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Cessation of Ultrafiltration Therapy by Treating with Tolvaptan in a Patient with Hypervolemic Hyponatremic Heart Failure

Kalp Yetersizliği ve Hipervolemik Hiponatremisi Olan Bir Hastada Tolvaptan Tedavisi ile Ultrafiltrasyonun Kesilmesi

ABSTRACT

Patients with heart failure (HF) often develop hyponatremia owing to the activation of many neurohormonal systems leading to decreased sodium levels. Treatment options for hyponatremia such as water restriction or the use of loop diuretics are present but patients do not always respond to treatment. Ultrafiltration (UF) is used in patients at an advanced stage of congestive HF and unresponsive to medical treatment. Tolvaptan, a vasopressin 2 receptor antagonist, has recently been used in hypervolemic hyponatremia in patients with heart failure. We report a 60-year-old man who had heart failure and hypervolemic hyponatremia that was resistant to medical treatment. Ultrafiltration was started but the treatment was stopped because of catheter infection. Tolvaptan was used for hyponatremia in this case and the patient did not need ultrafiltration again.

KEY WORDS: Heart failure, Hyponatremia, Tolvaptan, Ultrafiltration

ÖZ

Kalp yetersizliği (KY) hastalarında çok sayıdaki nörohumoral sistemin aktivasyonuna bağlı olarak kan sodyum değerinde azalma meydana gelmekte ve hiponatremi gelişmektedir. Tedavide su kısıtlaması ve kıvrım diüretikler kullanılmakta ancak tedaviye yanıt her zaman alınamamaktadır. Medikal tedaviye cevapsız ileri evre konjestif KY hastalarında ultrafiltrayon (UF) tedavisine başvurulmaktadır. Tolvaptan bir vasopressin 2 reseptör antagonistidir ve hipervolemik hiponatremik KY hastalarının tedavisinde son zamanlarda kullanılmaktadır. Biz 60 yaşında dekompanse KY olan ve dirençli hiponatremisi nedeniyle ultrafiltrasyon tedavisi başlanan ancak kateter enfeksiyonu gelişmesi üzerine UF tedavisi kesilen ve tolvaptan kullanımı sonrası hiponatremisi düzelen ve takipte ultrafiltrasyon ihtiyacı olmayan bir olguyu sunduk.

ANAHTAR SÖZCÜKLER: Kalp yetersizliği, Hiponatremi, Tolvaptan, Ultrafiltrasyon

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INTRODUCTION

Hyponatremia is an electrolyte imbalance that occurs when serum sodium (Na) concentration is lower than 135 mEq/L. It is a common complication of heart failure (HF) and usually presents as hypervolemic hyponatremia in HF. This condition occurs mostly in patients with symptomatic HF and reflects increased neurohormonal activation and especially increased Arginine Vasopressin hormone (AVP) that causes water retention (1). Tolvaptan is a selective oral vasopressin V2-receptor antagonist. Adding tolvaptan to standard treatment including diuretics increases fluid loss and it provides more weight loss than standard treatment without tolvaptan. This impact is achieved without affecting blood pressure, heart rate, renal functions and levels of electrolytes. Tolvaptan provides rapid and sustainable Na increase in patients with hyponatremia (2). Ultrafiltration (UF) is an alternative treatment option in patients with advanced stage congestive heart failure who do not respond to diuretics. Despite the widespread use, there is no large-scale, randomized controlled study investigating the efficacy and safety of UF treatment. In this case, we

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present our experience regarding the use of tolvaptan instead of UF therapy in a patient with hypervolemic hyponatremia who was hospitalized because ofacute decompensated heart failure.

