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Case Report

# Strategy for monitoring decompensated heart failure treated by an oral vasopressin antagonist with special reference to the role of serum chloride: A case report

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ABSTRACT

Compared with conventional diuretic therapy, monitoring decompensated heart failure (HF) under treatment with a vasopressin antagonist is problematic because (1) use of this medication usually allows the patient free water intake to prevent drug-induced hypernatremia and (2) this medication often induces only minimal changes in the hemodynamics and blood concentration. In a 68-year-old female HF patient, use of tolvaptan did not induce much change in the urine output, presumably because of the low water intake due to a lack of thirst, but she did achieve a profound weight loss. Both the changes in chloride and sodium were negatively correlated with changes in the hemoglobin and serum creatinine, and positively correlated with changes in the mean red blood cell volume, but changes in the serum chloride were better correlated with each variable than were changes in the serum sodium.
<**Learning objective:** The present case of heat failure therapy using a vasopressin antagonist highlights the importance of monitoring serum chloride concentration in relation to changes in the hemoglobin (to evaluate intravascular volume) and mean red cell volume (to estimate intracellular fluid status) in addition to changes in body weight.>



## Introduction

In heart failure (HF) patients with hypervolemic hyponatremia, an oral vasopressin $V_2$-receptor antagonist, such as tolvaptan, induces aquaresis in the kidney and a subsequent increase in the serum sodium concentration [1]. Fluid removal with a vasopressin receptor antagonist beneficially occurs with sparing or improvement of renal blood flow and the glomerular filtration rate, relative to treatment with a loop diuretic [2]. Compared with conventional diuretic therapy, monitoring of decompensated HF patients under treatment with a vasopressin antagonist is problematic, however, because this medication (1) usually allows a patient free water intake to prevent drug-induced hypernatremia and (2) often induces minimal changes in hemodynamics and blood concentration [3,4]. Therefore, it is important to elucidate suitable methods for monitoring HF patients during treatment with a vasopressin antagonist. In HF status, alterations in body fluid accompany changes in both the extracellular and intracellular fluid volumes. Treatment of HF patients requires clinical evaluation and monitoring of changes in each volume. We recently demonstrated that, in HF patients, serum chloride (Cl) is a key osmolyte for the regulation of intracellular volume [5] and distribution of body fluid between each compartment of extracellular and intravascular spaces [6]. Herein, we report the case of an HF patient treated with a vasopressin antagonist that highlights the importance of monitoring changes in serum Cl concentration in relation to changes in plasma hemoglobin to evaluate intravascular volume and changes in mean red blood cell volume (MCV) to estimate intracellular volume.

## Case report

A 68-year-old female, being treated for hypertension by another clinic, first visited (October, 2014) our outpatient clinic 9 months prior to the present admission because of the onset of decongestive HF. Cardiac examination revealed diastolic dysfunction of the preserved left ventricular ejection fraction (49%), non-dilated diastolic volume (133 cc), and moderate mitral and tricuspid regurgitation. A 12-lead electrocardiogram revealed atrial fibrillation with a heart rate of 110 beats/min. She was

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**Table 1** Findings of the study patient.

| | Out patient | | In hospital | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | July 10 | 31 | August 21 | 24 | 25 | 26 | 28 | Sept 4 | 7 | 11 |
| Body weight (kg) | 38.2 | 38.1 | 39.6 | – | – | – | 36.4 | 39 | 38.8 | – |
| Urine output (cc) | – | – | – | 1150 | 1200 | 1000 | 980 | 1200 | 600 | 1820 |
| Blood pressure (mmHg) | 97/68 | 109/73 | 98/78 | 107/77 | 117/79 | 109/68 | 111/69 | 96/71 | 97/75 | 103/79 |
| Heart rate (bpm) | – | 61 | 82 | 55 | 85 | 79 | 84 | 62 | 92 | 54 |
| HF related symptoms | | | | | | | | | | |
| Dyspnea | NYHA II | NYHA II | NYHA III | – | – | – | NYHA II | NYHA III | – | NYHA II |
| Physical findings | | | | | | | | | | |
| Wheezing on lung auscultation | Absent | Absent | Mild | Mild | – | – | Absent | Absent | Mild | Absent |
| Distribution of edema | Pedal | Pedal | Systemic | Systemic | – | – | Absent | Systemic | Systemic | Absent |
| Pleural effusion by ultrasound | Absent | – | – | – | – | – | Absent | – | Moderate | – |
| Peripheral blood findings | | | | | | | | | | |
| Hemoglobin (g/dL) | 14.2 | 14.1 | 14.1 | 15.1 | – | 13.9 | 13.1 | 12.3 | 11.9 | 12.7 |
| Hematocrit (%) | 41.5 | 40.3 | 39.7 | 42.5 | – | 40.1 | 39 | 37.2 | 36 | 37.6 |
| Mean red cell volume (fL) | 87 | 85 | 83 | 83 | – | 85 | 88 | 89 | 91 | 89 |
| Total protein (g/dL) | – | 6.3 | 5.7 | – | – | – | 5.8 | – | 5.4 | 5.6 |
| Albumin (g/dL) | – | 3.6 | 3.1 | – | – | – | 3.1 | – | 2.8 | 2.7 |
| Electrolytes (mEq/L) | | | | | – | | | | | |
| Sodium | 134 | – | 125 | 126 | – | 135 | 140 | 136 | 140 | 140 |
| Potassium | 4.2 | – | 5 | 4.3 | – | 4 | 4.3 | 5 | 4.6 | 3.9 |
| Chloride | 96 | – | 87 | 85 | – | 98 | 104 | 102 | 108 | 104 |
| Blood urea nitrogen (mg/dL) | 25 | 17 | 23 | 39 | – | 44 | 32 | 27 | 21 | 27 |
| Creatinine (mg/dL) | 1.13 | 0.91 | 1.01 | 1.15 | – | 1 | 0.91 | 0.91 | 0.85 | 0.91 |
| B-type natriuretic peptide (pg/mL) | 573 | – | 661 | – | – | – | 593 | – | 1014 | 749 |
| Loop diuretic | | | | | | | | | | |
| Azosemide | Azosemide 60 mg | | | | | | | | Azosemide 60 mg | |
| Mineralocorticoid antagonist | | | | | | | | | | |
| Spironolactone | Spironolactone 25 mg | | | | | | | | | |
| Vasopressin antagonist | | | | | | | | | | |
| Tolvaptan | Tolvaptan 7.5 mg → 15 mg | | | | | | | | | |

