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The Use of Terlipressin for Management of Dynamic Left Ventricular Outflow Tract Obstruction Complicating Othotropic Liver Transplantation: A Case Report

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ABSTRACT

We describe a patient with structurally normal heart who developed hemodynamic instability during orthotropic liver transplantation caused by severe dynamic left ventricular outflow tract obstruction. Successful management of this adverse event was facilitated by the use of intravenous terlipressin. The case highlights a role for terlipressin as a selective vasopressin receptor agonist with subsequent effects on systemic vascular resistance.

PROFOUND HEMODYNAMIC and metabolic changes occur during adult orthotopic liver transplantation.[1,2] During the dissection phase, the disturbance is mainly due to bleeding and hypovolemia[3] while in the anhepatic phase, there may be a 50% reduction of venous return during clamping of inferior vena cava.[4] Reperfusion of the graft during the neohepatic stage carries the risk of systemic hypotension (postreperfusion syndrome).[5] In this report, we have presented a case who developed severe dynamic left ventricular outflow tract obstruction (LVOTO), with hemodynamic instability that was successfully managed with terlipressin.

CASE REPORT

A 40-year-old male patient underwent living donor liver transplantation for end-stage liver disease resulting from Budd-Chiari. His medical history was unremarkable. Both resting and dobutamine stress echo (DSE) were performed during the routine preoperative evaluation, revealing no evidence of either ischemia or LVOTO at a maximum heart rate of 160 beats/min. Induction of anesthesia used propofol, fentanyl, and atracurium. Anesthesia was maintained with sevoflurane in an oxygen/air mixture, fentanyl infusion (1 to 2 g/kg/h), and atracurium infusion (0.5 mg/kg/h). A pulmonary artery catheter was inserted into the right internal jugular vein for continuous monitoring of cardiac output (CO) and mixed venous oxygen saturation (Svo2). Two hours after induction of anesthesia, there were brief episodes of hypotension that resolved with intravenous fluid administration. At the end of the dissection phase and before inferior vena cava clamping, the blood pressure fell to 80/40 with a sudden decrease in CO from 6.5 L/min to 1.7 L/min and Svo2 from 70% to 52% with a central venous pressure of 7 mm Hg, and a pulmonary artery occlusion pressure of 10 mm Hg. After aggressive intravascular volume resuscitation with albumin (5%) and hydroxyethyl starch, vasopressor therapy was initiated with norepinephrine (0.2 g/kg/min). However, hemodynamic instability persisted and the blood pressure dropped to 60/20 mm Hg despite increasing the norepinephrine dosage to 0.5 μg/kg/min. A transesophageal probe inserted to assess the left ventricular function revealed severe dynamic LVOTO with systolic anterior motion of the mitral valve with severe mitral regurgitation (MR; Fig 1A, 1B). Rapid infusion of 1000 mL of albumin (5%) and two packs of red cells did not improve the degree of MR. We then administered 1 mg of terlipressin (Glypressine; Ferring Company, Berlin, Germany) as an intravenous bolus followed by an infusion at 2 μg/kg/h. This moreover resulted in rapid reversal of hemodynamic instability with an increase in blood pressure to 120/60, CO to 4.2 L/min, and systemic vascular resistance from 1100 to 1500 dyn/s/cm.[5] SAM improved and the degree of MR was reduced to mild (Fig 1C). The norepinephrine was reduced to 0.1 μg/kg/min; the remainder of the intraoperative course was unremarkable. Postoperatively, terlipressin infusion was discontinued and bisoprolol prescribed orally. The patient had an uneventful recovery. Two blood samples were simultaneously obtained from the portal vein, hepatic vein, pulmonary artery catheter, and arterial catheter immediately after terlipressin injection, and at the end of the surgery. Blood gases were evaluated using a co-oximeter (ABL 700; Radiometer, Copenhagen, Denmark; Table 1).

DISCUSSION

Dynamic LVOTO has been previously described during liver transplantation[6]; however, it was uniquely managed with terlipressin in this case. Although LVOTO should be

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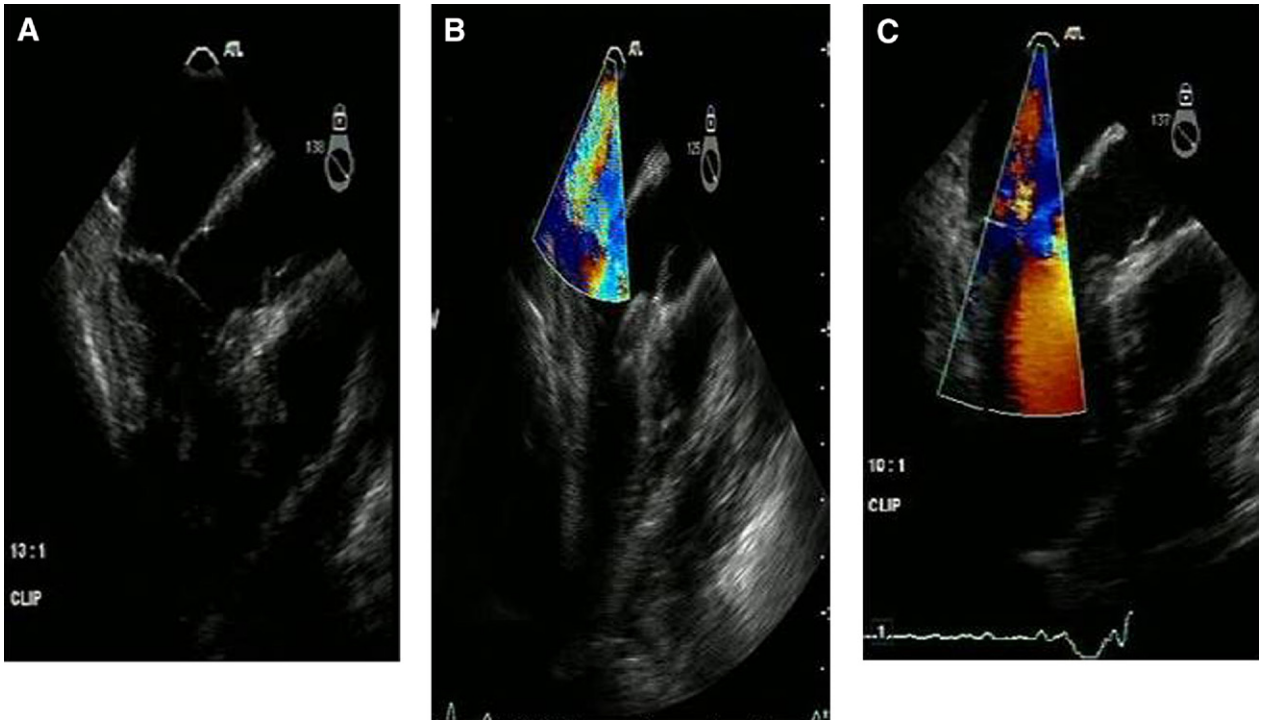

