K11 A Two-Month Stability and Distribution Study of the Benzodiazepine Phenazepam

Tracy Gastineau, BS, Department of Forensic Science, Sam Houston State University, 1003 Bowers Boulevard, Huntsville, TX 77341; Justin Schwane, MS, Southwestern Institute of Forensic Sciences, 2355 N Stemmons Freeway, Dallas, TX 75207; and Elizabeth L. Todd, PhD, Southwestern Institute of Forensic Sciences, 2355 N Stemmons Freeway, Dallas, TX 75207-2703*

After attending this presentation, attendees will better understand the extent to which 7-bromo-5-(2-chlorophenyl)-1,3-dihydro-2H-1,4-benzodiazepin-2-one (phenazepam) undergoes postmortem redistribution and its stability in blood and urine.

This presentation will impact the forensic science community by raising awareness concerning phenazepam distribution, stability, and the subsequent interpretation of toxicological results. As this drug is emerging as a controlled drug in Europe and a drug of concern in the United States, laboratories need to be aware of the concentration among biological specimens that can be encountered. Also, the stability study will aid in accounting for postmortem redistribution and putrefaction of the drug.

Outside of the United States, phenazepam has been prescribed as an anxiolytic, anticonvulsant, and sedative since its development in Russia in the 1970s. Compared to other 1,4-benzodiazepines, it is more potent and longer lasting with a half-life up to 60 hours. It has been recently controlled in parts of Europe and, although it has been declared a drug of concern in the United States, only a very small number of states have controlled its use.[1] Pharmacological studies on phenazepam are extremely limited and little is understood regarding its distribution in postmortem samples. In this study, the postmortem distribution of phenazepam is reported in a series of ten toxicology cases. Stability issues will also be addressed in blood and urine.

The distribution of phenazepam in postmortem femoral, subclavian and central blood, antemortem blood, urine, vitreous humor, and skeletal muscle was determined using liquid-liquid extraction and liquid chromatography-tandem mass spectrometry. The concentration ranges were as follows: 0.010-0.272mg/L for femoral blood; 0.024-0.171mg/L for subclavian blood; 0.202mg/L for antemortem blood; 0.067mg/L for chest blood; 0.001-0.030mg/L for urine; 0.001-0.016mg/L for vitreous humor; and 0.023-0.522mg/kg for skeletal muscle. Highest concentrations of phenazepam were observed in the skeletal muscle and the lowest concentrations were in the vitreous humor. Highest blood concentrations were seen in antemortem blood which were 6-10 times greater than urine and vitreous humor.

For the stability study, drug-free whole blood and urine were fortified with phenazepam (0.25mg/L) and stored at room temperature (20°C) and refrigerated (4°C) for two months. Samples were extracted at day 0, 1, 3, 7, and then weekly for the remainder of the two-month study. There was very little change in concentration over two months. Days 7 and 35 marked significant points in the concentration trend. On day 7, there was an overall decrease in concentration, and after day 35, there was an increase in concentration over all the fluids except blood at room temperature. There was a noticeable concentration variation between the specimens after day 35. However, at day 56, all the fluids had a concentration within 10% of each other. From the original day 0 concentration, the decrease in concentration ranged from 16-30%.

Reference:

1. Maskell PD, De Paoli G, Seetohul LN, Pounder DJ. Phenazepam: The drug that came in from the cold, J Forensic Leg Med. 2012;19:122-5.

Phenazepam, Stability, Distribution

 ** Presenting Author*