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Clonazepam and Fentanyl: What's in Your Local Drug Supply?

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On behalf of the ToxICFentalog Study Group

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Background

The fourth wave of the opioid epidemic is described as fentanyl PLUS many other substances, including designer benzodiazepines such as clonazepam, which is an analogue of clonazepam and a potent GABAA agonist. Co-exposure of designer benzodiazepines with illicit opioids may confound antidotal treatment, delay therapeutic response, and in the long term, lead to addiction and withdrawal. We report a regional clonazepam outbreak in ED patients with illicit opioid overdose.

Methods

This is a case series from the Toxicology Investigators Consortium (ToxIC) Fentalog study group, an ongoing cohort study at nine sites located across the United States. Consecutive adult ED patients from 5 participating facilities who presented following a suspected acute opioid overdose were screened for enrollment, which included comprehensive toxicological testing. Waste clinical specimens were analyzed via liquid chromatography quadrupole time-of-flight mass spectrometry for the presence of over 900 psychoactive substances and their metabolites. Cases with clonazepam identified in biologic samples were included in this series, and medical records review was performed.

Results

In patients evaluated between 10/6/20–3/9/21, out of 141 samples taken from presumed opioid overdoses from 5 clinical sites encompassing 4 states (Missouri, Oregon, New York, and Pennsylvania), 11 blood samples detected the presence of clonazepam. Of these 11 patients, 8 (72.7%) were positive in Pennsylvania, 2 (18.2%) in Missouri, and 1 (9.1%) in Oregon. All ranged between ages 18–65 (mean age = 37) and the majority occurred in men (N = 8, 72.7%). Age, sex and geographic location are reported in Table 1. Current sedative/hypnotic use (use < 30 days prior) was reported in 1 (9.1%) and unknown use history in the other 10 (90.9%). Confirmed opioid analytes found in clinical specimens are listed in Table 1. Naloxone was given in 9 (81.8%) and the response after treatment with the first dose was known in 7 of these cases. Out of these 7 patients, no response with first dose was noted in 4 (57.1%), and improved level of consciousness was noted in 2 (28.6%). There were no deaths.

CLONAZOLAM DETECTED IN

11 of 141

BLOOD SAMPLES

Conclusion

This case series confirms an ongoing clonazepam outbreak. Clinicians should recognize that illicit opioid overdoses may not fully respond to naloxone due to the presence of designer benzodiazepines.

TABLE 1

OVERDOSES CONTAINING CLONAZOLAM			
AGE	SEX*	LOCATION	OPIOID ANALYTES DETECTED
31	M	Pennsylvania	Methadone
47	F	Pennsylvania	Methadone
39	F	Pennsylvania	None
42	M	Pennsylvania	Methadone, Trazodone
57	M	Pennsylvania	Methadone
27	M	Pennsylvania	Methadone, Heroin, Para-Fluorofentanyl, Acetyl Fentanyl
37	M	Oregon	Heroin, Codeine
32	F	Pennsylvania	Methadone
35	M	Pennsylvania	Fentanyl
27	M	Missouri	Fentanyl, Para-Fluorofentanyl
36	M	Missouri	Bromphine, Fentanyl

*M = male, F = female