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## 51. Clonazepam and fentanyl: what's in your local drug supply?

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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) Fentanyl 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%). Current sedative/hypnotic use (use < 30 days prior) was reported in 1 (9.1%) and unknown use history in the other 10 (90.9%). 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.

**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.