H67 Emerging Trends: Deaths Associated With the Novel Synthetic Opioid U-47700 at the Tarrant County Medical Examiner's Office in Fort Worth, Texas

Tasha Zemrus Greenberg, MD, Tarrant County MEO, 200 Feliks Gwozdz Place, Fort Worth, TX 76104-4919; Barrie Miller, MD, Tarrant County Medical Examiner, 200 Feliks Gwozdz Place, Fort Worth, TX 76104; Richard C. Fries, DO, 200 Feliks Gwozdz Place, Fort Worth, TX 76104; Chris Heartsill, BS, Tarrant County Medical Examiner's Office, 200 Feliks Gwozdz Place, Fort Worth, TX 76104; and Robert D. Johnson, PhD, Tarrant County MEO, 200 Feliks Gwozdz Place, Fort Worth, TX 76104*

After attending this presentation, attendees will better understand the increasing trend in opioid deaths in the United States and specifically the presence of synthetic opioid analogs in forensic practices.

This presentation will impact the forensic science community by aiding public health agencies and law enforcement in addressing outbreaks of drug overdoses.

The Centers for Disease Control and Prevention reported in the January 1, 2016, Morbidity and Mortality Weekly Report that there was a 200% increase in the rate of opioid overdose deaths since 2000.[1] In addition, this Report notes that the age-adjusted rate of death from synthetic opioids other than methadone increased 80% from 2013-2014. There are many different synthetic opioids available on the internet, sold for research purposes, not for human consumption. These drugs may not readily be identified in forensic laboratories, as they are not on many general drug screens. This was the case in the laboratory at the Tarrant County Medical Examiner's Office (TCME) in Fort Worth, TX until 2016, when the standard for the synthetic opioid U-47700 was obtained from Cayman Chemicals and incorporated into the drug-testing library.

In 2016 at the TCME, there have been three cases in which the synthetic opioid U-47700 was identified. In two of those cases, the cause of death was associated with use of the drug. In the third case, the circumstances of death are still under investigation and further information is not available at this time. In all cases, initial enzyme-linked immunosorbent assay screening was negative for opioids.

The first case was a 38-year-old found unresponsive in the living room. He had a history of seizures, anxiety, and testicular cancer with hypofunction. Autopsy revealed pulmonary congestion and edema, mild cerebral edema, cardiomegaly, and moderate coronary atherosclerosis. A plastic bag containing white powder was found at the scene, reportedly field test positive for cocaine. This substance was analyzed in the forensic chemistry laboratory and was identified as U-47700. Toxicology testing on the decedent was positive for U-47700 in the femoral blood and urine by Gas Chromatography/Mass Spectrometry (GC/MS), as well as Tetrahydrocannabinol (THC) and ibuprofen in urine and alprazolam, 7 aminoclonazepam, and gabapentin in femoral blood. The cause of death was ruled as sudden death associated with synthetic opioid use with cardiomegaly as a significant contributory condition.

The second case was a 30-year-old male with a history of intravenous drug use and hepatitis C, found unresponsive at a friend's home. He was transported to the hospital and expired the next day. Hospital toxicology screen was reported positive for U-47700, THC, and amphetamine. Autopsy revealed pulmonary congestion and edema, cerebral edema with herniation, and moderate coronary atherosclerosis. At the scene, police found two syringes, a spoon with residue, and a plastic bag containing white powder reportedly labeled U-47700 that were brought to the forensic laboratory at the TCME for testing. The spoon tested positive for heroin while one syringe and the powder tested positive for U-47700. Hospital blood samples were tested by GC/MS and were positive for

norfentanyl and U-47700. The cause of death was ruled sudden adult death associated with synthetic opioid use (U-47700) with coronary artery disease a significant contributory condition.

U-47700 (3,4-dichloro-N-[2-(dimethylamino)cyclohexyl]-N-methylbenzamide), is a non-prescription synthetic opioid derived from AH-7921. AH-7921 was synthesized in the 1970s by Allen and Hanburys Ltd. as a potential analgesic medicine; however, development was abandoned due to addictive properties. In animals, it has m opioid receptor agonistic activities, though studies have not been performed in humans with activities similar to those of morphine, including analgesia, hypothermia, respiratory depression, and addictive behavior. U-47700 was synthesized from AH-7921 in the 1970s by Upjohn Laboratories and is currently marketed as a research chemical, not for human consumption. Due to structural similarity, the properties are assumed to be similar. Animal studies show a potency of approximately 7.5 times that of morphine. Recently, there have been a few cases of acute intoxication associated with death reported in the literature, one due to the combined use of fentanyl and U-47700. There are no established reference ranges for this drug.

In summary, there is a growing problem of synthetic opioid use in the United States that can be associated with death. It is important for forensic pathologists to consider this in the setting of an apparent opioid death, even with a negative general opiate screen.

Reference(s):

1. Rudd R.A., Aleshire N., Zibbell J.E., Gladden R.M. *Increases in Drug and Opioid Overdose Deaths – United States, 2000-20014.* Morbidity and Mortality Weekly Report. 2016:64(50).

U-47700, Synthetic Opioid, Opioid Overdose