



### H108 Loperamide Abuse: A Rising Public Health Concern?

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**Learning Overview:** After attending this presentation, attendees will better understand the pharmacology and toxicology of loperamide and its rising popularity as an opioid drug of abuse.

**Impact on the Forensic Science Community:** This presentation will impact the forensic science community by providing a case report of a young woman who died of loperamide toxicity and by allowing for increased recognition of this potential drug of abuse that is readily available over the counter.

**Introduction:** Loperamide is a well-known, cheap, anti-diarrheal medication with  $\mu$ -opioid agonist activity that has been available over the counter in the United States since 1988.<sup>1</sup> Loperamide achieves an anti-diarrheal effect through binding opioid receptors in the wall of the bowel and inhibiting the release of chemical mediators, such as prostaglandins and acetylcholine, which leads to a reduction in peristalsis activity.<sup>2</sup> In addition, loperamide is thought to block calcium channels, which also contributes to a decrease in gastrointestinal motility.<sup>2</sup> This medication was originally thought to have little misuse potential for several reasons. These reasons include poor oral bioavailability, rapid hepatic first pass metabolism by the cytochrome P450 complex, and p-glycoprotein mediated efflux out of the central nervous system.<sup>3</sup> However, an opioid toxidrome, including euphoria, has been reported when taking large doses of up to 50–100 2mg pills.<sup>3</sup>

**Materials and Methods:** The decedent was a 27-year-old woman with chronic pain due to severe interstitial cystitis that was being treated with a sacral neurostimulator. She was found by her live-in boyfriend after complaining of nausea and vomiting throughout the day. Based on prescribed medication at the scene and medical records, the decedent may have had an opiate abuse or dependence problem.

**Results:** At autopsy, there was no evidence of significant trauma. Toxicology results revealed the decedent was positive for loperamide at levels of 630ng/ml and diphenhydramine at 2,000ng/ml. A single standard 2mg dose of loperamide gives an average peak plasma loperamide level of 0.24ng/ml at approximately six hours.<sup>5</sup> The toxicology results indicated the decedent took a dose of loperamide at orders of magnitude higher than the recommended dose. The amount of diphenhydramine was also unusually high. It is unknown if this drug played any role in potentiating the effect of the loperamide. The cause of death was determined to be due to the combined toxic effects of loperamide, diphenhydramine, and dextromethorphan.

**Conclusion:** This case report illustrates the potential toxic effects of loperamide when ingested in quantities that are far above the recommended dosing levels. Documented adverse effects from loperamide overdose include fatal cardiac arrhythmia, loss of consciousness, Electrocardiogram (ECG) alterations, and hypokalemia.<sup>4</sup> The opioid crisis occurring in the United States is undeniable. As greater restrictions are put on traditional opiate medications, addicts will likely increasingly turn to more available alternatives and over-the-counter medications such as loperamide. This has already begun to occur. Internet posts about illicit loperamide use have increased from 50 posts a quarter in 2005 to more than 275 posts per quarter in 2011, with an associated increase in published case reports of ten-fold by 2014.<sup>2,4</sup> Recognition and greater awareness of using these widely available alternative medications for obtaining a high is crucial for the public health.

#### Reference(s):

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#### Loperamide, Overdose, Forensic Pathology