THE DUAL EFFECT OF TOLVAPTAN ON DIURESIS AND AZOTEMIA IN ACUTE KIDNEY INJURY WITH FUROSEMIDE RESISTANCE AFTER CORONARY ARTERY BYPASS GRAFTING: A CASE REPORT

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Abstract

Background: Acute kidney injury (AKI) following coronary artery bypass grafting (CABG) occurs in up to 30% of patients and is associated with increasing morbidity and mortality. Escalation of furosemide dose, which blocks sodium, potassium, and chloride reabsorption, paradoxically enhances urea reabsorption to preserve medullary osmolarity. This urea retention may reduce diuretic responsiveness and worsen azotemia. Tolvaptan, a vasopressin V2 receptor antagonist, indirectly inhibits Urea Transporter A1 (UT-A1), potentially counteracting this mechanism. **Case Presentation**: A 67-year-old man developed AKI after CABG with inadequate diuresis despite high-dose furosemide infusion (20 mg/hour). Following extubation, he experienced progressive dyspnea, positive fluid balance, elevated central venous pressure (CVP), and a rapid rise in creatinine (0.97 to 4.74 mg/dL). Dialysis was planned on Day 3 due to KDIGO stage 3 AKI. However, concomitant hyponatremia and oliguria raised suspicion for syndrome of inappropriate antidiuretic hormone (SIADH); dialysis was therefore deferred, and tolvaptan was administered. After treatment, urine output increased, CVP decreased, and creatinine improved to 2.11 mg/dL. The patient subsequently recovered without complications. **Discussion**: This case illustrates the potential use of tolvaptan as an adjunct to furosemide to enhance diuresis and reduce urea reabsorption in diuretic-resistant AKI. **Conclusion**: Tolvaptan may augment diuretic response and improve azotemia, potentially reducing the need for dialysis. Further studies are required to confirm this therapeutic approach in broader clinical settings.

Keywords: vasopressin V2 receptor, urea transporters, diuretic resistance, fluid overload

Introduction

Acute Kidney Injury (AKI) is a serious and frequent complication following coronary artery bypass grafting (CABG), affecting up to 30% of patients and significantly increasing hospital stay and mortality.[1] AKI is associated with increased short-term mortality, especially when dialysis is required.[2] Standard management commonly includes loop diuretics such as furosemide; however, diuretic resistance is common, leading to persistent fluid overload and potential progression to dialysis[2].

Several mechanisms have been proposed to explain diuretic resistance in AKI. Activation of the renin-angiotensin-aldosterone system (RAAS) may enhance the activity of urea transporter A1 (UT-A1), increasing urea reabsorption to preserve medullary interstitial osmolarity and thereby offsetting the natriuretic effect of furosemide[3,4]. Tolvaptan, a vasopressin V2 receptor antagonist, may counteract this process by indirectly inhibiting UT-A1.[5] However, its role as adjunctive therapy to improve diuresis and promote urea clearance in severe post-CABG AKI with furosemide resistance remains poorly defined.

Here, we present the case of a 67-year-old male who developed severe furosemide-resistant AKI and azotemia following CABG. This report highlights the dual beneficial effects of tolvaptan in augmenting diuresis and improving urea clearance, underscoring its potential role as a strategy to avert the need for dialysis in this challenging clinical scenario.

Case Report

A 67-year-old man with coronary artery disease was scheduled for CABG. His medical history included hypertension, type 2 diabetes mellitus, dyslipidemia, and prior smoking. During the preceding two months, he experienced chest pain even at rest. He had a previous admission for impending acute pulmonary edema complicated by AKI and junctional bradycardia. Preoperative echocardiography demonstrated preserved cardiac function with an ejection fraction of 58%, grade 1 diastolic dysfunction, no regional wall motion abnormalities, concentric left ventricular hypertrophy, and mild mitral regurgitation due to tenting. Preoperative laboratory tests were within normal limits except for mild hyponatremia (130 mmol/L). His initial lab results related to kidney function and fluid physiology included albumin 4.03 g/dL, BUN 38.2 mg/dL, and creatinine 0.97 mg/dL. Chest radiography showed no evidence of fluid overload.

Intraoperatively, the patient developed ventricular tachycardia requiring two direct-current shocks (10J each) and experienced bradycardia with a nadir heart rate of 30 bpm. The intraoperative fluid balance was +630 ml (input 5680 ml and output 5050 ml). The remainder of the procedure was uneventful, and the patient was transferred to the intensive care unit (ICU).

