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Cibenzoline attenuates systolic anterior motion of the mitral valve after mitral valvoplasty

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Abstract
We report a patient in whom severe hemodynamic instability occurring after mitral valvoplasty (MVP) was successfully treated with cibenzoline. Left ventricular outflow tract obstruction (LVOTO) with mitral regurgitation (MR) resulting from the systolic anterior motion (SAM) of the mitral valve that occurs after MVP often leads to hemodynamic collapse. Patients who develop SAM after MVP have been managed with intravenous volume loading, reduction/discontinuation of inotropic drugs, and with increased afterload, but these strategies were often ineffective. Cibenzoline decreased myocardial contraction, attenuated SAM, and improved hemodynamics in our patient. We recommend that cibenzoline be administered before further surgical manipulation is considered for patients who develop SAM after MVP.

Key words Cibenzoline · Systemic anterior motion of mitral valve (SAM) · Mitral valvoplasty (MVP)

Introduction

Systolic anterior motion (SAM) of the mitral valve can develop after a patient is weaned from extracorporeal circulation during mitral valvoplasty (MVP) to treat mitral regurgitation (MR). SAM often leads to left ventricular outflow tract obstruction (LVOTO) with MR, resulting in severe circulatory collapse due to reduced forward left ventricular stroke volume. Although a β-blockade can attenuate SAM and can resolve circulatory collapse after MVP [1,2], it also can exert adverse effects such as bronchospasm. Hamada et al. [3] have reported that the class Ia antiarrhythmic drug cibenzoline eliminates SAM in patients with hypertrophic obstructive cardiomyopathy. We found that this drug, cibenzoline, attenuated SAM and improved hemodynamics in a patient with SAM after MVP that resulted in circulatory collapse.

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Case report

A 74-year-old woman (weight, 56 kg; height, 150 cm) with a long history of bronchial asthma was administered with a β-stimulant and developed dyspnea upon exertion. Preoperative echocardiography confirmed severe MR due to prolapse of the middle scallop of the posterior leaflet, and MVP was scheduled. The ejection fraction was 72.9%, the preoperative posterior leaflet of the mitral valve was elongated to 21 mm (normal length, 12.8 ± 1 mm) [4], and the ratio of anterior-to-posterior leaflet length was decreased to 1.1 (normal ratio, 1.95) [5]. Diazepam (10 mg) was administered per os (p.o.) before the induction of anesthesia with intravenous (i.v.) midazolam (4 mg), fentanyl (250 μg), and vecuronium (8 mg). Anesthesia was maintained with a continuous infusion of propofol (6 mg·kg^{-1}·h^{-1}), and injections of fentanyl (total, 1000 μg) were intermittently administered under 40%–100% oxygen [6]. The patient was monitored using five-lead electrocardiography, pulse oximetry, and capnometry. Hemodynamic variables, including mean arterial pressure (MAP), mean pulmonary artery pressure (MPAP), cardiac index (CI), pulmonary capillary wedge pressure (PCWP), central venous pressure (CVP), and mixed venous O_2 saturation (Sv_{O_2}) were measured; MAP was measured after inserting a catheter into the radial artery. An Opti Q Sv_{O_2}/CCO catheter (Hospira, North Chicago, IL, USA) was inserted to measure PAP, PCWP, CVP, Sv_{O_2}, and CI. A Q2 Continuous Cardiac Output/S_{O_2} computer (Hospira) was used to measure Sv_{O_2}, and transesophageal echocardiography (TEE) was performed using a multiplane transducer and a ProSound SSD-4000SV device (Aloka, Tokyo, Japan). An echocardiographer later reviewed videotapes of the TEE. Baseline hemo-

Table 1. Hemodynamic changes after cibenzoline administration

	MAP (mm Hg)	HR (bpm)	CI (l $min^{-1} \cdot m^2$)	SV (ml)	MPAP (mmHg)	PCWP (mmHg)	Sv_{O_2} (%)
Baseline	76	72	3.3	66	22	15	76
Before cibenzoline	53	92	1.4	23	31	23	57
After cibenzoline	85	83	3.4	61	14	10	81