CASE PRESENTATION

A sixty-year-old male patient was admitted to emergency department for exertional dyspnea and orthopnea. He had medical history of type 2 diabetes mellitus and hypertension for twenty years. She was diagnosed with acute anterior myocardial infarction and coronary artery bypass surgery was performed after primary percutaneous balloon angioplasty in 2003. He had multiple admissions to our hospital for acute decompensated heart failure and severe hyponatremia for last one year. In the last three hospitalizations, conventional medical treatment resistant hyponatremia had been treated with UF therapy. At the current admission, physical examination revealed severe pretibial edema, distended abdomen with ascyte and pleural efusion. His axillary temperature was 37.2°C, blood pressure 100/50 mmHg, heart rate 95 beats/min, and respiratory rate 24 breaths/min. He was taking following medications: carvedilol 12.5 mg bid, ramipril and hyrochlorothiazide 10 and 25 mg qd, furosemide 40 mg bid, insulin glargine 20 IU/day, spironolactone 25 mg qd, aspirin 100 mg qd, and metformin 100 mg bid. Serum Na was 116 mmol/L, serum creatinine 1.14 mg/dL, urea 120 mg/dL, serum potassium 4.8 mmol/L, and pro-BNP 1423 ng/mL in laboratory tests. Echocardiography was performed revealing anterior akinesia, apical aneurism of left ventricle with low ejection fraction (EF: %25), moderate-severe mitral regurgitation (MR), severe tricuspid regurgitation (TR), and high estimated systolic pulmonary artery pressure (70 mmHg). Water restriction (500 mg/day) and combination of high dose furosemide (500 mg/day) and positive inotropic agents were started. Despite urine output of 3000 mL/day, serum Na decreased to 104 mmol/L and mental confusion was observed. Then hypertonic saline was added to treatment, but it further deteriorated to heart failure. Therefore, UF therapy was started by catheter. By UF therapy, his symptoms reduced and his pretibial edema was diminished, but on 10th day of UF therapy catheter infection was detected and catheter was removed. Aggressive diuretic treatment was again initiated. On the 5th day of diuretic treatment, serum Na decreased to 105 mmol/L, then tolvaptan 15 mg/day was started. With tolvaptan treatment, patient's serum Na level increased to 125 mmol/L within 3 days. It was 135 mmol/L on the 6th day. The patient's quality of life improved following relief of ascites, pleural effusion and peripheral edema; he became mobilized, was able to be discharged, and was satisfied with tolvaptan 15 mg/day and furosemide 80 mg/day. His serum creatinine and Na levels remained in normal ranges during weekly follow-up (Figure 1, 2). 3 months after discharge, he was good in clinical condition without fluid overload beside a normal Na level.

DISCUSSION

Congestive heart failure (CHF) is a clinical condition characterized by intravascular and extravascular volume overload. Several pathophysiological mechanisms are activated secondary to decreased effective blood volume to increase cardiac output. Neurohormonal activation results an increase in AVP level. AVP causes myocardial fibrosis/hypertrophy and vasoconstriction viaV1 receptors, and water retention in the kidney collecting duct via V2 receptors(3).

CHF is an important problem causing high mortality and recurrent hospitalizations. Management of volume overload in patients with decompensated heart failure is very difficult. Fluid restriction is difficult to maintain, so efficiency is low. Loop diuretics cause an isotonic urine output. Despite existence of multiple beneficial medications for the treatment of chronic CHF, no therapy reducing mortality in acute decompensated heart failure has been developed. High doses of diuretics are related with increased mortality probably due to diuretic resistance, neurohumoral activation, or electrolyte changes rather than the dose itself.