The patient arrived in the ICU at approximately 22:00 on postoperative Day 1. Despite adequate mean arterial pressure (MAP), urine output remained low (**Figure 1**). Increasing

the furosemide dose did not improve urine output. Serial measurements of BUN and creatinine (**Table 1**) demonstrated progressive deterioration of kidney function. Although fluid balance improved, the patient remained alert and responsive, maintaining a high SpO2/FiO2 ratio. The patient was extubated on postoperative Day 2.

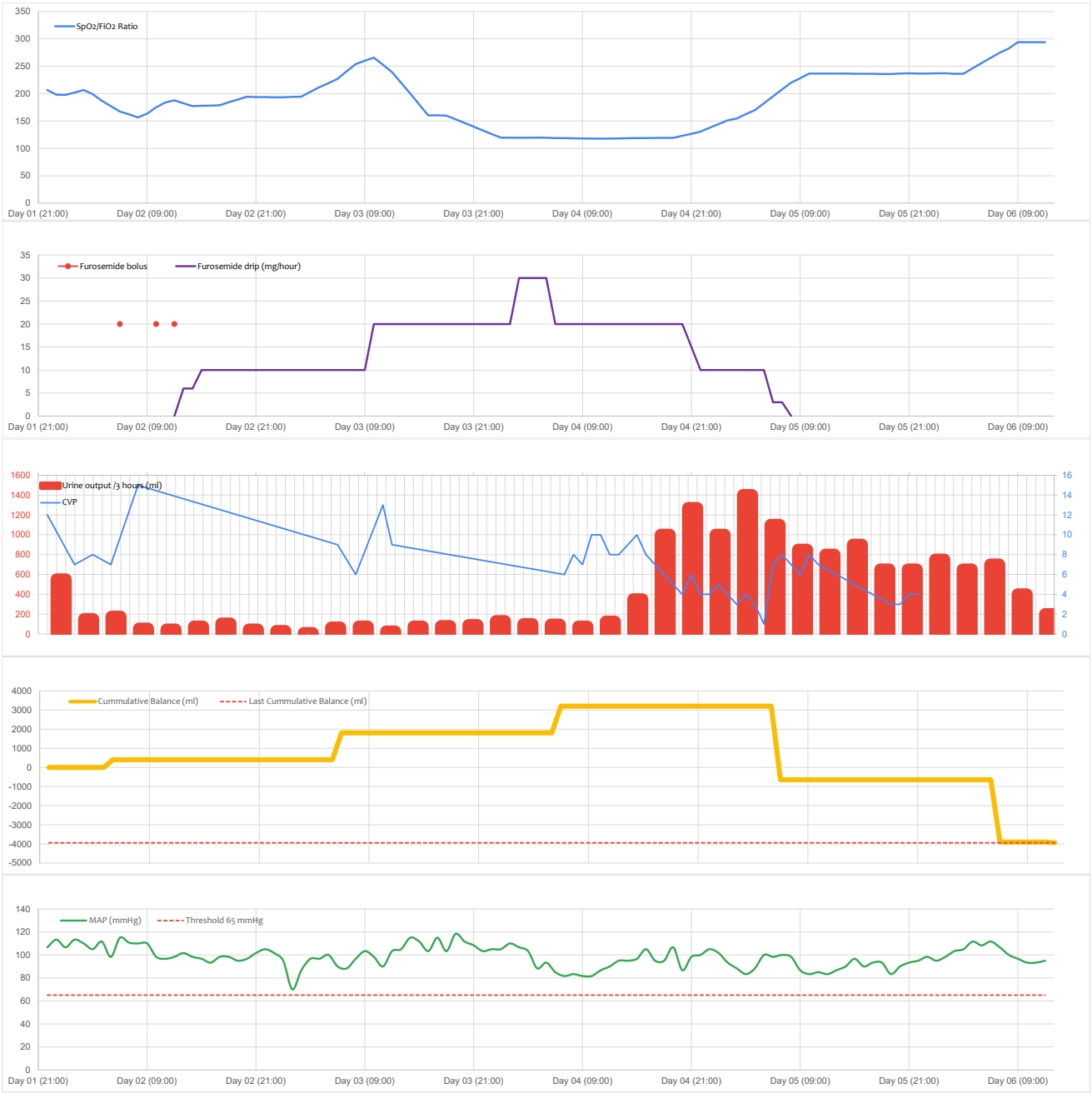

Figure 1: SpO2/FiO2 ratio, Furosemide dose, CVP, Urine Production, Fluid balance, Hemodynamic Trends

