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Diet-Exercise-Induced Hypokalemic Metabolic Alkalosis

To the Editor:

The combination of endurance exercise and an alkaline diet may cause hypokalemic metabolic alkalosis,[1] but little is known regarding this uncommon cause of hypokalemic metabolic alkalosis.

A healthy 49-year-old female with no medical history, on no medication, and no history of substance abuse presented with a convulsive syncope secondary to hypokalemic metabolic alkalosis (plasma potassium 2.7 mEq/L and plasma bicarbonate 29 mEq/L) with prolonged QT interval (503 ms). She was admitted for telemetry monitoring and treatment with intravenous potassium chloride. After the correction of hypokalemia, the QT interval normalized, and no signs of arrhythmia were observed. She was discharged and followed-up as outpatient.

In the outpatient setting, hypokalemia and metabolic alkalosis persisted and were further characterized by normal blood pressure, normal kidney function, normal plasma magnesium, high urine pH (8-9), high fractional potassium excretion (>15%), low fractional excretions of sodium and chloride (<1%), and normal plasma renin and aldosterone (see Table 1 for complete laboratory results). Because these findings were not characteristic for a specific cause, we formally excluded common causes of hypokalemic metabolic alkalosis, including primary aldosteronism, hypercortisolism, tubulopathies, Pendred syndrome, cystic fibrosis, vomiting, eating disorders, and the use of diuretics, laxatives, or licorice. Because she performed daily multihour

Table 1 Complete Laboratory Results

Setting	Outpatient	Hospital		R1	A1	R2		A2	Reference
Diet	Alkaline	Alkaline	Acidic	Alkaline	Acidic	Alkaline	Alkaline	Acidic	
Exercise	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	
Plasma									
Na^+	139	137	138	140	143	136	140	139	136-145
K^+	3.4	3.4	4.3	4.3	4.0	4.2	3.0	3.7	3.5-5.1
Cl^-	98	93	105	102	109	99	97	100	97-107
HCO^{3-}	30.1	36.2	23.4	29.4	25.3	28.8	33.8	29.9	21.0-27.0
eGFR	56	55	66	62	65	61	69	69	>60
Renin	26.6	60.3	22.3	43.9	6.2	44.9	18.2	8.3	6-63
Aldosterone	130	<50	217	209	<50	278	<50	<50	139-694
Urine									
pH	9	9	7	9	8	8	8	—	
Osmolality	705	399	67	717	210	763	84	—	
Na^+	84	52	9	33	53	62	20	—	
K^+	156	63	9	162	14	131	9	—	
Cl^-	35	18	11	28	30	25	9	—	
Fractional Excretions*									
Na^+	0.4	0.4	0.6	0.1	0.7	0.2	1.2	—	
K^+	28.2	19.5	18.6	21.5	6.6	16.1	25.8	—	
Cl^-	0.2	0.2	0.9	0.2	0.5	0.1	0.8	—	

All units in mEq/L, except for eGFR (mL/min/1.73m^2), renin (μU/mL), aldosterone (pmol/L), osmolality (mOsm/kg), and fractional excretions (%).

*Fractional excretions were calculated as (urine electrolyte concentration * plasma creatinine) / (plasma electrolyte concentration * urine creatinine) × 100.

A = dietary adjustment; Cl^- = chloride; eGFR = estimated glomerular filtration rate; HCO_3^- = bicarbonate; K^+ = potassium; Na^+ = sodium; R = rechallenge.

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endurance exercise and consumed a healthy diet, we finally considered this as the cause of hypokalemic metabolic alkalosis. Nutritional assessment showed that she was well-nourished and consumed the required calories and proteins, ~1800 kcal/d, ~88 g/d, respectively, for her theoretical needs, ~1650 kcal/d and ~65 g/d, respectively. Calculation of her potential renal acid load showed that she consumed an alkaline diet (-5.1 mEq/d), which was mainly explained by fruits, vegetables, and dairy. Her body mass index was 20.2 kg/m^2 and was stable over time (observation time >2 years).

During hospital admission for analysis, hypokalemic metabolic alkalosis resolved by refraining from exercise and consuming the hospital diet (Figure 1A). During 2 rechallenges of her diet-exercise combination (potential renal acid load −26 mEq/d), she again developed hypokalemic metabolic alkalosis. Serial measurements of plasma bicarbonate correlated strongly with plasma chloride (r^2 0.8, P = 0.0009), suggesting chloride depletion maintained the alkalosis (Figure 1B). Her urine composition showed low excretion of ammonium and high excretion of bicarbonate and organic anions (Figure 1C). A switch to a more acidic diet (potential renal acid load +10.6 mEq/d) prevented hypokalemic metabolic alkalosis and allowed her to continue exercise.

