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Case Report

Treatment of hypochloremia with acetazolamide in an advanced heart failure patient and importance of monitoring urinary electrolytes

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ABSTRACT

Chloride was recently recognized to play an important role in the pathophysiology of heart failure (HF). Chloride manipulation, including the use of acetazolamide, may be a requisite therapeutic target in HF treatment. An 87-year-old male patient with advanced HF and hypertrophic cardiomyopathy was admitted to the hospital due to hypochloremia (94 mEq/L) and hyponatremia (134 mEq/L) under diuretic treatment with azosemide, spironolactone, and tolvaptan. On admission, HF-related signs of overhydration were lacking, but B-type natriuretic peptide was moderately elevated. The etiology of the hypochloremia/natremia state was depletion of both electrolytes based on serum analysis and spot urinary concentrations. Immediately after admission, acetazolamide (500 mg/d) was prescribed to correct the hypochloremia in parallel with cessation of the preceding administration of azosemide and spironolactone, and tapering off of the tolvaptan over 7 days. Under treatment, both serum chloride and sodium concentrations recovered to normal (108 mEq/L and 148 mEq/L, respectively), and the serum potassium concentration decreased from 3.9 mEq/L to 2.4 mEq/L. Urinary concentrations of sodium and potassium increased from 18 mEq/L to 31 mEq/L and from 19 mEq/L to 51.5 mEq/L respectively, in concordance with the changes in serum concentrations, but the chloride concentration decreased from 18 mEq/L to 12 mEq/L, opposite the changes in the serum concentration.

<**Learning objective:** The present case confirms that the classic drug acetazolamide, although rarely used now for HF treatment, is a potent "chloride-regaining" or "chloride-retaining diuretic" with concomitant activity to reduce serum potassium. Additionally, this case study highlights the importance of monitoring both serum and urinary electrolyte concentrations to determine the electrolyte disturbance and efficacy of diuretic treatment through analytic evaluation of changes in the serum electrolytes and their tubular reabsorption in the kidney.>

Introduction

Chloride was recently identified as having an important role in heart failure (HF) pathophysiology. Grodin et al. reported that upon admission for worsening HF, the serum chloride concentration, but not the serum sodium concentration, is an independent prognostic marker of acutely decompensated HF [1]. I recently proposed a unifying hypothesis of the "chloride theory" for HF pathophysiology during worsening HF and its therapeutic resolution [2,3]. According to the "chloride theory" [2], chloride manipulation, including the use of acetazolamide [4–6], may be an essential therapeutic target in HF treatment.

Case report

An 87-year-old man with advanced HF patient (New York Heart Association functional class III) and hypertrophic cardiomyopathy was admitted to the hospital due to complaints of general fatigue and loss of appetite. Physical examination on admission revealed no HF-related physical signs of neck vein distension, peripheral edema, extra-cardiac sounds, or bilateral pulmonary rales, but he presented with weight loss of 2 kg over 3 months, hypotension (92/72 mmHg), irregular pulse (98 bpm), and peripheral coldness. A 12-lead electrocardiogram revealed atrial fibrillation with an irregular heart rate of 106 beats/min and a complete right bundle branch pattern. A chest X-ray revealed moderate cardiomegaly (cardiothoracic ratio, 63%), but no signs of pulmonary congestion or pleural effusion. Ultrasonography showed diastolic dysfunction with reduced left ventricular ejection fraction (40%), non-dilated diastolic volume (74 cc), marked asymmetric left ventricular

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hypertrophy (interventricular septum, 35 mm; posterior wall, 20 mm), and a moderately enlarged left atrium. Ultrasound revealed no pleural effusion, but a moderately expanded inferior vena cava with minimal respiratory change. Blood examination revealed a modestly increased serum B-type natriuretic peptide concentration (720 pg/ml), reduced renal function (estimated glomerular filtration rate of 31 mL/min), and a moderate degree of hyponatremia (134 mEq/L) and hypochloremia (94 mEq/L) under diuretic treatment with a combination of azosemide (90 mg/d), spironolactone (12.5 mg/d), and tolvaptan (22.5 mg/d).

