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# Case report: New treatment with Tolvaptan for heart failure after cardiac surgery

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## ABSTRACT

The vasopressin $V_2$ receptor antagonist (Tolvaptan) is a new diuretic that selectively promotes the excretion of water. It has been reported to be effective for patients in cardiology, but there have been no reports of its use in the perioperative period after cardiac surgery. We report the usefulness of Tolvaptan for postoperative fluid management in a patient with severe mitral regurgitation due to ischemic cardiomyopathy. Marked improvement was achieved after administration of Tolvaptan for heart failure in the postoperative period.

## INTRODUCTION

Tolvaptan is a vasopressin $V_2$ receptor antagonist that has attracted attention as a new diuretic selectively promoting the excretion of water. Japan is the only country where this drug is approved for the treatment of cardiac failure, and it has been reported to be effective for patients in cardiology [Pang 2011; Imamura 2013]. However, there have been no reports of its use in the perioperative period after cardiac surgery. We previously observed strong cardiac and renal protection, renin-angiotensin-aldosterone system (RAAS) inhibition, prevention of left ventricular remodeling, and antiarrhythmic activity with continuous low-dose infusion of carperitide in patients undergoing cardiac surgery and found that not only the early results, but also the long-term outcome showed improvement [Sezai 2010; Sezai 2009; Sezai 2013]. We subsequently used Tolvaptan to treat heart failure occurring after cardiac surgery, and significant improvement was achieved. Accordingly, we are reporting this case since Tolvaptan seems to be useful for control of heart failure after cardiac surgery.

## CASE REPORT

A 57-year-old man with disturbance of consciousness after the sudden onset of chest pain was brought to the emergency unit of our hospital. He had a clear sensorium on arrival, so urgent coronary angiography was performed for suspected myocardial infarction because ST elevation was detected on an electrocardiogram (leads $aV_1$ and $V_{2\text{-}5}$). Since the left main trunk was totally occluded, thrombus was aspirated while the patient was supported by an intra-aortic balloon pump (IABP) and percutaneous coronary intervention (PCI) was conducted using a bare-metal stent. After PCI, he was treated with Dobutamine and a PDE III inhibitor as well as the IABP for pulmonary congestion and pulmonary hypertension, but no improvement was observed. Echocardiography revealed a left ventricular ejection fraction of only 19 percent, as well as severe mitral regurgitation and a left atrial thrombus. We considered it difficult to continue treatment with the IABP and drugs since the patient's blood pressure was 91/51 mmHg, his pulmonary atrial pressure was 58/30 mmHg, his PCWP was 36 mmHg, and his urine volume was 200 mL/day. Therefore, we performed mitral valve replacement (ATS 31 mm), left atrial thrombectomy, and left atrial appendectomy in the second month of hospitalization. Ultrafiltration was performed and carperitide was administered intraoperatively (0.02μg/kg/min) due to preoperative anasarca with weight gain of 8 kg. As a result, the intraoperative fluid balance was -238 mL. After surgery, Dopamine (5μg/kg/min), Dobutamine (5μg/kg/min), Norepinephrine (0.02μg/kg/min), a PDE III inhibitor (0.2μg/kg/min), carperitide, and the IABP were employed for management of the patient. His daily urine volume was 3000 mL or more, and he was weaned from the IABP on Day 4 and from the ventilator on Day 7. Norepinephrine was discontinued on postoperative Day 4, the PDE III inhibitor and carperitide were stopped on Day 6, and Dopamine and Dobutamine were ceased on Day 8. Furosemide was administered orally at 40 mg/day and intravenously at 20 mg/day to 80 mg/day, but intravenous administration was discontinued on postoperative Day 9 and the oral dose was increased to 60 mg/day. His fluid balance was negative up to postoperative Day 7, but became positive from Day 8 with a decrease of the urine volume to 2000 mL/day. The fluid balance was +993 mL on postoperative Day 10 along with respiratory discomfort and lower limb edema. Oral administration of Tolvaptan (3.75mg/day; Otsuka Pharmaceutical Co., Ltd, Tokyo, Japan) was started from postoperative Day 11. Subsequently, the urine volume was maintained at 3000 mL/day or more and the fluid balance was -500 mL/day or more, with marked improvement of his respiratory discomfort and lower limb edema. Tolvaptan was administered for 24 days (Figure 1). The patient developed phlegmon at the central venous catheter site, but there was no worsening of heart failure. Echocardiography performed

