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60. Additional morbidity of co- exposure to novel psychoactive benzodiazepines in Emergency Department patients with confirmed opioid overdose

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Objective: Although prescription and novel psychoactive sub- stances (NPS) classified as benzodiazepines are structurally simi- lar, NPS benzodiazepines can have different pharmacological characteristics. Additionally, NPS benzodiazepines may have potent clinical side effects [1]. The objectives of this analysis in emergency department patients with confirmed opioid overdose, were to examine the association with adverse clinical effects for NPS benzodiazepines compared to 1) prescription benzodiaze- pines and 2) all patients without NPS benzodiazepines.

Methods: The Toxicology Investigators Consortium (ToxIC) Fentalog Study is an ongoing prospective multicenter cohort study consisting of 9 medical centers across the US. Patients are enrolled if they present with acute suspected opioid overdose. Clinical data are obtained via chart review and blood samples are collected for qualitative toxicological analysis using liquid chromatography quadrupole time-of-flight mass spectrometry for the presence of over 1100 psychoactive substances. Laboratory analyses are performed by the Center for Forensic Science Research and Education. Adverse clinical effects included death, intubation, naloxone requirements, and neurological effects. Neurological effects included the presence of agitation, cerebral hemorrhage, coma/central nervous system depression, delirium, dystonia, hallucinations, hyperreflexia, hypoxic or anoxic brain injury, seizures, and/or slurred speech. Bivariate statistical tests were conducted for each comparison (chi square tests for categorical variables and Mann-Whitney U Tests for continuous variables). All analyses were conducted in R 4.2.2 and approved by a central institutional review board (IRB) (WIRB).

Results: Between 21 September 2020 and 13 May 2023, 1541 patients met the inclusion criteria, and 1266 cases had blood analytes. A total of 113 patients (8.9%) had at least one NPS benzodiazepine. The most common NPS benzodiazepines (N 1⁄4 113) were bromazolam

(40.7%), clonazolam (38.9%), etizolam (19.5%), and flubromazepam (15.0%). NPS benzodiazepine over- doses were significantly more likely to have neurological effects within 4h of hospital presentation (77.0%) compared to neuro- logical effects among those without NPS benzodiazepines (55.2%; p 1⁄4 0.008). Furthermore, NPS benzodiazepines were also more likely to result in adverse neurological effects within 4 h of hospital presentation compared to prescription benzodiazepines (77.0% versus 63.4%; $p < 0.001$).

Conclusion: Neurological effects were much more likely in patients testing positive for NPS benzodiazepines among patients presenting after acute opioid overdose to emergency departments.