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لم ترد بالأصل

HOSSAM MAGHRABY

RELATIVE STABILITY AND PATTERNS OF CHANGE OF AMINO ACIDS IN POST-MORTEM BLOOD

Thesis

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Table of Abbreviations

Ala -	Alanine
Asp -	Aspartic acid
ASN-	Asparagine
ARG-	Arginine
Ca-	Coronary artery
Cys -	Cysteine
GC-	Gas chromatography
GC/MS-	Gas chromatography /Mass spectrometry
Gln -	Glutamine
Glu -	Glutamic acid
Gly -	Glycine
His -	Histidine
ILE-	Isoleucine
IVC -	Inferior vena cava
IVC(ir) -	Infrarenal inferior vena cava
LEIV -	Left external iliac vein
Leu -	Leucine
LPV -	Left pulmonary vein
LSCV -	Left subclavian vein
Lys-	Lysine
MET -	Methionine
MI-	Mycardial infarction
MTBSTFA-	N-(Tertbutyldimethylsiyl-n-methyltrifuoroacetamide)
PA -	Pulmonary artery
PF -	Pericardial fluid
Phe -	Phenylalanine
Pro -	Proline
RA -	Right atrium
RPV -	Right pulmonary vein
RSCV -	Right subclavian vein
Ser -	Serine

SIM-	Selective ion monitoring
SVC -	Superior vena cava
Thr -	Threonine
Trp -	Tryptophan
TYR-	Tyrosine
Val -	Valine

Introduction

Recently, it has become increasingly apparent that drugs accumulate in the blood following death so that the levels measured at autopsy may be significantly higher than if they had been measured antemortem. Moreover, the concentrations of drugs in postmortem blood specimens often exhibit sample collection site dependence, particularly for drugs with a high apparent volume of distribution. These findings are an obvious source of concern for toxicologists, as drugs circulating at therapeutic levels during life may rise after death to toxic levels and be wrongly interpreted as a cause of death.

This phenomenon has many components, the majority of which are difficult to quantify. Diffusion of drugs into blood from organs where they are sequestered during life, or cell death releasing drugs into the blood, contribute. There have been many attempts to eliminate these factors. For example, by taking blood from a peripheral site which is less prone to diffusion from the organs in order to gain accurate blood measurements of drugs in the postmortem period. Efforts have also been made to use other specimens, e.g. muscle, to interpret drug levels or corroborate blood results. However, neither of these methods have given a satisfactory means of determining accurate postmortem drug levels.

A putative peripheral blood sample may not be truly representative of a peripheral site as sampling techniques vary between pathologists and a sample simply identified as blood may originate from a number of vessels. To

further confuse matters, a peripheral blood sample drawn without cross clamping may result in a siphoning of blood from the more central vessels. Thus a sample which is purportedly obtained from a peripheral site and is thus assumed to be more representative of perimortem drug level may in fact be either contaminated by blood of central origin or be in fact sampled from a central vessel.

An alternative way to tackle this situation is by asking if a correlation exists between drug concentrations found at different sites and endogenous biochemical markers at these sites. This would be based on the premise that any factors affecting a drug postmortem would affect an endogenous substance proportionally. Such biochemical markers could be used to track the rise of a drug in the postmortem period. Moreover, if such markers showed a pattern unique to that vessel, especially the peripheral vessels, they may be used to distinguish a sample derived from a peripheral vessel from one which has actually come from a central site.

A study designed to look into this hypothesis[1] found amino acids to be the most promising biochemical markers. This study forms the basis for our investigation