This case illustrates that the combination of endurance exercise (chloride loss) and an alkaline diet (bicarbonate gain) can cause metabolic alkalosis with secondary hypokalemia. Metabolic alkalosis can only persist if the ability to excrete excess bicarbonate in urine is impaired because of chloride depletion, hypovolemia, reduced glomerular filtration rate, or mineralocorticoid excess. In our case, chloride depletion maintained the metabolic alkalosis (Figure 1). The characteristics of our case are similar to those reported previously, including the low urine chloride and ammonium excretions and high excretion of organic anions.[1] We also measured urine bicarbonate and α-ketoglutarate, which is secreted by the proximal tubule during alkalosis.[2] The distribution of bicarbonate and organic anions during hypokalemic metabolic alkalosis is compatible with experimental data analyzing urinary composition after heavy base loading.[2] It is unclear how common hypokalemic metabolic alkalosis is among subjects with similar diet-exercise combinations. Hypokalemic metabolic alkalosis may be relatively mild and, therefore, remain asymptomatic. Furthermore, individual susceptibility may be determined by differences in the sodium chloride content of sweat or the gastrointestinal absorption or production of organic anions and bicarbonate.[3]

In summary, diet-exercise combinations can cause hypokalemic metabolic alkalosis when loss of chloride is replaced by base and nonreabsorbable anions promote kaliuresis. We believe that the detailed analysis of this case including challenge-dechallenge-rechallenge testing sheds further light on the pathogenesis of diet-exercise-induced hypokalemic metabolic alkalosis and will assist physicians to recognize and treat future cases.

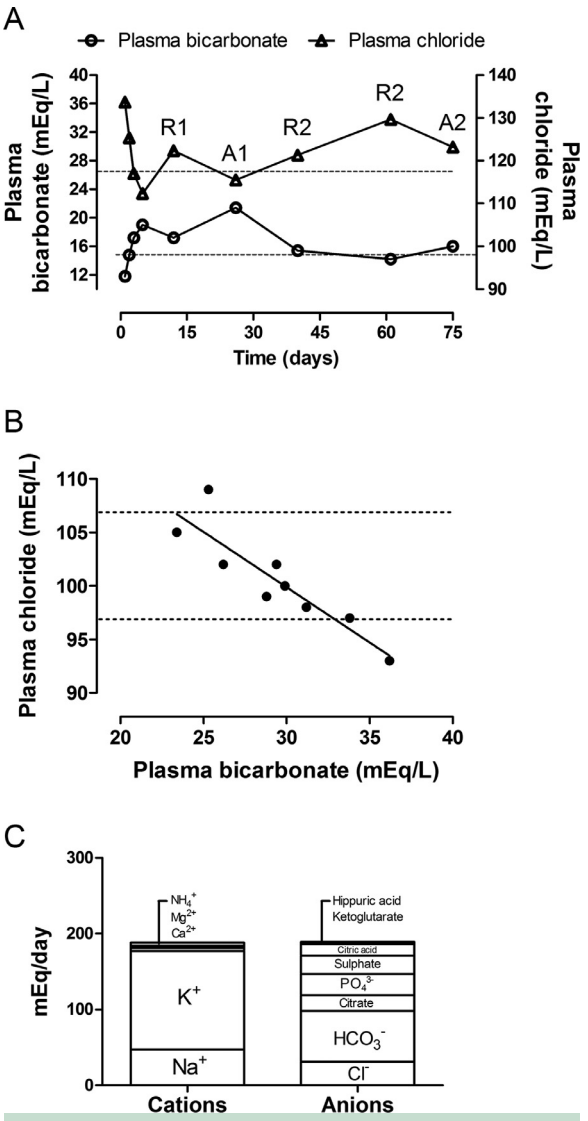

Figure 1 Plasma bicarbonate, plasma chloride, and urinary composition during hypokalemic metabolic alkalosis. **(A)** The first 4 days represent the hospital admission for analysis. Subsequently, the diet-exercise combination was rechallenged twice (R1, R2), and alternated with adjustment to a more acidic diet (A1, A2). **(B)** Correlation between the serial measurements of plasma bicarbonate and plasma chloride measurements (r^2 0.8, P = 0.0009); **(C)** 24-hour urine composition during hypokalemic metabolic alkalosis.

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References

1. Kamel KS, Ethier J, Levin A, Halperin ML. Hypokalemia in the "beautiful people". *Am J Med* 1990;88:534–6.
2. Packer RK, Curry CA, Brown KM. Urinary organic anion excretion in response to dietary acid and base loading. *J Am Soc Nephrol* 1995;5:1624–9.
3. Remer T. Influence of diet on acid-base balance. *Semin Dial* 2000;13:221–6.