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## H121 Poor Man's Methadone: A Case Report of Loperamide Toxicity

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After attending this presentation, attendees will understand the recreational abuse of the antidiarrheal drug, loperamide (Imodium®), its mechanism of action, and the typical findings in cases of loperamide toxicity.

This presentation will impact the forensic science community by discussing the abuse of loperamide, a commonly used over-the-counter antidiarrheal drug, in order to increase awareness in the forensic and medical communities of the possible role of loperamide in cases suspicious for opioid toxicity but that have no evidence of toxic concentrations of commonly abused opioids.

The case of a 19-year-old male with a history of drug abuse who was found dead at his residence, possibly after recently attending a party, is presented. Bottles for his medications (including cyclobenzaprine, benzonatate, and nabumetone) were found at the scene, along with bottles for medications prescribed to other people. No other illicit drugs or paraphernalia were noted at the scene.

At autopsy, the major significant finding was massive urinary retention, seen frequently in opioid toxicity, with the bladder containing at least 750 milliliters of urine. Initial routine toxicology testing revealed non-toxic concentrations of alprazolam and fluoxetine as well as marijuana metabolites. Based on the strong suspicion of a drug-related death, further analysis utilizing the Liquid Chromatography/Time-Of-Flight/Mass Spectrometry (LC/TOF/MS) was requested.

The LC/TOF/MS analysis identified an unusual set of split isotope peaks, consistent with chlorine, and a molecular formula ( $C_{29}H_{33}ClN_2O_2$ ) suggestive of the chemical composition of loperamide. A comparative sample of loperamide from a drugstore was analyzed by LC/TOF/MS, resulting in a mass and retention time matching the compound in the decedent's sample. Confirmatory and quantitative testing by an outside reference laboratory using gas chromatography detected 63ng/mL of loperamide, more than six times the therapeutic peak concentration. Based on these results, the cause of death was determined to be "Toxic effects of loperamide with fluoxetine and alprazolam" and the death was classified as accidental.

Loperamide (Imodium®), a synthetic phenyl piperidine opioid, is available as an Over-The-Counter (OTC) antidiarrheal medication. Like other opioids, loperamide acts in the gastrointestinal tract at mu-opioid agonist receptors, the myenteric plexi, by slowing intestinal motility. The opiate effects in the central nervous system with other opiates, such as euphoria, analgesia, and respiratory depression, are avoided with loperamide because of its decreased central nervous system penetration. Because of its decreased central nervous system effects and low abuse potential compared to other opioid drugs, loperamide was removed from Schedule V classification and can currently be dispensed without a prescription.

Loperamide is a substrate of P-glycoprotein, which causes it to be actively pumped out of the central nervous system at the blood-brain barrier; however, when P-glycoprotein is inhibited, loperamide can cross the blood-brain barrier freely and exert central nervous system effects similar to more commonly used opiates. P-glycoprotein is inhibited by many substances, including protease inhibitors, quinines, and even high doses of loperamide. Although normally poorly absorbed at therapeutic doses, loperamide ingested in massive doses can circumvent the inhibitory mechanism, remain in the central nervous system, and cause central opiate effects.

According to various sources, recreational loperamide abusers describe taking massive doses (50-200 pills) of the standard over-the-counter 2 milligram formulation, resulting in a cumulative dose of 100 to 400 milligrams. This concentration is frequently used to obtain a euphoric high, but it can be used to avoid symptoms of opiate withdrawal; for this reason, loperamide is also known as "poor man's methadone."

Loperamide toxicity in children is frequently reported to poison control centers for accidental ingestion. Most cases of adult loperamide toxicity report gastrointestinal symptoms and drowsiness with infrequent fatal outcomes. Due to its unrestricted access and low cost, loperamide abuse may be more common than the medical community realizes. Loperamide could be relatively unnoticed at a scene investigation and the drug may go undetected with routine drug screening.

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### Loperamide, Toxicology, Opioid Abuse