Case Report

Sildenafil Improves Right Ventricular Function in a Cardiac Transplant Recipient

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We report the case of a male patient who underwent orthotopic cardiac transplantation. A marginal donor was used, because the recipient's clinical condition was critical. He experienced cardiogenic shock due to right ventricular dysfunction secondary to pulmonary hypertension associated with vasoplegia. After the introduction of sildenafil, the patient recovered hemodynamically, his pulmonary vascular resistance decreased, the vasoactive drugs were withdrawn, and his right ventricular function improved.

The use of inhaled nitric oxide reduces pulmonary artery pressure, increasing the production of guanosine 3',5'-cyclic monophosphate (GMPc) in the smooth muscle cells of the lung [1]. Specific inhibitors of GMPc phosphodiesterase (PDE5), which hydrolyzes GMPc in vascular smooth muscle, cause pulmonary vasodilation [2-4].

Sildenafil is a specific inhibitor of PDE5 that increases the pulmonary vasodilating effect of inhaled nitric oxide [5-8], prevents pulmonary hypertensive crises after weaning of nitric oxide in patients with severe pulmonary hypertension [5,9], and has its own pulmonary vasodilating effect [10,11] by increasing the GMPc levels [12].

Molina et al [11] reported a 20% reduction in the PAP of a patient with pulmonary hypertension due to systemic lupus erythematosus, who had suprasystemic pulmonary pressure levels, with elevated doses of sildenafil (1600 mg per day). The authors reported a good tolerance to the medication.

In an experimental study, Weimann et al [10] showed that the pulmonary vasodilating effect of sildenafil is dose-dependent, beginning 5 minutes after its administration and reaching its maximum effect in 10 minutes.

Michelakis et al [12] showed that patients with pulmonary hypertension who are candidates for cardiac transplantation had a decrease in pulmonary vascular resistance that was more prominent with sildenafil alone, at the dosage of 75mg, than with inhaled nitric oxide in 80 ppm, associated with a significant increase in GMPc levels.

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The use of a female donor for a male recipient is known to have a greater early mortality (OR=1.11, P=0.3), similarly to that of a recipient using vasoactive drugs and waiting in the intensive care unit (OR=2.51, P<0.0001)[13-15].

We report the case of a patient undergoing orthotopic cardiac transplantation, who experienced cardiogenic shock due to right ventricular dysfunction secondary to pulmonary hypertension associated with vasoplegia. Because the recipient's clinical condition was critical, a marginal donor was used.

In the national literature, we did not find reports of the use of sildenafil for pulmonary hypertension in the postoperative period. The objective of this report is to propose a new and safe manner to treat right ventricular failure secondary to pulmonary hypertension in the postoperative period of cardiac transplantation.

Case Report

The patient was a 33-year-old man with idiopathic dilated cardiomyopathy, who had been in NYHA functional class IV for the preceding 2 years and was hospitalized with low cardiac output and was using catecholamines (dobutamine, 6.6 mcg/kg/min, and dopamine, 8 mcg/kg/min). The patient was hypotensive (blood pressure of 70x40 mmHg), slightly dyspneic at rest, and had hepatomegaly and pulmonary congestion (basal rales in both bases).

The patient underwent orthotopic cardiac transplantation on 08/02/2003. Due to his rapid clinical worsening, a marginal organ was used. The marginal donor was a 60-kg female, who had experienced cardiac arrest for 15 minutes 3 days before, was using 12 mcg/kg/min of dopamine, and, on the echocardiogram, had diffuse, mild hypokinesia and preserved overall function.

The transplantation was performed according to the bicaval technique with 165 minutes of extracorporeal circulation and 117 minutes of anoxia, under mild hypothermia (32ºC) and use of intermittent anterograde blood cardioplegia. The patient was removed from the extracorporeal circulation after the third attempt and sent to the ICU receiving 0.11 mcg/kg/min of isoproterenol, 0.75 mcg/kg/min milrinone, and 20mcg/kg/min of dobutamine. His mean blood pressure was 40 mmHg and mean pulmonary arterial pressure was 45 mmHg. His right ventricular contractility was very poor, and he received adrenaline in bolus during transportation and in the first hours at the ICU. Twelve hours after transplantation, the patient was receiving 10mcg/kg/min of dobutamine, 0.96 mcg/kg/min of adrenaline, 0.13 mcg/kg/min of isoproterenol, and 0.41 mcg/kg/

Table I - Hemodynamic measures for thermodilution with the Swan-Ganz catheter and catecholamines used in the postoperative period

