K54 Xylazine Alone and in Combination With Opioid Drugs in Forensic Toxicology Casework

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Learning Overview: After attending this presentation, attendees will understand the frequency of xylazine detection in forensic toxicology casework, the potential effects of the drug alone, and the combined effects with opioids.

Impact on the Forensic Science Community: This presentation will impact the forensic science community by informing attendees about the pharmacology of xylazine and its detection in forensic toxicology casework.

Illicit drugs are often "cut" prior to being sold to the end user. Diluents such as lactose are used to dilute the drug and add bulk to the preparation, but have no pharmacological impact. Adulterants such as procaine may ease the pain of injection and diphenhydramine may enhance the sedative effects of heroin while helping with side effects such as itching. The purpose of this study was to evaluate the frequency of xylazine, a veterinary anesthetic/analgesic, detected alone or in combination with heroin, fentanyl ,or fentalogs in blood samples submitted to a large reference laboratory.

Data from cases received between May 1, 2013, and June 30, 2019, and screened by liquid chromatography/time-of-flight/mass spectrometry were extracted from the NMS Labs Laboratory Information Management System. Xylazine was included in the scope of this assay, but routine confirmation and quantification of xylazine did not begin until January 2019. Based on the confirmation rate (approximately 90%) of presumptive positive cases after the availability of the confirmation test, the entire data set was used to evaluate the frequency of xylazine in casework.

One thousand twenty-five cases had a presumptive positive finding for xylazine. Seven cases had no opioids detected and two contained xylazine and methadone. The remaining cases contained one or more of the following opioid drugs: fentanyl (796), heroin (461), morphine (139), 2-furanylfentanyl (26), fluoroisobutyryl/para-fluorobutyrylfentanyl (23), carfentanil (25), 3-methylfentanyl (7), methoxyacetylfentanyl (6), valerylfentanyl (6), cyclopropylfentanyl (5), butyryl/isobutyrylfentanyl (5), U-47700 (3), acrylfentanyl (2), and fluorofentanyl (1). Quantitative data for xylazine were available for 236 cases that had comprehensive screening performed. The mean (range) xylazine concentrations in postmortem (*N*=226) and driving under the influence of drugs (*N*=10) cases were 73 (5–9,100) and 25 (5.3–53) ng/mL, respectively. Fentanyl concentrations were 0.84–420ng/mL in 228 of these cases. Ninety-five cases contained morphine and 40 of these also had 6-Monoacetylmorphine (6-MAM) reported in blood. Mean concentrations for morphine and 6-MAM were 130 and 20ng/mL, respectively. Three postmortem cases that underwent comprehensive screening at NMS Labs and had quantitative confirmation of xylazine contained xylazine in the absence of fentanyl, morphine, or 6-MAM. The information available about these cases is summarized below.

Xylazine (ng/mL)	Other Drugs	History
16	Cis-3-methylfentanyl=0.12ng/mL Bupropion=14ng/mL Hydroxybuproprion=360ng/mL Diphenhydramine=150ng/mL Citalopram/Escitalopram=76ng/mL	Suspected overdose.
9,100	Citalopram/Escitalopram=85ng/mL	Found in truck with bottle of xylazine and suicide note.
6.6	Metaxlone=0.15µg/mL Citalopram/Escitalopram=390ng/mL	Found having seizures. History of opioid use.

Blood/plasma xylazine concentrations in individuals known to be exposed to xylazine and survived ranged from 570–4,600ng/mL and a postmortem blood xylazine concentration of 16,000ng/mL was reported in a case of intentional intravenous administration. In this study, the xylazine concentrations in cases where opioids were detected are low compared to the reported concentrations in fatal cases, but the potential combined effects cannot be ignored. Reported adverse effects of xylazine include obtundedness, bradycardia, cardiac arrhythmias, and respiratory depression. Therefore, when combined with other central nervous system depressants such as fentanyl or heroin, xylazine may increase risk of overdose in otherwise opioid-tolerant individuals.

Xylazine, Opioids, Fentalogs

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