



Clinical Pharmacology & Toxicology Pearl of the Week

~ Xylazine ~

Case:

- A 40-year-old male crushes and snorts an unknown amount of a pink powder. He is brought to the ED by his roommate. Vitals: HR 80, BP 100/70, RR 6, O₂ sat 83% r/a, glucose 5.0, temp 36.5 C, pupils 2mm, GCS 9.
- He receives an appropriate amount of naloxone and has an incomplete response to same, with persistent decrease in his level of consciousness despite improvement in pupil size and respiratory rate.
- Other than opioids and novel benzodiazepines, what other medications could be present in his drug supply that are contributing to his persistent clinical findings?

Background:

- Xylazine is used in veterinary medicine, often in combination with ketamine, opioids, or barbiturates for anesthetic purposes.
- It is structurally similar to clonidine, phenothiazines, and imidazolines (see Figure 1 below).
- It acts primarily as a presynaptic alpha-2 adrenergic agonist, inhibiting release of norepinephrine and dopamine in the CNS.
- These receptor interactions ultimately result in sedation, muscle relaxation, and analgesia.
- Xylazine has emerged as a drug of misuse/abuse and as an adulterant in the unregulated drug supply in Alberta. One of its street names is “tranq.”
- Xylazine has also been increasingly detected among overdose fatalities in post-mortem studies.

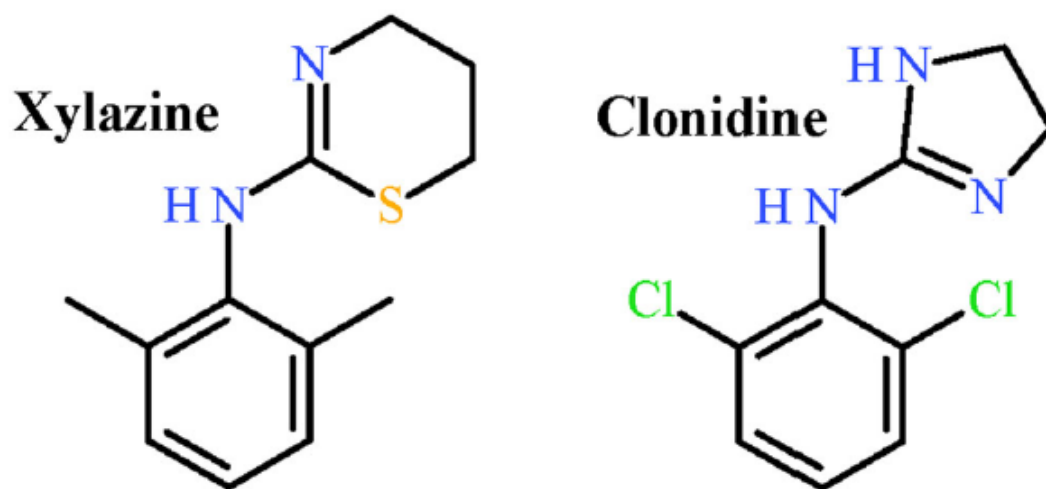
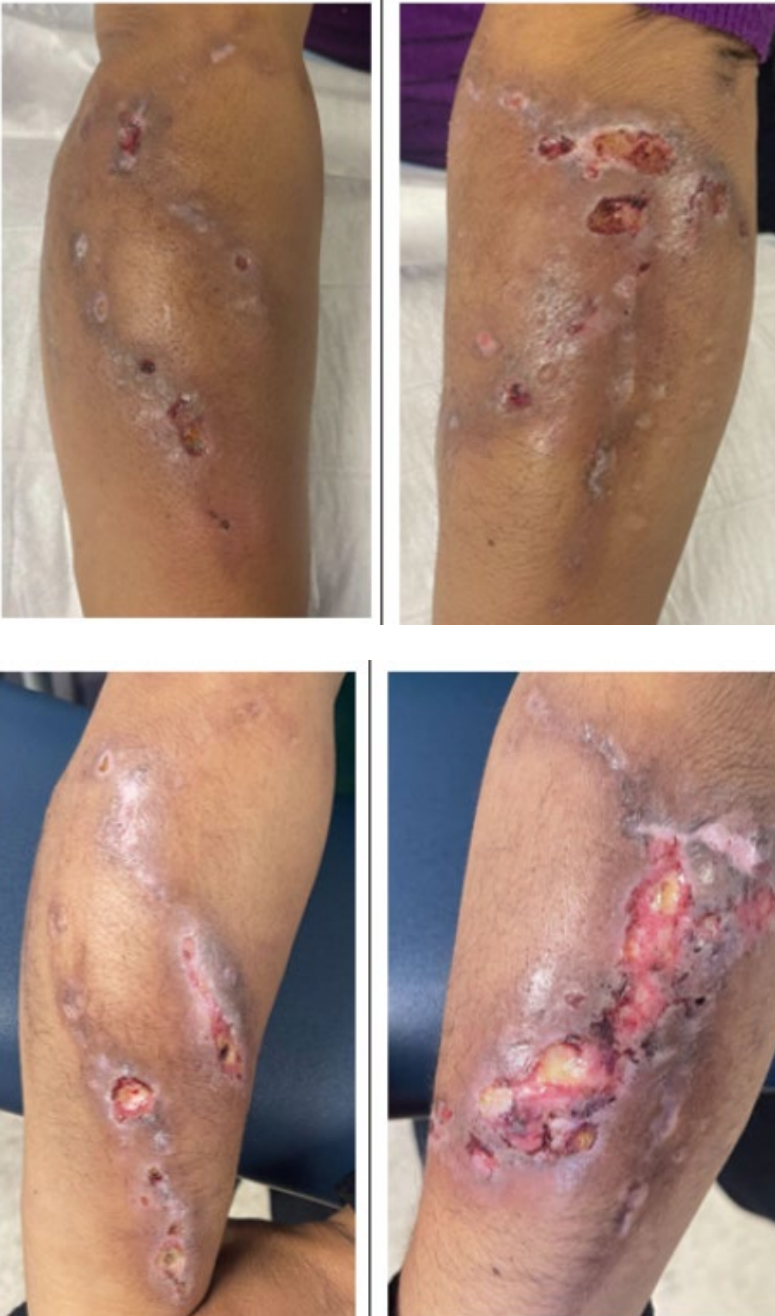