		Sildenafil			
	08/03/03 11:20	08/03/03 16:35	08/03/03 20:30	08/04/03 01:15	08/04/03 15:00
MBP (mmHg)	65	62	92	93	66
PAP (mmHg)	38	35	33	31	27
CVP (mmHg)	36	34	30	26	23
PCP (mmHg)	22	21	26	21	21
SVR (D.s/cm^5)	368	238	762	939	603
PVR (D.s/cm^5)	203	155	86	140	84
Dobutamine (mcg/kg/min)	9.6	16.0	16	16	16
Adrenaline (mcg/kg/min)	0.87	0.39	0.39	0.39	0.29
Noradrenaline (mcg/kg/min)	0.41	1.23	2.0	2.0	1.34

MBP - mean blood pressure; PAP - pulmonary arterial pressure; CVP - central venous pressure; PCP - pulmonary capillary pressure; SVR - systemic vascular resistance; PVR - pulmonary vascular resistance.

min of noradrenaline, and his mean blood pressure was 63 mmHg. His clinical condition was clearly worsening, with pulmonary hypertension associated with vasoplegia. The use of vasoconstrictors for vasoplegia (systemic vascular resistance = 238 D.s/cm^5) was hindered by pulmonary hypertension.

As the patient evolved with aggravation of the hemodynamic condition and oliguria, 150 mg of sildenafil was administered through a nasogastric probe (4:30 PM on 08/03/03). The pulmonary vascular resistance significantly decreased (tab. I), allowing the use of greater doses of vasoconstrictors (noradrenaline) for treating vasoplegia, and the following values were obtained: pulmonary vascular resistance of 86 D.s/cm^5 (1.08 Wood) and systemic vascular resistance of 762 D.s/cm^5. Sildenafil was maintained at the dosage of 50mg every 8 hours, allowing, on the following day, a significant drop in pulmonary arterial pressure and in CVP, without pulmonary hypertension even with the use of noradrenaline.

The echocardiograms in the immediate postoperative period and third postoperative day showed a significant right ventricular deficit. However, the hemodynamic measurements showed an improvement in right ventricular performance and a sustained drop in pulmonary vascular resistance. The suspension of the vasoactive drugs was progressive, and the echocardiogram on the sixth postoperative day showed a mild right ventricular deficit. The patient was discharged from the ICU on the eighth postoperative day, and the use of sildenafil was maintained until the 15th postoperative day. The echocardiogram of the 17th postoperative day showed a preserved biventricular function, mild tricuspid regurgitation, and pulmonary arterial pressure of 45 mmHg. The immunosuppressive scheme used comprised prednisone, mycophenolate mofetil, and cyclosporine. So far, the endomyocardial biopsies have shown no sign of rejection.

Discussion

The patient studied had preoperative pulmonary hypertension (PAP=52 mmHg) even while using dobutamine. Despite the short period of ischemia (117 minutes), severe right ventricular dysfunction developed, being attributed to pulmonary hypertension. The overlapping vasoplegia, secondary to either extracorporeal circulation or the use of vasodilators (dobutamine, isoproterenol, milrinone), made the patient's management difficult, because the increase in the doses of vasoconstrictors aggravated pulmonary hypertension.

The use of sildenafil caused significant pulmonary vasodilation without causing systemic vasodilation. Its specific pulmonary vasodilating effect allowed the use of high doses of vasoconstrictors (noradrenaline and adrenaline) for the treatment of vasoplegia without causing pulmonary vasoconstriction. The catecholamines were suspended and the right ventricular function recovered, which was evident on serial echocardiography.

Patient candidates for cardiac transplantation, in whom a pulmonary vascular resistance lower than 2.5 Wood units is not obtained with a vasodilator without systemic hypotension or with elevated pulmonary arterial pressure (PAP >50 mmHg), have a significant increase in early mortality due to graft failure after transplantation [14,15]. Graft failure accounts for 38.7% of the deaths in the first 30 days after transplantation [13].

Mychaskiw et al [9] reported a surprising hemodynamic improvement in a patient with a device for left and right ventricular support waiting for cardiac transplantation, who was experiencing clear hemodynamic worsening due to a pulmonary hypertension crisis, 20 minutes after receiving 50 mg of sildenafil. The authors managed to interrupt the treatment with nitric oxide and catecholamines, and extubate the patient who seemed to have an irreversible clinical worsening.

Sildenafil is rapidly absorbed through the gastrointestinal tract, even in critically ill patients [6]. High doses (400 mg, 4 times a day) of sildenafil are well tolerated and have few significant side effects (hypotension, significant cephalea) [11].

Therefore, we believe that sildenafil may be adequate for the postoperative period of patients undergoing cardiac transplantation, who have significant right ventricular dysfunction, and even in patients in critical condition, as long as the drug is adequately absorbed, even in poor clinical conditions.

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