Failure of Cilostazol in the Prevention of Ventricular Fibrillation in a Patient with Brugada Syndrome

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Cilostazol Does Not Prevent VF in Brugada Syndrome. The ECG appearance in Brugada syndrome is caused by failure of the dome of the action potential to develop. Increased activity of the I(to) current in epicardial cells generates a transmural gradient with repolarization dispersion between the epicardium and the endocardium in the right ventricular wall, thus favoring the development of VF by a phase 2 reentry mechanism. The efficacy of cilostazol for the management of these arrhythmias has been reported. This drug is a phosphodiesterase inhibitor with positive chronotropic properties, thus blocking outward potassium currents I(to) in the myocardial tissue. We present a patient with Brugada syndrome with an implantable cardioverter defibrillator (ICD), who suffered multiple ICD discharges due to VF during therapy with this drug. (*J Cardiovasc Electrophysiol, Vol. 17, pp. 210-212, February 2006*)

**Brugada syndrome, ventricular fibrillation, cilostazol**

**Introduction**

Brugada syndrome is a clinical and electrocardiographic entity characterized by a pattern of right bundle branch block with ST segment elevation in the right precordial ECG leads and syncope or sudden death, associated with polymorphic ventricular tachycardia (PVT) and ventricular fibrillation (VF).1 Although different antiarrhythmic drugs have been postulated for the therapy of lethal arrhythmias in patients with this syndrome, the implantable cardioverter defibrillator (ICD) remains as the only effective option. Specifically, there are previous experiences on the efficacy of cilostazol.2 However, in this report we communicate its failure in this regard.

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**Case Report**

The patient is a 30-year-old man who was evaluated in August 2001 due to episodes of syncope. He was otherwise healthy, but his father died suddenly at the age of 42. Physical examination was normal, and the baseline electrocardiogram (ECG), as well as the tracing recorded after an ajmaline test, showed a pattern characteristic of Brugada syndrome, exclusively in the high, right-sided precordial leads (Fig. 1).

An echocardiographic study, exercise scintigraphy (single photon emission computed tomography [SPECT]), and cardiac MRI were normal. A single-lead ICD was implanted to prevent sudden death.

In October 2003, the patient was admitted to the coronary care unit (CCU) after suffering several ICD discharges while sleeping. The ICD discharges were initially interpreted as due to VF (continuous electrocardiographic monitoring), and cilostazol at a dose of 200 mg/day was initiated. After 3 days, when the ICD was actually interrogated, it was felt that the discharges were inappropriate and were due to atrial fibrillation (AF). Discontinuation of cilostazol was recommended but the patient refused since he felt that the drug offered some protection against arrhythmias.

The drug therapy continued, and he remained asymptomatic until September 2004, when he received several shocks from the ICD within a 24-hour period. On the event counter, an episode

**Figure 1.** ECG recording in the baseline state and 5, 10, and 20 minutes postintravenous ajmaline administration (1 mg/kg). The characteristic pattern of this syndrome is expressed exclusively in the high, right-sided precordial leads. 3rd IS = third intercostal space. 4th IS = fourth intercostal space.
thought to be AF was recorded (10:24 am) (Fig. 2), followed by four episodes of VF (11:07 am, 2:00 pm, 4:40 pm, 0:30 am), all successfully treated by the device. The episodes of VF were initiated by a ventricular extrasystole with a similar morphology and coupling interval (360 msec) (Fig. 3). Cilostazol was discontinued and oral quinidine at a dose of 1,000 mg/day was initiated.

**Discussion**

The genetic defect responsible for the functional inhibition of cardiac sodium channels \( I(na) \) is the arrhythmogenic substrate in the Brugada syndrome. Increased activity of the \( I(to) \) current in epicardial cells generates a transmural gradient with repolarization dispersion between the epicardium and the endocardium in the right ventricular wall, thus favoring the development of malignant ventricular arrhythmias by a phase 2 reentry mechanism.3-5

A variety of drugs with the ability to block these currents have been reported to be efficient for the management of these arrhythmias.6-9 The efficacy of cilostazol in the case reported by Tsuchiya et al.2 was demonstrated, but this drug was not able to prevent VF in our patient. As seen in other genetically based electrical abnormalities, despite the phenotypical (electrocardiographic and arrhythmic) similarities, different genotype variants10-11 could generate dissimilar electrophysiological substrates with a different sensitivity to certain antiarrhythmic drugs. It is also likely that autonomic influences12 and other biological variables (body temperature),13-14 provoke dynamic variations within the arrhythmic substrate, thus modifying the long-term response to the drug. For these reasons, added to the lack of controlled studies with adequate follow-up time allowing for an establishing of the true efficacy of these agents in the prevention of PVT and VF, ICDs are the only effective and safe therapy for high-risk
patients, while antiarrhythmic drugs should be used as an adjuvant therapy only for completely symptomatic patients.

The VF crises seen in this patient were preceded by an episode of AF. The association with specific mutations having a higher degree of malignancy and their role as factors triggering or conditioning the development of PVT or VF are aspects related to AF that have not been thoroughly assessed. Therefore, either a casual or a causal relationship between the two arrhythmias is difficult to determine. Future investigations in this field will define the true meaning of AF and its relationship to the risk of sudden death in this population.

References