To identify the background mechanisms of the hypochloremia and hyponatremia in this patient, longitudinal changes in serum and spot urinary electrolytes [7] before and after the present hospital admission were examined in parallel with evaluation of changes in other laboratory tests (Table 1). Approximately four months prior to the present hospital admission, he was admitted to another hospital (March, 2017) and underwent evaluation of dietary effects on the changes in serum and spot urinary solutes under a high- (12 g/d) or low-salt (6 g/d) diet. That evaluation clearly revealed high and low urinary excretion of both sodium and chloride in accordance with the amount of dietary salt. The etiology of hypochloremia and hyponatremia at the present admission (July, 2017) was determined to be the depletion of both sodium and chloride electrolytes from the body based on the evaluation of serum and spot urinary concentrations of the solutes, i.e. excretion of both chloride and sodium was extremely reduced compared with the previous examination. Acetazolamide (500 mg/d) was prescribed on day 1 of the present admission to correct the hypochloremia, and replace the previously prescribed diuretics. In parallel, the preceding administration of azosemide (90 mg/d) and spironolactone (12.5 mg/d) was discontinued immediately, and tolvaptan was tapered off over 7 days from 22.5 mg/d before admission to 15 mg/d, 7.5 mg/d, and ultimately cessation. Under such treatment, both the serum chloride and sodium concentrations recovered to normal values (108 mEq/L and 148 mEq/L, respectively), and the serum potassium concentration decreased from 3.9 mEq/L to 2.4 mEq/L on day 8 of hospitalization. Urinary concentrations of sodium and potassium were increased (sodium, from 18 mEq/L to 31 mEq/L; potassium, from 19 mEq/L to 51.5 mEq/L) in accordance with the changes in the serum concentrations, but the urinary chloride concentration was decreased (from 18 mEq/L to 12 mEq/L) opposite the changes in the serum concentration. Thereafter, the hypokalemia was treated by increasing the dose of oral spironolactone (37.5 mg/d) and administering a potassium supplement (Slow-K, 1200 mg/d). As shown in Table 1, the serum potassium concentration returned to the normal range (4.5 mEq/L) on day 14 of hospitalization. At this time, the appetite loss and hypotension improved, worsening of

Table 1 Changes in serum and urinary electrolytes before and after administration of acetazolamide.

	Admission to another hospital (March/2017)		Admission to the present hospital (July/2017)			
			Before acetazolamide therapy — day 1	After acetazolamide therapy		
	High-salt diet (12 g/d) (March 15)	Low-salt diet (6 g/d) (March 21)	(July 4)	Day 4 (July 8)	Day 8 (July 12)	Day 14 (July 18)
A. Heart failure-related examination						
Body weight (kg)	50	–	48.1	–	–	–
Blood pressure (mmHg)	115/82	–	92/71	85/66	94/67	104/77
Heart rate (bpm)	91	–	98	95	83	80
Sings of body fluid retention	No	–	No	No	No	No
B-type natriuretic peptide (pg/mL)	711		720	–	–	–
B. Peripheral blood examination						
Hemoglobin (g/dL)	14	14.6	14.4	14.5	14.8	13.5
Hematocrit (%)	42.2	42.4	42.1	42.8	44.8	39.7
MCV (fL)	100	98.6	102	105	107	106
Serum electrolytes						
Sodium (mEq/L)	142	138	134	138	148	147
Potassium (mEq/L)	4.1	4.3	3.9	3.2	2.4	4.5
Chloride (mEq/L)	104	105	94	102	108	109
Serum blood urea nitrogen (mg/dL)			48	50	66	45
Serum creatinine (mg/dL)	1.64	1.8	1.67	1.78	2.38	1.47
C. Urinary examination						
Urinary electrolytes						
Sodium (mEq/L)	92	54.3	18	–	31	–
Potassium (mEq/L)	10.8	17.9	19	–	51.5	–
Chloride (mEq/L)	90	59.1	18	–	12	–
Urinary creatinine (mg/dL)	25.8	–	46.7	–	71.2	–
Urinary electrolytes corrected by urinary creatinine						
Sodium/Cr (10mEq/g Cr)	3.57	–	0.39	–	0.44	–
Potassium/Cr (10mEq/g Cr)	0.42	–	0.41	–	0.72	–
Chloride/Cr (10mEq/g Cr)	3.49	–	0.39	–	0.17	–
D. Diuretic treatment (daily dose)						

Cr, Creatinine; d, day; MCV, mean corporeal red cell volume.

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