HF, heart failure.

initially treated with loop diuretics (60 mg azosemide and 25 mg spironolactone every morning) to control body fluid retention and β-blockade (10 mg carvedilol twice daily) for control of heart rate and blood pressure. The subsequent clinical course was uneventful up to the present admission and her serum B-type natriuretic peptide (BNP) levels fluctuated between 241 and 573 pg/mL without worsening of HF status except for occasional mild pedal edema.

Owing to worsening of the HF and progressive hyponatremia, she was admitted to our hospital on August 21, 2015. Clinical course and physical signs, peripheral blood, serum electrolytes, and measurement of BNP are shown in Table 1. Upon admission, she complained of a mild dyspneic sensation at rest and her body weight had increased by 1.5 kg compared to that at a recent outpatient clinic visit (July 31, 2015). Physical examination revealed mild systemic edema and bronchial wheezing on chest auscultation. Upon admission, the dosage of a β-blocker was reduced (2.5 mg carvedilol twice daily) due to progressive hypotension. To correct the overhydrated hyponatremia, we discontinued the azosemide and initiated oral administration of tolvaptan on August 25. The dose of tolvaptan was 7.5 mg on day 1, and increased the following day to 15 mg every morning. This medication did not noticeably increase the patient's urine volume, but modestly reduced her body weight by 3 kg and resolved the systemic edema within 3 days of beginning the treatment. During this period, the serum sodium and Cl concentrations concomitantly increased to a normal range and the hemoglobin concentration gradually decreased. The patient's dyspneic sensation improved, but her serum BNP level did not change significantly (from 661 to 593 pg/mL). Seven days after initiating the tolvaptan treatment (September 4), she complained of dyspnea and presented with systemic edema, a concomitant body weight gain of 2.6 kg, and an increase in the serum BNP level to 1014 pg/mL. We began to re-administer 60 mg azosemide every morning and the patient's symptoms improved gradually thereafter.

Table 2 shows the correlations between changes in serum Cl or sodium and changes in hemoglobin, serum creatinine, and MCV during the clinical course. Both the changes in Cl or sodium were negatively correlated with changes in the hemoglobin and serum creatinine, and positively correlated with changes in the MCV, but changes in the serum Cl (Fig. 1) were better correlated with each variable than were changes in the serum sodium.

**Table 2** Correlations between changes in serum chloride or sodium and changes in hemoglobin, serum creatinine, and mean red cell volume during the clinical course.

| | *r* | *p* value |
|---|---|---|
| Chloride (mEq/L) | | |
| Hemoglobin (g/dL) | −0.898 | 0.0025 |
| Serum creatinine (mg/dL) | −0.826 | 0.012 |
| Mean red cell volume (fL) | 0.946 | 0.0004 |
| Sodium (mEq/L) | | |
| Hemoglobin (g/dL) | −0.795 | 0.018 |
| Serum creatinine (mg/dL) | −0.729 | 0.04 |
| Mean red cell volume (fL) | 0.901 | 0.002 |

## Discussion

Under the usage of a vasopressin receptor blockade in HF patients, monitoring of urine volume alone may have a limited value because this medication allows for the patient's free water intake to prevent drug-induced hypernatremia. In such cases, monitoring the change in body weight would be more advantageous because fluid is the body component with the ability to undergo the most rapid change, so a substantial change in body weight over a short period would relate most directly to fluid status [7]. In our patient, use of tolvaptan did not induce much change in the urine output, presumably because of the low water intake due to a lack of thirst, but she did achieve a profound weight loss, indicating that monitoring changes in body weight is more

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