CASE REPORT

Sinus Standstill in a Patient after Intracoronary Papaverine Administration for a Coronary Fractional Flow Reserve

Masahiro Nauchi, MD, Tsuyoshi Sakai, PhD, Masahiro Yamawaki, MD and Yoshiaki Ito, MD

Summary
A 78-year-old woman had paroxysmal atrial fibrillation and effort angina. Two months before she was admitted for a coronary angiography, she had been feeling dizzy. A Holter 24-hour electrocardiography monitor exhibited an asymptomatic episode of 2.9 seconds of RR interval. She underwent a coronary angiography, which showed intermediate stenosis in the left descending artery. Fractional flow reserve (FFR) measurement using intracoronary papaverine administration was performed. After intracoronary papaverine (12 mg) administration, pause of 4 seconds led to polymorphic ventricular tachycardia (VT), although the VT terminated spontaneously. Premature ventricular beat occurred and led to sustained polymorphic VT. In cardiac electrophysiology study, pacing from the right atrium showed that the maximum sinus node recovery time (SRT) was 910 ms. After procainamide (10 mg/kg) administration, the maximum SRT was 16.3 seconds with some junctional escapes. After intravenous papaverine administration, there was a slight change. Intracoronary papaverine administration induced about 9-seconds pause with some junctional escapes. We conclude that intracoronary papaverine administration reveals potential sinus node dysfunction. The patient has been asymptomatic since the implantation of the pacemaker. Patients with suspicious sinus dysfunction should be careful.

Key words: Sick sinus syndrome

Fractional flow reserve (FFR) measurement is used for assessing moderate coronary artery stenosis. Papaverine hydrochloride is administered intracoronary and induce the maximal hyperemia in FFR measurement. It is known that papaverine may induce ventricular tachyarrhythmia (VTA). The incidence of VTA ranges from 1.3% to 2.8%.\textsuperscript{1,2} This mechanism is unclear. One of its several causes is suggested to be a QT prolongation. We report a case of a patient who experienced papaverine-induced pause.

Case Report
A 78-year-old woman had a history of paroxysmal atrial fibrillation, type 2 diabetes mellitus, hypertension, hypothyroidism, and effort angina for which a zotarolimus-eluting stent was implanted. Her conditions of these diseases were stable, but she had been feeling dizzy. A Holter 24-hour electrocardiography monitor exhibited an asymptomatic episode of 2.9 seconds of RR interval. Total heart beats of the day were 85,793 with bisoprolol 5 mg/day. As diuretic agents were reduced, her symptoms improved.

Two months later, she was admitted for a follow-up coronary angiography (CAG). On physical examination, there was no abnormal findings. Electrocardiogram showed normal sinus rhythm and QT interval of 448 ms (QTc 452 ms). Laboratory data showed normal values, except those for liver dysfunction aspartate aminotransferase, 97 U/L; alanine aminotransferase, 83 U/L; $\gamma$-glutamyltransferase, 76 U/L). Serum potassium and calcium levels were within the reference range (4.4 mEq/L and 8.8 mg/dL, respectively). CAG revealed an intermediate stenosis in the left descending artery. Then, FFR measurement using intracoronary papaverine administration was performed. After papaverine (12 mg) administration as usual dosage into the left coronary artery over a period 15 seconds, a pause of 4 seconds with polymorphic ventricular tachycardia (VT) occurred, though the VT terminated spontaneously (Figure 1). Premature ventricular beat occurred, leading to sustained polymorphic VT (Figure 2). Sinus rhythm was resumed by a DC shock delivery at 150 J. Following papaverine administration, QT interval was prolonged from 440 ms (QTc, 491 ms) to 770 ms (QTc, 550 ms). Then, bisoprolol was stopped, because it might effect bradycardia.

A month later, cardiac electrophysiology study was performed. A-A interval, A-H interval, and H-V interval were within thereference range (570, 85, and 35 ms, respectively). The paced cycle length of the A-V nodal Wenckebach-type block was 353 ms. Pacing from the right atrium at a basic cycle length of 600 ms for 30 sec-
Figure 1. Papaverine administration induced sinus standstill. Sinus arrest led to polymorphic ventricular tachycardia.

