Xylazine Masking Benzodiazepine Withdrawal

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Xylazine, or "tranq," is a veterinary anesthetic recognized as a highly potent and potentially lethal adulterant in community supplies of opioids, benzodiazepines, and cocaine.[1] Here, we report a case that suggests a xylazine-induced masking of benzodiazepine withdrawal, which resulted in a withdrawal seizure in our patient. The importance of vigilant monitoring for withdrawal symptoms in patients using multiple substances and the value of drug testing for impurities and additives in the community drug supply are highlighted.

Case Report

A 35-year-old man with a history of polysubstance use disorder (opioids, cocaine, benzodiazepines, THC, methamphetamine, and tobacco), including a recent hospitalization for opioid overdose, presented to the emergency department after being found cyanotic at home. He was successfully resuscitated with 3 doses of naloxone, returning to his clinical baseline. His hospitalization was otherwise complicated by asymptomatic bradycardia with heart rates consistently in the 40s and 50s, upon which no clinical action was taken. During subsequent interactions, the patient reported injecting an unknown quantity of what he described as "black tar heroin," as well as benzodiazepines prior to his presentation.

On hospital day 3, he reported subjective benzodiazepine withdrawal symptoms, but given bradycardia, normal blood pressure, and lack of overt tremulousness or other objective signs of withdrawal, the decision was made to forego lorazepam or phenobarbital for treatment of γ-aminobutyric acid (GABA) ergic withdrawal. That evening, the patient suffered a generalized tonic-clonic seizure, confirmed by bedside observation of the event and laboratory evaluations revealing a lactate level of 14 mmol/L and creatine kinase level of 1,010 U/L. Of note, a prolactin level was not obtained since all other clinical and laboratory data pointed toward this being a seizure episode. The patient's seizure aborted spontaneously after 1 to 2 minutes, and he received a total of 4 mg of intravenous lorazepam for postictal agitation. He was subsequently started on gabapentin 600 mg 3 times/day. Follow-up electroencephalogram, brain magnetic resonance imaging, echocardiogram, and blood cultures revealed no etiology of the seizure.

Testing of the patient's drug supply demonstrated numerous impurities and additives including xylazine, fentanyl, and bromazolam among others. We hypothesize that xylazine masked our patient's expected adrenergic benzodiazepine withdrawal symptoms, consequentially resulting in a seizure. Subsequently, the patient had no further seizure activity, and opioid withdrawal symptoms were well-managed with buprenorphine. He was discharged to an inpatient substance use rehabilitation treatment center.

Discussion

There is growing academic and community recognition of the deadly impact of xylazine, including a recent public health report in the *New England Journal of Medicine*[2] and segments on National Public Radio.[3,4] Xylazine is a centrally acting alpha-2 adrenergic agonist that exerts its pharmacologic effects in the central nervous system, resulting in sedation, analgesia, and muscle relaxation. Xylazine could therefore mask the expected physiological effects of GABAergic withdrawal such as hypertension, tachycardia, and tremulousness, without providing the needed GABAergic effect to prevent a withdrawal seizure. To our knowledge, this is the first described possible case of xylazine masking benzodiazepine withdrawal resulting in a withdrawal seizure. This case demonstrates the importance of closely monitoring patients suspected of having ingested both opioids and GABAergic substances, and the need to be hypervigilant for withdrawal symptoms even several days after the acute opioid withdrawal phase has passed. Furthermore, our case underscores the utility of drug testing for impurities and additives, allowing both patients and providers to be familiar with the contents of the community drug supply.

Article Information

Published Online: February 8, 2024.
https://doi.org/10.4088/PCC.23cr03619

Submitted: August 23, 2023; accepted: October 18, 2023.

To Cite: Robbins-Welty G, Hart J, Dussault N, et al. Xylazine masking benzodiazepine withdrawal. *Prim Care Companion CNS Disord*. 2024;26(1):23cr03619.

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Relevant Financial Relationships: None.

Funding/Support: None.

Acknowledgements: The authors would like to thank Jonathan Komisar, MD (Department of Psychiatry, Duke University School of Medicine, Durham, North Carolina; Dr Komisar has no relevant financial relationships to report.) for his clinical care of this patient. We also acknowledge and appreciate the University of North Carolina Street Drug Analysis Lab (https://www.streetsafe.supply) for assistance in drug testing.

Patient Consent: The patient provided written consent to publish this case report, and information has been de-identified to protect anonymity.

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References

1. Delcher C, Anthony N, Mir M. Xylazine-involved fatal overdoses and localized geographic clustering: Cook County, IL, 2019-2022. *Drug Alcohol Depend*. 2023;249:110833.
2. Gupta R, Holtgrave DR, Ashburn MA. Xylazine-medical and public health imperatives. *N Engl J Med*. 2023;388(24):2209–2212.
3. Zamora K. The drug fueling another wave of overdose deaths. Yenigun S, Raney A, de Leon A, eds. *National Public Radio*. Published online June 15, 2023. Accessed July 23, 2023. https://www.npr.org/2023/06/14/1182219327/the-drug-fueling-another-wave-of-overdose-deaths
4. Mann B, Beck M, Kiefer P. A deadly new street drug caught the U.S. off guard. Experts say it'll happen again. *National Public Radio; Public Radio from UA Little Rock*. Published online June 17, 2023. Accessed July 23, 2023. https://www.ualrpublicradio.org/npr-news/2023-06-17/a-deadly-new-street-drug-caught-the-u-s-off-guard-experts-say-itll-happen-again