Table 1: Sodium, BUN, and Creatinine Trend

Time (Post op)	Sodium (mEq/L)	BUN (mg/dL)	Creatinine (mg/dL)
Preoperative	130	38.2	0.97
Day 1 (0 hour)	132	-	-
Day 1 (3 hours)	135	-	-
Day 1 (6 hours)	138	-	1.67
Day 1 (10 hours)	127	89.6	3.27
Day 1 (18 hours)	129	-	-
Day 2 (33 hours)	128	144.8	4.74
Day 4 (105 hours)	143	136.2	2.11
Day 6 (153 hours)	131	-	-
Day 7 (177 hours)	-	-	1.12

The patient had worsening dyspnea as the fluid balance started to increase. On postoperative Day 3, creatinine rose to 4.74 mg/dL, and dialysis was planned. However, given concurrent hyponatremia, syndrome of inappropriate antidiuretic hormone (SIADH) was suspected. Tolvaptan 15 mg daily was initiated for three days, and dialysis was deferred. Around four hours after the first dose, urine output gradually increased from 25 ml/hour to 500 ml/hour. Furosemide infusion was gradually tapered and discontinued by postoperative Day 5.

With reduced fluid balance, the patient's clinical status improved markedly. Oxygen requirements and central venous pressure (CVP) decreased steadily. Creatinine declined from 4.74 mg/dL to 2.11 mg/dL after three days of tolvaptan (postoperative Day 4). The patient was transferred to the ward on postoperative Day 6, and recovery thereafter was

uneventful. At discharge, the creatinine level had normalized to 1.12 mg/dL without further intervention.

Discussion

We report a 67-year-old male who developed stage 3 AKI after CABG, who exhibited resistance to furosemide, yet demonstrated improvement in kidney function following administration of tolvaptan. This patient presented with oliguria and creatinine exceeding 4 mg/dL. Based on guidelines on AKI management, this corresponds to stage 3 AKI and constitutes an indication for dialysis.[2] However, elevations in creatinine do not always reflect irreversible parenchymal injury, especially in the context of severe congestion.[7]

Diuretic resistance is variably defined as failure to achieve adequate sodium and fluid excretion despite the maximum daily dose of loop diuretics (80 to 240 mg).[8] Furosemide inhibits the sodium-potassium-chloride (Na+/K+/2Cl-) cotransporter (NKCC2) in the thick ascending limb of the loop of Henle in the kidneys, which increases tubular water excretion.[9] When intravascular osmolarity rises or effective circulating volume declines, activation of the RAAS and vasopressin release occurs. Angiotensin II and vasopressin, acting via the V2 receptor, stimulate UT-A1, thereby enhancing urea reabsorption into the medullary interstitium[3,4]. This compensatory mechanism preserves osmolarity when sodium transport is blocked. As a result, BUN may rise despite ongoing diuresis.

Increased medullary urea elevates interstitial osmolarity, promoting water movement from the tubular lumen into the interstitium[10]. In other words, increasing urea will reduce furosemide's effectiveness. While the balance between sodium inside the kidney tubule and urea in the interstitial space is appropriate, the sodium chloride concentration inside the kidney tubule is normal. But when water shifts more into the interstitial space due to higher osmolarity from increasing urea concentration, the sodium chloride concentration inside the kidney tubule will increase. This increase will be "seen" by the macula densa, and it will send a signal through the juxtaglomerular pathway to constrict the afferent and reduce GFR, which in turn will reduce creatinine elimination[11].

Tolvaptan acts by selectively inhibiting vasopressin V2 receptors in the kidney, thereby decreasing the expression of aquaporin channels[12]. This will lead to more urine production. The V2 receptor also interacts with UT-A1, which is responsible for reabsorbing urea to increase interstitial osmolarity.[5] Tolvaptan will indirectly reduce urea reabsorption, decreasing interstitial osmolarity, and promoting water shift into the kidney tubules. When the water shifts more into the kidney tubules, the sodium chloride concentration inside the kidney tubules will become appropriate. This condition will be "seen" by the macula densa, which will then signal the afferent to dilate and increase the GFR[11]. This is in line with recent research that shows adding tolvaptan to furosemide therapy might reduce the risk of persistent AKI[13].

Although these observational findings align with known physiology, they remain susceptible to confounding factors. This case serves as hypothesis-generating rather than definitive causal evidence. The potential of tolvaptan to improve diuresis and reduce urea reabsorption might help reduce the need for dialysis. It might also help differentiate an increase in creatinine caused by our body's response to furosemide from actual kidney tissue damage. Further research is needed to confirm this theoretical effect with a focus on kidney function.

Competing Interests

All authors declare no competing interests. This case report was done without external funding.

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Generative AI Declaration

In the development of this manuscript, the author(s) made use of Gemini 2.5 to identify sentence redundancy and optimize structure for clarity. All outputs were carefully reviewed and revised by the author(s), who take full responsibility for the accuracy, originality, and integrity of the final published version.

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