CLINICAL VIGNETTE

Intentional Overdose with Loperamide

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Case Presentation

A 25-year-old male with an extensive history of depression, anxiety, neuropathic pain, and heroin addiction was taken by ambulance to the emergency room after his family found him sluggish and minimally responsive at home. In his room, the family found two empty loperamide boxes which had contained 150 tablets of 288 mg strength.

The patient regularly took escitalopram, gabapentin, and quetiapine. However, the patient also had a well-documented history of heroin, hydrocodone/acetaminophen, and tramadol abuse. He had no pertinent surgical history. Family history was significant for substance abuse in his father, with no family history of cardiac arrhythmias or sudden cardiac death. The patient had no prior syncope and did not abuse alcohol.

Upon arrival in the emergency room, he was hemodynamically unstable with a blood pressure of 100/52. 12-lead EKG revealed a wide complex undetermined atrial rhythm at a rate of 66 bpm with prolonged QT and QTc intervals. The patient was hyponatremic with a serum sodium of 130. Urine toxicology screen was positive for opiates. Chest x-ray and non-contrast computed tomography (CT) of the head were unremarkable.

The patient was intubated for airway protection. The regional Poison Control Center was notified and recommended sodium bicarbonate and lipid infusions. Electrolytes were maintained within normal limits through intravenous supplementation. On hospital day 3, the patient progressively improved and was extubated without any residual neurologic deficit. He remained slightly bradycardic until the day of discharge. Serial repeat EKGs showed progressive shortening of the QTc and QT intervals. Cardiology recommended outpatient resting transthoracic echocardiogram and monitoring. He was discharged in stable condition and transferred into a rehabilitation facility for continued treatment of addiction.

Discussion

Loperamide is a μ-opioid receptor agonist that is available over-the-counter as an anti-diarrheal agent. Initially placed in Schedule V of the US Controlled Substances Act in 1977, loperamide was taken off schedule and made available without a prescription in 1982 due to its low risk of physical dependence.[1] At recommended doses (4 mg orally for acute diarrhea followed by 2 mg after each loose stool; maximum daily dose of 8 mg/day for the over-the-counter formulation and maximum daily dose of 16 mg/day for prescription formulation), loperamide is considered safe and effective. Opiate-like effects are rare and loperamide is considered to have low abuse potential.[2-4] However, at higher than recommended doses, it may cause central nervous system (CNS) effects and doses of up to 50 to 300 mg may induce euphoria.[5]

Loperamide abuse and overdose, as in doses of 70 mg per day or higher, increases the risk of adverse effects such as CNS depression, respiratory depression, and cardiac toxicity. Cardiac toxicity from overdoses may include life-threatening QTc and QRS prolongation, torsades de pointes, Brugada syndrome, ventricular arrhythmias, and cardiac arrest.[5] The FDA released drug safety communications in 2016 and 2018 addressing the increased reports of cardiac toxicity, urging healthcare providers to advise patients about this risk. The agency has encouraged manufacturers to use blister packs or single-dose packaging.[6,7] With its diversion potential in self-treatment for opioid withdrawal, the medication has been now coined the “poor man’s methadone”.[8,9]

Current evidence suggests that loperamide abuse is becoming more prominent. Individuals may take large doses to achieve euphoria or to self-treat opioid withdrawal, at the risk of cardiac toxicity, respiratory depression, and death. Patients may also be taking other prescription medications, such as antidepressants or substances that synergistically increase plasma concentrations of loperamide, magnifying risk of toxicity. Presentating symptoms of loperamide overdose may be generic and lead to misdiagnosis. With the opioid crisis highly publicized and the FDA receiving more abuse reports, physicians need to recognize loperamide abuse and intoxication. Education of patients and healthcare workers, identifying patient behaviors of abuse and diversion, appropriate physician prescribing, and strong communication between retail pharmacists and physicians are all crucial to preventing unnecessary toxicity and harm from this easily accessible over-the-counter substance.

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