Cardiac Consequences of the Heroin Epidemic: Loperamide Causing Torsades de Pointes

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INTRODUCTION

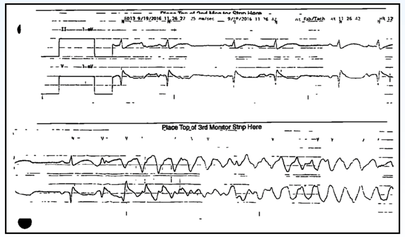
Heroin and drug related overdoses have increased by over 20% annually since 2014 in the state of Pennsylvania. Fueled by addiction to prescription drugs, addicts have turned to alternative methods to get high. According to a report in the Annals of Emergency Medicine, there has been a 10-fold increase in internet posting regarding the abusive potential of loperamide. 70% of postings discussed loperamide for opiate withdrawal, while approximately 25% focused on using loperamide to get high.[1] We present a case of a patient who abused loperamide with dangerous consequences.

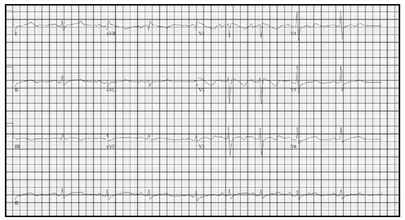
CASE REPORT

A 39 year old female with a history of opiate abuse and hepatitis C, presented to the ER after witnessed syncope and tonic-clonic seizure like activity.

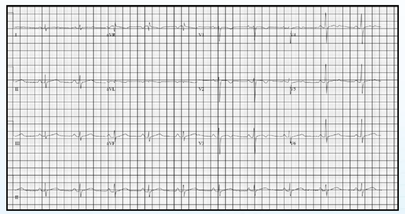
In the emergency department, the patient had another seizure like episode and was found to have torsades de pointes on telemetry. An EKG revealed sinus bradycardia with QTc of nearly 700ms. The patient reported recreational loperamide abuse, taking 100 tablets daily for the past 3 months. The patient was admitted to the cardiac intensive care unit for hemodynamic monitoring. Isoproterenol infusion was initiated. Heart rate was maintained greater than 80 BPM. Admission potassium was 3.0 and magnesium 1.7. Electrolyte levels were closely monitored and repleted.

An echocardiogram revealed hyperdynamic LV function, without any chamber enlargement or valvular disease. The patient remained on isoproterenol drip for 96 hours. EKGs were routinely performed and isoproterenol was eventually weaned off. No subsequent episodes of torsades were noted. On the day of discharge, the QTc was 466ms. The patient was discharged with instructions to avoid QT prolonging agents and avoid any further use of loperamide.





Admission ECG



Discharge ECG

Table 1.

Hospital Day	Loperamide Level	Desmethylloperamide
1	76 ng/mL	630 ng/mL
2	30 ng/mL	350 ng/mL
3	9.3 ng/mL	230 ng/mL
4	Not detected	120 ng/mL
5	Not detected	74 ng/mL
6	Not detected	47 ng/mL
7	Not detected	27 ng/mL

DISCUSSION

Loperamide is an opioid derivative and common over-the-counter antidiarrheal drug. At high doses, loperamide crosses the blood-brain barrier and reaches opioid receptors in the brain, leading to central opiate effects including euphoria and respiratory depression. Approximately 40% of the drug is absorbed into the bloodstream after oral administration. The drug is metabolized to inactive products and is eliminated through both the urine and the feces.

Drug-induced TdP typically results from the development of early afterdepolarizations and triggered activities from prolonged repolarization. This is usually caused by a ventricular premature beat falls on a prolonged repolarization cycle.[2]

The mechanism of QTc prolongation due to loperamide is unclear. QTc prolongation related to synthetic opioids is due to blockade of the cardiac 'human ether-a-go-go' (hERG) potassium channel. Loperamide may block hERG, leading to prolonged QT.[2]

The half-life of loperamide is 9-14 hours. We maintained the patient on isoproterenol to maintain a heart rate of >80. No further episodes of torsades were seen after admission.

Loperamide is categorized as a QTc-prolonging drug in the public registry http://www.crediblemeds.org. In June 2016, the FDA issued a warning regarding loperamide abusive potential and cardiac toxicity.

In patients with unexplained syncope, QT prolongation, and malignant ventricular arrhythmias, loperamide abuse should be considered in the differential diagnosis.

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