Successful Treatment of Intractable Fluid Retention Using Tolvaptan After Treatment for Postoperative Mediastinitis in a Patient With a Left Ventricular Assist Device

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Summary

The use of implantable continuous-flow left ventricular assist devices (LVADs) as a bridge to transplant is effective for patients with congestive heart failure (HF). However, some patients develop congestive symptoms due to right-sided HF even with LVAD support. Tolvaptan, a vasopressin type 2 receptor antagonist, corrects both congestion and hyponatremia in patients with advanced HF. We report herein a case involving a patient who underwent LVAD implantation and developed hyponatremia and congestive symptoms after negative-pressure wound therapy and omental transposition for postoperative mediastinitis. Hemodynamic evaluation performed after negative-pressure wound therapy revealed elevation of both right arterial pressure and pulmonary capillary wedge pressure, and suggested biventricular dysfunction despite LVAD support. Symptoms improved after starting administration of tolvaptan. Tolvaptan may be useful for correcting hyponatremia and volume overload in patients under LVAD support. (Int Heart J 2015; 56: 574-577)

Key words: Congestive symptom, Hyponatremia, Volume overload negative-pressure wound therapy

The use of implantable continuous-flow left ventricular assist devices (LVADs) is effective as a bridge to transplant for patients with congestive heart failure (HF).1,2 Some patients with stage D HF can reduce or discontinue diuretics after LVAD implantation. However, some patients develop congestive symptoms due to right-sided HF even with LVAD support. Tolvaptan (Otsuka Pharmaceutical Co., Ltd., Tokyo), a vasopressin type 2 receptor antagonist,4,5 effectively corrects both congestion and hyponatremia in patients with advanced HF.6-8 We describe herein a case of successful treatment with tolvaptan in a patient with LVAD implantation complicated by intractable fluid retention after negative-pressure wound therapy (NPWT) and omental transposition for postoperative mediastinitis.

Case Report

A 42-year-old woman with congenital bicuspid aortic valve and aortic stenosis underwent aortic valve replacement with a mechanical valve at a local hospital in August 2012. She developed acute myocardial infarction of the left main trunk in November 2012. Coronary angiography performed after initiation of percutaneous cardiopulmonary support system showed reperfusion of the left coronary system, but cardiac function did not recover and she underwent implantation of a NIPRO paracorporeal VAD (Nipro Corporation, Osaka, Japan) at the other hospital. The patient was placed on a heart transplantation waiting list and transferred to our hospital for surgical conversion to an implantable LVAD. Echocardiography demonstrated a left ventricular ejection fraction (LVEF) of 21% by the Teichholz method and a left ventricular end-diastolic diameter (LVDd) of 48 mm. Right heart catheterization showed a right atrial pressure (RAP) of 10 mmHg and pulmonary capillary wedge pressure (PCWP) of 7 mmHg with NIPRO LVAD support (Table). The plasma B-type natriuretic peptide (BNP) level was 287.2 pg/mL. She underwent surgical conversion from the NIPRO VAD to a HeartMate II (Thoratec Corp., Pleasanton, CA, USA) and aortic valve re-replacement with a bioprosthetic valve in May 2013. Nine days postoperatively, she developed methicillin-resistant Staphylococcus epidermidis mediastinitis and underwent NPWT. Sternal closure and omental transposition were performed on day 53.

The patient developed fluid retention following sternal closure. The estimated pump flow was 3.2 to 3.6 L/minute at a pump speed of 8800 rpm. Furosemide (60 mg/day) and spironolactone (50 mg/day) were administered. Her serum sodium concentration decreased to < 130 mEq/L. Chest computed tomography on day 70 revealed bilateral pleural effusion, ascites, and hepatic congestion (Figure 1). She underwent tho-
## Table. Results of Right Catheterization

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Before conversion (NIPRO VAD support)</th>
<th>After conversion (HeartMate II support)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pump speed (rpm)</td>
<td>8800</td>
<td>9200</td>
</tr>
<tr>
<td>BP (mmHg)</td>
<td>104 / 75 / 86</td>
<td>80 / 57 / 65</td>
</tr>
<tr>
<td>RAP (mmHg)</td>
<td>10</td>
<td>21</td>
</tr>
<tr>
<td>RVP (s/EDP) (mmHg)</td>
<td>30 / 12</td>
<td>36 / 19</td>
</tr>
<tr>
<td>PAP (s/d/m) (mmHg)</td>
<td>25 / 6 / 14</td>
<td>36 / 18 / 25</td>
</tr>
<tr>
<td>PCWP (mmHg)</td>
<td>7</td>
<td>15</td>
</tr>
<tr>
<td>PVR (Wood)</td>
<td>2.31</td>
<td>3.98</td>
</tr>
<tr>
<td>CI (L/minute/m²)</td>
<td>1.91</td>
<td>1.57</td>
</tr>
<tr>
<td>SvO₂ (%)</td>
<td>55</td>
<td>38</td>
</tr>
</tbody>
</table>

