Presented at the North American Congress of Clinical Toxicology 2024 – Denver, Colorado

Published in Clinical Toxicology 2024;62:23

47. Bromazolam blood concentrations in patients presenting to the emergency department after an opioid or stimulant overdose

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Background: Bromazolam is a psychoactive benzodiazepine that was first detected in the United States in 2019 and has since been increasingly detected among antemortem and postmortem toxicological samples, with a thirteen-fold increase noted between 2021 and 2022. Despite its increased detection, limited research has been conducted on bromazolam in patients experiencing severe or life- threatening opioid or stimulant overdose. This analysis aims to examine the prevalence and geographical distribution of patients with confirmed bromazolam exposures who present with a severe or life-threatening opioid or stimulant overdose to emergency departments (EDs). Secondary objectives are to examine bromazolam blood concentration levels, concurrent drug exposures, and to compare patients' self-reported drug use with confirmed toxicology results for those with bromazolam.

Methods: The Toxicology Investigator's Consortium (ToxIC) Drug Overdose Toxico-Surveillance (DOTS) reporting program (Food and Drug Administration Contract #75F40122D00028/75F40123F19002) is an ongoing multicenter project that prospectively collects data on patients presenting with a severe/life-threatening opioid or stimulant overdose to one of 17 participating EDs across the United States. DOTS consists of data collected from direct subject interviews, medical record reviews, and toxicological analysis of blood samples using liquid chromatography tandem quadrupole mass spectrometry. Only patients with confirmed bromazolam exposures were included in this study. Descriptive statistics were computed to assess the prevalence of bromazolam, concurrent drug exposures, and patient-reported characteristics. Central/site IRBs have approved this study, and patients provided informed consent.

Results: Among 293 patients with laboratory analyses (N 1⁄4 285 with completed records), 20 patients had confirmed bromazolam exposures (7%). The majority were male (75%) and Black (75%), and the average age was 50 years old. To date, bromazolam has been detected in 9 of 17 surveillance sites across the country: Baltimore (35.0%), Iowa City (5.0%), Jackson (5.0%), Minneapolis (5.0%), Philadelphia (5.0%), Pittsburgh (20.0%), Portland (5.0%), San Francisco (5.0%), and St. Louis (15.0%). Among the 16 cases with bromazolam above the level of quantitation (5ng/mL), the median detected bromazolam level was 50.0ng/mL (range: 14– 310 ng/mL). Fentanyl was detected in 17 of 20 patients with any bromazolam, with fentanyl concentrations above 1ng/mL in 12 patients. The median fentanyl concentration in these patients was 6.8ng/mL (range 1⁄41.4–17.0). In 75% of cases (n 1⁄415), the patient believed they had utilized an opioid leading to the over- dose, while only two (10%) believed they had

taken alprazolam, and none reported using bromazolam. Nineteen out of the 20 patients (95%) also had stimulants detected.

Conclusion: In our cohort of patients presenting with severe/ life-threatening opioid or stimulant overdoses, bromazolam was confirmed in 20 out of 293 patients. Bromazolam was detected across multiple sites in the U.S., with most cases presenting in Baltimore and the Northeastern U.S. Only 10% of patients in our study reported taking alprazolam, for which bromazolam may be substituted in counterfeit sources. Future analyses are planned to examine clinical outcomes associated with benzodiazepines such as bromazolam in the context of polydrug overdoses.