K26 Postmortem Distribution of Acetyl Fentanyl

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After attending this presentation, attendees will have a better understanding of the analysis of biological specimens for acetyl fentanyl and the postmortem distribution of acetyl fentanyl.

This presentation will impact the forensic science community by providing medical examiners and toxicologists with an analytical method and postmortem concentrations for acetyl fentanyl, a relatively new drug of abuse in the United States.

Acetyl fentanyl (*N*-(1-phenethylpiperidin-4-yl)-*N*-phenylacetamide) is a potent synthetic opioid with structural similarity to fentanyl. Animal studies have estimated acetyl fentanyl to be about one-third as potent as fentanyl.[1] Acetyl fentanyl has recently gained public attention when it was linked to 12 fatal overdoses in Rhode Island.[2]

The Office of the chief Medical Examiner of the State of Maryland has investigated three deaths related to acetyl fentanyl use. The cause and manner of death was acetyl fentanyl intoxication/undetermined for each of the three following cases.

Case 1: A 23-year-old White male college student was found unresponsive on his bedroom floor. He had attended a banquet the night before, visited a few bars, then returned home where he watched television with a friend for several hours before going to bed. The friend found him later the next day and he was pronounced deceased at the scene. The decedent's bedroom contained pills, powders, and drug paraphernalia. It was reported that the decedent had a history of drug abuse and had been in rehab approximately one year prior.

Case 2: A 36-year-old African American male was found lying on the floor with vomit and blood on the carpet next to him. He was reportedly visiting with friends and had used cocaine with them. It was also reported that he may have used heroin. He was transported to the hospital where resuscitation attempts were unsuccessful. The decedent did have prior arrests for possession of a controlled substance.

Case 3: A 17-year-old Hispanic male was at a friend's house. He was reportedly offered a powder that another individual was snorting. Soon after, the decedent became unresponsive. Treatment with Narcan™ and resuscitative efforts were unsuccessful.

Acetyl fentanyl was identified in an alkaline drug screen, which involved an alkaline extraction of specimens followed by detection with Gas Chromatography/Nitrogen Phosphorous Detection (GC/NPD) and confirmation by Gas Chromatography/Mass Spectrometry (GC/MS). Acetyl fentanyl elutes shortly before fentanyl on an HP-5 column and prominent GC/MS ions are 231, 146, and 188. Further evaluation of the standard liquid-liquid alkaline extraction screening procedure in use in the laboratory indicated adequate sensitivity for the detection of acetyl fentanyl, which was detected at concentrations less than 5ng/mL. Subsequently, a quantitation method was developed for acetyl fentanyl. Briefly, internal standard (d5-fentanyl) was added to specimens which were alkalinized and extracted with n-butyl chloride:ether then back extracted into sulfuric acid and finally alkalinized and extracted into methylene chloride, evaporated and reconstituted with methanol. The extract was injected into the GC/MS which was operated in the selected ion monitoring mode. The ions monitored included 231, 146, 188 (acetyl fentanyl) and 250, and 194 (d5-fentanyl). The method was linear from 25ng/mL to 800ng/mL. Case specimens with concentrations above 800ng/mL were diluted with distilled water to ensure the results were within the calibration curve. The results (ng/mL or ng/g) are summarized below.

Case	Heart Blood	Femoral Blood	Liver	Kidney	Urine	Vitreous Humor	Additional Toxicology Findings
1	700	460	1800	1200	1600	500	Urine: alpha-pyrrolidinovalerophenone positive
2	180	180	180	250	380	160	Blood Benzoylecgonine 1.3 mg/L
3	500	430	430	220	1500	350	None

Acetyl fentanyl was detected at much higher concentrations relative to what is typically seen for fentanyl intoxications, which is consistent with its lower potency relative to fentanyl. Although there were some differences between heart blood and femoral blood concentrations, the greatest difference was seen in the case with the highest concentration, and the heart blood concentration was within 35% of the femoral blood concentration. The liver and vitreous humor concentrations were close to the blood concentrations. Urine also contained a higher concentration of acetyl fentanyl relative to blood, making it a suitable specimen to screen for acetyl fentanyl use.

References:

1. Higashikawa, Y, Suzuki, S. Studies on 1-(2-phenethyl)-4-(N-propioylanilino) piperidine (fentanyl) and its related componds. VI. Structure-analgesic activity relationship for fentanyl, methyl-substituted fentanyls and other analogues. *Forensic Toxicol* (2008) 26:1-5
2. Acetyl Fentanyl Overdose Fatalities - Rhode Island, March–May 2013. *Centers for Disease Control and Prevention Morbidity and Mortality Weekly Report*, **August 30, 2013, 62(34); 703-704.**

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