Abuse of OTC Antidiarrheal Meds Linked to Cardiac Deaths

Liam Davenport | May 12, 2016

Abuse of over-the-counter, opioid-based antidiarrheal drugs is a growing problem that is placing individuals at risk for cardiac dysrhythmia and death, says a US pharmacist, who describes two illustrative cases in a new report.

Loperamide (*Imodium*, J and J Consumer Health Care Products) is a low-cost, over-the-counter antidiarrheal medication that inhibits intestinal peristalsis via µ-opioid receptor agonism, calcium channel blockade, calmodulin inhibition, and reduced paracellular permeability. It was thought that the potential for abuse with the drug was limited by its poor oral systemic bioavailability and central nervous system penetration.

However, two recent cases of loperamide abuse and subsequent death have raised a red flag. Despite standard advanced cardiac life support, both patients were pronounced dead on arrival at the emergency department (ED).

Lead author William Eggleston, PharmD, Upstate New York Poison Center, Syracuse, New York, told *Medscape Medical News* that these two cases "highlight the severity of the issue in the US of opioid abuse.

"It's a growing problem, and we're doing our best to manage it by limiting access to opioid medications, but unfortunately, addiction is something that's not that easily overcome, and so folks are finding other avenues, whether that be heroin or whether that be, in this case, loperamide.

"I think what makes loperamide so unique and so dangerous is that, in addition to being an opioid, it's a cardiac toxin, and something that's pretty unique to loperamide," he added.

The article was published online April 29 in the Annals of Emergency Medicine.



The first case was that of a 24-year-old man with a history of substance abuse that was managed by buprenorphine (multiple brands). The patient was found at home exhibiting seizurelike activity. He was pulseless and aphetic. Six empty boxes of loperamide were found at the scene. Manual cardiopulmonary resuscitation (CPR) and administraiton of naloxone (multiple brands) were ineffective, and intubation was unsuccessful. He was pronounced dead shortly after arrival at the ED.

Postmortem analysis revealed that the patient had been abusing loperamide orally to self-treat his opioid withdrawal. The concentration of loperamide in his cardiac blood of 77 ng/ml (therapeutic range, 0.24 - 3.1 ng/ml). Pulmonary and cerebral edema, urinary retention, moderate cardiomegaly, and lower-extremity venous thrombi were found on autopsy.

The second case involved a 39-year-old man who also had a history of opioid addiction, which was also managed with buprenorphine. The patient was reported to have collapsed and to be gasping for breath. Emergency medical services identified asystole. CPR was initiated, and resuscitative efforts were continued on the way to the hospital. The man was pronounced dead on arrival at the ED.

The patient's family reported that he had been self-treating his opioid addiction with an over-the-counter antidiarrheal medication after discontinuing buprenorphine 3 years earlier.

Cardiomegaly and severe pulmonary edema were identified on autopsy. Postmortem toxicology revealed a femoral blood concentration of loperamide of 140 ng/ml.

Dr Eggleston said that it is not clear whether the drug's over-the-counter status should be revised and noted that it is



difficult to determine the long-term impact of a drug on the basis of animal models and preclinical studies.

"But I think what it does highlight is the need for us to revamp how we look at drugs once they've hit the market and how we assess the impact they are having on the population," he said.

Watch Patient Forums

Dr Eggleston believes the problem with relying on the US Food and Drug Administration's (FDA's) voluntary MedWatch reporting program is that it is "passive" and that "it doesn't have a lot of teeth. "So that makes it difficult for the FDA to track these agents once they've hit the market," he said.

In the article, Dr Eggleston and colleagues highlight the fact that abuse of oral loperamide was reported on online message boards in 2005. A recent study of 1290 messages posted on a single website indicated a 600% increase in such messages between 2009 and 2011. This tallies with data from the poison center at Dr Eggleston's institution, where there was a sevenfold increase in calls related to loperamide abuse or misuse between 2011 and 2015.

One study revealed that in the majority of cases (70%), loperamide was discussed as a method of self-treating opioid withdrawal. Approximately one quarter of individuals who posted messages on the message boards said they abused the drug because of its euphoric properties.

"I think these message boards are something that healthcare professionals and public officials really need to be made aware of," Dr Eggleston said. "They're a tool that we can use to do our best to keep up with what our patients are doing."

He noted that loperamide abuse has been occurring for more than a decade and that "here in the healthcare community, we are finally, in 2015-2016, getting our act together and catching up with it.

"We need to do our best to stay ahead of the curve, and the forums are a great way to do that," he said.

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