CLINICAL VIGNETTE

"Getting High" From Loperamide Can Cause Cardiac Arrhythmias

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A 24-year-old female with history of substance abuse was transported to the emergency department after experiencing a syncopal episode at home lasting about 10 seconds. According to her husband, she was walking to the bathroom when she suddenly collapsed. In the emergency department, she was slightly lethargic with slurred speech complaining of generalized fatigue. She denied chest pain, shortness of breath, or palpitations. She denied current use of illicit drugs such as heroin or cocaine but admitted to recreational use of large doses of loperamide. The patient reported taking in excess of eighty 2 mg tablets (160 mg) daily over the last 2 months, including the day of admission.

On arrival, her temperature was 36°C, blood pressure 88/45 mmHg, and pulse was 64/min. Her respiratory rate was 18/min with 96% saturation on room air.

On physical exam, she was a slightly somnolent but in no distress. Her cardiopulmonary examination was normal except for mild bradycardia. Her abdominal exam exhibited mild distension with minimal tenderness and urinary retention with a post void residual of 400 cc, requiring the placement of a Foley catheter. Her neurological exam was essentially normal except for her decreased alertness.

Her initial EKG had a ventricular rate of 94, QRS of 90milliseconds (msec) and prolonged QTc of 650 msec. EKG was also noted to have a possible type 1 Brugada morphology (Figure 1).

Approximately two hours after presentation, the patient had 2 short runs of non-sustained ventricular tachycardia and then an episode of torsade de pointe requiring administration of 1 gram of magnesium sulfate, one external defibrillation with resulting return to normal sinus rhythm. Subsequent suppressive treatment with amiodarone was initiated. Her lab tests were normal except for a potassium of 3.3 mEq/L and magnesium of 1.6 mEq/L. These electrolytes were replaced intravenously. Loperamide concentration was 110 ng/ml (normal < 1.2 ng/ml). Urine toxicology test was negative for other drugs. A bedside echocardiogram was significant for an ejection fraction of about 30% with global hypokinesis. The patient was admitted to the ICU for close monitoring and consideration for an implantable cardioverter defibrillator (ICD). In the ICU, the patient was continued on the amiodarone infusion, and after 2 days there were no further malignant arrhythmias. Her initial prolonged QTc normalized to 450 msec within 48 hours. Upon consultation with cardiology, it was decided that her arrhythmia was from a reversible cause, abuse of loperamide, and an ICD placement was not necessary. She was later discharged to a drug rehabilitation program.

Discussion

The above case describes loperamide-induced QTc prolongation, torsade de pointe and a Brugada pattern, which resolved after removal of the offending drug. Loperamide is an over-the-counter opiate marketed as an anti-diarrheal agent and deemed safe with low abuse potential when used at the recommended dose of about 2 mg. Intranet sites directed to recreational users suggest doses between 70 to 200mg a day to achieve euphoric effects.[1] Taking the therapeutic dose will yield serum concentrations of about 0.24 ng/ml within 5-6 hours.[2] The patient above presented with serum levels that were nearly 500 times the therapeutic level.

Such supra-therapeutic doses of loperamide have been associated with significant, dose-dependent cardiac effects.[3] The QT prolongation and subsequent torsade de pointe have been linked to delays in repolarization of the ventricular myocardium with blockade of the potassium rectifying current, I_{kr}. The human ether-a-go-go related gene (HERG) encodes the protein that makes up the I_{kr} channel and many drugs associated with QT prolongation block this gene.[4] Loperamide has been implicated as one of the drugs that can inhibit the HERG gene, leading to potentially lethal arrhythmias at high doses.[5]

The type 1 Brugada pattern noted in this patient is defined as ≥ 2mm ST elevation with a coved appearance and inverted T-waves in the right precordial leads. The presence of Brudaga can be congenital but can also be unmasked or provoked by agents such as cocaine, antiarrhythmic drugs, anti-depressants as well as fever and electrolyte abnormalities.[6] The acquired Brugada pattern has been associated with sodium channel inhibition, which can lead to ventricular arrhythmias and sudden death.[7] The presence and subsequent resolution of the Brugada pattern suggests loperamide may have a role in sodium channel blockade as well.

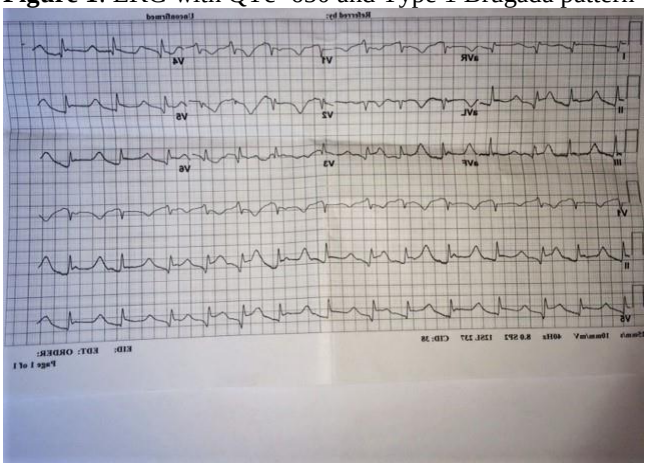
The treatment of high dose loperamide ingestion is primarily based on EKG findings and removal of the offending drug. The acquired QT prolongation and subsequent torsades de pointe is treated by correcting all electrolyte abnormalities (especially magnesium), temporary transvenous cardiac pacing and isoproterenol infusion.[8] Defibrillation and use of antiarrhythmic agents may be used as indicated.

In conclusion, it is important for physicians to recognize loperamide as a non-prescription opioid drug of abuse

especially with recent efforts to curb prescription drug abuse by state and federal agencies. Clinicians should be aware of the significant cardiac toxicities associated with consumption of large quantities of this over-the-counter drug in order to help diagnose, treat, and counsel.

Figures

Figure 1: EKG with QTc=650 and Type 1 Brugada pattern



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Submitted October 11, 2016