BRIEF REPORT

Dysrhythmias with Loperamide Used for Opioid Withdrawal

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The antidiarrheal loperamide has had a recent, drastic increase in off-label use as an alternative treatment for symptoms of opioid withdrawal. The concept of this is easily discovered on the Internet and social media, where there are multiple blogs and forums promoting loperamide use at doses of 70 to 200 mg per day. Unfortunately, the serious side effects are not well recognized. Multiple cases of cardiac dysrhythmias contributing to death have been highlighted in recent literature. In November 2016, the US Food & Drug Administration released a statement highlighting the potential heart effects and risk of death with high doses of loperamide.[1] This case regards a 22-year-old who took 200 mg of loperamide per day for 2 years as an alternative to methadone in her attempts to wean off heroin. Her subsequent spontaneous collapse, dysrhythmias, and acute hospital treatment are reviewed in detail as they were contradictory to standard therapy and required a multidisciplinary approach. Her outpatient management addressed the complex biological, psychological, and social aspects of her addiction. (J Am Board Fam Med 2017;30:832–834.)

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The use of loperamide at high doses to avoid symptoms of heroin withdrawal has been steadily increasing since 2003. In a recent statement, the US Food & Drug Administration (FDA) addressed the association between high dose loperamide and adverse cardiac events including QT interval prolongation, torsades de pointes, ventricular arrhythmias, and cardiac arrest.[1]

Loperamide is available OTC for the symptomatic treatment of diarrhea. The approved daily dose is 8 mg per day. Loperamide at higher doses has found a reputation as an alternative to standard opioid withdrawal therapy. Information on this use is shared publicly through unregulated Internet forums and blogs without additional caution regarding adverse effects.[2,3,4] Forty-eight documented cases of cardiac problems associated with loperamide misuse were reported to the FDA from 1976 to 2015, 10 of which were fatal.[1]

We report a case of loperamide used to alleviate symptoms of heroin withdrawal. The patient self medicated with up to 200 tablets a day of loperamide for 2 years. She presented to the Emergency Department in cardiac arrest. After successful resuscitation she had a prolonged QTc which progressed to torsades de pointes, which resolved with isoproterenol and transvenous pacing. Her dysrhythmias have not recurred after cessation of loperamide use.

Case Presentation

A 20-year-old female with a history of heroin use presented to the emergency department with a wide complex tachycardia following a brief syncopal episode. On questioning, she admitted to regularly taking large quantities of loperamide (Imo-

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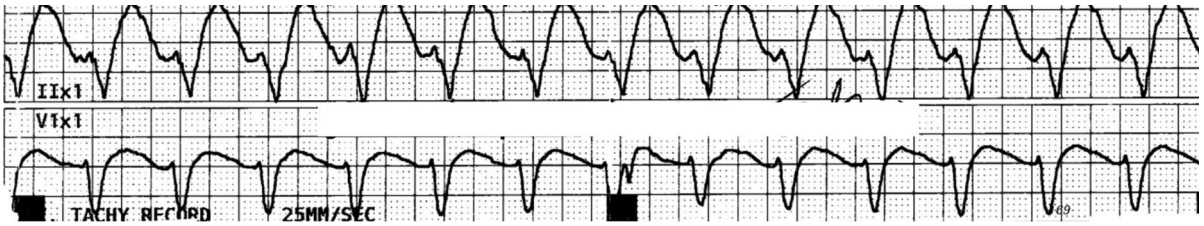
Figure 1. Electrocardiogram in ambulance.



dium) for the past several years as a cheaper alternative to methadone therapy. She had an ongoing history of substance use including heroin, tobacco, and alcohol. Citing a lack of insurance to cover standard therapy, she used the Internet to find alternate means of self detoxification. This led her to acquire and ingest large quantities (75 to 200 2-mg tablets) of loperamide daily over a 2-year span before her presentation.

Following a brief syncopal episode at home, Emergency Medical Services were activated by a friend who found the patient awake, but drowsy. On arrival, her initial rhythm strip showed a wide QRS and tachycardia with a prolonged QTc interval (Figure 1). During transport to the hospital, she became unresponsive, was pulseless, and her rhythm showed a wide-complex tachycardia. Cardiopulmonary resuscitation was initiated with return of her pulse.

