



Loperamide-Induced Ventricular Tachycardia Storm

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Abstract

Loperamide is an over-the-counter antilaxative medication with minor opioid properties. For this reason, it has recently become a drug of concern for the Food and Drug Administration due to its potential for abuse. In addition, further apprehension pertaining to its over-the-counter availability has developed due to the recent increase in reported cases of loperamide overdose or prolonged use leading to arrhythmias. We described a rare case of loperamide-induced ventricular tachycardia storm.

Keywords

- ▶ loperamide
- ▶ ventricular tachycardia storm
- ▶ ventricular arrhythmias
- ▶ opioid

Background

Loperamide is an over-the-counter (OTC) antilaxative medication with some opioid properties. It was deemed low risk for abuse in 1982 and was dropped off the prescription drug list.¹ Recently, it has received attention due to its potential for abuse, especially with the ongoing opioid crisis. The Food and Drug Administration (FDA) warns about the abuse potential in its labeling for this drug. It also warns that cases of Qt/QTc interval prolongation, *Torsades de Pointes*, other ventricular arrhythmias, and cardiac arrest have been reported in adults who take higher than recommended doses.² In this article, we describe a case of loperamide-induced ventricular tachycardia (VT) storm.

Case Report

A 40-year-old female with a past medical history of depression and irritable bowel syndrome presented to the emergency department via emergency medical services (EMS) after a syncopal episode while driving. She was initially taken to an outside hospital where she was found to have a new left bundle branch block (LBBB) and an episode of nonsustained VT, so she was transferred to a higher level of care. In the ambulance, she developed incessant, polymorphic VT (▶ **Fig. 1**) and went into cardiac arrest. EMS performed a precordial thump and gave a bolus of amiodarone 150 mg which achieved return of spontaneous circulation (ROSC). On arrival at the tertiary facility, she was alert and oriented. She

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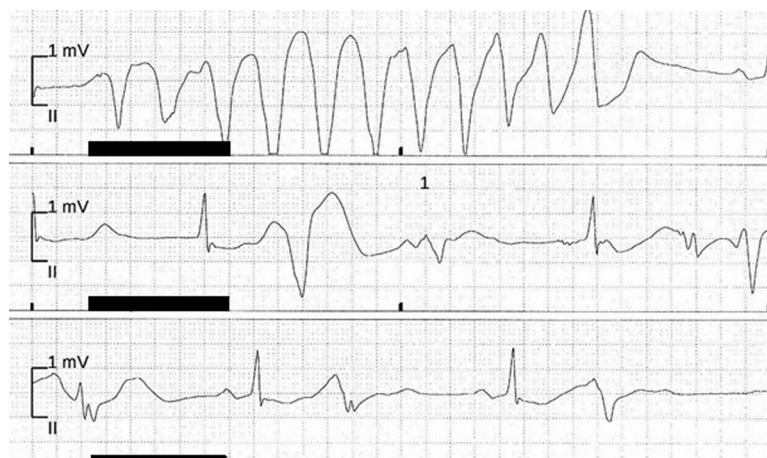


Fig. 1 Telemetry rhythm strip—incessant polymorphic ventricular tachycardia.

denied taking any prescription medications except duloxetine 90 mg daily, which she had been on for several months. She denied suicidal ideations or intentional overdose. She subsequently went into ventricular fibrillation (VF) cardiac arrest, and cardiopulmonary resuscitation (CPR) was initiated. She received amiodarone 150 mg IV (intravenous), lidocaine 100 mg IV, and defibrillation which again achieved ROSC. A lidocaine infusion was begun, she was intubated for airway protection and transferred to the intensive care unit.

