A Snapshot of Xylazine Prevalence in Drivers in Central Virginia

Introduction: Xylazine is a non-narcotic drug that was synthesized by Bayer in 1962 [(1)]. In clinical trials xylazine was seen to have central nervous system depressant effects. However, due to negative effects causing hypotension and bradycardia, xylazine was never approved for use in humans by the Food and Drug Administration in the United States [(2)]. Since xylazine was approved for veterinary use only it is not a controlled substance under the U.S. Controlled Substance Act [(3)]. Although, due to the rise in human consumption over the past decade some states have adopted legislation that identifies xylazine as a scheduled drug. In the early 2000s, the Drug Enforcement Administration (DEA) reported that xylazine was used as an adulterant in Puerto Rico [(4)]. Due to its low price point and psychoactive effects, addition of xylazine allows drug traffickers to increase profits while reducing the amount of fentanyl or heroin in a sold product [(4)]. A study conducted in 2008, in Puerto Rico where syringes were collected and analyzed found that xylazine was present in 36% of syringes. Xylazine was most commonly found in "speedball preparations," containing heroin and cocaine in the analyzed syringes [(5)]. Almost a decade later, a review of drug material between 2015 and 2020 in New Jersey found xylazine was frequently found mixed with heroin and fentanyl [(6)]. A DEA report released in October of 2022 indicated the prevalence of xylazine was increasing across the country, with some regions in the U.S. reporting a doubling in positive cases from 2020 to 2021 [(4)]. Due to the increase in xylazine presence around the country, there has been an increased interest in Virginia to identify the presence of xylazine in toxicological samples for public health purposes. In early 2024, a validated quantitative method for xylazine was applied to casework at the Virginia Department of Forensic Science to aid in the determination of prevalence.

Objective: This study was conducted to better understand the prevalence of xylazine in the driving population in Central Virginia.

Methods: This study was performed at the Virginia Department of Forensic Science's Central Laboratory, located in Richmond, Virginia. The laboratory services forty-nine surrounding counties/cities in Central Virginia. On average, the Central Laboratory analyzes 125 impaired driving cases a month. Impaired driving cases are defined by the Code of Virginia §§ 18.2 268.2-268.7. These case types are first analyzed for ethanol. If an ethanol concentration is greater than or equal to 0.100%, these cases are screened by enzyme linked immunosorbent assay (ELISA) for cannabinoids only. Samples with ethanol concentrations below 0.100% are tested by ELISA for eighteen drug targets/panels. Blood samples with ethanol concentrations below 0.100% which screen positive on ELISA for one or more of the following drug targets/panels: cocaine metabolites, opiates, oxymorphone/oxycodone, fentanyl, tramadol, and methadone are further analyzed by the Opioid, Cocaine, Benzoylecgonine, and Cocaethylene Quantitation and Confirmation by LCMSMS method (OpiCoc method). The limit of detection and quantitation for xylazine is 1 ng/mL and the upper limit of quantitation is 200 ng/mL. Additional details of the protocols and methods used by the Virginia Department of Forensic Science are available on the Department's website [(7)]. Data included in this study was mined from samples tested by the OpiCoc method on an Agilent 6460 Triple Quadrupole LC/MS between late February 2024, when the xylazine assay was first placed online, through the end of May 2024. Monitoring casework for approximately three months enabled any potential trends to be identified in a timely manner.

Results: During the approximately three-month period, seventy-four driver cases were analyzed for xylazine by the OpiCoc method along with morphine, oxymorphone, hydromorphone, oxycodone, hydrocodone, 6-acetylmorphine, codeine, fentanyl, acetylfentanyl, methadone, tramadol, cocaine, benzoylecgonine, and cocaethylene. Fourteen of these cases (19%) were positive for xylazine with an average (median) concentration of 34 (9.7) ng/mL. Xylazine concentrations ranged from 1.1 to 201 ng/mL. All fourteen positive xylazine cases were also positive for fentanyl with an average (median) concentration of 36 (18) ng/mL. The average (median) concentration for all forty-four fentanyl positive cases analyzed was 19 (7.1) ng/mL, with 32% of those cases testing positive for xylazine. Benzoylecgonine was the second most frequently co-detected drug at 86% with an average (median) concentration of 799 (690) ng/mL. Fifty-two of the cases analyzed were positive for benzoylecgonine and 23% of those cases also contained xylazine. The third most prevalent drug detected in xylazine positive cases was cocaine (57%) followed by methadone (36%).

