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Nicorandil Successfully Abolished Intraoperative Torsade de Pointes

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TORSADE DE POINTES (TdP), polymorphic ventricular tachycardia with QT interval prolongation, is one of the life-threatening arrhythmias and may occur in association with intracranial disorders.[1-6]

Nicorandil, a potassium-channel opener, has been used as a coronary vasodilator.[7] Recently antiarrhythmic therapy using nicorandil has been attempted. Chinushi *et al.*[8] reported that nicorandil suppressed TdP in patients with idiopathic long QT syndrome. We experienced a case in which TdP occurred during surgery and was clearly abolished by nicorandil.

Case Report

A 70-yr-old woman weighing 50 kg was admitted for evaluation of Parkinson's disease. She had ataxia for 1 yr without other neurologic signs. Examination revealed a cerebellopontine angle meningioma, and she was scheduled for surgery. She underwent long-term therapy with levodopa for Parkinsonism and complicated mild hypertension for ≈10 yr. Results of routine laboratory tests were within normal limits. The preoperative electrocardiogram showed a sinus rhythm without marked prolongation of the QT interval. The QT and QTc intervals were 0.38 and 0.46 s, respectively. She had no history of arrhythmias, ischemic heart disease, or syncope.

The patient was premedicated with 0.5 mg atropine and 25 mg hydroxyzine administered intramuscularly. She had an uneventful anesthetic induction with propofol and was intubated after the administration of vecuronium. Continuous electrocardiogram (fig. 1A), SpO_2, $ETCO_2$, invasive and noninvasive arterial pressures, and rectal temperature were monitored. After induction of anesthesia, no obvious electrocardiographic change was noted. Anesthesia was maintained with isoflurane and nitrous oxide in oxygen. The patient was placed in the lateral position for surgery.

The surgery proceeded uneventfully. At 1.0-1.5% concentrations of isoflurane, blood pressure and heart rate remained at ≈100/60 mmHg and 60-70 beats/min, respectively. SpO_2 was >97% during anesthesia. Ventilation was controlled to keep $ETCO_2$ at 30-35 mmHg. Approximately 7 h after induction of anesthesia, however, premature ventricular contractions appeared (fig. 1B). Two or three consecutive premature ventricular contractions were observed. Premature ventricular contractions persisted after administration of lidocaine (50 mg given intravenously).

Subsequently, nonsustained TdP occurred (fig. 1C). The electrocardiogram revealed markedly prolonged QT (0.62 s) and QTc (0.69 s) intervals. Arterial blood drawn at this time yielded arterial oxygen tension at 189.8 mmHg, arterial carbon dioxide tension at 33.9 mmHg, *p*H at 7.44, and normal concentrations of sodium, potassium, and calcium in serum. Blood pressure was 100/60 mmHg, and heart rate was 60 beats/min. Rectal temperature was 36.6°C.

The patient was initially treated with lidocaine (50 mg given intravenously followed by 1-2 $mg \cdot kg^{-1} \cdot h^{-1}$), but nonsustained (lasting several minutes) TdP recurred. The incidence of the TdP was several times per hour. Then the anesthetic agent was changed from 0.8% isoflurane to 1.5% sevoflurane. This was ineffective in controlling the arrhythmias. The patient continued to have several episodes of TdP per hour. Thereafter, lidocaine was discontinued, and magnesium (1 g given intravenously followed by 1 g/h) was administered. This also failed to prevent the attacks, and the patient continued to have nonsustained TdP over the next 2 h. Finally we decided to use nicorandil to treat TdP. After intravenous administration of nicorandil (4 mg/h), TdP was completely suppressed (fig. 1D). Neither TdP nor premature ventricular contractions developed again. During treatment with nicorandil, blood pressure and heart rate were maintained at 100/60 mmHg and 70-80 beats/min, respectively. The patient was extubated uneventfully in the operating room and transferred to the ward.

A postoperative 12-lead electrocardiogram showed QT prolongation (QT, 0.48 s; QTc, 0.54 s). Administration of nicorandil was terminated the next day. The patient experienced no further arrhythmias. The QT prolongation returned to the approximate preoperative length (QT, 0.40 s; QTc, 0.47 s) on the electrocardiogram on the seventeenth postoperative day.