On arrival in the Emergency Department, her vital signs were normal. A complete physical examination and initial laboratory workup were also within normal limits. A 12-lead electrocardiogram showed a QTc interval of 766 ms (upper limit of normal, 440 ms for her age and sex). Poison control was contacted and magnesium and sodium bicarbonate were recommended to treat the prolonged QTc interval.

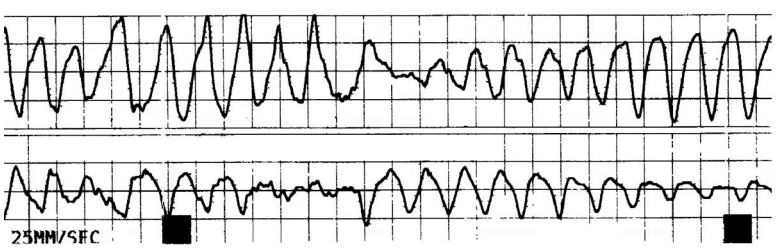
The patient was admitted to the intensive care unit and isoproterenol was added to treat the prolonged QTc interval. Despite this, she continued to have a wide-complex tachycardia with a markedly prolonged QTc interval (730 ms; Figure 2) which degenerated into torsades de pointes requiring repeated defibrillation. A temporary pacemaker was ultimately placed for overdrive pacing. This patient's course was deemed a probable adverse drug reaction per the Naranjo Adverse Drug Reaction scale.[5]

Over the next several days, her QTc interval gradually decreased to 462 ms with no further dysrhythmias. On discharge from the hospital, she was in good health and her electrocardiogram showed normal sinus rhythm. Since discharge, she has had no relapses of heroin or loperamide use.

Discussion

Loperamide is an FDA-approved antidiarrheal medication. It is currently on the World Health Organization list of essential travel medicines.[6] It is available over the counter (OTC) or with prescription, and comes in tablet, capsule, and liquid formulations. A typical dosing schedule involves a 4-mg loading dose followed by 2 mg after each loose stool thereafter.[7] Packaging recommends an 8-mg maximum daily dose for OTC preparations. Up to 16 mg/day is indicated by prescription.[7] Loperamide exerts its clinical effects through the stimulation of gastrointestinal opiate receptors. This slows down intestinal peristalsis and decreases the number of stools. Loperamide is metabolized

Figure 2. Wide complex tachycardia progressing to torsades de pointes.



by a P-glycoprotein pump and does not cross the blood brain barrier. The most notable side effects include dry mouth, nausea, vomiting, dizziness, and constipation.[8]

Since 1976, the FDA has received formal reports of 48 cases of cardiovascular morbidity and mortality associated with loperamide use. In June 2016, the FDA released a statement regarding a warning about high-dose loperamide, and the association with a prolonged QTc.[1] Other cases in the literature describe patients who also used loperamide at high doses for heroin withdrawal.[9–12] Most of these cases reported ventricular arrhythmias and torsades de pointes, which were treated with isoproterenol and transvenous pacing, as other therapies were often unsuccessful. In surviving patients, dysrhythmias generally resolved after discontinuation of loperamide.[9]

Multiple unregulated blogs and online forums contain opinions and personal accounts of using loperamide as an off-label use for heroin withdrawal.[2–4] In our case, the patient used the Internet to find loperamide as a potential form of self treatment for heroin addiction. She was unable to afford methadone maintenance and psychotherapy, which could have prevented her sequence of events. She reported her search strategy of "home remedies, heroin withdrawal" uncovered multiple sites, blogs, and chat rooms describing loperamide use to manage heroin withdrawal symptoms. One blog post claims that loperamide is a "godsend" for patients who cannot afford standard therapy.[2] Another forum "highly recommends" using loperamide for opiate withdrawal diarrhea and cramping.[3] Another reports that "with loperamide [I] avoided 90% of heroin withdrawal symptoms, with very few complications."[4]

The Internet and social media outlets can plant the seed for off-label use of OTC medicines. Loperamide is just 1 example. Although most commonly used for the treatment of diarrhea, loperamide is being used for other reasons including self-management of opioid withdrawal. Misuse of loperamide is associated with potentially serious side effects (cardiac arrhythmias; QT prolongation) and even death.

To see this article online, please go to: http://jabfm.org/content/30/6/832.full.

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