15 - Interpreting postmortem blood concentrations

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Pharmacokinetics CHAPTER 11 Interpreting postmortem blood concentrations Much is known about the distribution of drugs in the body during life but relatively little about these same parameters after death. A great many drugs are subject to postmortem distribution changes but, for obvious practical reasons, research into the mechanisms and extent of these effects is very limited. The best that can be said is that a drug plasma concentration measured during life may be very different from the concentration measured at some time after death (usually in whole blood from the femoral artery). A number of processes are responsible for these changes. In life, active mechanisms serve to concentrate some drugs in certain organs or tissues. After death, passive diffusion occurs as cell membranes break down and this will mean that postmortem blood samples will, for some drugs, show higher concentrations than were seen during life. This is known as postmortem redistribution (PMR). In addition, central blood vessels surrounding major organs often demonstrate much higher drug concentrations than relatively distant peripheral samples.1 PMR and other processes are temperature- and time-dependent so time since death and conditions of storage are important determinants of blood concentration changes.2 PMR tends to be greater with drugs with a large volume of distribution (i.e. those for which tissue concentrations in life vastly exceed blood concentrations) especially when given over a long period during life. Other processes of importance3 include the postmortem synthesis of certain compounds. For example, the body is able to generate gamma-hydroxybutyrate. Trauma may allow the introduction of yeasts that metabolise glucose to alcohol. Another phenomenon is the degradation of drugs by bacteria (e.g. clonazepam and nitrazepam) or fungi. Also, the metabolism of some drugs (cocaine, for example) appears to continue after death (although this may be simple chemical instability of the parent compound). All of the processes described here contribute to an overall direction of change of concentration postmortem. Antidepressant concentrations tend to increase in postmortem samples whereas those of benzodiazepines invariably decrease.4 Mirtazapine concentrations also appear to decrease.5,6 Antipsychotic concentrations both increase and decrease depending on the drug.4

Thus, when an isolated postmortem concentration is considered (i.e. one which cannot be compared with a concentration measured in life), it can only be said that the in-life concentration would have been higher or lower.7 Table 11.3 lists some of the factors relevant to drug concentration changes after death and the possible consequences of these processes. Generally speaking, an isolated postmortem blood concentration cannot be sensibly interpreted. Even where in-life levels are available, for most drugs in most circumstances, interpretation of blood levels after death is near impossible. High postmortem concentrations should certainly not be taken, in the absence of other evidence, to indicate death by overdose, for example. Two valuable reference sources for interpretation of postmortem sample analysis are the systematic reviews of Ketola and Kriikku8 and Ketola and Ojanperä.9 Expert advice should always be sought when considering the role of medication in a death.10

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