

## K59 The First Case of Loperamide Toxicity in Jefferson County, Alabama

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After attending this presentation, attendees will be aware of the potential for loperamide toxicity and of loperamide's emerging presence and significance in communities in which opioids are commonly abused.

This presentation will impact the forensic science community by emphasizing the importance of considering loperamide toxicity in deaths of individuals with histories of opioid abuse.

Shortly after being treated and released from a drug rehabilitation center, a 23-year-old male with a long history of heroin abuse was found dead, sitting in a chair. No drug paraphernalia was discovered at the scene. Upon examination, the only evidence of recent injury to the body was a punctate needle mark on the right antecubital fossa. Autopsy did not reveal any underlying disease.

Toxicological analysis of blood from the iliac veins detected therapeutic and subtherapeutic concentrations of trazodone (385ng/mL), citalopram (105ng/mL), diazepam (9ng/mL), and nordiazepam (43ng/mL). Loperamide was detected at a concentration of 374ng/mL (therapeutic range is up to 10ng/mL).<sup>1</sup> All analytes were quantified via Gas Chromatography/Mass Spectrometry (GC/MS) following n-butyl chloride liquid-liquid extraction. Death was attributed to accidental loperamide toxicity. Review of medical examiner cases in Alabama from 2013 to 2016 revealed six additional cases in which loperamide was detected at toxic concentrations (130ng/mL to 1,400ng/mL).

Loperamide is an over-the-counter diphenoxylate analogue that is commonly used for its anti-diarrheal effects. Loperamide is an opioid receptor agonist and, at therapeutic concentrations, acts on  $\mu$ -opioid receptors along the gastrointestinal tract, causing suppression of normal bowel motility that ultimately results in increased water absorption from the small and large intestines; however, at particularly high concentrations or in cases in which another drug reduces the integrity of the blood-brain-barrier, loperamide exhibits a more centralized opioid action.

Drug discussion forums on the internet suggest that loperamide is thus being used recreationally to simulate the effects of other opioids like heroin and morphine or even to mitigate withdrawal symptoms associated with heroin and prescription opioid disuse.<sup>2</sup> Naloxone can even be given to reverse loperamide's effects in cases of suspected toxicity. Recently, loperamide has also been shown to produce both QRS and QT prolongation at high concentrations, and deaths have been reported directly related to its cardiotoxic effects.<sup>3,4</sup> Some toxicologists even advocate putting restrictions on the sale of loperamide, likening its potential for abuse in a manner similar to pseudoephedrine's when commercial sales limits were implemented in 2006 due to its non-intended use in the manufacturing of methamphetamine.

It is certainly possible that an increasing number of loperamide-related deaths are related to the current opioid epidemic, and it is important that investigators, forensic toxicologists, and medical examiners consider the possibility of loperamide toxicity in decedents with histories of drug abuse.

## **Reference(s):**

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Loperamide Toxicity, Withdrawal, Opioids

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