MAP, mean arterial blood pressure; HR, heart rate; CI , cardiac index; SV, stroke volume; MPAP, mean pulmonary artery pressure; PCWP, pulmonary capillary wedge pressure; Sv_{O_2}, mixed venous O_2 saturation

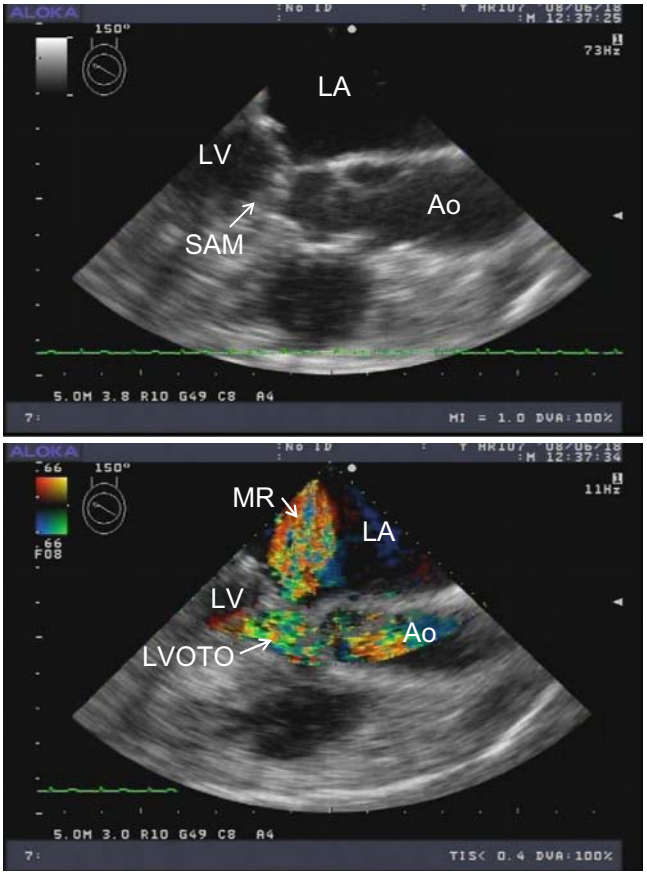

Fig. 1. Transesophageal echocardiography mid-esophageal long-axis view before cibenzoline administration, showing systolic anterior motion (*SAM*), left ventricular outflow tract obstruction (*LVOTO*), and mitral regurgitation (*MR*). *LA*, Left atrium; *LV*, left ventricle; *Ao*, aorta

