

#### **46. Fentanyl and norfentanyl blood concentrations among severe/life-threatening opioid overdose patients stratified by self-reported opioid use patterns**

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**Background:** Fentanyl overdoses often include concomitant exposures to stimulants and other drugs. Interpretation of fentanyl concentrations following these polydrug overdoses can be challenging due to differences in opioid amounts consumed, timing since the overdose, and post-mortem redistribution. Previously reported fentanyl concentrations were frequently obtained following therapeutic applications or from postmortem samples. This study aims to describe fentanyl and norfentanyl concentrations stratified by self-reported opioid use patterns and examine fentanyl concentrations stratified by norfentanyl concentrations among patients presenting to emergency departments (EDs).

**Methods:** The Toxicology Investigators Consortium (ToxIC) Drug Overdose Toxicology Surveillance (DOTS) Reporting Program (Food and Drug Administration (FDA) Contract #75F40122D00028/ 75F40123F19002) enrolls patients ages 13 years and older following a severe/life-threatening opioid or stimulant overdose presenting to one of 17 U.S. EDs. Patient characteristics, clinical information, and quantitative blood drug concentrations are assessed. This analysis consists of patients enrolled from April 2023 to March 2024 who had detectable fentanyl and/or norfentanyl blood concentrations determined by liquid chromatography tandem quadrupole mass spectrometry. Fentanyl concentrations were stratified by the frequency of self-reported opioid use within the previous 30 days (categorized into “everyday use” and “less than everyday use”). Additionally, fentanyl concentrations were stratified by time of ED presentation to blood collection and norfentanyl concentration ranges: none, <1.00ng/mL, 1.00–9.00ng/mL, and >9.00ng/mL. Central/site IRBs approved this project, and patients provided informed consent.

**Results:** Among 293 patients with completed laboratory results, 226 patients had any fentanyl detected; 78.8% patients had fentanyl levels >1 ng/mL. Norfentanyl was detected in 206; 68.4% had norfentanyl levels >1 ng/mL. Among patients with both fentanyl >1 ng/mL and detectable norfentanyl concentrations (n = 174), the average age was 43 years (IQR 1/423) and 79% were male. In these patients, mean fentanyl concentrations were calculated based on the following norfentanyl concentration ranges: 2.25ng/mL (no norfentanyl), 3.00 ng/mL (<1 ng/mL norfentanyl), 4.95 ng/mL (1.00–9.00 ng/mL norfentanyl), and 17.00 ng/mL (>9.01 ng/mL norfentanyl). Among those who

completed interview questions on the overdose drug (n 1/4 201), 122 (60.7%) had fentanyl levels >1 ng/mL and 89 (44.3%) had detectable norfentanyl levels. For those who reported everyday use (with blood samples obtained <6hours from ED visit), the median fentanyl and norfentanyl concentrations were 8.70 and 3.20ng/mL, respectively. Among those with less than everyday use, the median fentanyl and norfentanyl concentrations were 4.50 and 2.30 ng/mL, respectively. Fentanyl/norfentanyl ratios were similar between groups (2.44 for everyday use and 2.47 for less than everyday use).

**Conclusion:** To our knowledge, these preliminary data are the first to report fentanyl and norfentanyl concentrations following severe/life-threatening overdose within the context of the patient's opioid use history. From descriptive analyses, higher fentanyl concentrations correspond to higher norfentanyl concentrations, and patients reporting everyday opioid use have higher fentanyl and norfentanyl concentrations overall compared to those with less than everyday use. Examining concentrations of fentanyl and nor- fentanyl based on patients' opioid use patterns may help better understand opioid tolerance, which is important in understanding the contribution of opioids to polydrug overdoses.