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An Over-the-Counter Treatment for Diarrhea Leading to Euphoria and Fatal Arrhythmia

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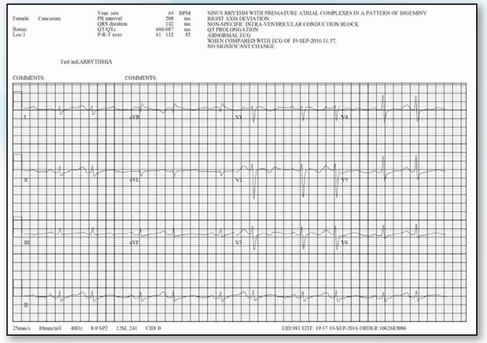
BACKGROUND

- Loperamide is a non-prescription anti-diarrhea medication
- Mechanism of action involves opioid agonism to inhibit intestinal peristalsis, calcium channel blockade, and a decrease in paracellular permeability
- At therapeutic doses, loperamide has low oral bioavailability and minimal central nervous system (CNS) penetration
- At supratherapeutic doses, loperamide can penetrate the CNS and is being increasingly used recreationally to alleviate the symptoms of opioid withdrawal as well as induce euphoria.

CASE PRESENTATION

A 39 year-old woman with past medical history of intravenous drug and alcohol abuse and hepatitis C presented to the emergency room due to seizure-like activity. Family reported loss of consciousness with associated tonic-clonic movements of her upper extremities. The patient had eight similar episodes of seizure-like activity while at work prior to presenting to the emergency department where she had an additional witnessed event. Telemetry monitoring during the episode revealed torsades de pointes. Her admission electrocardiogram (EKG) revealed a QTc of 687 ms. Urine drug screen was negative, however she admitted to abusing loperamide. Initially taking 20 pills per day, she increased the dose over several months to 100 pills per day. The patient was admitted to the cardiac intensive care unit and placed on an isoproterenol drip to maintain a heart rate greater than 100 beats per minute to prevent R-on-T phenomenon and therefore further episodes of torsades de pointes. Serum magnesium and potassium levels were closely monitored and repleted as appropriate. The patient's serum loperamide level on admission was lethally elevated at 76 ng/mL and trended down significantly to 30 ng/mL on day two, 9.3 ng/mL on day three, and was undetectable on day four. She was gradually weaned off isoproterenol after 5 days of therapy. Her QTc normalized and she was discharged home in stable condition after seven days.



Day	Loperamide Level (ng/mL)	QTc (ms)
1	76	687
2	30	691
3	9.3	442
4	none	366
5	none	498

DISCUSSION

- Loperamide's half-life at therapeutic doses is 9-13 hours with 30-40% fecal excretion
- Due to Loperamide's mu-receptor agonism, gastrointestinal motility is reduced and therefore loperamide overdose likely leads to prolonged toxicity from delayed absorption and reduced elimination of the drug
- It is important for physicians to recognize the abuse potential of loperamide and to understand the treatment of its toxic effects during an era of growing opioid epidemic
- The relatively low cost of loperamide coupled with its opioid-like effects at high doses has made it an emerging drug of abuse with potentially lethal consequences

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