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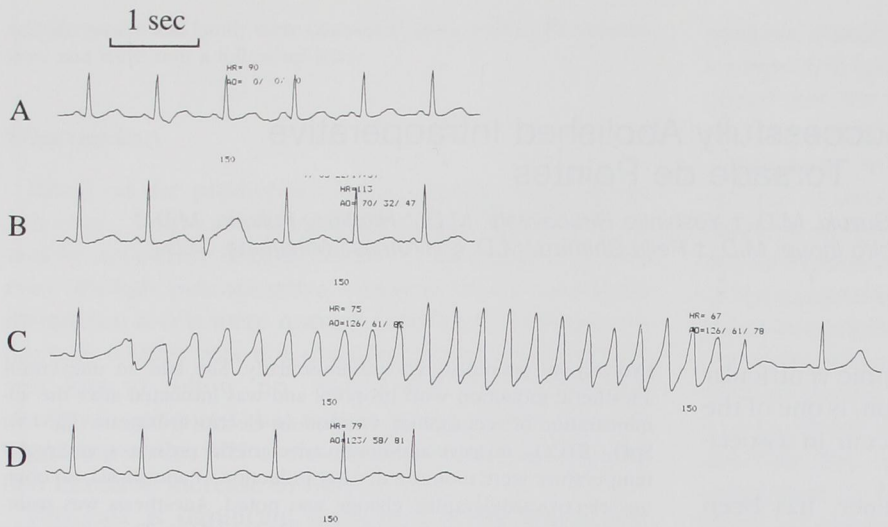

Fig. 1. Two-lead electrocardiogram recorded sequentially. (*A*) Preinduction of anesthesia (QT, 0.44 s; QTc, 0.50 s). (*B*) Premature ventricular contraction with marked prolonged QT interval (QT, 0.50 s; QTc, 0.57 s). (*C*) Torsade de pointes (TdP) terminated spontaneously. (*D*) After administration of nicorandil (QT, 0.54 s; QTc, 0.60 s).

Discussion

In this patient, nicorandil clearly abolished TdP during surgery. Nicorandil has potent vasodilating action and has been used as a coronary vasodilator.[7] Nicorandil increases the outward potassium current of not only vascular smooth muscle but also of cardiac muscle. In recent studies suppression of this outward potassium current has been shown to produce early after depolarizations and TdP concomitantly with QT interval prolongation.[3] Triggered activity originating from early after depolarizations has been proposed as a mechanism responsible for TdP.[3] In one experimental model, potassium channel openers including nicorandil have been shown to suppress early after depolarizations and ventricular arrhythmias.[3,9,10] In the clinical setting, nicorandil suppresses early after depolarizations and TdP in patients with idiopathic long QT syndrome.[8,11] To our knowledge, however, the current report is the first to describe the usefulness of nicorandil to treat ventricular tachycardia or TdP during anesthesia.

There are several principles of treatment for ventricular tachycardia. Electrolyte abnormalities and hypothermia should be looked for and appropriately corrected. Although magnesium concentrations were not measured, other electrolyte imbalances were not present, and magnesium did not successfully treat her dysrhythmia. The patient remained normothermic. Another approach is to decrease adrenergic tone.[3] Isoflurane is vagolytic and can increase sympathetic tone.[12,13] Sevoflurane is not associated with sympathetic activation.[14] Therefore, in the current patient, isoflurane was discontinued and sevoflurane was administered. Again this was unsuccessful. Although antiarrhythmic therapy for TdP begins with lidocaine or magnesium,[1,3,15] these agents were ineffective in the current patient. β-Blockers have been used to treat TdP in congenital long QT syndrome.[1-3] Conversely, β-stimulation may be effective and β-blockers contraindicated with acquired long QT syndrome.[2,3] Therefore, β-blocker therapy was not attempted in our patient.

In controlling TdP in this patient, marked QT prolongation received attention. We postulated that this phenomenon reflected prolongation of the action potential duration. Therefore, we thought potassium channel activation may shorten action potential duration and be effective for this arrhythmia, and we decided to use nicorandil. The antiarrhythmic action of nicorandil is considered to be attributable not only to shortening action potential duration but also to hyperpolarization of the resting potential and suppression of automaticity.[16] Therefore, nicorandil may be effective for treating arrhythmias originating from enhanced automaticity and reentry.[16] In the current patient, nicorandil successfully terminated TdP without obvious hemodynamic change, providing additional evidence that potassium channel agonists may have a place in the treatment of TdP.

