The Prevalence of Nutritional Deficiencies in Philadelphia's Xylazine ("Tranq") Users: A Retrospective Chart Review

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Background

- Opioid use disorder (OUD) continues to be a major public health concern, particularly in urban centers like Philadelphia. Recently, the presence of xylazine, an alpha-2 agonist primarily used in veterinary medicine, has become a growing issue within the opioid supply in the city.
- Xylazine has been increasingly used as an adulterant in fentanyl, extending its effects and contributing to the rising number of opioid-related overdoses . This combination increases the risk of respiratory depression but also contributes to severe necrotic wounds due to its vasoconstrictive properties, which complicates treatment for individuals with OUD (1)
- Individuals with OUD often face significant nutritional challenges. Chronic opioid use has been linked to impaired neuroadaptation and decreased appetite, resulting in unhealthy eating patterns such as meal skipping and reliance on nutrient-poor foods (3). This problem is exacerbated by socioeconomic factors like food insecurity and limited access to nutritious food, particularly in communities severely impacted by the opioid epidemic (5). Furthermore, metabolic changes associated with opioid use contribute to deficiencies in vital nutrients such as iron, zinc, and vitamins A, C, and D, all of which are critical for proper wound healing (13).
- Research on the prevalence of specific vitamin and mineral deficiencies in individuals with xylazine use remains limited. Addressing these deficiencies may improve outcomes such as wound healing, immune function, and cardiovascular health (7).
- This study aims to assess the nutritional status of patients seen by the Addiction Service at Thomas Jefferson University Hospital (TJUH) who use xylazine . By doing so, we seek to enhance our understanding of the relationship between nutrition and xylazine use, and to explore the potential benefits of targeted nutritional interventions.

Methods

- We collected the medical record numbers (MRNs) of patients for whom the Jefferson Addiction Medicine Service (JAMS) was consulted between August 2022 and May 2024. This project was given exempt status by Jefferson IRB
- Each patient encounter was reviewed individually in the EPIC electronic medical record system, specifically searching for Urine Drug Screen (UDS) results. Fentanyl was used as a surrogate marker for Xylazine, so patients who tested negative for fentanyl or did not have a UDS collected during the encounter were excluded from our dataset.
- We collected specific demographic information (age, sex) and various laboratory results (magnesium, calcium, zinc, B12, B6, folate, B1, Vitamin C, Vitamin D, ferritin, iron, iron binding capacity, phosphorus, hemoglobin, prealbumin, albumin, total protein, erythrocyte sedimentation rate [ESR], and C-reactive protein [CRP]) and compiled this data into a shared Excel sheet. Each lab value was recorded and noted whether it was within, above, or below the reference range as indicated by EPIC's reference standards.
- Some patients were consulted by JAMS multiple times during the study period. We retained only the encounter with the most complete data. In cases where the data collected was equivalent between encounters, we retained the most recent encounter and excluded the older ones.
- After filtering and excluding encounters, the final dataset consisted of 354 patient encounters. We analyzed the data by comparing lab values across encounters and calculating the percentage of values that fell within, above, or below EPIC's reference ranges. The compiled data was then organized into a chart to visualize the distribution of laboratory values across patient encounters, as presented in the results section.
- Finally, we compared all the principal diagnoses across the collected patient encounters and identified the top three principal diagnoses on admission using an inductive coding approach, which are presented in the results section.

Results

Demographics

- A total of 353 patients were included in the study, with a mean age of 41.6 years (range: 21–93 years).
- The number of patients with available laboratory values varied depending on the specific test, ranging from 31 patients for vitamin B6 levels to 351 patients for hemoglobin measurements.
- Of the cohort, 131 patients (37.1%) were assigned female sex at birth, and 222 patients (62.9%) were assigned male sex at birth.

Top 3 Principal Diagnoses on Admission

#1 Sepsis
105 patients
29.7%

#2 Cellulitis
31 patients 8.8%

#3 Opioid Use/ dependence with withdrawal
29 patients, 8.2%

Distribution of Laboratory Values: Percentage of Patients with High, Low, and Normal Levels

