Adverse Effect of Nifedipine on Left Ventricular Obstruction Detected by Pulsed Doppler Echocardiography

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SUMMARY
The effect of nifedipine on the ejection flow pattern in the left ventricular outflow tract was observed using pulsed Doppler echocardiography in 6 patients with hypertrophic cardiomyopathy. After sublingual administration of nifedipine (10 mg) to 1 patient, the turbulent ejection flow pattern became more marked and increased in duration compared with the initial state. An increase in turbulence in the left ventricular outflow tract may increase the pressure gradient between the left ventricle and the aorta. Nifedipine appeared to have the potential of adverse action on left ventricular outflow obstruction.

Additional Indexing Words:
Hypertrophic cardiomyopathy Pressure gradient Turbulent ejection flow

INTRAVENOUS administration of verapamil, which is a slow channel ion flux inhibitor, reduces left ventricular (LV) outflow obstruction in patients with hypertrophic cardiomyopathy (HCM). A lessening of the obstruction, together with an improvement of the LV diastolic function, may contribute to symptomatic improvement in patients taking oral verapamil. However, verapamil has also the potential of adverse effects. A paradoxical increase in LV outflow obstruction can occur when verapamil causes a marked drop in blood pressure. We have observed a similar sequence of events in one of 6 patients with HCM to whom nifedipine (another slow channel inhibitor) was administered, by using pulsed Doppler echocardiography.
Case Report

A 52-year-old male was admitted with a heart murmur and shortness of breath. Auscultation of the heart revealed a grade 3/6 systolic ejection murmur over the left cardiac base. A carotid pulse tracing manifested a mid-systolic retraction with amyl nitrite inhalation. Echocardiograms showed evidence of LV hypertrophy (posterior wall thickness: 16 mm; interventricular septum thickness: 19 mm), a systolic anterior movement of the anterior mitral leaflet and an early closure of the aortic valves. Cardiac catheterization showed a LV outflow tract pressure gradient (20 mmHg) in the resting state and an elevated LV end-diastolic pressure (17 mmHg).

The ejection flow in the LV outflow tract was observed using pulsed Doppler echocardiography (ultrasonic frequency: 2.75 MHz; repetition rate: 4.4 KHz) combined with two-dimensional echocardiography, before and after sublingual administration of nifedipine (10 mg). The transducer position was at the apical region where the LV long-axis plane was clearly visible. The sampling site of the Doppler signal was the LV outflow tract, and the sampling volume was $5 \times 5 \times 2.5 \text{ mm}^3$. Initially, the LV ejection flow revealed a turbulent pattern only in the late ejection phase. However, 30 min after administration of nifedipine, the turbulent ejection flow pattern became more marked and increased in duration (Fig. 1). The heart rate increased from 70 to 75 beats/min. Blood pressure fell from 150/90 to 125/75 mmHg.

![Fig. 1. Effect of nifedipine on the ejection flow pattern in the left ventricular outflow tract. Before administration of sublingual nifedipine (10 mg), left ventricular ejection flow showed a turbulent flow pattern only in the late ejection phase. At 30 min after administration, the turbulent flow pattern became more marked and manifested itself throughout the ejection phase.](image-url)
DISCUSSION

The mechanisms by which the administration of verapamil decreases the LV outflow tract obstruction are unknown. However, it is assumed that this action is probably related to depressed myocardial contractility caused by the drug's pharmacological effect of inhibiting slow channel ion flux. On the other hand, an increase in the velocity of the LV ejection flow, derived from both a decrease in the afterload and the resulting reflex increase in sympathetic stimulation of the heart caused by the slow channel inhibitor, may facilitate the turbulence of blood flow in the LV outflow tract in patients with obstruction. An increase in turbulence results in an increased pressure gradient between the LV and the aorta caused by an increase in the kinetic energy of the blood. Nifedipine has a lower negative inotropic potential, but has a more potent vasodilatory action than verapamil. Thus, the potential of an adverse effect with nifedipine may be higher than with verapamil, though changes of the ejection flow pattern were not detected in 5 other patients to whom nifedipine was also given in our laboratory. Lorell and co-workers have recently reported that nifedipine elicited systolic obstruction in 1 of 8 patients with HCM studied during cardiac catheterization, although abnormal LV diastolic properties were favorably modified by nifedipine in patients with HCM. These results indicate that nifedipine should be given to patients with HCM cautiously, even though it has the relative advantage of a lack of drug-induced conduction disturbances compared with verapamil.

The abnormal LV ejection flow pattern in patients with HCM was monitored using pulsed Doppler echocardiography. Intracardiac phonocardiograms have been recorded in patients with LV obstruction. Identification of an ejection murmur of maximal intensity within the LV outflow tract implied the presence of an intraventricular obstruction sufficient to disturb flow. Intracardiac turbulent flow is readily detected using pulsed Doppler echocardiography. This non-invasive technique is useful in evaluating pharmacological effects on LV outflow obstruction.

REFERENCES