

Correction of Dialysis-Induced Metabolic Alkalosis

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Normal saline solution infusion with concurrent removal by ultrafiltration successfully corrected pretreatment metabolic alkalosis when other measures were inadequate for a patient on dialysis.

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Metabolic alkalosis, a disorder that causes elevations in serum bicarbonate and arterial pH, is a common metabolic abnormality found in nearly half of hospitalized patients but is rare in patients with end-stage renal disease (ESRD) on hemodialysis (HD) during the pretreatment state. The problem seems to arise due to a high rate of older patients with multiple comorbidities and malnutrition who are undergoing HD. Metabolic alkalosis is associated with increased morbidity and mortality. In this report, we present a case of metabolic alkalosis, describe an innovative approach to manage metabolic alkalosis in the dialysis population, and review the pathophysiology.

CASE PRESENTATION

A 63-year-old female with emphysema, diabetic nephropathy, and ESRD on regular HD for 2 months by a tunneled subclavian vein catheter was admitted with 2 weeks of orthopnea and leg swelling. The review of systems was negative for chest pain, cough, wheeze, or sputum production. She was a former smoker with no alcohol or drug misuse. The patient was taking carvedilol 25 mg daily, furosemide 20 mg twice daily, basal insulin premeal, lisinopril 40 mg daily, pantoprazole 40 mg daily, calcium carbonate 400 mg 3 times daily, ferrous sulphate 325 mg daily, and a vilanterol/tiotropium inhaler once daily. Her dialysate outpatient prescription included sodium 140 mEq/L, potassium 2 mEq/L, calcium 2.5 mEq/L, and bicarbonate 36 mEq/L. Our dialysis unit used NaturaLyte dry pack for bicarbonate dialysis.

The patient appeared tachypneic with 26 respirations/min, oxygen satura-

tion of 89% on room air, which improved to 94% on a 2 L nasal cannula. Her heart rate was 89 beats/min, blood pressure was 129/72 mm Hg, and body mass index was 21.2. The physical examination revealed jugular venous distension, lung crackles, reduced air entry, and pedal edema. Muscle wasting was noted in the arms and thighs. The tunnel catheter did not appear infected.

The patient's blood work showed sodium, 136 (reference, 132-140) mmol/L; potassium, 4.3 (reference, 3.5-5.0) mmol/L; chloride, 89 (reference, 98-111) mmol/L; total CO₂, 36 (reference, 24-28) mEq/L; blood urea nitrogen, 21 (reference, 7-21) mg/dL; creatinine 3.4 (reference, 0.5-1.4) mg/dL; and albumin, 2.7 (reference, 3.7-5.0) mg/dL. Arterial gases showed pH, 7.56 (reference, 7.35-7.45), partial CO₂, 47 (reference, 35-45) mm Hg; bicarbonate, 42 (reference, 22-26) mEq/L; partial O₂, 54 (reference, 75 to 100) mm Hg. Brain natriuretic peptide was 2,800 (normal, < 100) pg/mL with a normal troponin. X-rays showed pulmonary congestion and bilateral pleural effusions that were transudative on fluid analysis. An echocardiogram showed ejection fraction of 20 to 25% with normal valves (baseline ejection fraction of 60%-65%). A coronary arteriogram revealed severe nonischemic cardiomyopathy.

Treatment

To reduce bicarbonate levels, 3 L of normal saline solution were infused prefilter during HD, and ultrafiltration (UF) of 4.5 L achieved a net UF of -1.5 L over 3.5 hours on lower dialysate bicarbonate (30 mEq/L). Good catheter flow was achieved with a blood flow rate of 350 mL/min and a dialysate flow of 700 mL/min. Venous blood gases and basic

serum metabolic panels were obtained throughout the first HD session (Table 1). Improvement in pH from 7.5 to 7.43 and in total CO₂ from 36 to 30 mEq/L were noted after the treatment. Subsequently, we used the same membrane (Optiflux F160NRe) for 2 consecutive daily treatments to remove excess fluid and prevent worsening alkalosis using the same minimal bicarbonate bath, but no further normal saline solution was given.

Outcome

Volume overload was controlled as needed with UF. The bicarbonate did not drop after the second HD session, suggesting low organic acid production in the intradialytic period. By shortening the duration of dialysis to 3 hours and improving nutritional intake, we achieved dry weight, and the patient was discharged home with a total CO₂ of 25 mEq/L. Outpatient dialysis sessions were arranged to run at shorter duration (3 hours compared with 3.5 hours) and use low bicarbonate dialysate. The patient was admitted several times afterward for acute decompensated heart failure, but in all those admissions, her bicarbonate was in the normal-to-high range, between 23 and 30 mEq/L.

