ToxTalks: Substances of Abuse and Misuse
Highlights from the Field

Blue Ridge Poison Center | University of Virginia Health | April 2023

Xylazine

This is a special edition dedicated to substance use & misuse. Look for more of these editions as we encounter emerging and growing concerns. Funding support provided by the CDC's Prescription Drug Overdose: Prevention for States program in partnership with the Virginia Department of Health.

Case Example

A 29-year-old woman injected a substance intravenously and became unresponsive. EMS arrived and naloxone 2 mg was administered with no effect. The patient was apneic in the emergency department and she underwent endotracheal intubation and mechanical ventilation. Spontaneous respirations did not return until I8 hours after admission. The patient fully recovered and on extubation she admitted to injecting xylazine.

Overview

Xylazine is a veterinary anesthetic that is emerging as both a drug of abuse and as an additive to illicit fentanyl, heroin and cocaine. Sporadic cases of overdose have been reported in the literature dating back to the 1980s. More recently, there has been an increase in cases in certain regions of the country, including Virginia. Common street names for the drug include: tranq, tranq dope, sleep cut, or anestesia de caballo (horse anesthesia).

What is xylazine?

Xylazine (trade names: Rompun, Sedazine, AnaSed, Chanazine) is a non-narcotic drug used in veterinary medicine as a sedative, anesthetic, analgesic, and muscle relaxant in both wild and domesticated animals. It was first synthesized in 1962 in Germany by Bayer as a possible anti-hypertensive agent in humans, however trials were terminated due to its ability to cause severe hypotension and central nervous system (CNS) depression. It is currently not approved by the FDA for use in humans, meaning it cannot be classified as a controlled substance under the Controlled Substances Act.

How does xylazine work?
Xylazine is a lipophilic drug with a chemical structure similar to phenothiazines, tricyclic anti-depressants, and clonidine. Like clonidine, it is an alpha-2 adrenergic receptor agonist which causes decreased sympathetic outflow from the CNS by modulating the release of norepinephrine (NE). Increase in vagal tone is reported in veterinary literature. Xylazine also acts on alpha-2 receptors in pancreatic beta cells, inhibiting insulin release.

How is xylazine abused?
Xylazine is most likely to be encountered as either a known or unknown additive to common illicit drugs. Xylazine/fentanyl is the most common combination, followed by xylazine/fentanyl/heroin, xylazine/cocaine, and xylazine/fentanyl/ cocaine. Exposures to xylazine were sporadically reported in the literature in the 1980s and 1990s, with widespread use first noted in Puerto Rico in the early 2000s. Known by the name anestesia de caballo (horse tranquilizer), it was most commonly used as part of a speedball (xylazine/heroin/cocaine).

Injection of pure xylazine by users led to the development of abscesses, skin ulcerations, and other skin lesions. Users claimed to recognize xylazine in drugs by its odor, color (dark brown), effects, taste, and crystallization during preparation. Use has since spread to the US mainland, with first widespread use documented in Philadelphia in 2007 where it was known as tranq. From there, it spread further into the Northeast and is now found throughout the country.

What symptoms are expected from xylazine?
The alpha-2 agonist effects of xylazine are expected to cause symptoms similar to other well-known alpha-2 agonists like clonidine and dexmedetomidine. Decreased outflow of NE leads to sedating effects, bradycardia, and hypotension. Similar to effects seen in alpha-2 agonists used in humans, xylazine is reported in veterinary literature to cause transient hypertension followed by bradycardia and hypotension. Significant respiratory depression can occur if combined with opioids due to synergistic effects. Increased vagal tone can lead to sinus bradycardia as well as AV blocks. Blockade of pancreatic alpha-2 receptors leads to inhibition of insulin release, causing hyperglycemia. While injection is the most common route of exposure, ingestion, inhalation, and accidental ocular exposure have all been reported to produce clinically significant symptoms.

How long do effects last?
In animals, onset of action occurs within a few minutes with a duration of effect lasting between 3 and 4 hours. In human overdoses, duration of effect ranges from 8 to 72 hours. Withdrawal from xylazine has been reported with chronic users, producing symptoms similar to clonidine withdrawal with autonomic instability and hypertension.

How are symptoms treated?

Supportive care is the mainstay of treatment. Like overdoses of other alpha -2 agonists, CNS depression and bradycardia may be responsive to tactile stimulation. Administration of naloxone does not appear to be effective in reversing respiratory depression associated with xylazine, but should still be given if co-ingestion with an opioid is suspected. If not responsive, consider intubation and mechanical ventilation for respiratory support. Bradycardia may require atropine. Hypotension not responsive to IV fluids may require vasopressor support. Because xylazine is a lipophilic drug, hemodialysis is not effective at removal.

While veterinary literature cites the use of alpha-2 antagonists (yohimbine, tolazoline, idazoxan, atipamezole) to reverse the effects of xylazine, no antidote is currently approved for human use.

In cases of withdrawal from xylazine for chronic users, case reports have shown benefit in the use of other alpha-2 agonists such as dexmedetomidine and clonidine in helping to control symptoms.

If overdose or toxicity is encountered, please contact the poison center at 1-800-222-1222. Our center is collecting data associated with xylazine human exposures and can help with management questions.

References available upon request.