PLEASE POST

POISON Help 1-800-222-1222

The Blue Ridge Poison Center

Tox Talks

October 2013 | A Bulletin for Health Care Professionals Who Manage Poisoned Patients | www.brpc.virginia.edu

BRPC STAFF

Director
Christopher Holstege, MD

Nursing Director
Beth Mehring, BSN

Medical Toxicologists
Nathan Charlton, MD
Andy Baer, MD

Medical Toxicology Fellows
Lewis Hardison, DO
Josh King, MD
William Rushton, MD

Certified Poison Specialists
Brenda Beech, RN, CSPI
Andre Berkin, BSN, CSPI
Joyce Brown, RN, CSPI
Jennifer Horn, BSN, CSPI
Sue Kell, Ph.D, M.Ed, CSPI
Christie Lee, RN, SPI
Kathy Mayo, RN, CSPI
Scott Wiley, BSN, CSPI

Epidemiologist
Priyanka Vakkalanka, ScM

Public Health Educator
Kristin Wenger, MT, BS

Administrative Specialists
Heather Collier
Robert Walters

To receive this newsletter via email: Kristin Wenger: KLW2S@virginia.edu.

Archived issues online: www.healthsystem.virginia.edu/medtox

'MOLLY' LATEST SUBSTANCE ABUSE TREND

Recently news outlets have reported an alarming number of deaths related to the street drug "Molly". The name is allegedly derived from the word "molecule" as the drug is touted as a pure form of 3,4-methylenedioxy-N-methylamphetamine (MDMA). However, it is essentially a rebranded form of ecstasy, which fell out of favor with many users in the late 1990s over rising concerns of contamination with other substances.

MDMA was originally patented by Merck pharmaceutical company in 1914. It was introduced into the clinical setting by psychotherapists in the United States in the mid 1970's and found acceptance as a method to reportedly enhance insight-oriented therapy. Until 1985, MDMA was unscheduled and not regulated. Concerns voiced by Texas senators over rampant and unrestricted use reached the U.S. Food and Drug Administration (FDA). On July 1, 1985 the drug was placed on Schedule 1 on an emergency basis until investigations into its potential for abuse and therapeutic benefit could be performed. While initial recommendations from the investigational committees recommended rescheduling to Schedule III, the DEA ultimately decided that MDMA should remain permanently on Schedule I over concerns for neurotoxicity and potential for abuse.

Over the past 5 years Molly has gained popularity in association with the electronic dance music movement. Several of the most recent deaths have occurred at music festivals and nightclubs along the East coast, with two occurring at the Electric Zoo music festival in New York, one at a Boston nightclub and a fourth at a club in Washington, D.C. These fatalities have received significant media attention.

Many of the substances sold as Molly are not pure MDMA as touted, but more often contain toxic substances such methylone, a synthetic cathinone found in "bath salts". Other contaminants are often also present in MDMA including highly toxic paramethoxymethamphetamine (PMMA) or paramethoxyamphetamine (PMA).

This trend of selling substances other than MDMA as Molly is financially more beneficial to the dealers. MDMA is reportedly expensive to produce. By cutting it with a cheaper substances or not including MDMA at all in Molly, the dealers can increase profits. It is this adulteration which makes it difficult to know for certain whether the recent overdose deaths have occurred due solely to MDMA, to its interaction with other pharmaceuticals, or to other chemicals that may have been sold as Molly.

MDMA stimulates both the sympathetic nervous system and central nervous system (CNS) by catecholamine release. Methoxylation and methylenedioxylation of the catechol ring is responsible for the hallucinogenic activity. It also depletes serotonin receptors in the brain, with a disruption in behavior. This methamphetamine analogue is a potent indirect sympathomimetic agent. A double blind placebo controlled trial showed a dose-related increase in myocardial oxygen demand without an increase in contractility which may lead to a higher risk of cardiovascular complications.

Acute Toxicity

Most cases of MDMA use develop mild sympathomimetic symptoms of anxiety, mydriasis, hypertension, tachycardia, increased respiratory rate, and diaphoresis. Similar to other sympathomimetics like cocaine, methamphetamine, and ephedrine, overdoses are characterized by hyperthermia, arrhythmias, hyperreflexia, seizures, metabolic acidosis, rhabdomyolysis, and renal failure.

At one institution MDMA accounts for the second most common cause of liver injury in patients under the age of 25. While the vast majority of these cases have spontaneous recovery, an increasing number of fulminant hepatic failure reports are now appearing in the literature. Hyponatremia is a frequently described complication that is thought to have several contributing factors including sodium loss through excessive sweating, hemodilution with large free water volume intake, and inappropriate secretion of antidiuretic hormone leading to water retention.

Chronic Toxicity

MDMA use can cause massive serotonin release which can lead to hallucinations and psychosis acutely, but also causes chemical damage to serotoninergic nerves. PET scans of previous users of MDMA showed a decrease in the structural component of the brain 5-HT neurons. These changes are of unknown consequences but may include depression, anxiety, and memory impairment. Chronic paranoid psychosis, depression, flashbacks, panic disorders, and some

impairment of cognitive function have been related to long-term use.

Clinical Management

The major complications seen in MDMA intoxication are hyperthermia, aspiration pneumonia, rhabdomyolysis, hepatotoxicity, hyponatremia, seizures, end-organ ischemia (stroke and myocardial infarction), hypertension and it's sequelae (aortic dissection and stroke).

There is no antidote for MDMA poisoning. Beyond basic and advanced life-support, the treatment is similar to other sympathomimetic poisonings. The use of the butyrophenone haldoperidol may be a useful adjunct for the immediate management of an acutely agitated or psychotic patient that poses an immediate threat to healthcare staff or self. There may be a benefit from switching from haloperidol to benzodiazepines after gaining control of the patient so as not to obscure the clinical picture if the patient becomes hyperthermic. Benzodiazepines may also be used to treat neuromuscular hyperactivity, seizures, and hyperthermia. Similar to cocaine toxicity, there may be a benefit to decreasing central sympathetic activity with benzodiazepines.

Hypertensive emergencies with end-organ ischemia may be treated in a traditional manner with the exception of not using beta blockers. Phentolamine may be useful in cases of hypertensive emergencies or end-organ ischemia refractory to traditional nitrate infusions and benzodiazepines.

Hypothermic blankets, ice water baths, chilled intravenous fluids, gastric and bladder lavage with cooled fluids may be needed to reduce body temperature. Acetaminophen is not routinely recommended because the etiology of the hyperthermia is thought to be a combination of increased psychomotor activity and peripheral vasoconstriction rather than a central effect. Controlling agitation is important to prevent rhabdomyolysis. Measuring creatine phosphokinase levels is helpful in recognizing those at risk of developing acute renal failure. Ensuring adequate urine output with intravenous fluids is the mainstay of treatment for preventing acute tubular necrosis.

For guidance in treating patients with suspected Molly use, or any other substance of abuse, contact the Blue Ridge Poison Center 24 hours a day, every single day, at 800-222-1222. Cell users may use 800-451-1428. Calls are free and confidential.

ToxTalks is funded in part through a grant from the U.S. Department of Health and Human Services Health Resources Services Administration.