DISCUSSION

Metabolic alkalosis is relatively rare in ESRD patients on HD. Particularly in the predialysis period, but with the growing number of older patients undergoing HD and the aggressive treatment of acidosis with relatively higher buffer concentrations; there has been an increase in the incidence of metabolic alkalosis in patients on HD. In the Fresenius Medical Care (FMC) prevalent HD patient study, predialysis bicarbonate levels have increased overtime from a mean (SD) 22.9 (3.1) mEq/L in 2004 to a mean (SD) 24.1 (3.5) mEq/L in September 2011, with 25% of patients > 26.0 mEq/L compared with only 6% in 2004.¹ The condition has been associated with cardiac arrhythmia, intradialytic hypocalcemia, hypokalemia, hypercapnia, hypoxia, accelerated hypertension, and seizure.²⁻⁴ Metabolic alkalosis may be associated with increased mortality.⁵⁻⁷ However, the effect dissipated after adjusting for inflammation and nutritional status.⁶

Our patient had primary metabolic alkalosis evident by her high pH of 7.56 and

TABLE 1 First Dialysis Session Results

Components	Hemodialysis		
	Before	During	After
pH	7.50	7.47	7.43
PCO ₂ , mm Hg	42	48	47
Total CO ₂ , mEq/L	36	36	30
Sodium, mmol/L	137	137	136
Chloride, mmol/L	91	100	101

high total CO₂ of 36 mEq/L. The serum total CO₂ reflects the metabolic status more accurately than the blood gas bicarbonate, which is prone to calculation error by the Henderson-Hasselbalch equation. Her respiratory compensation for the metabolic alkalosis was appropriate, with an increase of arterial PaCO₂ to 47 mm Hg (expected PaCO₂ = 40 + 0.7[HCO₃⁻-24] = 48.4). She had normal baseline PaCO₂ in the weeks prior to admission. Due to lack of residual urine output, < 50 mL/d, her metabolic alkalosis could not be attributed to the generation of bicarbonate by the kidneys, or ameliorated by dumping of excess bicarbonate, which explained why her metabolic alkalosis was severe. On the other hand, respiratory distress may have hindered the appropriate CO₂ retention.

In patients with ESRD on HD who have no residual urine output, causes of metabolic alkalosis are limited to loss of net acid or gain of alkali through the gastrointestinal tract; our patient had none of these. Similarly, all renal causes of metabolic alkalosis are not applicable to our patient, including mineralocorticoid excess and contraction alkalosis. In patients with preserved kidney function, loop diuretics can induce alkalosis through enhanced tubular absorption of HCO₃⁻. While acetazolamide can mitigate this scenario by blocking carbonic anhydrase in the luminal border of the collecting ducts resulting in excretion of bicarbonate in the urine, our patient had negligible urine output despite being on furosemide 20 mg twice daily, making this an unlikely cause.

Severe metabolic alkalosis in dialysis patients has been reported with cocaine use, pica ingestion, and citrate load as in plasma exchange, massive transfusions, and

TABLE 2 Contents of Acid Concentrates by Manufacturer^a

Manufacturers	Acid Concentrate	Acetic acid, mEq/L	Acetate, mEq/L ^b	Citric acid, mEq/L ^b	Sum of Acetic Acid, Acetate, and Citric Acid (mEq/L) ^b
Fresenius Medical Care	Naturalyte	4	–	–	4
	GranuFlo	4	4	–	8
	Citrasate	–	0.3	2.4	2.7
Minntech	Centrisol	4	–	–	4
	Renasol	4	–	–	4
Diasol	Diasol	4	–	–	4
	Dryasol	4	–	–	4

Adapted from Fresenius Medical Care North America Bicarbonate Dialysis Update.¹

^aAll available dialysates have either acetic acid, acetate, citric acid or combinations of these elements.

^bActual value may vary slightly depending on postreaction bicarbonate and sodium settings.

regional anticoagulation.^{2,8-11} Although calcium carbonate intake can contribute to alkalosis, her small daily dose of 1,200 mg contains approximately 12 mEq of carbonate, which is not a significant contributor to the alkalosis.

With all other causes excluded, the metabolic alkalosis in our patient is presumed to result from the bicarbonate-rich dialysate. Since the majority of patients with ESRD are acidotic before dialysis, the dialysate bicarbonate is set at a higher than normal physiologic level to bring the pH close to or even higher than normal after dialysis. The patient had been dialyzed with Naturalyte as an outpatient, which was set at the dialysis unit default mode of 36 mEq/L. This form of alkalosis has been reported to peak immediately after treatment but in most patients returns to the predialysis acidotic state due to endogenous acid production.^{1,4,12} Normally, muscles play a significant role in buffering excess bicarbonate in patients with non-functioning kidneys; hence, malnutrition with muscle wasting tends to propagate and maintain alkalosis, as in our patient.