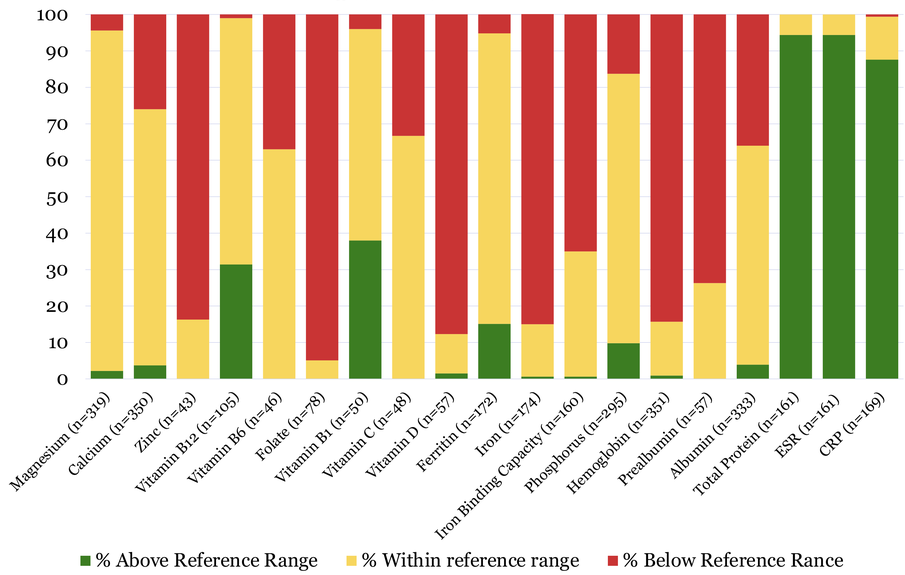

Table 1: Percentage of participants who were above, within, and below laboratory reference ranges per vitamin level.

Additional Highlights:

- The mean total protein level was 7.5 g/dL, with a range of 4.2 to 10.6 g/dL.
- The mean erythrocyte sedimentation rate (ESR) was 68.8 mm/hr (range: 1–130 mm/hr).
- The mean C-reactive protein (CRP) level was 9.4 mg/L, ranging from 0.3 to 64.7 mg/L.
- Zinc levels had a mean of 48 µg/dL, with a range of 25 to 80 µg/dL.
- Folate levels averaged 10.5 ng/mL, with values ranging from 2 to 20 ng/mL.
- The mean vitamin D level was 17.9 ng/mL, with a range of 6 to 54.3 ng/mL.
- Iron levels averaged 29.8 µg/dL (range: 6–158 µg/dL), while the mean total iron-binding capacity (TIBC) was 222.5 µg/dL (range: 88–459 µg/dL).
- Hemoglobin levels had a mean of 10.8 g/dL, with a range of 5 to 17.4 g/dL.

Discussion

- Xylazine use is rapidly increasing in the United States, and can potentially cause addiction and subsequent withdrawal. It is known that individuals with substance use disorders (SUDs) show more signs of clinical malnutrition than the average person without an SUD, and that, in general, clinical signs of malnutrition have been associated with nutrient deficiencies on a laboratory level (6). Similarly, with our xylazine-using population:
  - A large percentage of people (>80%) had folate, zinc, vitamin D, iron, hemoglobin, and pre-albumin deficiencies
  - A large percentage of people (> 80%) had elevated protein, ESR, and CRP levels
- There appears to be different prevalences of deficiencies than in non-xylazine opioid users. Although there is not much data, studies have suggested the frequency in heroin users of folate deficiency to be 37% (lower than our study), B6 deficiency to be 45% (higher than our study), and B12 deficiency to be 16% (higher than our study) (el-Nakah et al., 1979). Another study found rates of Vit C and D deficiencies in the broad category of drug users to be 50% (higher than our study) and 70% (lower than our study), respectively (Saeland et al., 2011).
- The above trends of deficiencies, normal values, and values above the reference range are of unclear clinical significance. It is not unknown whether they correlate with clinical symptoms or if they are chronic patterns as opposed to acute markers of illness.
- Limitations: No control population (non-IVDU vs opioid-only users)
  - Did not account for hospital intervention (vitamin supplementation, blood transfusions, etc)
  - We did not quantify use patterns or stratify based on amount of use
  - Surrogate UDS is also an imperfect measure of xylazine use (for example, a small number of people may have received fentanyl while in hospital for pain)
  - All patients are acutely ill, by virtue of being admitted medically to the hospital and having a JAMS consult placed. Other reasons for illness may account for some amount of observed nutritional deficiencies. However, the majority of principal diagnoses appear to be sequelae of substance use disorders

Conclusions and Future Directions

We aim to establish a link between xylazine and nutrition and to establish a pattern of clinically relevant nutritional deficiencies.