Fig 1. **(A)** Midesophageal aortic valve long-axis view showing anterior mitral leaflet obstructing left ventricular outflow tract. **(B)** Midesophageal aortic valve long-axis view showing severe eccentric mitral regurgitation due to systolic anterior motion of mitral valve. **(C)** Mild degree of mitral regurgitation after terlipressin injection.

triggered during preoperative DSE testing, in this case the DSE was negative despite increasing the heart rate to 160 beats/min. A previous report attributed the development of LVOTO during liver transplantation to the uptake of blood by the donor liver[6]; however, in the present case the LVOTO occurred at the end of the dissection phase and before the inferior vena cavae clamping. In the present scenario, the possible contributing factors to the development of LVOTO were peripheral vasodilatation, together with hypovolemia, which are classical complications of the dissection phase.[3]

Table 1. Arterial and Regional Acid Base Status

	Immediately After Terlipressin	At the End of Surgery
PHart	7.24	7.35
PHmv	7.21	7.33
PHpv	7.24	7.34
PHhv	7.22	7.33
SaO2 (%)	100	100
SVO2 (%)	72	80
pvO2 (%)	91	91
hvO2 (%)	61	60
BEart (mmol/L)	−8	−6
BEmv (mmol/L)	−7	−5
BEhv (mmol/L)	−10	−7
BEpv (mmol/L)	−7	−6
Lactate-art (mmol/L)	4.5	2.6
Lactate-mv (mmol/L)	4.3	2.4
Lactate-pv (mmol/L)	4.4	2.4
Lactate-hv (mmol/L)	4.3	2

PHart, arterial PH; PHmv, mixed venous PH; pHpv, portal venous pH; PHhv, hepatic vein PH; SaO2, arterial saturation; SVO2, mixed venous saturation; pvO2, portal vein oxygen saturation; hvO2, BEart, arterial base excess; BEmv, mixed venous baseexcess; BEpv, portal vein base excess; BEhv, hepatic vein base excess; Lactate-art, arterial lactate; Lactate-mv, mixed venous lactate; Lactate-PV, portal vein lactate; Lactate-hv, hepatic vein lactate.

Typically, LVOTO can be treated using intravascular volume expansion together with vasoconstriction. In our case, the hemodynamics did not improve despite adequate fluid loading. Patients with cirrhosis and portal hypertension have an altered blood volume distribution with pooling in the splanchnic circulation. Rapid expansion of the blood volume in these patients increases the splanchnic venous congestion, with little effect on the systemic circulation.[7]

We routinely used norepinephrine as a first-line medication to manage hemodynamic instability during liver transplantation. In this case, there was a deterioration of hemodynamics despite an escalating, stepwise increase in the dose of norepinephrine up to 0.5 μg/kg/min. Nearly all of the commonly used vasopressors for hypotension display significant inotropic effects; when they are administered before ensuring adequate volume repletion, they may precipitate dynamic LVOTO.[8]

In the present case, intravenous terlipressin administration resulted in an increased SVR with a subsequent decrease in LVOTO and an improvement in blood pressure and CO.

Terlipressin (tricyl-lysine vasopressin) is a synthetic analogue of arginine vasopressin. It is rapidly metabolized by endopeptidases to form the vasoactive lysine vasopressin, which shows greater selectivity for the V1 vasopressin receptor than arginine vasopressin.[9] V1 receptor's which are involved in smooth muscle contraction, are particularly abundant in the splanchnic area.[10] Thus, it was postulated that terlipressin attenuated the hyperdynamic circulation due to an increased effective arterial blood volume following splanchnic arteriolar vasoconstriction. Previous studies have demonstrated that injection of terlipressin was associated with an increase in mean arterial blood pressure and systemic vascular resistance among patients with portal hypertension.[11,12]

Nonetheless, administration of terlipressin has been associated with several adverse effects in both preclinical and clinical studies. One of these adverse effects is terlipressin-induced impairment of intestinal perfusion in patients with esophageal variceal hemorrhage[13] and portal hypertension.[14] In this case, we did not detect any sign of splanchnic hypoperfusion, such as worsening metabolic acidosis or increased lactate levels in the portal or hepatic vein.

In conclusion, our case illustrated successful management of dynamic LVOTO complicating orthotopic liver transplantation using intravenous administration of terlipressin; however, its safety is yet to be determined.

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