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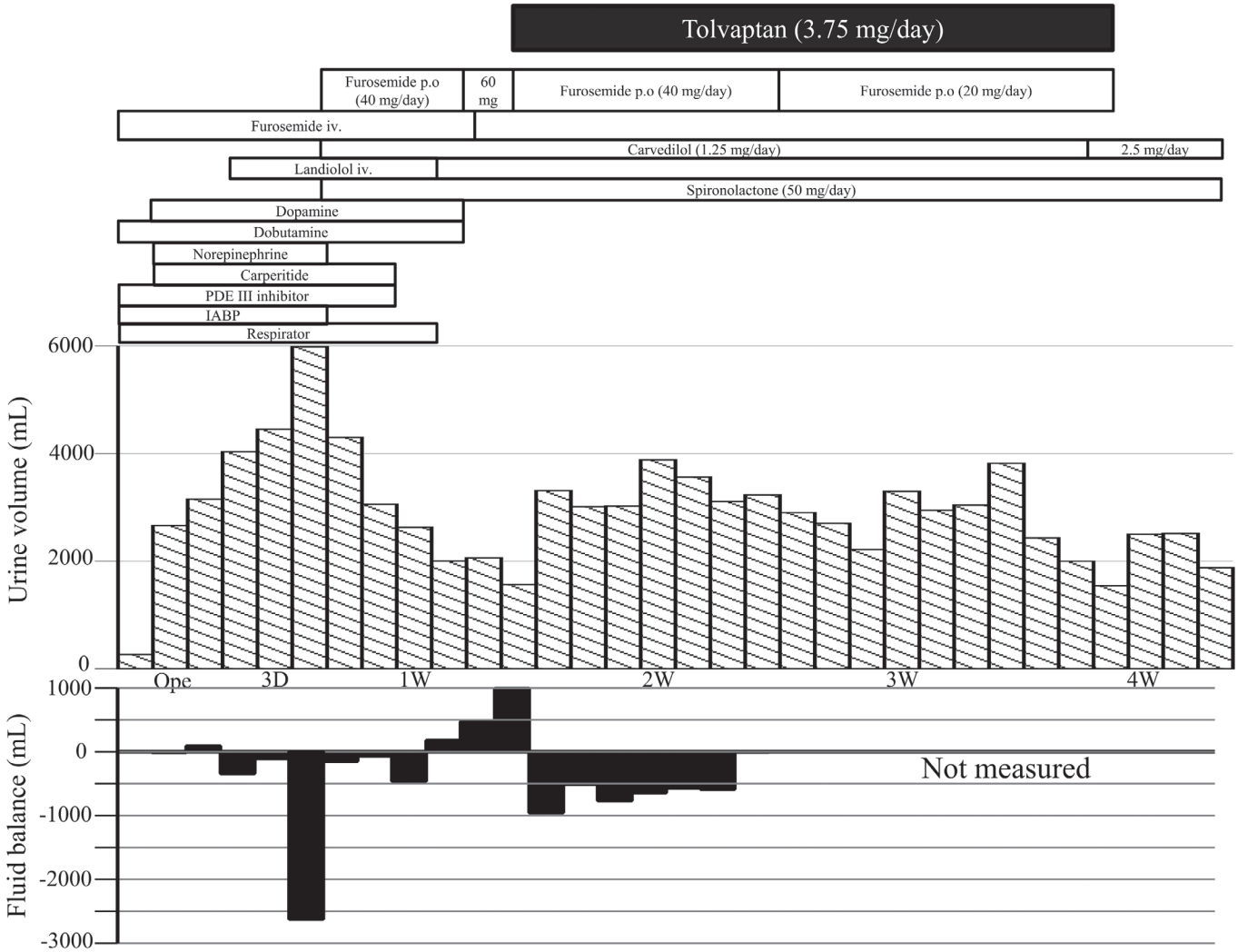
before discharge showed improvement of the ejection fraction (33 percent) and a decrease of the estimated right ventricular pressure assessed by TRPG (45mmHg) compared with the preoperative results. The patient was discharged on postoperative Day 67. His oral medications at discharge were Furosemide (40 mg/day), Spironolactone (50 mg/day), Carvedilol (3.75 mg/day), Pimobendan (5 mg/day), and Perindopril Erbumine (1 mg/day).

## COMMENT

In patients with heart failure or cardiac surgery, increased RAAS activity and sympathetic hyperactivity are observed, and an increase of vasopressin may also be seen sometimes. While carperitide is effective for reducing RAAS activity and sympathetic hyperactivity as a β-blocker, Tolvaptan is effective for patients whose vasopressin levels are increased and are not controlled by other drugs. Administration of Tolvaptan was effective in our patient with cardiac dysfunction, perioperative heart failure, and a significantly positive postoperative fluid balance, suggesting that earlier use of this drug was warranted because a significantly higher urine volume could be maintained after its administration.

A large-scale clinical study of Tolvaptan in patients with heart failure showed that weight loss, improvement of edema, and improvement of dyspnea were significantly greater in the Tolvaptan group than the conventional treatment group. Although there was no difference of the long-term prognosis, and it was reported that Tolvaptan promotes pure water diuresis and causes fewer electrolyte abnormalities and less RAAS activation [Gheorghiade 2007; Konstam 2007]. When diuretic therapy is administered to patients with heart failure after cardiac surgery, who generally have massive water retention due to a positive intraoperative fluid balance, Furosemide frequently is selected as the first-line drug. Although Furosemide is a potent diuretic, it has been reported that frequent, high-dose, and long-term administration leads to increased RAAS activity and deterioration of renal function [Eshaghian




Postoperative course of the patient

2006; Abdel-Qadir 2010]. In addition, Furosemide may cause intravascular volume depletion due to its natriuretic effect and this sometimes leads to hypotension. In contrast, Tolvaptan is an aquaretic and has been reported to cause less blood pressure reduction because it equally promotes the excretion of intracellular and extracellular fluid, making it the most appropriate agent for use in the perioperative period when patients show hemodynamic instability. Therefore, for patients in whom fluid overload cannot be controlled by Furosemide, the dosage should not necessarily be increased and use of Tolvaptan should be considered. However, since the efficacy of Tolvaptan for perioperative management of heart failure after cardiac surgery has not been proven, it will be necessary to conduct a prospective study for validation of our findings.

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