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Maryland Poison Center
UNIVERSITY OF MARYLAND SCHOOL OF PHARMACY

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The Maryland Poison Center's Monthly Update: News, Advances, Information

Loperamide

Loperamide, a nonprescription antidiarrheal medicine with peripheral mu opioid receptor activity, is gaining attention as a drug with abuse potential. It causes minimal CNS effects in therapeutic doses because the transporter P-glycoprotein prevents it from crossing the blood brain barrier. Thus, sedation, euphoria, and respiratory depression are not seen in therapeutic doses. It's site of action is the GI tract; it has poor oral bioavailability. The normal dose of the drug is 4 mg (two tablets) followed by one tablet after each loose stool, up to 16 mg/day.

Although purported to lack abuse potential, opioid abusers have discovered it as an easily accessible opioid agonist. Since the early 2000s, there has been online discussion among substance abusers about how to increase CNS penetration for the purpose of obtaining a high or relief from opioid withdrawal. Abusers may chronically take hundreds of milligrams a day. Sometimes this is done in conjunction with P-glycoprotein inhibitors such as quinidine, quinine, verapamil, or cyclosporine A. Other routes, such as insufflation, may be used to increase absorption.

Emerging case reports demonstrate that loperamide abuse and misuse is dangerous. Syncope has been reported, presumably as a result of dysrhythmias and hypotension. Serious cardiac conduction disturbances have occurred including QTc and QRS prolongation progressing to ventricular dysrhythmias including recurrent torsade de pointes (TdP). The mechanism is unknown but postulated to be due to blockade of potassium, sodium, and calcium channels. CNS penetration in an opioid naïve individual can lead to miosis, sedation, respiratory depression, bradycardia, and hypotension. Young children (<3 years) may be more susceptible because their blood brain barrier is more easily traversed.

Obtaining a history is important for diagnosis as urine toxicology screens do not detect loperamide as an opiate. Use of opioids and other sodium or potassium channel blocking drugs (e.g. methadone, quinidine, tricyclic antidepressants) should be considered in the differential diagnosis. Activated charcoal has little or no benefit in the setting of chronic toxicity and should not be used in the presence of an ileus, which can result from loperamide abuse. In addition to supportive care, management includes naloxone for respiratory depression and sodium bicarbonate for QRS widening. For QTc prolongation, potassium and magnesium should be monitored and repleted if low. If TdP occurs, administer magnesium 1-2 g IV. For resistant or recurring TdP, cardiac pacing either electrically or with isoproterenol may be effective. At 97% protein binding, loperamide is not removed by dialysis. Although lipophilic (LogP ~5.5), there are no data on the use of lipid emulsion to reverse toxicity.

Gina L Stassinos, PharmD
Clinical Toxicology Fellow
Maryland Poison Center
University of Maryland School of Pharmacy

Did you know?

Loperamide (Imodium®) was a schedule V drug when it was approved by the FDA in 1973.

In 1988, loperamide became an over-the-counter product when studies deemed it to be safe with a low risk of dependence. It is currently sold as oral tablets, chewable tablets, capsules, caplets, and liquid. It is a relatively inexpensive drug; the cost for 1200 of the 2 mg caplets is as low as $25.

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