Department of Mental Health & Substance Abuse Services

Published
May 15, 2023

Xylazine Overview and Frequently Asked Questions

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the TDMHSAS Division of Substance Abuse Services

What is xylazine? How does it work in the body/what systems are impacted by it?

Xylazine (pronounced "zai·luh·zeen") is a non-opioid used for its tranquilizer, sedative, and pain relieving with muscle relaxant properties in animal (veterinary) medicine. It was synthesized by Bayer Pharmaceuticals in 1962 and is FDA-approved ONLY for use in animal medicine. Bayer studied xylazine for use in humans, but it was found to **have serious side effects like the occurrence of very low blood pressure** (severe hypotension) and **severe central nervous system depressant effects. It is not approved by the FDA for use in humans.**

Chemically it is not an opioid; therefore, naloxone is not known to be effective in reversing the toxic effects of xylazine. However, **naloxone should always be administered if an overdose is suspected.** Xylazine also has chemical properties similar to drugs commonly used for high blood pressure, like clonidine, and has similar clinical effects. Like clonidine, xylazine decreases heart rate and contractility. In the central nervous system, xylazine also causes a rapid decrease in the release of the neurotransmitters norepinephrine and dopamine which leads to sedation, analgesia, and muscle relaxation.

Xylazine **appears to be absorbed, metabolized, and eliminated extremely rapidly in animals, but has not been fully studied in humans.** After intravenous administration in animals, xylazine rapidly distributes, concentrating in the kidney and the central nervous system. The duration of effects begins within a few minutes and last up to 4 hours. These values indicate that the xylazine concentration would decrease to an undetectable level within a few hours.

Routine toxicology screens do not identify xylazine and it may be difficult to determine if it is involved in an overdose without additional, more advanced analytical measures like gas chromatography–mass spectrometry (GC-MS). In addition, xylazine is rapidly removed from the body (half-life of 23 to 50 minutes), which may make detection even more difficult.

Why are the wound issues/necrosis/skin damage and rotting so much worse with xylazine than other substances?

The mechanism is thought to be mediated by its direct vasoconstricting effect by shrinking smaller blood vessels, resulting in decreased oxygen delivery to the skin. In addition to vasoconstriction, it causes low blood pressure, slow heart rate, and shallow breathing, leading to lower tissue oxygenation in the skin. Thus, **chronic use of xylazine can** progress the vasoconstriction and reduction of oxygen to the skin, **leading to severe skin and soft tissue infections, including abscesses, cellulitis, and skin ulceration.** Repeated exposure to Xylazine has been found to cause characteristic necrotic skin ulcers (death and loss of skin tissue) in patients. Decreased oxygen delivery to the skin also leads to impaired healing of wounds and a higher chance of infection of these ulcers by bacteria that is very difficult to treat with conventional antibiotics.

Xylazine-related skin infections and most other skin and soft tissue infections require medical treatment. They are typically Methicillin-resistant Staphylococcus aureus (MRSA) and need to be **treated from the inside out with intravenous antibiotics or complex oral medication combinations**.

Topical treatments and general wound care, while helpful, are **ineffective at stopping skin necrosis** or treating the underlying infection.

Is it true that xylazine can do similar skin damage to areas other than where xylazine is being injected?
Yes, a high prevalence of abscesses and painful skin ulcers developed over various body parts irrespective of the IV injection site has been reported. Some individuals who inject fentanyl with xylazine may repeat injections into infected tissues to relieve the pain from the infection.

Are there types of tissue that are more vulnerable to xylazine?
Due to the vasoconstrictive effects, any tissue that comes in direct contact will be more vulnerable than non-exposed tissues. In rat models, intramuscular injections resulted in muscle necrosis in all exposed rats.

How does xylazine cause/contribute to an overdose?
Xylazine-induced bradycardia (slow heart rate/beat) and hypotension (low blood pressure/perfusion) are the primary contributors linked to overdose deaths. Concurrent administration of other drugs in combination with Xylazine, specifically opioids like fentanyl, intensifies the challenges of managing intoxication and significantly increases overdose risk and lethality.

Xylazine is shown to impair the anticonvulsant properties of medications used for seizures, such as, phenobarbital, phenytoin, and diazepam in rats. Thus, Xylazine can impede the clinical treatment of withdrawal seizures and further increases the risk death or serious harm.

What happens if there is an overdose with both xylazine and opioid(s), and naloxone is administered? What happens in the body?
At this time, **there is no known xylazine antidote** for safe and effective use in humans. **Xylazine is NOT an opioid and not likely to be reversed by naloxone** (Narcan, Kloxxado, Zimhi, generics), an opioid antidote. **However, bystanders should still administer naloxone whenever someone is suspected to be experiencing an overdose.** Bystanders should also provide appropriate supportive care (CPR) to patients who do not respond adequately to naloxone administration. In cases where Xylazine is used in conjunction with opioids, naloxone's effectiveness in reversing the effects of opioids may indirectly contribute to patient recovery by mitigating the impact of opioid intoxication.

Harm reduction strategies to be utilized with xylazine
Harm reduction measures that are generally utilized for intravenous drug use should be considered, including practices to reduce the risk of blood-borne infections. Wound care kits containing antiseptic solutions, bandages, and antibiotic ointments can prevent infections and promote healing in cases of skin abscesses or injection-related injuries, especially if treated early.

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Xylazine-related information from the Tennessee Department of Health
Emerging Trends Brief-published 11/22/2022
https://www.tn.gov/content/dam/tn/health/documents/pdo/infographics/Emerging_Trends_Xylazine.pdf

Other Resources:
Drug Enforcement Administration, Xylazine
https://www.deadiversion.usdoj.gov/drug_chem_info/Xylazine.pdf

National Institute on Drug Abuse (NIDA), Xylazine https://nida.nih.gov/research-topics/xylazine

Public Health Alerts
FDA "FDA warns about the risk of xylazine exposure in humans"
https://www.fda.gov/drugs/drug-safety-and-availability/fda-alerts-health-care-professionals-risks-patients-exposed-xylazine-illicit-drugs

Drug Enforcement Administration Public Safety Alert "DEA Reports Widespread Threat of Fentanyl Mixed with Xylazine" https://www.dea.gov/alert/dea-reports-widespread-threat-fentanyl-mixed-xylazine

Office of National Drug Control Policy "Biden-Harris Administration Designates Fentanyl Combined with Xylazine as an Emerging Threat to the United States"
https://www.whitehouse.gov/ondcp/briefing-room/2023/04/12/biden-harris-administration-designates-fentanyl-combined-with-xylazine-as-an-emerging-threat-to-the-united-states/

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