# Cilostazol - 2015

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Dr. Tsuchiya et al (Tsuchiya T, Ashikaga K, Honda T, Arita M. Prevention of ventricular fibrillation by cilostazol, an oral phosphodiesterase inhibitor, in a patient with Brugada syndrome. J Cardiovasc Electrophysiol 2002; 13:698-701) reported a case of 67-year-old man with BrS, in whom daily episodes of VF occurred early in the morning for 4 consecutive days.
The episodes of VF were completely prevented by an oral administration of cilostazol, (Cebralat$^{R}$ Libbs , Pletal$^{R}$). This drug is a quinolinone derivative that inhibits cellular phosphodiesterase type III (PDE III inhibitor).
This effect was confirmed by the on-and-off challenge test, in which discontinuation of the drug resulted in recurrence of VF and resumption of the drug again prevented VF. This effect may be related to the suppression of I(to) activity secondary to the increase in heart rate and/or to an increase in $Ca^{2+}$current (I(Ca)) due to an elevation of intracellular cyclic AMP concentration via inhibition of phosphodiesterase activity.
This drug might have an anti-VF potential in patients with BrS. Concomitant administration of quinidine with a single dose of cilostazol 100 mg did not alter cilostazol pharmacokinetics.
Both drugs associated in patiens with BrS could theoretically have more potency in inhibiting $I_{TO}$ channel and abolishing arrhythmias by phase 2 reentry.

Oral denopamine, atropine or cilostazol all increase ICa-L, and for this reason may be effective in reducing episodes of VF.
Cilostazol is used in clinical for intermittent claudication. The drug and several of its metabolites are cyclic AMP (cAMP) phosphodiesterase III inhibitors, inhibiting phosphodiesterase activity and suppressing cAMP degradation with a resultant increase in cAMP in platelets and blood vessels, leading to inhibition of platelet aggregation and vasodilation, respectively.
Cilostazol reversibly inhibits platelet aggregation induced by a variety of stimuli, including thrombin, ADP, collagen, arachidonic acid, epinephrine, and shear stress.
Effects on circulating plasma lipids have been examined in patients taking Cilostazol. After 12 weeks, as compared to placebo, Cilostazol 100 mg b.i.d. produced a reduction in triglycerides of 29.3 mg/dL (15%) and an increase in HDL-cholesterol of 4.0 mg/dL (10%).
Cilostazol affects both vascular beds and cardiovascular function. It produces non-homogeneous dilation of vascular beds, with greater dilation in femoral beds than in vertebral, carotid, or superior mesenteric arteries. Renal arteries were not responsive to the effects of cilostazol.
Experimental study in swine shows that cilostazol administration of 6 mg/kg significantly increased the diastolic pacing threshold, which was associated with significantly reduced the defibrillation threshold and the upper limit of vulnerability.(Kanlop N, Shinlapawittayatorn K, Sungnoon R, Weerateerangkul P, Chattipakorn S, Chattipakorn N. Cilostazol attenuates ventricular arrhythmia induction and improves defibrillation efficacy in swine. Can J Physiol Pharmacol. 2010 Apr;88:422-428.).
Abud et al from Santa Fe, Argentina observed failure of cilostazol in the prevention of ventricular fibrillation in a patient with Brugada syndrome.
(Abud A, Bagattin D, Goyeneche R, Becker C. Failure of cilostazol in the prevention of ventricular fibrillation in a patient with Brugada syndrome. J Cardiovasc Electrophysiol. 2006 Feb;17(2):210-2.)