Acquired Long QT and Torsades de Pointes Induced by Loperamide Toxicity

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Introduction

- Loperamide is an antidiarrheal agent with peripheral µ-opioid receptor activity.
- When taken in large quantities, loperamide crosses the blood-brain barrier, leading to euphoric and analgesic effects.
- Between 2010-2015, there was a 91% increase in the nonmedical use of loperamide in the U.S.
- Loperamide abuse has been reported to cause significant cardiotoxicity, including arrhythmias, syncope, and sudden death.

Case Presentation

HPI: A 38-year-old male with a history of opioid use disorder presented to the emergency department (ED) with multiple episodes of syncope within 48 hours. While in the ED, he had recurrent episodes of sustained ventricular tachycardia (VT), beginning as TdP and organizing into monomorphic VT. He remained hemodynamically stable.

Exam: Irregularly irregular rhythm with no murmurs, rubs or gallops; normal PMI. No JVD. Lungs clear to auscultation. Skin clammy, extremities cool distally with no edema. Alert and oriented, anxious.

Pertinent Labs & Imaging: Potassium (K) 3.1 mg/dL; Magnesium (Mg) 1.7 mg/dL; Troponin I undetectable. Bedside echocardiogram was largely unremarkable.

Initial Management: Prior to transfer to our institution, he was given an amiodarone bolus as well as atropine. We administered potassium, magnesium and calcium intravenously, as well as a lidocaine bolus and infusion. He underwent amiodarone bolus as well as atropine. We administered potassium, magnesium and calcium intravenously, as well as a lidocaine bolus and infusion. He underwent temporary transvenous pacing (TVP) was initiated with a balloon tipped catheter at a rate of 80 beats per minute. VT was successfully terminated, and no further episodes of VT occurred during his hospitalization.

Definitive Management: Temporary transvenous pacing (TVP) was initiated with a balloon tipped catheter at a rate of 80 beats per minute. VT was successfully terminated, and no further episodes of VT occurred during his hospitalization.

Further discussion with the patient and his family revealed that he had been taking approximately 70 pills of loperamide 2mg daily for several months.

The patient unfortunately left the hospital against medical advice on hospital day 3, and his TVP was removed. Prior to discharge, his QRS had normalized, and QTC had shortened to 500 msec. He was subsequently lost to follow up.

Discussion

- The arrhythmogenic effects of loperamide are thought to be due to inhibition of both sodium and potassium channels in cardiac myocytes. Loperamide inhibits the sodium channel (Na1.5) responsible for the fast depolarization current (iNa), leading to widening of the QRS interval. Loperamide also antagonizes the human ether-a-go-go (HERG) potassium channel, which regulates the delayed rectifier repolarization current (iKr), prolonging the QT interval.
- Patients with toxicity variably demonstrate QRS widening, QT prolongation, or both, which can lead to ventricular arrhythmias. The rhythm disturbances commonly lead to syncope, or in extreme cases, sudden cardiac death.
- Cardiogenic shock has also been reported.
- There are no evidence-based therapies specifically for loperamide cardiotoxicity.
- Suggested management based on available literature:
  - Follow Advanced Cardiovascular Life Support guidelines.
  - Provide intravenous electrolyte replacement (K, Mg, calcium).
  - Utilize isoproterenol or temporary venous pacing to help prevent long-short sequence initiation of TdP.
  - Temporary mechanical support may be required in cases of refractory cardiogenic shock.
  - Antiarrhythmics have not been found to be consistently helpful in reducing or preventing recurrence of arrhythmias.
  - Genetic testing for long QT syndromes is not necessary if the patient’s QT interval normalizes after the medication has cleared.

Conclusions

- Loperamide overdose can prolong the action potential in cardiac myocytes, causing significant cardiotoxicity such as malignant arrhythmias, cardiogenic shock and sudden cardiac death.
- Provider awareness of these effects can facilitate recognition of loperamide toxicity, and thereby help direct appropriate supportive therapies.
- Increasing the heart rate with isoproterenol or temporary pacing can terminate and prevent recurrence of the arrhythmias while loperamide is metabolized by the body.

References