VAD indicates ventricular assist device; BP (s/d/m), systemic blood pressure (systolic, diastolic, mean); RAP, right atrial pressure; RVP (s/EDP), right ventricular pressure (systolic, end-diastolic pressure); PAP (s/d/m), pulmonary artery pressure (systolic, diastolic, mean); PCWP, pulmonary capillary wedge pressure; PVR, pulmonary vascular resistance; CI, cardiac index; and SvO₂, mixed venous oxygen saturation.

**Figure 1.** Computed tomography after surgical conversion demonstrated bilateral pleural effusion (A, B), ascites (D), hepatic congestion (C), and an omental flap (B).

**Figure 2.** Clinical course after tolvaptan administration. The patient was discharged from the hospital on day 115 and visited the outpatient clinic on days 129 and 143. BW indicates body weight; sNa, serum sodium; sCr, serum creatinine; and BNP, B-type natriuretic peptide.
Tolvaptan in a patient with right-sided HF caused by postoperative mediastinitis and remained categorized as NYHA class I for more than 1 mg/day (Figure 2). The patient continued to take tolvaptan on day 36, and serum sodium level decreased to < 120 mEq/L on day 129, and tolvaptan was thus restarted at 3.75 mg/day. However, her serum sodium concentration decreased to < 120 mEq/L on day 129, and tolvaptan was thus restarted at 3.75 mg/day (Figure 2). The patient continued to take tolvaptan on LVAD with a serum sodium concentration of 135 to 139 mEq/L and remained categorized as NYHA class I for more than 1 year.

**DISCUSSION**

Use of implantable continuous-flow LVADs offers an effective bridge to transplant for patients with congestive HF. Pump pocket infection or postoperative mediastinitis in patients with LVAD may constitute a life-threatening adverse event. NPWT followed by omental transposition is reportedly effective against such complications. In one report, use of NPWT induced healthy granulation tissue formation and bacterial clearance. This treatment may improve the survival rate of patients with postoperative mediastinitis. However, whether granulation tissue formation or fibrosis of the cardiac surface induced by long-term use of NPWT affects cardiac function remains unclear. In the present case, the HeartMate II showed an estimated pump flow of about 5.0 L/minute on day 7; however, this flow decreased to < 4.0 L/minute after sternal closure at the same pump speed. Hemodynamic evaluation performed after NPWT and sternal closure revealed a high RAP and PCWP and relatively small left ventricular size. Pulmonary vascular resistance was elevated, reflecting decreased cardiac output. We performed NPWT for 44 days. Long-term use of NPWT may affect cardiac function. To the best of our knowledge, however, no studies have described the hemodynamic effects after NPWT.

Tolvaptan, an oral arginine-vasopressin type 2 receptor antagonist, has demonstrated advantages in ameliorating congestion through increasing excretion of free water, thus stabilizing the hemodynamic state and correcting hyponatremia. In Japan, Matsuzaki, et al reported that tolvaptan reduced volume overload and improved congestive symptoms associated with HF.

Kanaya, et al reported a case of successful treatment with tolvaptan in a patient with right-sided HF caused by postoperative constrictive pericarditis. The present patient showed congestive symptoms with hyponatremia despite LVAD support. Her hemodynamic state was considered to be mimicking constrictive pericarditis. Her pericardium had been removed in a previous operation, but the epicardium might have undergone hardening. Several studies have demonstrated a response after administration of tolvaptan under various clinical conditions. Imamura, et al reported that a baseline urine osmolality of > 352 mOsm/L was a good predictor of positive treatment outcome with tolvaptan. Baseline urine osmolality in the present patient was 536 mOsm/L, and this was one of the reasons for starting tolvaptan. Tolvaptan effectively corrected the volume overload and improved the congestive symptoms under LVAD support. This case suggests that tolvaptan might be effective for relief of congestive symptoms despite LVAD support.

In conclusion, patients with intractable fluid retention under LVAD support may benefit from treatment with tolvaptan to correct hyponatremia and volume overload.

**DISCLOSURES**

Dr. Teruhiko Imamura and Dr. Koichiro Kinugawa belong to the Department of Therapeutic Strategy for Heart Failure, which is an endowed department sponsored by 13 companies including Otsuka Pharmaceutical (Tokyo). Koichiro Kinugawa was a consultant for Otsuka Pharmaceutical and has received honoraria from Otsuka Pharmaceutical for lectures. The other authors have no conflicts of interest to declare.

**REFERENCES**