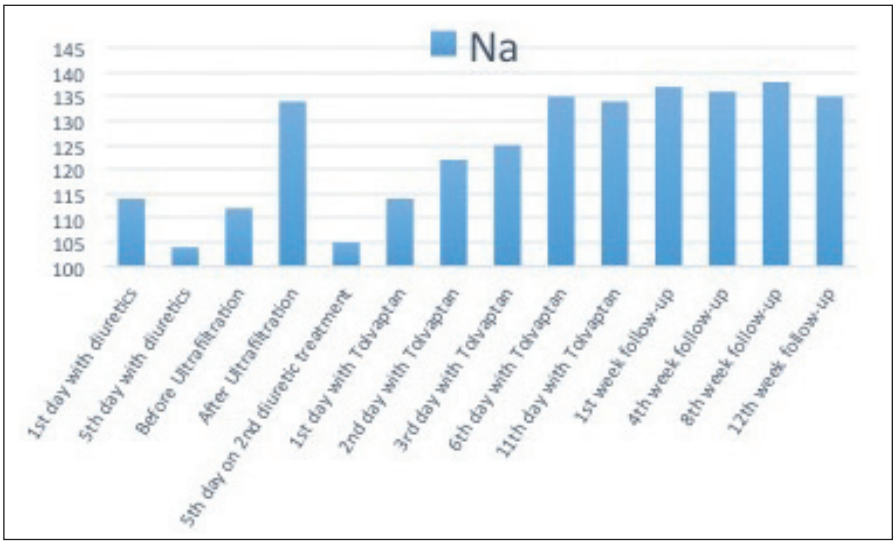

Figure 1: *Serum sodium level before and after tolvaptan treatment.*

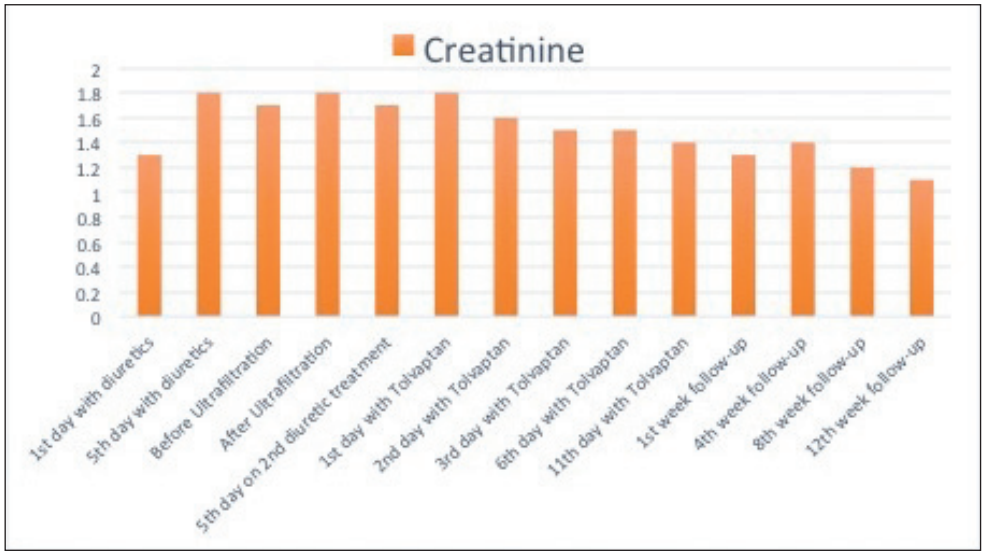

Figure 2: *Serum creatinine level before and after tolvaptan treatment.*

In patients with CHF, edema and congestion often occurs due to fluid retention. Hypervolemic hyponatremia is a common condition in about 20% of the patients. Hyponatremia is an indicator of advanced disease and poor outcome in CHF (4). Loop diuretics do not increase serum sodium level where fluid restriction is not effective; hyponatremia became more prominent (1). So the presence of hyponatremia also limits the usage of loop diuretics.

In case of hypervolemic hyponatremia resistant to medical therapy, UF has been an option for patients older than 30. But, UF is potentially associated with risks of hypotension, catheter-related complications, bleeding due to systemic anticoagulation. Current guidelines consider UF as a reasonable approach in advanced decompensated heart failure patients with unresolved congestion despite optimal medical therapy and/or hyponatremia (3-5).

Arginine vasopressin levels are elevated in congestive heart failure patients. Tolvaptan is a selective oral vasopressin V2-receptor antagonist. It has been approved by the FDA for the treatment of euvolemic and hypervolemic hyponatremia (per FDA label "serum sodium<125 mEq/L or less marked hyponatremia that is symptomatic and has restricted correction with fluid restriction"). Tolvaptan is effective at aquaresis (free water removal), safe and not associated with increased morbidity such as renal failure and arrhythmias (5).

In this case, because of diuretic resistant symptomatic hyponatremia, the patient received recurrent UF therapy. UF therapy was terminated due to catheter infection. After termination of UF therapy more prominent hyponatremia occurred and so tolvaptan was started. In time, the patient's symptoms due to congestion and hyponatremia disappeared. Though tolvaptan has no effect on survival, it may alleviate congestion without disturbing renal function. Additionally, it may reduce UF requirement in patients with acute decompensated heart failure. Furthermore, tolvaptan may help us to stop UF therapy in selected patients group with hypervolemic hyponatremia.

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