Given the high prevalence of multiple vitamin deficiencies, this study could be used to advocate for routine nutritional screening and consider the benefits of prophylactic vitamin supplementation

In future studies, determining clinical significance will be paramount and will likely vary depending on the particular lab value of interest. Future directions could include:

- Replicating this study at an earlier period of time (such as 2016-2018), when xylazine adulteration was less prevalent, in order to establish an OUD control population
- Link between malnutrition and infection, restlessness, impaired wound healing, or cardiac function
- Link between xylazine and chronic wounds: Is there something unique to xylazine (such as the hypothesized splenic sequestration of RBCs leading to impaired wound healing, chronic inflammation, and anemia (Kullmann et al., 2014)) that leads to malnutrition?
- Is this independent of already established psychosocial factors (food and housing insecurity, reduced appetite) associated with individuals with OUD (Chavez & Rigg 2020)?
- Role for treatment (such as iron infusions) in an inpatient setting (pilot interventions in place)
- Role for nutrition-informed treatment recommendations in the outpatient setting

References

1. Akoh, C. C., & Orlow, S. J. (2020). A Review of Vitamin D and Scarring: The Potential for New Therapeutics. Journal of Drugs in Dermatology: JDD, 19(7), 742-745.
2. BETTIGOLE, C., Best, A., & TEIXEIRA DA SILVA, D. (2022, December 8). *Health Update Xylazine (tranq) exposure among people who use substances in Philadelphia.* Philadelphia Department of Public Health Substance Use Prevention and Harm Reduction. https://hip.phila.gov/document/3154/PDPHHAN_Update_13_Xylazine_12.08.2022.pdf/
3. Chavez, M. N., & Rigg, K. K. (2020). Nutritional implications of opioid use disorder: A guide for drug treatment providers. *Psychology of Addictive Behaviors*, *34*(6), 699.
4. el-Nakah, A., Frank, O., Louria, D. B., Quinones, M. A., & Baker, H. (1979). A vitamin profile of heroin addiction. *American journal of public health*, *69*(10), 1058-1060.
5. Evans, A., Banks, K., Jennings, R., Nehme, E., Nemec, C., Sharma, S., ... & Yaroch, A. (2015). Increasing access to healthful foods: a qualitative study with residents of low-income communities. International Journal of Behavioral Nutrition and Physical Activity, 12, 1-12
6. Islam, S. N., Hossain, K. J., Ahmed, A., & Ahsan, M. (2002). Nutritional status of drug addicts undergoing detoxification: prevalence of malnutrition and influence of illicit drugs and lifestyle. *British Journal of Nutrition*, *88*(5), 507-513.
7. Kiani, A. K., Dhuli, K., Donato, K., Aquilanti, B., Velluti, V., Matera, G., ... & Bertelli, M. (2022). Main nutritional deficiencies. Journal of preventive medicine and hygiene, 63(2 Suppl 3), E93.
8. Kullmann, A., Sanz, M., Fosgate, G. T., Saulez, M. N., Page, P. C., & Rioja, E. (2014). Effects of xylazine, romifidine, or detomidine on hematology, biochemistry, and splenic thickness in healthy horses. *The Canadian veterinary journal*, *55*(4), 334.
9. Malayala, S. V., Papudesi, B. N., Bobb, R., & Wimbush, A. (2022). Xylazine-induced skin ulcers in a person who injects drugs in Philadelphia, Pennsylvania, USA. Cureus, 14(8)
10. MacKay, D., & Miller, A. L. (2003). Nutritional support for wound healing. Alternative medicine review, 8(4).
11. Saeland, M., Haugen, M., Eriksen, F. L., Wandel, M., Smehaugen, A., Böhmer, T., & Oshaug, A. (2011). High sugar consumption and poor nutrient intake among drug addicts in Oslo, Norway. *British journal of nutrition*, *105*(4), 618-624.
12. Wang, T. Y., Lu, R. B., Lee, S. Y., Chang, Y. H., Chen, S. L., Tsai, T. Y., ... & Hong, J. S. (2023). Association between inflammatory cytokines, executive function, and substance use in patients with opioid use disorder and amphetamine-type stimulants use disorder. International Journal of Neuropsychopharmacology, 26(1), 42-51.
13. Zinder, R., Cooley, R., Vlad, L. G., & Molnar, J. A. (2019). Vitamin A and wound healing. Nutrition in Clinical Practice, 34(6), 839-849

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