Challenges in Interpretation of Postmortem Drug Levels

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Accurate interpretation of postmortem drug levels is a complex science that involves far more than just detection and quantitation of drugs. Given there are multiple physiologic variables in the postmortem context, the interpreter must be careful when correlating drug levels to toxic ranges provided in “standard” charts and tables. Additionally, accurate interpretation can necessitate communication with the clinician, especially in regards to the decedent's pharmacologic history, including prescription history, social habits, and even pharmacogenetic profile. The toxicologist must be cognizant of confounding factors like postmortem redistribution, drug interaction, and variations in host response.

The toxicologist receives several types of tissue for drug analysis including blood, urine, vitreous, bile, muscle, hair, nails, and other organs that most commonly include the liver. Blood is generally considered the most important of these because it is the usual mode of distribution of drugs and toxins and most accurately reflects the pharmacologic state of the person when he or she died. However, after anatomic functions cease the blood is subject to change. Postmortem redistribution refers to diffusion of fluids between body compartments after death. Pounder et al. demonstrated postmortem redistribution by instilling amitriptyline into the stomach of a cadaver and detecting the drug in adjacent tissue, such as lung and pericardial fluid, only 48 hours later.1 As a result of studies like this, it is standard practice to harvest blood for toxicology studies from the more peripherally located femoral or subclavian vessels. Since, in some cases, postmortem blood is difficult or impossible to obtain, it is prudent for health care personnel to take any available blood in the period preceding death.

The interaction of multiple substances used together can present an additional confounding factor. The presence of multiple substances causes interpretive challenges in that no one substance may be outside of its “therapeutic range.” The interpreter must take into account pharmacologic principles like synergism and additive effects.2 Alcohol is a common substance found concomitant with other drugs. The significance of the presence of alcohol is two-fold. First, alcohol can be deadly when used acutely in combination with other drugs due to exacerbation of CNS effects.3 Second, if the decedent was a chronic alcohol abuser, normal liver and kidney function could have been compromised, altering the normal metabolism and excretion of drugs. While signs of chronic alcohol abuse can be detected grossly and histologically, a thorough clinical and social history is certainly helpful in these cases.

Over the last several years, advances in genetics have introduced another factor for consideration in the interpretation of postmortem drug levels. Pharmacogenetics is the study of genetic differences that affect an individual’s response to certain drugs. Studies have shown many drugs to undergo different metabolisms as a result of genetic variations, particularly in the cytochrome p450 family of enzymes, which is responsible...
for phase 1 metabolism of many drugs. This can potentially result in adverse or toxic effects from drugs administered at therapeutic dosages. This not only emphasizes a further confounding factor in the interpretation of postmortem drug levels, but also emphasizes an additional consideration for clinicians when prescribing certain medications.

In some cases, both the toxicologist and clinician share equally vital roles in contributing important information about the decedent. It is only then that confounding factors can be sufficiently accounted for and postmortem drug levels most accurately interpreted.

References


