

## Postmortem Drug Redistribution

Iain M McIntyre\* and Christina Meyer Escott

County of San Diego Medical Examiner's Office, 5570 Overland Ave., Suite 101, San Diego, CA 92123, USA

Postmortem drug concentrations in blood may not always reflect antemortem drug concentrations in blood due to the movement of the drugs after death. The phenomenon is referred to as Postmortem Redistribution (PMR). Mechanisms involved in postmortem redistribution are both complicated and poorly understood. However, postmortem drug concentrations in blood do follow some generally accepted trends that aid with interpretation; the characteristics of the drug itself can be used to indicate if a drug is subject to PMR. Large changes in blood drug concentrations are predicted for basic, lipophilic drugs with a high volume of distribution (>3L/kg). When PMR occurs, blood specimens drawn from the central body cavity and heart generally will have higher drug concentrations postmortem than specimens drawn from peripheral areas, most commonly the femoral vein. The diffusion of drugs from organ tissue into the blood may explain the observed phenomenon [1]. To compensate for PMR, postmortem blood specimens are recommended to be collected from at least two areas of the body at autopsy; a peripheral area and a central area (often the heart), so that a comparison can be made. While antemortem blood specimens are especially helpful in interpreting postmortem blood drug concentrations, relevant specimens are only very rarely available. In a set of case studies of six drugs, drug concentrations in postmortem femoral blood specimens always exceeded the antemortem concentrations in five cases, suggesting that even peripheral blood may still exhibit some redistribution [2]. The study did not, however, report the postmortem interval been death and autopsy.

It appeared that a partial answer to the difficulties associated with interpretation of postmortem drug concentrations was provided by two papers published in the 1990s. The first provided detailed information about blood drug concentrations attained from different sites for over fifty drugs [3]. The second provided a tabular list of the drug concentrations from both cardiac and peripheral blood samples expressed as a ratio of cardiac to peripheral blood (C/P) for over one hundred drugs [4]. The C/P ratio became the accepted benchmark with the accepted guideline that "high ratios" were associated with "potential for redistribution" [4]. This guideline was repeated in a review published a few years later that republished the C/P ratios for many of the drugs included in the Dalpe-Scott and coworker's paper [5].

Limitations of the C/P model, however, have been noted. While drug properties such as volume of distribution, protein binding, and pKa are thought to contribute to PMR, a relationship between C/P and drug properties has not been established [6]. In addition, "there has been little agreement as to what ratio actually defines that a compound is prone to PMR, or not" [7]. Reports of a C/P ratio greater than 1.0 have been published for tramadol, which is not prone to redistribution [8]. Arterio-venous differences, anatomic variability within individuals, and statistical chance may result in a C/P ratio greater than 1.0 in drugs that do not redistribute. In addition, resuscitation attempts may result in a C/P ratio less than 1.0 [9]. Inaccurate ratios may also be obtained as an artifact of sampling when the cardiac blood volume is

depleted by the collection of blood from connected blood vessels, or in cases of acute overdose where the drug has not undergone complete distribution.

The liver to peripheral blood (L/P) ratio has been recently proposed as a marker for PMR, with ratios exceeding 20 indicative of a propensity for significant PMR, and ratios less than 5 indicating no propensity towards PMR [7]. Some scientists have already obtained and published liver data as auxiliary data to aid in the interpretation of cardiac and peripheral blood concentrations [10-14]. However, there has been no compilation for liver and peripheral blood data from the literature nor has there been a group that has published a large body of liver and peripheral blood data for reference.

A major advantage of this proposed model is the magnitude of the liver concentration compared to blood. This is in contrast to the conventional C/P ratios which are frequently not dissimilar among many compounds. Additionally, the previously established C/P ratios are often subjected to confounding interferences such as specimen contamination, overdose (incomplete distribution), and relatively few case numbers. These shortcomings often make the C/P ratio approach difficult to deduce a drugs' propensity for PMR.

Future directions for research to evaluate this potential model include a compilation of L/P ratios established from a single laboratory. The research should include drugs that have known propensity for PMR (including one or more tricyclic antidepressants and selective serotonin reuptake inhibitors), drugs without a known propensity for PMR (such as tramadol), as well as other drugs with suspected moderate PMR.

### References

1. Pounder DJ, Jones GR (1990) Post-mortem drug redistribution--A toxicological nightmare. *Forensic Sci Int* 45: 253-263.
2. Cook J, Braithwaite RA, Hale KA (2000) Estimating antemortem drug concentrations from postmortem blood samples: the influence of postmortem redistribution. *J Clin Pathol* 53: 282-285.
3. Prouty RW, Anderson WH (1990) The Forensic science implications of site and temporal influences on postmortem blood-drug concentrations. *J Forensic Sci* 35: 243-270.
4. Dalpe-Scott M, Degouffe M, Garbutt D, Drost M (1995) A Comparison of drug concentrations in postmortem cardiac and peripheral blood in 320 cases. *Journal of the Canadian Society of Forensic Sciences* 28: 113-121.

\*Corresponding author: Iain M McIntyre, County of San Diego Medical Examiner's Office, 5570 Overland Ave., Suite 101, San Diego, CA 92123, USA, E-mail: [Iain.McIntyre@sdcounty.ca.gov](mailto:Iain.McIntyre@sdcounty.ca.gov)

Received April 19, 2012; Accepted April 19, 2012; Published April 21, 2012

Citation: McIntyre IM, Meyer Escott C (2012) Postmortem Drug Redistribution. *J Forensic Res* 3:e108. doi:[10.4172/2157-7145.1000e108](https://doi.org/10.4172/2157-7145.1000e108)

Copyright: © 2012 McIntyre IM, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

5. Leiken JB, Watson WA (2003) Post-mortem toxicology: What the dead can and cannot tell us. *J Toxicol Clin Toxicol* 41: 47-56.
6. Ferner RE (2008) Post-mortem clinical pharmacology. *Br J Clin Pharmacol* 66: 430-443.
7. McIntyre IM, Sherrard J, Lucas J (2012) Postmortem carisoprodol and meprobamate concentrations in blood and liver: lack of significant redistribution. *J Anal Toxicol* 36: 177-181.
8. Moore KA, Cina SJ, Jones R, Selby DM, Levine B, et al. (1999) Tissue distribution of tramadol and metabolites in an overdose fatality. *Am J Forensic Med Pathol* 20: 98-100.
9. Pélessier-Alicot AL, Gaulier JM, Champsaur P, Marquet P (2003) Mechanisms underlying postmortem redistribution of drugs: A Review. *J Anal Toxicol* 27: 533-544.
10. Anderson D, Reed S, Lintemoot J, Kegler S, DeQuintana S, et al. (2006) A first look at duloxetine (Cymbalta) in a postmortem laboratory. *J Anal Toxicol* 30: 576-580.
11. Anderson DT, Fritz KL, Muto JJ (2002) Oxycontin: The concept of a "ghost pill" and the postmortem tissue distribution of oxycodone in 36 cases. *J Anal Toxicol* 26: 448-459.
12. Anderson DT, Fritz KL (2000) Quetiapine (Seroquel) concentrations in seven postmortem cases. *J Anal Toxicol* 24: 300-304.
13. Kirkton C, McIntyre IM (2006) Therapeutic and toxic concentrations of mirtazapine. *J Anal Toxicol* 30: 687-691.
14. Vance CS, McIntyre IM (2009) Postmortem tissue concentrations of olanzapine. *J Anal Toxicol* 33: 15-26.