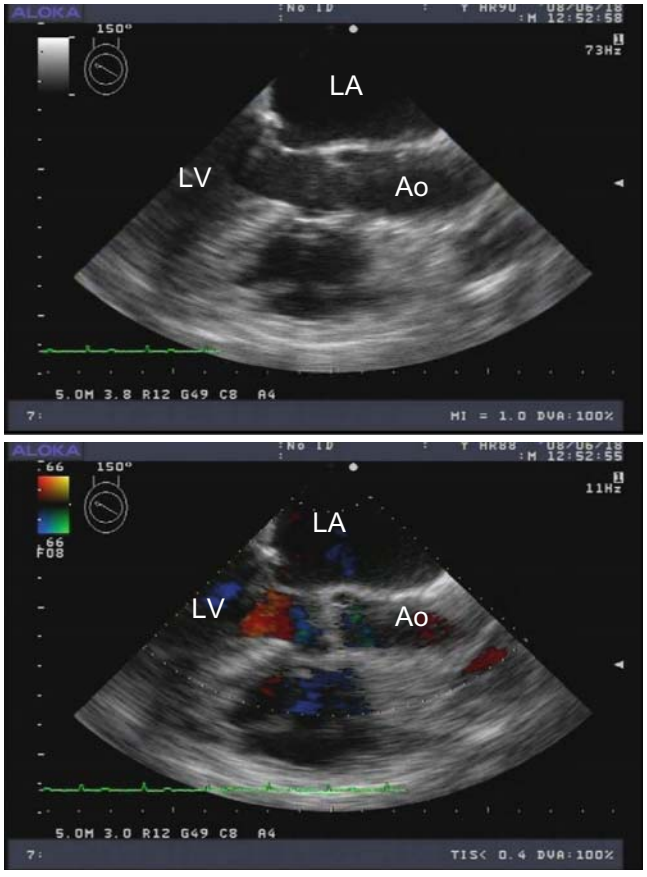

Fig. 2. Transesophageal echocardiography mid-esophageal long-axis view after cibenzoline administration. Neither residual obstruction of left ventricular outflow tract nor mitral regurgitation is evident. *LA*, Left atrium; *LV*, left ventricle; *Ao*, aorta

dynamic data were obtained after the induction of anesthesia and before sternotomy. Values at each point were averaged after three measurements. We performed triangular resection of the posterior leaflet of the mitral valve and the valve ring was sutured. A slightly larger artificial valve ring, no ring at all, or a sliding technique that narrows the width of the posterior leaflet can be applied to a long posterior leaflet to avoid SAM developing during surgery [7,8]. Due to the high risk of SAM in our patient, we performed triangular resection of the posterior leaflet of the mitral valve and applied a slightly larger artificial valve ring than usual. The patient was weaned from cardiopulmonary bypass (CPB) without catecholamine. After separation from CPB, TEE confirmed SAM, which led to LVOTO with severe MR (Fig. 1). A deep transgastric view showed that the peak pressure gradient across the left ventricular outflow tract (LVOT) reached 148 mmHg. Table 1 shows the hemodynamic variables indicating the development of SAM, LVOTO, and MR and subsequent circulatory collapse. Because of suspected hypovolemia, a blood transfusion to 10 mmHg of CVP was followed by noradrenaline administration, but this did not result in any improvement. Ten minutes later, cibenzoline (70 mg) was administered intravenously over a period of 2 min. Another 5 min later, TEE (Fig. 2) confirmed that left

Table 2. Changes in echocardiographic parameters after cibenzoline administration

	LVPG (mmHg)	LVDd (mm)	LVDs (mm)	VS–MV distance (mm)	EF (%)
Baseline	0	49	25	22	71
Before cibenzoline	142	48	24	18	68
After cibenzoline	0	49	29	22	52

LVDd, left ventricular dimension at diastole; LVDs, left ventricular dimension at systole; VS, ventricular septum; MV, mitral valve; EF, ejection fraction ratio (%), determined by modified Simpson method

ventricular myocardial contractility had decreased, with the ejection fraction decreased from 68% to 52%, left ventricular dimension at systole increased from 24 to 29 mm, and the distance between the ventricular septum and the mitral valve increased from 18 to 22 mm (Table 2). Subsequently, SAM, LVOTO, and MR disappeared and the hemodynamic variables also substantially improved (Table 1). The peak pressure gradient across LVOT also disappeared. The patient did not receive further treatment for SAM, which did not reappear; and MVP was completed without hemodynamic decompression.

