January 12, 2016: Concerns Over Loperamide Abuse

Over the past year, there have been a growing number of cases of loperamide abuse within the area of Virginia covered by the Blue Ridge Poison Center, with two serious cases in the past week. Loperamide is a synthetic opioid with poor bioavailability and central nervous system (CNS) penetration; it is used therapeutically for constipation, as it largely acts on the gastrointestinal tract and produces opioid-induced slowing of gut motility. However, in recent years, loperamide abuse has become a growing problem with several reports of cardiac conduction disturbances and arrhythmias, some fatal.

In therapeutic doses, loperamide rarely achieves significant CNS levels and thus does not produce any of the effects one would expect from use of other opioids (e.g., sedation, respiratory depression). A major reason why loperamide does not build up inside the CNS is that it is avidly excreted from the CNS by P-glycoprotein, a drug efflux pump found within the CNS and gastrointestinal tract. P-glycoprotein normally acts to prevent accumulation of substances within the CNS, or to limit absorption of potentially toxic substances from the gut. Drugs that inhibit P-glycoprotein, such as azithromycin and quinine, may result in increased levels of drugs that are transported in large amounts by P-glycoprotein, such as digoxin or colchicine. However, it seems that in recent years “recipes” for increasing loperamide levels have been widely available on the internet, facilitating drug abuse.

Drug users who abuse loperamide typically take it in such a way to increase the amount of loperamide that crosses the CNS, thus producing an opioid “high.” This is done by: 1) taking a very high dose of loperamide, such as an entire box of seventy-two 2 mg pills; 2) taking a cytochrome P450 inhibitor such as grapefruit juice, which inhibits the metabolism of loperamide and increases drug levels; 3) taking a P-glycoprotein inhibitor such as tonic water (which contains quinine), which decreases removal of
loperamide from the CNS by P-glycoprotein; or 4) some or all of the above.

The toxicity of loperamide in abuse includes both opioid toxicity as well as the potential for life-threatening arrhythmias. Loperamide, like any opioid such as morphine or heroin, can produce an opioid toxidrome characterized by respiratory depression, sedation, bradycardia and hypotension. Opioid overdose may result in severe events such as anoxic brain injury, aspiration pneumonitis or pneumonia, or multi-organ dysfunction due to hypotension and hypoxia. In addition to opioid effects, at high concentrations loperamide has been found to inhibit cardiac potassium rectifier currents. Clinically, this may lead to a very long corrected QT interval on an electrocardiogram. Coupled with the bradycardia that loperamide overdose usually causes, a long QT interval puts patients at high risk for development of torsades de pointes (bradycardia increases the risk for torsades at any QT length). This has been reported in the literature as well as seen in patients referred to the Blue Ridge Poison Center.

Treatment of loperamide overdose involves supportive care, with securing of the airway and respiratory support as needed, consideration of naloxone to reverse opioid toxidrome, IV fluids for hypotension, electrocardiography, laboratory studies, and contacting the poison center for additional information and recommendations. Patients with QT intervals longer than 500 msec should be treated with IV magnesium sulfate to decrease the risk of torsades de pointes, especially if bradycardia is present. If patients develop torsades de pointes, they should be treated with IV magnesium. Some patients may require overdrive pacing to induce tachycardia, which reduces the risk of torsades de pointes; this may be achieved electrically (through the insertion of a temporary pacemaker wire) or chemically (using isoproterenol). Loperamide is not detected on usual urine drug screening, so providers treating patients who present with long QT intervals, sedation, and/or a history of drug abuse should have a low index of suspicion that patients may be abusing this drug.

The Blue Ridge Poison Center provides free phone consultation with medical toxicologists for assistance with any case of loperamide overdose or other drug overdose; we strongly recommend contacting us at 1-800-222-1222 (or 800-451-1428 from cellular phones) to assist with any case of known or suspected loperamide poisoning.