Figure 2. A: Monitor before intracoronary papaverine administration. QT interval 440 ms (QTc 491 ms). B: Monitor after papaverine administration, premature ventricular beat lead to polymorphic ventricular tachycardia. Papaverine-induced QT prolongation. QT interval 800 ms (QTc 577 ms).

onds showed that the maximum sinus node recovery time (SRT) was 910 ms (the corrected sinus node recovery time [CSRT] was 290 ms). Sinoatrial conduction time could not be evaluated because of some premature atrial beats and unstable sinus cycle length.

After intravenous papaverine (12 mg) administration, the maximum SRT at paced cycle length of 330 ms for 30 seconds was 1690 ms (CSRT, 1110 ms). By pharmacologic denervation using atropine (0.04 mg/kg) and propranolol (0.2 mg/kg), the intrinsic heart rate was normal at 85 bpm. The paced cycle length of the A-V nodal Wenckebach-type block was 375 ms and the maximum SRT at paced cycle length of 375 ms for 30 seconds was 2035 ms (CSRT, 1235 ms).

After procainamide (10 mg/kg) was administrated intravenously, the measured values were as follows: A-A interval, 770 ms; A-H interval, 120 ms; H-V interval, 40 ms; and cycle length of A-V nodal Wenckebach-type block rate, 428 ms. The maximum SNRT at paced cycle length of 333 ms was 16.3 seconds with some junctional escapes (Figure 3). Intracoronary papaverine (12 mg) administration showed 9.3 seconds of sinus standstill and QT prolongation (QT interval, 370 ms; QTc, 530 ms).

The cardiac electrophysiology study indicated the following: 1) SRT was abnormal, especially with procainamide; 2) intracoronary papaverine administration induced
sinus arrest reproducibility; and 3) autonomic tone slightly affected SRT.

We considered that sinus node dysfunction was revealed by papaverine administration at the time of FFR measurement and the adaptation for pacemaker. Permanent pacemaker was implanted. After that, the patient has been followed up uneventfully.

Discussion

In this case, papaverine hydrochloride induced long pause and QT prolongation. Although QT prolongation is a well-known adverse effect, long pause is not. Larger dose of papaverine leads to sinus slowing or standstill, active ectopic ventricular rhythms, and even ventricular fibrillation. In this case, the usual dose of papaverine-induced sinus standstill.

Procainamide causes SRT prolongation in patients with sinus node dysfunction. Sinoatrial exit block is reported to cause long SRT. In this case, we were not able to measure sinoatrial conduction time. Therefore, we could not assess whether the papaverine-induced sinus arrest was caused by abnormality of automaticity or conduction.

Papaverine inhibits delayed rectifying potassium currents (IKr) and prolongs the action potential duration, resulting in QT prolongation. At cardiac electrophysiology test, several drugs such as atropine and propranolol were administrated. Therefore, QT interval was not quite prolonged and VT did not occur. Atropine is reported to be effective on QT interval prolongation. It was uncertain that propranolol was effective in this case. Patients with drug-induced long QT syndrome have a mutation rate similar to those with congenital LQT. Slow heart rate, which aggravates the dispersion of ventricular repolarization, is likely to induce VA in patients with LQT. Papaverine can prolong QT interval and decrease the heart rate. It may decrease the heart rate in suspected patients with slow heart rate or sinus dysfunction more strongly and worsen QT prolongation directly and indirectly. That may be the reason why papaverine is likely to induce VA in patients with a relatively slow heart rate.

In this case, papaverine is considered to reveal the potential sinus node dysfunction. Previous symptom of dizziness was related to sick sinus syndrome. In the end, we thought that her symptoms could be improved by pacemaker. Papaverine should be administered carefully in patients with sinus node dysfunction. In instantaneous flow reserve (iFR), there is no need for intracoronary papaverine administration. Therefore, we should use iFR for assessing moderate coronary artery stenosis in suspected patients with sinus dysfunction.
Disclosures

Conflicts of interest: None.

References


