Nicorandil Suppresses a Hump on the Monophasic Action Potential and Torsade de Pointes in a Patient with Idiopathic Long QT Syndrome

Masaomi Chinushi, M.D., Yoshifusa Aizawa, M.D., Hiroshi Furushima, M.D., Hiroshi Inuzuka, M.D.,* Kenji Ojima, M.D.,* and Akira Shibata, M.D.

Summary

The patient was a 71-year-old female with Torsade de Pointes (TdP) associated with idiopathic long QT syndrome. TdP and polymorphic nonsustained VT were frequently observed at bedside and an electrophysiologic study was performed. The QT (and QTU) interval was abnormally prolonged, and alternation of the QT interval was also recorded on the electrocardiogram. Monophasic action potential (MAP) from the right ventricle showed a hump on the falling limb of the MAP following a long RR interval of more than 1.0 sec. Intravenous administration of nicorandil (2 mg) resulted in disappearance of the hump, and ventricular arrhythmia was no longer observed. The QT interval at a PP interval of 720 msec was slightly shortened. She was treated with a DDD-pacemaker and given nicorandil. No recurrence of TdP was observed during the follow-up period of 8 months. This drug might be effective in patients with idiopathic long QT syndrome. (Jpn Heart J 36: 477-481, 1995)

Key words: TdP Idiopathic long QT syndrome Nicorandil

Torsade de Pointes (TdP) is found in patients with long QT syndrome, and early afterdepolarization (EAD) has been shown to be related to this arrhythmia.1)

Recently, we observed that a K-channel opener, nicorandil, suppressed TdP and eliminated the hump of the monophasic action potential (MAP)2,3) in a patient with idiopathic long QT syndrome.
CASE REPORT

A 71-year old female was referred to our hospital on March 28, 1994, because of frequent syncopal attacks. On admission, her pulse rate was 55 beats per minute and blood pressure was 150/88 mmHg. The electrocardiogram revealed a markedly prolonged QT interval up to 760 msec and T wave abnormality (Figure 1A). Alternations in the QT interval and T wave were also observed most clearly in V5. Serum electrolytes were normal as were other blood chemistry tests. Drugs were not related to the QT prolongation.

After admission to our hospital, TdP recurred frequently and the patient lost consciousness. A temporary pacing lead was inserted to prevent recurrence of ventricular arrhythmia by increasing the heart rate, and an electrophysiologic study was performed. During the study, spontaneous ventricular premature complexes and nonsustained polymorphic VTs occurred at the terminal portion of the prolonged T waves (Figure 2A). However, no ventricular tachyarrhythmia was induced by electrical stimulation which consisted of 1–3 extrastimuli and rapid pacing up to a rate of 210 per minute.

Figure 1. Twelve-lead electrocardiogram. Upon admission to our hospital, the QT interval was observed to be between 560–760 msec and QTc interval was 580–790 msec (Panel A). T wave abnormality was noticed in several leads. After oral administration of nicorandil and DDD pacing, the QT and QTc intervals were shortened to 420 and 480 msec, respectively (Panel B). The QT and QTc intervals were again prolonged to 460 and 530 msec, respectively by the discontinuation of nicorandil for 2 days (Panel C).
Figure 2. Electrocardiogram monitoring and monophasic action potential (MAP). In the control state (Panel A), ventricular premature complexes and nonsustained ventricular tachycardia occurred at the terminal portion of prolonged T wave. A hump was obvious on the falling limb of MAP (arrow) when the preceding RR interval changed from 720 to 1120 msec (Panel B). After intravenous administration of nicorandil (Panel C), the hump was not evident when the preceding RR interval was prolonged from 720 to 1100 msec. The spontaneous sinus cycle length, AH and HV intervals remained constant after drug administration.

HBE = His bundle electrogram; MAP = monophasic action potential from the septum of the right ventricle.

MAP was recorded by the contact technique. The local electrogram was filtered at 0.05–500 Hz for MAP. The duration of the MAP was measured at 90% repolarization (MAP90). MAP90 obtained from the septum of the right ventricle was 460 msec at a basic cycle length of 720 msec (Figure 2B). As the preceding RR interval was prolonged to 1120 msec, MAP90 was prolonged to 570 msec and a hump was reproducibly observed on the falling phase on the
MAP (Figure 2B).

After intravenous administration of 2 mg of nicorandil, polymorphic nonsustained VTs were suppressed and the hump following a long RR interval disappeared (Figure 2C). Sinus rate and the A-H and H-V intervals were unchanged by the administration of nicorandil. At basic cycle length of 720 msec, MAP90 and QTc interval were 440 and 590 msec, respectively. Systemic blood pressure fell slightly after administration of nicorandil, from 132/90 to 128/84 mmHg.

The patient was implanted with a DDD-pacemaker, and nicorandil was prescribed. The QT and QTc intervals were 460 and 530 msec, respectively, and with pacing alone were further shortened by nicorandil (15 mg per day orally) to 420 and 480 msec, respectively (Figure 1B). However, the shortening of the QT interval was reversed when nicorandil was discontinued (Figure 1C). The drug was continuously administered thereafter. With the combined treatment of pacing and nicorandil, no recurrence of syncope or TdP was observed during the follow-up period of 8 months.

**DISCUSSION**

In this patient, MAP obtained from the septum of the right ventricle showed a hump at a long preceding RR interval, and the hump was considered to be consistent with EAD which triggers TdP or polymorphic VT.4) Previous reports have demonstrated that either a decrease in outward K-current, or an increase in inward Ca-current or Na-current was responsible for prolongation of the QT interval.5-7) In experimental models, a suppression of outward K-current by some drugs has been shown to produce EAD and TdP concomitantly with QT interval prolongation.5-7) In this instance, K-channel openers have been shown to suppress EAD and TdP. However, the antiarrhythmic action of the drugs is considered not only to be due to shortening of the action potential duration but also due to hyperpolarization of the resting potential or suppression of automaticity,8,9) because the prolonged QT interval was not completely reversed by the drugs.10)

Our findings are in agreement with some experimental reports,8-10) and the hump on MAP and ventricular arrhythmia in this case were suppressed after the administration of the K-channel opener nicorandil. A shortening of the QT interval was concomitantly observed, and transient discontinuation of the drug resulted in a prolongation of the QT interval. Although we are not sure whether this finding indicates a chronic antiarrhythmic effect of this drug, the drug has since been continuously used to shorten the QT interval in this patient.

With, or possibly without pacing treatment, a K-channel opener might be
used as a therapeutic tool in patients with idiopathic long QT syndrome to shorten the QT interval and also to prevent TdP. Further study with a larger number of patients is warranted to establish the antiarrhythmic effect of this K-channel opener in patients with idiopathic long QT syndrome.

REFERENCES