Her magnesium and potassium at presentation were 2.1 and 4.3, respectively. An initial electrocardiogram showed profound QTc prolongation and new LBBB (→Fig. 2). Transthoracic echocardiogram revealed a left ventricular ejection fraction of 45% with apical hypokinesis, grade 2 diastolic dysfunction, moderate mitral valve regurgitation, and moderately dilated left atrium with a volume index of 46.8 mL/m². Despite aggressive IV magnesium repletion she continued to have frequent nonsustained VT with subsequent VF cardiac arrest. CPR was again initiated, and she was defibrillated twice prior to ROSC. At that time neuromuscular paralysis and deep sedation were initiated to lyse her adrenergic drive, which was thought to be contributing to recurrent VT/VF arrests. She remained intubated, sedated, and paralyzed for approximately 48 hours with IV lidocaine infusion and magnesium repletion until she was without arrhythmia on telemetry. Lidocaine was weaned and the

patient's paralysis and sedation were discontinued. She was extubated to nasal cannula on day 3 of hospitalization. A follow-up transthoracic echocardiogram was done at this time which demonstrated a normalized ejection fraction of 66%.

Upon further questioning, the patient endorsed taking an entire bottle (~200 tablets) of loperamide for intermittent diarrhea. She denied suicide attempt or taking additional OTC medications besides loperamide. Her LBBB resolved on day 3 of hospitalization, her QTc gradually improved, and she was without arrhythmia for the remainder of her hospital course (→Figs. 3 and 4). Coronary angiography performed prior to discharge showed nonobstructive coronary artery disease in the left anterior descending artery without significant stenosis. She was discharged on day 6 of hospitalization upon resolution of her QTc (→Fig. 5) with a wearable defibrillator and advised to follow up with the cardiology clinic where informed consent was provided.

Discussion

VT storm, defined as three or more episodes of VT within a 24-hour period, can be caused by ischemia, congenital heart disease, myocarditis, and medications.³⁻⁵ While in this case loperamide was the trigger for VT, it is important to rule out other causes including ischemia through coronary

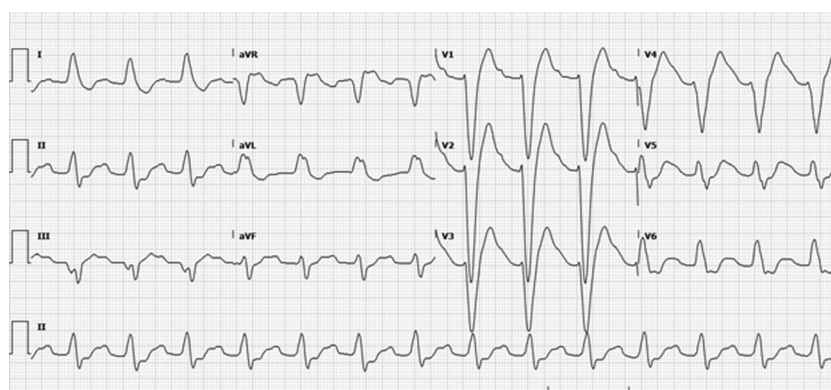


Fig. 2 EKG on arrival—severe QTc prolongation, new LBBB. EKG, electrocardiogram; LBBB, left bundle branch block.

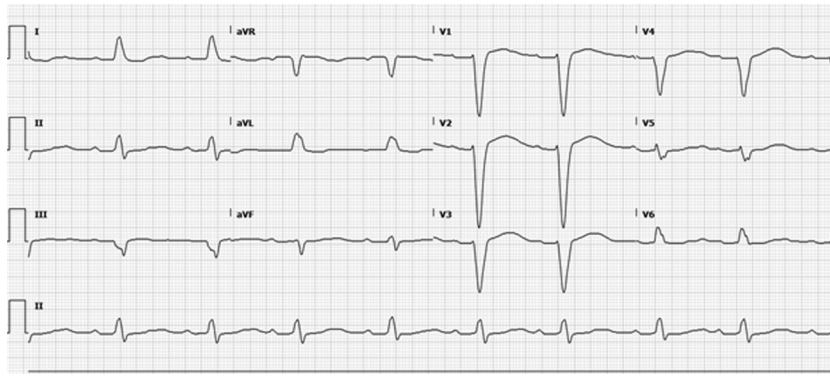


Fig. 3 Severe QTc prolongation, new LBBB. LBBB, left bundle branch block.