Managing alkalosis in patients on dialysis can be challenging and is often directed at identifying potential causes like overzealous bicarbonate dialysate and addressing comorbidities, especially malnutrition.^{6,7} Bicarbonate delivery can be set on dialysis machines as low as 20 mEq/L. However, the reliability of correcting serum bicarbonate by adjusting bicarbonate-based dialysis products is in question as these products deliver additional buff-

ering capacity through mixing and metabolism of acetate, acetic acid, or citric acid (Table 2).

We infused a high volume of sodium chloride during dialysis to create hyperchloremic metabolic acidosis while removing the volume by UF, thereby eliminating more bicarbonate by convection. Normal saline has a pH of 5.5 and a chloride of 154 mmol/L. We have compensated for an inherent lack of flexibility in HD as it is currently practiced: dialysates are virtually all deliberately alkaline because most of the patients coming to HD have varying magnitudes of metabolic acidosis and acidemia. The dialysate concentrate that dilutes to a bicarbonate level of 30 mEq/L would have only a modest effect against this magnitude of metabolic alkalosis that this patient had at dialysis. We have compensated for this structural inadequacy of current HD by repairing the patient's severe hypochloremic metabolic alkalosis by infusing a hyperchloremic sodium chloride solution and dialyzing off the excess sodium bicarbonate. This is the logical inverse of what usually happens in the severely acidotic patients seen prior to dialysis: dialyzing off an excess of normal saline and repairing the metabolic acidosis by transfer-in of sodium bicarbonate from the dialysate.

Fresenius Medical Care, which provides most HD machines and fluids in the United States, created charts to show the approximate degree that each contributes as additional buffer. That was in response to a class action lawsuit for metabolic alkalosis

due to overdelivery of bicarbonate that resulted in alleged cardiac arrests in patients with HD.¹³ Their report cast doubt on the ability of a lower bicarbonate bath to correct metabolic alkalosis in a predictable fashion.¹ We accordingly showed that normal saline delivery is a reliable option to promptly lower serum bicarbonate level. However, this is a temporary measure and long-term bicarbonate delivery during dialysis needs to be addressed.

Huber and Gennari demonstrated success in reducing severe alkalosis in patients with ESRD due to vomiting with the use of HCO₃ bath of 30 mEq/L.¹⁴ In their report, the calculated bicarbonate dropped from 94 to 39 mEq/L; after 3 hours of HD, their patient also was receiving 2 L of an isotonic saline infusion daily. These observations suggest that lowering bicarbonate in the bath is effective in much more severe cases than ours, and even then, extra measures are needed to bring it down to desirable levels. In the early days, some health care providers used a specially prepared high-chloride (123 mEq/L) and low-acetate dialysate (18 mEq/L), which increased serum chloride and hydrogen ion concentrations and decreased the serum bicarbonate concentration compared with those in commercially available high-acetate dialysate (containing 37 mEq/L acetate and 104 mEq/L Cl).¹⁵ However, this method requires special preparation of dialysate. Oral potassium chloride also was used to correct metabolic alkalosis, but the risk of potassium overload precludes this approach in patients with ESRD.¹⁶

Likewise, adding oral sodium chloride risks causing volume overload, especially in patients with cardiomyopathy; it may increase thirst, resulting in interdialytic excess volume gains.¹⁷ In our patient, respiratory compensation took place by correcting pulmonary congestion by UF, and the gentle bicarbonate removal in addition to boosting chloride levels promptly improved the metabolic alkalosis.

Notably adequate volume control achieved by HD in persons with small muscle mass and severe cardiomyopathy can require longer treatment duration than

required to achieve adequate clearance. Accordingly, more bicarbonate loading can take place, causing metabolic alkalosis. This problem is compounded by the potential overdelivery of bicarbonate than that entered by the physician's order.¹

CONCLUSIONS

Attention should be paid to detect elevated predialysis serum bicarbonate levels in ESRD patients on HD, especially those with values above 27 mmol/L due to higher mortality.^{6,7} Treatment of these patients is more challenging than for those who are acidotic predialysis, especially when alkalosis is compounded by malnutrition. Mitigation of this problem is achieved by using a lower bicarbonate bath and the shortest effective dialysis duration that achieves adequate clearance. Poor clearance also deleteriously affects patient nutrition and well-being. We have shown that normal saline solution infusion with concurrent removal by UF can correct pretreatment metabolic alkalosis when other measures are inadequate.

Author disclosures

The authors report no actual or potential conflicts of interest with regard to this article.

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