Postoperative usage of tolvaptan in a patient with aortic valve stenosis complicated by Child-Pugh classification B liver cirrhosis and hepatic edema

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Abstract We report the case of an 80-year-old woman with postoperative congestive heart failure (CHF) complicated by Child-Pugh classification B liver cirrhosis and hepatic edema successfully treated with tolvaptan. The patient suffered from liver cirrhosis and underwent partial hepatectomy for a hepatocellular carcinoma diagnosed together with a severe aortic valve stenosis. Aortic valve replacement was performed under cardiopulmonary bypass. The postoperative course was uneventful until CHF and hepatic edema symptoms appeared on postoperative day (POD) 2. The symptoms were treated with intravenous human atrial natriuretic peptide and oral diuretics. As the condition showed no improvement, oral tolvaptan was administered on POD 11 and thereafter, which markedly improved the symptoms. This is apparently the first report describing the effectiveness of tolvaptan for the postoperative management of fluid balance in a patient with cardiac and liver dysfunction.

Keywords Tolvaptan · Aortic valve stenosis · Liver cirrhosis · Competitive vasopressin nonpeptide V₂ receptor antagonist

Introduction

Liver cirrhosis is a major preoperative risk factor in patients undergoing cardiac surgery. Previous studies reported that morbidity and mortality progressively

increase with the severity of liver dysfunction; however, the lines of evidence come from limited studies with a small number of patients [1, 2]. Patients with Child-Pugh classification B or C liver cirrhosis have higher risks after open heart surgery using cardiopulmonary bypass. For the treatment of clinically significant hypervolemic or euvolemic hyponatremia or less marked hyponatremia in patients with CHF, liver cirrhosis, or syndrome of inappropriate antidiuretic hormone, tolvaptan (SamscaTM; Otsuka Pharmaceutical Co. Ltd., Tokyo, Japan), a selective and competitive vasopressin nonpeptide V₂ receptor antagonist, has been developed.

We successfully treated a patient with severe aortic valve stenosis (AS) and Child-Pugh classification B liver cirrhosis and hepatic edema, which deteriorated postoperatively, using tolvaptan as an add-on treatment to conventional diuretics.

Case report

An 80-year-old woman with Child-Pugh classification B liver cirrhosis and hepatic edema underwent aortic valve replacement for severe AS. The patient suffered from hypertension, dyslipidemia, autoimmune hepatitis which was diagnosed in 2011, and liver cirrhosis. She previously underwent partial hepatectomy to remove a hepatocellular carcinoma in 2012.

Preoperative chest X-ray showed cardiomegaly. Echocardiography revealed severe AS with a maximum/mean pressure gradient of 89/54 mmHg or an aortic valve area of 0.6 cm², which required operation. Following median sternotomy, cardiopulmonary bypass was established through the ascending aorta and a two-staged venous cannula from the right atrium. Under cardiac arrest with

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Fig. 1 **a, b** Postoperative chest X-rays revealed marked cardiomegaly and pleural effusion. **c** After tolvaptan administration, chest X-rays showed improvement of cardiomegaly and pleural effusion. **d** The chest X-ray at discharge demonstrated improved cardiomegaly with no sign of congestion

antegrade cardioplegia, the ascending aorta was opened and the three severely calcified cusps of the aortic valve were resected. A 19 mm bioprosthetic valve was implanted in the supra-annular position. Weaning from the cardiopulmonary bypass was smooth and the chest was closed routinely.

After extubation on POD 1, human atrial natriuretic peptide and oral diuretics were administered. However, chest effusion retention was observed and the condition deteriorated despite repeated chest drainage and increased amounts of diuretics. Postoperative chest X-rays revealed marked cardiomegaly and pleural effusion (Fig. 1a, b). On POD 11, tolvaptan (7.5 mg/day) was administered and continued for 2 weeks. Chest X-rays revealed cardiomegaly improvement (Fig. 1c). There was a marked increase in urine output, reduction in weight, and systemic edema improvement. There was no sign of electrolyte imbalance, and the NT-pro brain natriuretic peptide (BNP) level gradually decreased during the clinical course progression (Fig. 2). Abnormal systemic blood pressure and deterioration of the renal and liver functions were not evident (Fig. 3).

Tolvaptan administration was stopped as the patient's condition improved. There was no sign of water retention

thereafter. Postoperative echocardiography showed a decreased maximum/mean pressure gradient of 36/18 mmHg with an aortic valve area of 1.06 cm² and abdominal ultrasonography also showed decreased ascites. The patient was discharged without complications and showed no signs of deteriorated heart failure or liver cirrhosis postoperatively (Fig. 1d).

Discussion

Tolvaptan is indicated for volume overloaded heart failure at 15 mg/day in Japan [3]. It is indicated for hospitalized adults with clinically euvolemic or hypervolemic hyponatremia, including patients with heart failure, liver cirrhosis and syndrome of inappropriate secretion of antidiuretic hormone (SIADH). The administration does not exceed 30 days to minimize or avoid risk of liver damage. In patients with inability to feel or respond to thirst, hypovolemic hyponatremia, anuria, concomitant strong human cytochrome P450 (CYP) 3A4 inhibitors, requiring urgent correction of hypovolemia, and hypersensitivity such as anaphylactic shock or generalized rash, the administration of tolvaptan was regarded as a contraindication,

In our case, we administered tolvaptan postoperatively following aortic valve replacement for severe AS in a patient with Child-Pugh classification B liver cirrhosis and hepatic edema. Deterioration of cardiomegaly and water retention in the third space progressed rapidly postoperatively despite the increased dose of conventional diuretics. The timing of our tolvaptan administration from POD 11 was deemed to be late, resulting in late recovery and prolonged administration. Notably, the administration span of tolvaptan has limitations. As our patient's condition improved, we were able to discontinue tolvaptan during her admission. However, many patients may require long-term

We successfully treated a patient with severe AS and Child-Pugh classification B liver cirrhosis and hepatic edema by the add-on treatment of tolvaptan to the conventional diuretics used. This case indicates that tolvaptan administration at the early postoperative phase following cardiovascular surgery improves cardiac function, which usually deteriorates temporarily postoperatively. Tolvaptan also stabilizes a patient's general condition and shortens the admission time. Further research and analysis of the pharmacokinetics and clinical application of tolvaptan can increase its potential to expand the indication of cardiac surgery for patients with liver cirrhosis and hepatic edema.

Fig. 3 Transition of blood pressure and functional parameters of liver and kidney. *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *eGFR* estimated glomerular filtration rate, *AST* aspartate

aminotransferase, *ALT* alanine aminotransferase, *γ-GTP* gamma-glutamyl transpeptidase, *hANP* human atrial natriuretic peptide, *POD* postoperative day

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Conflict of interest None.

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