Figure 1. Chemical structures of xylazine and clonidine.

Source: Love et al.

Clinical features:

- The most common reported symptoms include decreased level of consciousness, bradycardia, hypotension, and hypertension.
- Rarely, cardiac arrest has been reported. Cardiac arrest is less likely when xylazine is present in an opioid exposure compared to opioids alone, possibly because of lower opioid concentrations in drugs where xylazine is added
- Leg wounds are commonly seen in patients who inject drugs containing xylazine.
 - Xylazine-induced skin ulcers may appear diffusely throughout the body, even at sites distant from the injection site. These ulcers are typically progressive, large, and necrotic.
 - The mechanism of injury is thought to be related to its vasoconstricting effect on local blood vessels, resulting in decreased skin perfusion.



Leg wounds in a patient who injects xylazine. Source: Warp et al.

Management:

- ABC's
- Be prepared to intubate if a reversible cause (i.e., hypoglycemia, opioids, etc.) is not identified and the patient cannot protect the airway.
- Suspicion of xylazine toxicity should occur in patients with presenting signs or symptoms of an opioid overdose who do not respond to a 2 mg dose of naloxone.
 - Higher dosing of naloxone, such as 0.1 mg/kg in pediatric patients or 10 mg in adults as recommended in clonidine poisonings may be considered.
- Administration of atropine is unlikely to have an effect in xylazine toxicity as xylazine does not interact with muscarinic receptors.
- Symptoms generally last between 4-12 hours.
- Patients arriving alive to the ED generally survive with supportive care.

References:

1. Noah S. Ball et al. Xylazine poisoning: a systematic review. *Clinical Toxicology*. 2022, 60:8, 892-901, DOI: 10.1080/15563650.2022.2063135.
2. Jennifer S. Love et al. Opioid overdoses involving xylazine in emergency department patients: a multicenter study, *Clinical Toxicology*. 2023, 61:3, 173-180, DOI: 10.1080/15563650.2022.2159427.
3. Warp et al. A Confirmed Case of Xylazine-Induced Skin Ulcers in a Person Who Injects Drugs in Miami, Florida, USA. *Res Sq [Preprint]*. 2023 Jul 26:rs.3.rs-3194876. [Version 1] doi: 10.21203/rs.3.rs-3194876/v1.

The Clinical Pharmacology (CP) physician consultation service is available Mon-Fri, 8am-5pm, excluding stat holidays. The on-call physician is listed in ROCA on the AHS Insite page. CP consultations are also available through Netcare e-referral, Specialist Link, and RAAPID. You can also find us in the [Alberta Referral Directory](#) (ARD) by searching “Pharmacology” from the ARD home page. Click [HERE](#) for more details about the service.

The Poison and Drug Information Service (PADIS) is available 24/7 for questions related to poisonings. Please call 1-800-332-1414 (AB and NWT) or 1-866-454-1212 (SK). Information about our outpatient Medical Toxicology Clinic can be found in [Alberta Referral Directory](#) (ARD) by searching “Toxicology” from the ARD home page.

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