H72 Postmortem Distribution and Detection of Butyryl Fentanyl

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After attending this presentation, attendees will have a better understanding of butyryl fentanyl analysis and postmortem concentrations.

This presentation will impact the forensic science community by providing medical examiners and toxicologists with information concerning an analytical method and postmortem concentrations for butyryl fentanyl.

Butyryl fentanyl (N-phenyl-N-[1-(2-phenylethyl)-4-piperidinyl]-butanamide, monohydrochloride) is a potent synthetic fentanyl analog with lower affinity for the μ-opioid receptor than fentanyl. While fentanyl is 54 times more potent than morphine, butyryl fentanyl remains at least seven times more potent than morphine. Butyryl fentanyl is not currently a scheduled drug under the Controlled Substances Act but may be considered a "controlled substance analog" due to its structural similarity to fentanyl. Neither fentanyl nor butyryl fentanyl is metabolized to the other and they are separate chemicals. Fentanyl analogs are increasingly more common, including acetyl fentanyl, which has been implicated in intoxication deaths nationwide. Butyryl fentanyl represents an emerging fentanyl analog relatively new to the United States and the Drug Enforcement Administration (DEA) reports that no cases have been identified in the Baltimore area prior to the one reported in this abstract and only four cases have been reported over the last several years in the United States. The State of Maryland Office of the Chief Medical Examiner (OCME) recently identified butyryl fentanyl in an inspection performed on June 25, 2015, of an overdose death where the cause of death was mixed drug (fentanyl, butyryl fentanyl, morphine, and alprazolam) intoxication and the manner of death was accident. The decedent was a 47-year-old White female found unresponsive by her son at home on June 22, 2015, at 3:15 a.m. She had a past medical history of lupus, high blood pressure, hepatitis C infection, hepatocellular carcinoma, gastrointestinal hemorrhage, and chronic back pain. Reportedly, she had not seen a physician in more than six months and would obtain drugs off the street for her pain control. An admission hospital urine drug screen on June 22, 2015, at 4:48 a.m. was positive for benzodiazepines and opiates and confirmation testing of the urine revealed an alpha-hydroxyalprazolam concentration of 870ng/mL and a morphine concentration of 2,400ng/mL. She spent three days in the intensive care unit at the hospital before being declared brain dead.

Butyryl fentanyl was identified at the OCME in an alkaline drug screen, which involved an alkaline liquid-liquid extraction of specimens followed by detection with Gas Chromatography — nitrogen-phosphorus detection and confirmation by gas chromatography — Mass Spectrometry (GC/MS). Butyryl fentanyl eluted after fentanyl on an HP-5 column and prominent GC/MS ions were 259, 189, and 146. Quantitation of butyryl fentanyl was performed using solid phase extraction followed by GC/MS. Briefly, internal standard (d5-fentanyl) was added to 1.0mL case specimen which was mixed with 2mL deionized water and 2mL of phosphate buffer (100mM, pH 6.0), centrifuged, and applied to conditioned CEREX® Trace-B columns. The columns were then washed with deionized water, 100mM acetic acid, and methanol and dried for five minutes at 50psi. Analytes were eluted with 3mL of 78:20:2 methylene chloride:isopropanol:ammonium hydroxide. Eluents were evaporated to dryness, reconstituted in 50μL ethyl acetate, and injected into the GC/MS. The GC/MS was operated in the selected ion monitoring mode, monitoring 259 (quantitation ion), 189, and 146 for butyryl fentanyl and 250 (quantitation ion) and 194 for d5-fentanyl. The limit of quantitation was administratively set at 5.0ng/mL and the method was linear to 400ng/mL. Butyryl fentanyl concentrations (ng/mL) in the case specimens are summarized below.

Postmortem Heart Blood	34
Postmortem Subclavian Blood	26
Postmortem Vitreous Humor	13
Antemortem Hospital Blood	40 (6/22/15 @ 04:45) & 32 (6/22/15 @ 20:20)

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Additional toxicology findings in this case	Postmortem Heart blood: Diphenhydramine: 700ng/mL Promethazine: 70ng/mL Fentanyl < 5ng/mL Alprazolam: < 25ng/mL Antemortem Hospital Blood: Free Morphine: <10ng/mL (6/22/15 @ 04:45)

Butyryl fentanyl is less potent than fentanyl and its concentrations were noted to be higher than typical fentanyl intoxications, but lower than the acetyl fentanyl intoxications investigated by the Maryland OCME. In addition, the postmortem blood concentrations are likely affected by the three-day interval between drug use and death in this case. This is the first reported case of butyryl fentanyl intoxication in the State of Maryland. The rarity of this new analog emphasizes the importance of recognizing emerging new drugs in postmortem toxicologic analysis.

Butyryl Fentanyl, Fentanyl, Toxicology

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