

Loperamide – Safety Concerns in Overdose

Loperamide is a commonly used OTC medication for self-treatment of diarrhea. A derivative of opioids, it was long thought to be much safer and have less abuse potential than opioids since it acts only on mu receptors in the intestinal tract and does not cross the blood brain barrier (BBB). (1,2,3)

However, high doses of loperamide can cross the BBB causing respiratory depression, central opioid effects and euphoria. Loperamide can also act as “poor man’s methadone”. That is, high doses can counteract opioid withdrawal and is increasingly being used by opioid addicts for that effect. (1,2,3,4) Descriptions of the use of 100 to 400mg to produce a high or avoid withdrawal symptoms can be found on the internet. (4)

The high doses necessary to produce the above effects can also be cardiotoxic. Loperamide can prolong the QT interval as well as the QRS interval due to blockage of the cardiac potassium and sodium channels. Cases of torsades de pointes, other ventricular dysrhythmias, cardiac arrest and fatalities have been reported and are becoming more common as abuse of loperamide increases. (1,2,3,4,9) There have also been cases of cardiac effects when OTC loperamide for diarrhea was accidentally overdosed (5) and when prescription loperamide was used for loop ileostomy and short bowel syndrome-associated diarrhea. (6)

The following drug interactions may also predispose loperamide users to cardiac toxicity:

- Medications which have the potential to prolong the QT or QRS interval - erythromycin, clarithromycin, citalopram, quinidine, etc.
- Medications which inhibit loperamide’s metabolism (metabolised by both the cytochrome P450 isoenzymes CYP3A4 and CYP2C8, and also a substrate for P-glycoprotein) – HIV protease inhibitors, ketoconazole, itraconazole, gemfibrozil, etc.

The U.S. Food and Drug Administration (FDA) has released a safety alert (June 2016) about these potential side effects in opioid abusers and also in people using more than the recommended OTC doses or in people who may have drug interactions with loperamide. Health care providers should consider loperamide, in doses higher than recommended, as a possible cause of unexplained cardiac events including QT interval prolongation, torsades de pointes or other ventricular arrhythmias, syncope, and cardiac arrest. (7,8)

Advise anyone using loperamide to watch for fainting, rapid heartbeat or irregular heart rhythm and to seek medical help immediately if they experience these symptoms. People using OTC loperamide for diarrhea should be advised to use it for no longer than 2 days. (7,8)

References:

1. Eggleston W, Clark KH, Marraffa JM. Loperamide Abuse Associated With Cardiac Dysrhythmia and Death. *Ann Emerg Med*. 2016 Apr 26. pii: S0196-0644(16)30052-X PMID: 27140747
2. Wightman RS, Hoffman RS, Howland MA, Rice B, Biary R, Lugassy D Not your regular high: cardiac dysrhythmias caused by loperamide. *Clin Toxicol (Phila)*. 2016 Jun;54(5):454-8. PMID: 27022002
3. Dierksen J, Gonsoulin M, Walterscheid JP. Poor Man's Methadone: A Case Report of Loperamide Toxicity. *Am J Forensic Med Pathol*. 2015 Dec;36(4):268-70. PMID: 26355852
4. Mukarram O, Hindi Y, Catalasan G, Ward J. Loperamide Induced Torsades de Pointes: A Case Report and Review of the Literature. *Case Rep Med*. 2016;2016:4061980. PMID: 26989420
5. Spinner HL, Lonardo NW, Mulamalla R, Stehlik J. Ventricular tachycardia associated with high-dose chronic loperamide use. *Pharmacotherapy*. 2015 Feb;35(2):234-8. PMID: 25645123
6. Hurtado-Torres GF, Sandoval-Munro RL. An Additional Clinical Scenario of Risk for Loperamide Cardiac-Induced Toxicity. *Am J Med*. 2016 Apr;129(4):e33 PMID: 26972143
7. FDA Safety Alert: Loperamide (Imodium): Drug Safety Communication - Serious Heart Problems With High Doses From Abuse and Misuse. [Posted 06/07/2016] Accessed at: <http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm505303.htm>. Cited 04Jul2016
8. Lexi-Comp Online™, Lexi-Drugs Online™ (Loperamide), Hudson, Ohio: Lexi-Comp, Inc.; 2013; July 4, 2016.
9. DRUGDEX® System (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. Available at: <http://www.micromedexsolutions.com> (cited: 04Jul 2016).