K69 A Case of Death by Diclazepam: Lorazepam in Disguise

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After attending this presentation, attendees will be informed regarding the metabolism and toxicity of diclazepam, a potent designer benzodiazepine not approved for medicinal use. In the past few years, new types of benzodiazepines have emerged for recreational use through online portals. These selections often include phenazepam, pyrazolam, etizolam, and diclazepam, among other offerings. Currently, there are no other reports of illicit diclazepam use or cases of fatal toxicity.

This presentation will impact the forensic science community by exploring the first report of a death involving the toxic effects of diclazepam and its associated metabolites.

Diclazepam (2-chlorodiazepam) is a functional analog of diazepam, which has been alleged by recreational users to have a ten-fold higher potency. Diclazepam powder and 1mg or 2mg compressed tablets are sold online as "research chemicals not for human consumption." Based on published data obtained from a human study, diclazepam has an average elimination half-life of 42 hours and metabolizes into several pharmacologically active benzodiazepines, namely delorazepam, lorazepam, and lormetazepam, which can be detected in urine for 6, 19, and 11 days, respectively.

This study reports the death of a healthy 27-year-old man who was discovered unresponsive at home by a friend. The decedent was observed to have a prominent white foam cone coming from his mouth and blood-tinged white foamy fluid coming from his nostrils. Several alcohol bottles, a jar of greenish-brown powder labeled "Mitragayna Speciosa," and a cup of greenish-brown powder-filled capsules were discovered at the scene. No other prescription, over-the-counter medication, or illicit drugs were noted. The decedent reportedly was a strong believer in the use of herbal medicine.

Autopsy findings were significant for pulmonary edema and congestion, white frothy fluid within the airways, brown-yellow granular gastric contents, urinary retention, and cerebral edema. Comprehensive forensic toxicology testing revealed the following: negative blood alcohol screen and a positive Enzyme-Linked Immuno-Sorbent Assay (ELISA) blood screen for benzodiazepines. Quantitation of benzodiazepines by Liquid Chromatography/Tandem Mass Spectrometry (LC/MS/MS) revealed 0.62mg/L and 0.44mg/L lorazepam in the blood and stomach contents, respectively. Additional drug screening by Gas Chromatography/Mass Spectrometry (GC/MS) was performed and found the presence of delorazepam and mitragynine in the blood and stomach contents. A breakdown product of lorazepam was also identified in both the blood and stomach contents, which is the result of thermal decomposition of lorazepam in the process of GC. The absence of prescription history for lorazepam and the positive identification of delorazepam in the postmortem samples triggered further investigation to elucidate the parent drug and other possible metabolites. The blood sample screened by Liquid Chromatography/Time-Of-Flight/Mass Spectrometry LC/TOF/MS revealed the presence of the parent drug diclazepam, as well as the active metabolites delorazepam, lorazepam, and lormetazepam in addition to ritalinic acid and mitragynine. The quantitation result of ritalinic acid by LC/MS/MS is 0.11mg/L in the blood. Quantitation of mitragynine was not pursued, because pharmacokinetic data from human study characterizing the toxic and lethal levels of mitragynine is not available. Since mitragynine has opioid activity, its presence with other sedatives is considered as contributory to the effect of sedation. Analysis by the Harris County Institute of Forensic Sciences (HCIFS) Drug Chemistry Laboratory on one of the capsules obtained from the scene revealed the presence of mitragynine, but no trace of diclazepam or any other substance.

Based upon the autopsy findings and toxicology results, the forensic pathologist classified the manner of death as accidental, with the cause considering the contributions of lorazepam and the other upstream benzodiazepine derivatives in combination with mitragynine. This is a prime example of a postmortem toxicology case whereby an extensive analytical workup utilizing sophisticated instrumentation played a paramount role in aiding the pathologist in the determination of the cause and manner of death when scene information yielded few clues about the origins of the toxic substances involved.

Diclazepam, Mitragynine, LC/MS/TOF

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