We postulate that the neurosurgical procedure may have caused QT prolongation in this patient. The patient had no history of arrhythmias or syncope attack. Preoperative electrocardiogram did not show obvious QT prolongation either. The patient did show marked

QT prolongation during operation, however. The influence of preexisting hypertension was unknown. Because blood pressure and heart rate were unchanged, we did not consider that the QT prolongation was secondary to cardiac ischemia. Instead surgery may have locally distorted various autonomic nuclei of the brain stem and perhaps hypothalamus. Stimulation of these areas can cause a variety of sympathetic and parasympathetic responses. Intracranial mass lesions often are associated with changes in the electrocardiogram, including QT prolongation and TdP,[2-6] and volatile anesthetic agents may prolong the QT interval.[17,18] At least some contribution of volatile anesthetic agents to the prolongation of the QT interval interval can not be excluded in this patient.

Ventricular tachycardia or TdP is an infrequent complication during anesthesia. Early treatment is of paramount importance. Nicorandil may, at least in part, play an important role in the treatment of TdP with long a QT interval during anesthesia, especially when lidocaine and magnesium are not effective.

References

1. Atlee JL: Perioperative cardiac dysrhythmias: Diagnosis and management. ANESTHESIOLOGY 1997; 86:1397-424

2. Janeira LF: Torsade de Pointes and long QT syndromes. Am Fam Phys 1995; 52:1447-53

3. Tan HL, Hou CJY, Lauer MR, Sung RJ: Electrophysiologic mechanisms of the long QT interval syndromes and Torsade de Pointes. Ann Intern Med 1995; 122:701-14

4. Stober T, Sen S, Anstätt T, Bette L: Correlation of cardiac arrhythmias with brainstem compression in patients with intracerebral hemorrhage. Stroke 1988; 19:688-92

5. Di Pasquale G, Pinelli G, Andreoli A, Manini G, Grazi P, Tognetti F: Holter detection of cardiac arrhythmias in intracranial subarachnoid hemorrhage. Am J Cardiol 1987; 59:596-600

6. Hust MH, Nitsche K, Hohnloser S, Böhm B, Just H: Q-T prolongation and Torsade de Pointes in a patient with subarachnoid hemorrhage. Clin Cardiol 1984; 7:44-8

7. Goldschmidt M, Landzberg BR, Frishman WH: Nicorandil: A potassium channel opening drug for treatment of ischemic heart disease. J Clin Pharmacol 1996; 36:559-72

8. Chinushi M, Aizawa Y, Furushima H, Inuzuka H, Ojima K, Shibata A: Nicorandil suppresses a hump on the monophasic action potential and Torsade de Pointes in a patient with idiopathic long QT syndrome. Jpn Heart J 1995; 36:477-81

9. Takahashi N, Ito M, Saikawa T, Arita M: Nicorandil suppresses early afterdepolarization and ventricular arrhythmias induced by caesium chloride in rabbits in vivo. Cardiovasc Res 1991; 25:445-52

10. Fish FA, Prakash C, Roden DM: Suppression of repolarization-related arrhythmias in vitro and in vivo by low-dose potassium channel activators. Circulation 1990; 82:1362-9

11. Sato T, Hata Y, Yamamoto M, Morita H, Mizuo K, Yamanari H, Saito D, Ohe T: Early afterdepolarization abolished by potassium channel opener in a patient with idiopathic long QT syndrome. J Cardiovasc Electrophysiol 1995; 6:279-82

12. Graves CL, McDermott RW, Bidwai A: Cardiovascular effects of isoflurane in surgical patients. ANESTHESIOLOGY 1974; 41:486-9

13. Okamoto H, Hoka S, Kawasaki T, Okuyama T, Takahashi S: Dose-dependent increases in the renal sympathetic nerve activity during rapid increase in isoflurane concentration in intact, lower airway-deafferented, and baroreceptor-deafferented rabbits. ANESTHESIOLOGY 1996; 84:1196-204

14. Ebert TJ, Harkin CP, Muzi M: Cardiovascular responses to sevoflurane: A review. Anesth Analg 1995; 81(6S):S11-22

15. Tzivoni D, Banai S, Schuger C, Benhorin J, Keren A, Gottlieb S, Stern S: Treatment of torsade de pointes with magnesium sulfate. Circulation 1988; 77:392-7

16. Imanishi S, Arita M, Aomine M, Kiyosue T: Antiarrhythmic effects of nicorandil on canine Purkinje fibers. J Cardiovasc Pharmacol 1984; 6:772-9

17. Riley DC, Schmeling WT, Al-Wathiqui MH, Kampine JP, Warltier DC: Prolongation of the QT interval by volatile anesthetics in chronically instrumented dogs. ANESTHESIOLOGY 1988; 67:741-9

18. Schmeling WT, Warltier DC, MacDonald DJ, Madsen KE, Atlee JL, Kampine JP: Prolongation of the QT interval by enflurane, isoflurane and halothane in man. Anesth Analg 1991; 72:137-44