Discussion

The reported incidence of SAM developing as a complication of MVP ranges between 2% and 14% [9–11]. Because SAM increases the likelihood of MR and LVOTO, and these complications often occur together during MVP, the risk of severe circulatory collapse during surgery is high. The reported causes of SAM after MVP include an elongated posterior leaflet of the mitral valve, a smaller ratio of the length of the anterior to the posterior leaflet, a nondilating left ventricle, and the sliding of small artificial valve rings [5,7,12]. After MVP, coaptations of the anterior and posterior leaflets of the mitral valve are anteriorly displaced. Insufficient ventricular volume increases the velocity of blood flow from the narrow left ventricle, thus resulting in Venturi effects. The anterior leaflet of the mitral valve is also drawn towards the ventricular septum, and SAM occurs. Force against the mitral valve might also be involved at this time. Sympathetic nervous system stimulation, particularly β-adrenergic stimulation, can also cause SAM. Surgical and CPB-induced stress may activate the sympathetic nervous system and increase circulating catecholamine levels, resulting in hypercontractility, which leads to SAM [13]. The appropriate timing for medication can be determined and SAM can be diagnosed by TEE [1,2,14].

Patients with SAM after MVP have generally been managed with i.v. volume loading, limited administration of inotropic drugs, administration of a β-blockade, and increased afterload. Transfusion could increase left ventricular capacity or β-blockade, limited catecholamine administration could suppress the velocity of the outflow tract flow, or vasoconstrictors could diminish the pressure gradient across the LVOT with SAM [9]. However, neither volume replacement nor the absence of catecholamine was effective against SAM in our patient. Although β-blockade is effective for patients who develop SAM after MVP, this blockade can also cause bronchospasm. Thus, alternative care without a β-blockade was required for our patient who had bronchial asthma.

Since Millar and Vaughan Williams [15, 16] found that cibenzoline exerted a negative inotropic action in rabbits, producing bradycardia, this agent has been used to treat SAM and LVOTO in patients with hypertrophic obstructive cardiomyopathy; consequently, the ejection fraction can be decreased. In our patient, although left ventricular end-diastolic dimension was little changed, the left ventricular end-systolic dimension was enlarged. The exact mechanism of the decrease in the pressure gradient across LVOT caused by cibenzoline remains to be determined. We have reported that the negative inotropic action of a β-blockade is related to a decrease in the pressure gradient across LVOT, and that landiolol produces great effects on the fall in the pressure gradient across LVOT [1]. However, a β-blockade is sometimes insufficient to treat SAM [1] and in SAM after MVP, the essential cause is not tachycardia but hypercontractility. A β-blockade and the calcium antagonist diltiazem both have negative inotropic actions in addition to a negative chronotropic action, so with these agents, the heart rate can sometimes become overly decreased before diastolic dysfunction is attenuated. On the other hand, the class Ia antiarrhythmic drug, cibenzoline, has more negative inotropic than negative chronotropic action [17] and it has improved diastolic function in patients with LVOTO, when a β-blockade had no effect [1,17]. Thus, cibenzoline is suitable for treating SAM after MVP. That the decrease in myocardial contractility associated with cibenzoline is closely related to a decrease in the pressure gradient across LVOT is quite conceivable. An obvious decrease in left ventricular excursion and enlargement of the LVOT area both contributed significantly to the decrease in the pressure gradient across LVOT in our

patient with SAM after MVP. To our knowledge, this is the first report of cibenzoline attenuating SAM after MVP. Other class Ia antiarrhythmic drugs such as disopyramide (a potent cardiodepressant) have been considered, but adverse effects such as dysuria and thirst result from its anticholinergic activities [18]. The class Ia antiarrhythmic drug cibenzoline has little anticholinergic activity, and has been applied as an antiarrhythmic agent.

Brown et al. [9] compared medical and surgical approaches to treat circulatory collapse due to SAM after MVP together with LVOTO and MR and they found that drug therapy resulted in a more favorable vital prognosis, because SAM tended to occur most frequently during the intraoperative period. Such therapy sufficiently ameliorated SAM and avoided the need for further surgery. Furthermore, the clinical outcomes of patients with SAM are comparable to the current norms for mitral valve repair [9]. Therefore, repeated surgery could be avoided if intraoperative SAM after MVP is medically controlled.

We conclude that when additional volume expansion fails to treat SAM after MVP, cibenzoline should be administered before proceeding with further surgical manipulation.

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