of nonsteroidal anti-inflammatory drugs. She also had a history of chronic hyperkalemia (treated with sodium polystyrene therapy), osteoporosis, and gastroesophageal reflux disease. Her medications are listed in Box 1. She denied recent medication changes, use of herbal or over-the-counter medications, change in diet, or nausea or vomiting. Blood pressure was 150/79 mm Hg, heart rate, 76 beats/min, respiratory rate, 24 breaths/min, and oxygen saturation, 92% breathing room air. On examination, she had jugular venous distension, bibasilar inspiratory rales, tenderness of the right chest wall, and pitting edema (2-3+) in the legs bilaterally. The radiograph of the chest showed new small bilateral pleural effusions and mildly displaced fractures of the right 8th, 9th, and 10th ribs attributed to severe coughing. Laboratory testing revealed an elevated bicarbonate level and hypokalemia (Table 1). Arterial blood gas showed pH of 7.55, P_{CO_2} of 52 mm Hg, P_{O_2} of 70 mm Hg, and bicarbonate level of 45 mEq/L.

- **What is the approach to metabolic alkalosis in this patient?**
- **What is the cause of the metabolic alkalosis in this patient?**
- **What is the role of potassium in this disorder?**
- **How should this disorder be treated?**

Box 1. Home medications

Alendronate (oral), 35 mg/wk
Amlodipine (oral), 10 mg/d
Aspirin (oral), 81 mg/d
Calcium carbonate/vitamin D_3 (oral), 600 mg/400 units 2×/d
Lisinopril (oral), 5 mg/d
Magnesium oxide (oral), 800 mg/d
Omeprazole (oral), 20 mg/d
Sodium polystyrene (oral), 30 g/d[a]

[a]Formulation changed from liquid to powder 1 month prior to admission.

Table 1. Patient's Laboratory Data Before and at Admission

Test	Time of Test		
	5 mo Prior to Admission	5 wk Prior to Admission[a]	At Admission
Sodium, mEq/L	138	138	138
Potassium, mEq/L	5.3	4.8	2.0
Chloride, mEq/L	101	96	82
Serum CO_2, mEq/L	27	25	46
Calcium, mg/dL	9.6	Not performed	8.3
Magnesium, mg/dL	1.6	Not performed	1.5
Albumin, g/dL	4.1	Not performed	3.0
Creatinine, mg/dL	1.36	1.2	0.93
eGFR,[b] mL/min/1.73 m^2	36	42	57
Urine pH	7	Not performed	7
Urine chloride, mEq/L	Not performed	Not performed	95
UACR, mg/g	400	Not performed	Not performed

Note: Conversion factors for units: calcium in mg/dL to mmol/L, ×0.2495; magnesium in mEq/L to mmol/L, ×0.5; creatinine in mg/dL to μmol/L, ×88.4; UACR in mg/g to mg/mmol, ×0.113.

Abbreviations: eGFR, estimated glomerular filtration rate; UACR, urine albumin-creatinine ratio.

[a]Laboratory tests were performed 1 week prior to the change in sodium polystyrene formulation.

[b]Calculated according to the Chronic Kidney Disease Epidemiology Collaboration.

DISCUSSION

What is the approach to metabolic alkalosis in this patient?

The patient's blood tests indicate a simple metabolic alkalosis characterized by 3 clinical features: an increase in plasma pH (to >7.40), an increase in plasma bicarbonate concentration, and an increase in P_{CO_2} due to adaptive hypoventilation. Although the differential diagnosis of metabolic alkalosis is broad, simple blood and urine tests combined with a detailed history can often lead to a diagnosis. Urine pH is an important and often overlooked initial step in this process. The patient's elevated urine pH indicates alkali loading, resolving metabolic alkalosis, or very recent vomiting prior to establishing a new steady state. With an alkaline urine pH, additional testing often is unnecessary because all other causes of metabolic alkalosis are associated with aciduria. It should be noted that although urine chloride is usually advocated as the initial diagnostic test,[2] in the case of alkali loading, urine pH can reveal the diagnosis prior to testing urinary chloride. Caution also should be used when interpreting urine chloride results after administration of diuretics because this would mask the presence of a chloride-dependent alkalosis. In our patient, urine chloride levels were found to be elevated on admission.

What is the cause of the metabolic alkalosis in this patient?

Further examination of the patient's history revealed that she was unsure of the dose of sodium polystyrene she took after the medication's formulation was changed from liquid to powder 1 month prior to admission. The patient's family believed that she might have been taking higher doses than prescribed. Coadministration of sodium polystyrene and antacids (calcium carbonate and magnesium oxide, in this case) has been reported to cause metabolic alkalosis in patients with end-stage renal disease and advanced stages of CKD.[3-6] The proposed mechanism for both antacids is shown in Fig 1. In the absence of sodium polystyrene, antacids containing calcium and magnesium first react with hydrogen chloride secreted in the stomach to form calcium chloride and magnesium chloride, respectively. These moieties enter the duodenum, where they react with the secreted sodium bicarbonate to subsequently form carbonates of the cations. Because there is equimolar secretion and consumption of hydrogen chloride and sodium bicarbonate, there is no change in the net acid-base balance.

When calcium-, magnesium-, or even aluminum-containing antacids are administered concomitantly with sodium polystyrene, there is a similar equimolar secretion of hydrogen chloride and sodium bicarbonate. However, the sodium bicarbonate secreted in the duodenum is not consumed; rather, it is reabsorbed, resulting in a salt and alkali load. Alkali loading in the presence of reduced kidney function leads to metabolic alkalosis despite alkaline urine pH.

It is not known yet whether the newer agents for management of hyperkalemia (patiromer and sodium zirconium cyclosilicate) may have a similar complication. Patiromer reportedly has nonspecific cation binding similar to sodium polystyrene, whereas sodium zirconium cyclosilicate selectively binds potassium.[7] Based on this consideration, we would hypothesize that a similar effect could be seen with patiromer use.

What is the role of potassium in this disorder?

Hypokalemia can contribute to maintenance of the metabolic alkalosis through several mechanisms including increased ammoniagenesis and increased hydrogen secretion at the intercalated A cell in the collecting duct.[2,8] In this case, we attributed hypokalemia to cellular shift along with enhanced gastrointestinal and kidney losses. It is difficult to know whether hypokalemia was contributing to maintenance of the metabolic alkalosis via increased tubular hydrogen secretion in the setting of alkaline urine.

How should this disorder be treated?

In previous case reports, it has been shown that stopping coadministration of sodium polystyrene and oral antacids results in improvement in metabolic alkalosis.[3-6] This should be adequate unless serum pH requires rapid correction for symptoms related to electrolyte abnormalities or alkalemia. This can be achieved by administration of acetazolamide (with close monitoring of serum potassium level) or rarely with dilute hydrochloric acid.[2] In our patient, both metabolic alkalosis and hypokalemia improved after