Danger of Use of Disopyramide in Patients with Hypertrophic Obstructive Cardiomyopathy

An Electrophysiologic Study

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SUMMARY

A 61-year-old man with hypertrophic obstructive cardiomyopathy with asymptomatic ventricular tachycardia underwent electrophysiologic study. Double extrastimuli at the right ventricular outflow tract induced polymorphic ventricular tachycardia which degenerated into fibrillation. After intravenous administration of 50 mg of disopyramide, the pressure gradient in the outflow tract disappeared, but the tachycardia inducing zone appeared at the right ventricular apex. Although disopyramide may be used in patients with hypertrophic cardiomyopathy to relieve the intraventricular pressure gradient, it should be used only after evaluating its safety and efficacy electrophysiologically.

Additional Indexing Words:

Hypertrophic cardiomyopathy   Ventricular tachycardia   Electro-
physiologic study   Disopyramide

POLLICK reported that the class Ia antiarrhythmic drug, disopyramide, relieves the outflow tract obstruction of hypertrophic cardiomyopathy.¹⁾ Since class Ia antiarrhythmic drugs can be a cause of malignant ventricular tachycardia,²⁾⁻⁴⁾ disopyramide should be proven to be safe before use. Such caution is mandatory because sudden death from ventricular tachyarrhythmias is well known in patients with hypertrophic cardiomyopathy.⁵⁾⁻⁸⁾ We report on a patient with hypertrophic obstructive cardiomyopathy in whom disopyramide widened the trigger zone of lethal ventricular tachycardia seen in an electrophysiologic study.

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CASE REPORT

Clinical features: The patient was a 61-year-old male who had been well until 56 years of age when he was diagnosed as having mild systolic hypertension in a range of 160/80 to 170/90 mmHg. Because of markedly depressed ST changes and high voltage on the surface electrocardiogram, he was referred to our hospital. His family history was noncontributory. He was admitted for further evaluation.

Two-dimensional echocardiogram revealed a thickened interventricular septum (36.0 mm) but normal posterior wall thickness (10.0 mm). Systolic anterior motion of the mitral leaflet was also observed. Cardiac catheterization showed a pressure gradient in the outflow tract of 40 mmHg. Coronary arteriogram was normal. A 24-hour ambulatory electrocardiogram showed infrequent nonsustained ventricular tachycardia.

Electrophysiologic study: He underwent an electrophysiologic study after written consent was obtained. Two quadripolar and one tripolar electrode catheters were introduced to stimulate the heart and to record intracavitary electrograms (USCI His Bundle electrode and Josephson multipurpose electrodes). Incremental and programmed electrical stimulations were done first in the right atrium.^{9),10)} The effective refractory period or time intervals were measured in the standard manner. Then, programmed stimulation was applied to the right ventricle using single and double extrastimuli. Incremental pacing up to 210 beats/min was also given.

Results: The effective refractory period of the atrium was 320 msec at a basic cycle length of 600 msec and that of the atrioventricular node was not measurable because of the functional refractory period of the atrium, 340 msec. The Wenckebach point was reached at 190 beats/min. A-H and H-V intervals were 80 and 45 msec, respectively. No atrial arrhythmia or ventricular tachycardia was induced by atrial pacing.

The right ventricle was paced at the apex and at the outflow tract. The effective refractory period was 260 msec at a basic cycle length of 600 msec at the apex and 240 msec at the outflow tract. No ventricular tachycardia was induced by the programmed extrastimuli or by incremental pacing at the apex. When double extrastimuli were given after eight basic stimuli at the outflow tract, rapid ventricular tachycardia was induced which soon degenerated into ventricular fibrillation (Fig. 1). Disopyramide was then given intravenously at a dose of 50 mg. The effective refractory period of the right ventricle was prolonged to 260 msec at the outflow tract and to 300 msec at the apex (the basic drive was 600 msec). However, ventricular tachycardia became more easily inducible at the apex, where no ventricular tachycardia

Fig. 1. Induced rapid polymorphic ventricular tachycardia (VT) at the right ventricular outflow tract before disopyramide. VT soon degenerated into fibrillation.

Fig. 2. Induced VTs after disopyramide. In the control state, no VT was induced at the right ventricular apex (Panel A). After intravenous disopyramide (50 mg), VT became inducible at the echo zone (Panel B) but not at the outflow tract. VT terminated spontaneously several times as shown in Panel B, but finally degenerated into fibrillation (Panel C).

had been induced before administration of disopyramide (Fig. 2, A to C). Rapid ventricular tachycardia induced by double extrastimuli became polymorphic but terminated spontaneously several times (Fig. 2, B). Following rapid pacing at 210 beats/min, the induced ventricular tachycardia degenerated into fibrillation and required DC shock (Fig. 2, C).

DISCUSSION

Recently, Pollick reported a hemodynamically beneficial effect of disopyramide in hypertrophic obstructive cardiomyopathy.¹⁾ This drug might

be used as an alternative to reduce the outflow pressure gradient and to improve clinical symptoms¹¹⁾ but before its use, the safety must be proven.

Patients with hypertrophic cardiomyopathy are subject to sudden death⁵⁾⁻⁸⁾ and they are unusually vulnerable to ventricular arrhythmia.¹²⁾ Kowey et al performed an electrophysiologic study in 7 patients with hypertrophic cardiomyopathy.¹³⁾ They had episodes of either syncope or cardiac arrest. In a previous study from our unit, rapid lethal ventricular tachycardia was induced in 3 of 8 patients with hypertrophic cardiomyopathy.¹⁴⁾ In 3 patients with inducible ventricular tachycardia, class Ia antiarrhythmic drugs (procainamide in 3.0 gm/day or disopyramide 300-400 mg/day) were not effective. On the contrary, disopyramide widened the ventricular tachycardia inducing zone as in the present case (Fig. 2), although the pressure gradient was reduced. The inducibility of such lethal ventricular tachycardia seems very high in frequency in patients with hypertrophic cardiomyopathy since we have had inducible rapid ventricular tachycardias which degenerated into fibrillation in only 3 of 42 patients with recurrent sustained ventricular tachycardia (12 with old myocardial infarction, 12 with non-ischemic left ventricular aneurysm or regional wall motion abnormality, 9 with idiopathic ventricular tachycardia with CRBBB and left axis deviation which characteristically responded to verapamil, 3 with arrhythmogenic right ventricular dysplasia, 4 with ventricular tachycardia of undetermined cause and 2 postoperative cases of tetralogy of Fallot).^{15),16)} Only 3 of these patients (all with previous myocardial infarction) showed inducible rapid and polymorphic ventricular tachycardia. In 56 patients with frequent nonsustained ventricular tachycardia, only repetitive ventricular response was induced in some cases. Though disopyramide may be used to reduce the outflow pressure gradient as well as for arrhythmias,¹⁷⁾ this drug should be used only after determining electrophysiologically that disopyramide is safe and effective in preventing ventricular tachyarrhythmias. This principle is also applied to other antiarrhythmic drugs.¹⁸⁾

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