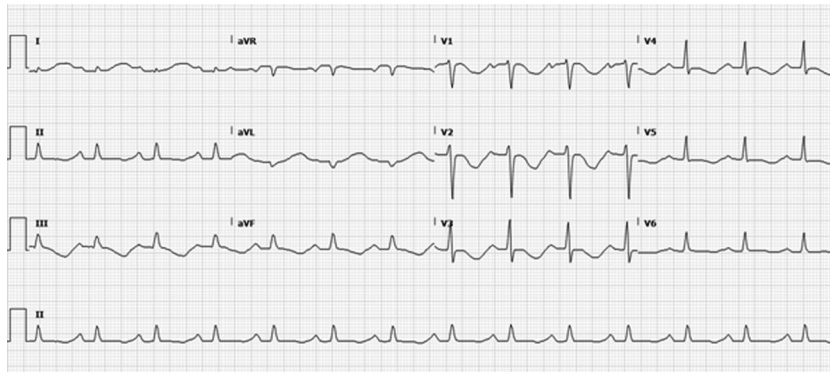


Fig. 4 Resolution of LBBB, continued QTc prolongation. LBBB, left bundle branch block.

angiography, which in this case proved to show no obstructive coronary artery disease.

Loperamide is an FDA-approved antidiarrheal medication. It can be obtained OTC or prescribed. It binds to opiate receptors in the gut wall. It also slows intestinal transit time and affects the water and electrolyte movement through the bowel, thus decreasing the number of stools.² In the current opioid epidemic, loperamide has been used to alleviate withdrawal symptoms. The doses that are used range from 70 to 100 mg per day, significantly higher than the maximum recommended daily dose of 16 mg.⁶ The National Poison

Data System reported 91% increase in loperamide exposures from 2010 to 2015.

Overdose of loperamide has been reported to cause life-threatening cardiac events, including ventricular arrhythmias, *Torsades de Pointes*, Brugada syndrome, and prolongation of QT/QTc/QRS.² Prolongation of QTc happens due to disturbances of the cardiac action potential. Multiple hypotheses have been proposed, but the exact mechanism of loperamide-induced cardiac events is unknown. Other medications that are known to cause prolonged QT interval include sotalol, haloperidol, methadone, and erythromycin.⁷



Fig. 5 Discharge EKG—normalization of QTc. EKG, electrocardiogram.

While the underlying mechanism by which loperamide induces QT/QTc prolongation, and ultimately VT storm, is not fully understood, theories have been postulated throughout the literature and in previous case reports. One of the most widely accepted and scientifically supported propositions is loperamide's action on the human ether-a-go-go (hERG) potassium channel. Loperamide shares structural features with both methadone, a known QT-prolonging drug, and terfenadine, a potent hERG-channel blocker. Each contains multiple phenyl rings, which may be a contributing factor to their shared QT-prolonging effects. Furthermore, terfenadine and loperamide possess a piperidine nitrogen molecule within their structure which is believed to inhibit the hERG channel.⁸ This proposed mechanism has yet to be verified in formal studies but should be the topic of future research. In several case reports pertaining to loperamide-inducing VT storm, patients were taking additional medications, including those known to prolong the QT segment. In addition, the dosing and duration of loperamide ingestion has led to ambiguity.

Conclusion

Loperamide-associated VT storm is a rare but serious toxicity of this medication. With the ongoing opioid epidemic, physicians should remain alert for its potential for abuse and side effects, especially cardiac toxicity when taken in high doses. QT prolongation precedes this arrhythmia and should lead to suspected toxicity/abuse.

Funding

None.

Conflict of Interest

None declared.

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