H136 Multi-Site Aspects of Postmortem Redistribution (PMR) and Their Combination With Pathological Findings to Determine Cause of Death (COD) in Suspected Diazepam, Methadone, and Morphine Drug-Related Cases

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After attending this presentation, attendees will understand: (1) that blood as well as other sampling sites (i.e., gastric contents and liver parenchyma) may all contribute to variations of drug blood concentration after death to some degree; and, (2) their combination with pathological findings is required in suspected drug-related deaths.

This presentation will impact the forensic science community by demonstrating that a multi-site approach of PMR in combination with pathological findings is useful in assessing the COD in selected drug-related cases.

There were 24 autopsied cases, sampled as follows: Intracardiac Blood (ICB), Subclavian Blood (SCB), Femoral Blood (FB), Popliteal Blood (PB), Gastric Contents (GC), and Liver Parenchyma (LP). PB was sampled after dissection and clamping of the popliteal vein because of its deep localization in the popliteal fossa, whereas LP was always sampled in the middle part of the liver. Selected substances (diazepam, methadone, and morphine) were sampled in all sites, whereas a complete drug screening was concomitantly performed on FB. GC and LP were homogenized before analysis; LP was also treated with subtilisin. For all sampling sites, morphine and methadone samples were prepared with solid phase extraction and quantified with Ultra Performance Liquid Chromatography-Tandem Mass Spectrometry (UPLC-MS/MS); diazepam was quantified with High-Performance Liquid Chromatography- Diode Array Detection (HPLC-DAD) after liquid-liquid extraction.

To assess PMR of selected substances, mean concentrations ratios were calculated as follows: ICB/SCB, ICB/FB, ICB/PB, SCB/FB, SCB/PB, and FB/PB. To assess the influence of other sampling sites on PMR, LP/FB and LP/PB as well as the correlation between GC and LP concentrations and the blood mean concentrations were obtained in concerned cases. In addition, for all cases, pathological findings were summarized and compared to toxicological findings in order to determine COD.

Toxicological results indicate that popliteal site is less subject to PMR as suggested by mean concentrations ratios FB/PB (diazepam (N=3) mean ratio = 1.84; methadone (n=15) mean ratio = 1.44; morphine (n=14) mean ratio = 1.86); mean LP/FB and LP/PB ratios are also in accordance (diazepam (n=1): mean LP/FB = 0.05, mean LP/PB=0.07; methadone (n=13): mean LP/FB=26.96, mean LP/PB=36.59; morphine (n=4): mean LP/FB=5.34, mean LP/PB=9.09). Results also suggest that GC and LP concentrations may influence blood concentrations, as seen with the following significant positive correlations observed between methadone GC and ICB, SCB, FB and PB (n=14; r=0.62, r=0.59, r=0.57, r=0.58; $p < 0.05$), as well as between methadone LP and ICB (n=13, r=0.55, $p < 0.05$).

Pathological findings are mostly non-specific in 16 cases in which toxicological findings suggest obvious intoxication to one or more substance(s), and compatible with usual drug-related fatalities findings (pulmonary edema and alveolar hemorrhage (n=14), terminal subendocardial ischemia (n=10), acute hepatic congestion (n=7), acute renal tubular necrosis (n=7)). In four cases in which toxicological findings are equivocal, the non-specific pathological findings may be observed, but considering PB instead of FB concentrations for selected substances

may allow clarifying COD (e.g., case #5: methadone FB=240µg/L-PB=103µg/L; case #21: morphine FB=46µg/L-PB=17µg/L). In four cases, COD is natural according to both toxicological and pathological findings (disseminated intravascular coagulation (DIC) and sepsis (*n*=1), cardiovascular diseases (CVD's) (*n*=3)), but considering PB instead of FB concentrations still allows helping to determine COD (e.g., case #6: COD=CVD, morphine FB=30µg/L-PB=18µg/L; case #9: COD=DIC and sepsis, methadone FB=265µg/L-PB=123µg/L).

In conclusion, this study is the first to suggest a multi-site approach of the PMR of selected drugs, including popliteal blood sampling in combination with pathological findings, in order to establish COD in drug-related fatalities. These results illustrrate that popliteal vein blood sampling is less prone to PMR, that other sampling sites may significantly influence postmortem blood concentrations, but also that the interpretation of toxicological findings alone, especially with FB instead of PB concentrations, may lead to confusion in determining COD in such cases.

Postmortem Redistribution, Sampling Sites Popliteal Blood, Pathological Findings