Discussion: The aim of this study was to gain knowledge on the prevalence of xylazine in the driver population in Central Virginia and to identify any trends. Since initially being identified as an adulterant in Puerto Rico in the early 2000s, xylazine has steadily increased in prevalence across the U.S. In 2015, xylazine was identified by the DEA in 149 items. Fast-forward to 2021 and that number has increased to 8,938 [(2)]. In the subset of seventy-four cases that were analyzed by the OpiCoc method in the present study, 19% of those driver cases were positive for xylazine compared to the 3.6% seen in the Kacinko et al. study in 2021 [(3)].

Other studies previously identified that exposure to xylazine is most common among heroin, fentanyl, and cocaine abusers [(2)]. A needle exchange program conducted in 2008 in Puerto Rico found that 91% of syringes that were positive for xylazine were also positive for heroin and cocaine [(5)]. The data from the present study shows that xylazine positive cases were also positive for fentanyl in 100% of cases and positive for benzoylecgonine in 86% of cases. Similarly, Kacinko et al. found that 100% of their impaired driving xylazine positive cases also contained an opioid, primarily fentanyl or fentanyl biproduct [(3)]. Additionally, the present study's fentanyl concentrations when xylazine was present were similar to the findings between January 2019 to June 2021 in the Kacinko et al. study with an average (median) concentration of xylazine in drivers of 36 (15) ng/mL [(3)]. A limitation of the current study is that samples were only analyzed by the OpiCoc method if they tested presumptive positive via ELISA analysis for the following kits: cocaine metabolites, opiates, oxymorphone/oxycodone, fentanyl, tramadol, and/or methadone. This is because the OpiCoc method is also the confirmation method for the kits listed above. Since xylazine has predominately been found concurrently with opioids and cocaine, this targeted approach would still provide useful information into the prevalence of xylazine in the area.

Both the current study and Kacinko et al. study showed that, in driver cases, xylazine was detected 100% of the time with an opioid, primarily fentanyl. Although xylazine and opioids produce similar psychoactive effects, their mechanisms of action differ. Xylazine acts as an agonist at the alpha-2 adrenergic receptor [(1)]. The alpha-2 stimulation decreases the release of dopamine and norepinephrine resulting in sedation, muscle relaxation, and pain relief [(1)]. Symptoms from human reported cases showed central nervous system depression, respiratory depression, bradycardia, hypotension, and hyperglycemia [(1)]. These symptoms are similar to those of heroin and fentanyl, along with other opioids, that bind at the opioid receptor sites. When opioids and xylazine are co-consumed they may cause synergistic effects which could increase the likelihood of adverse effects [(1)], which could in turn increase

potential impairment. Additionally, xylazine does not respond well to naloxone, a common antidote to reverse opioid overdoses, due to its limited activity at the opioid receptor sites [8].

In regard to xylazine and impaired driving, there is limited published information. A literature search identified only one case study where a man was found passed out in his car that was located on a freeway median. The individual's speech was slurred, movements were sluggish, and he needed help exiting his vehicle. The observed symptoms were consistent with that of a central nervous system depressant. His blood was drawn approximately two hours later and contained 570 ng/mL of xylazine and 20 ng/mL of paroxetine [9]. In the present study there were no cases where xylazine was detected in the absence of other drugs. Since xylazine is almost always found present with another opioid, as shown in the present study as well as Kacinko at et al., additional studies are needed to more fully characterize the extent which xylazine may cause or contribute to impairment.

References:

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