



### **K34 Concentrations of Amphetamine and Morphine in Femoral Blood in Overdose Deaths Compared With Venous Blood From DUID Suspects**

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After attending this presentation, attendees will learn about two of the major drugs of abuse in Sweden (amphetamine and heroin) and gain firsthand knowledge about the concentrations of these substances in blood in overdose deaths as well as in people arrested for driving under the influence of drugs (DUID suspects). This presentation compares and contrasts the concentrations of two major recreational drugs, namely amphetamine and morphine (derived as a metabolite of heroin), in peripheral blood samples from the living and the dead.

This presentation will impact the forensic science community by enabling medical examiners and toxicologists to compare the concentrations of amphetamine and morphine in blood. The large size of the present material, the sampling and analysis of drugs in peripheral blood (femoral or venous) and use of modern analytical methods are some of the major strengths of this research. The results will impact attendees when they are called upon to interpret drug concentrations in overdose deaths or to testify in court in cases of drug-impaired driving.

Interpreting the concentration of drugs determined in postmortem blood in terms of acute toxicity and whether an overdose and a drug poisoning was a likely cause of death is fraught with difficulties. The circumstances surrounding the death, the police reports, eye-witness statements, findings at the scene, and the autopsy all need careful consideration. People differ widely in their response to the same dose of a drug depending on factors such as absorption rate, dosage form, routes of administration, ethnicity, enzyme polymorphism, least previous experience with the drugs in question, and the development of central nervous tolerance.

Unlike in the United States where methamphetamine is the preferred central stimulant amine subjected to abuse, in Sweden it is the primary amine amphetamine that has topped the list of illicit drugs over many decades. Elevated blood-amphetamine is a common finding in postmortem (PM) toxicology as well as in apprehended drivers. Information about amphetamine concentrations in the living and the dead was retrieved from a forensic toxicology database (TOXBASE) using a cut-off concentration for positive results of 0.03 mg/L. Amphetamine was determined in blood by isotope-dilution GC-MS. The use of heroin was verified by identification of the unique metabolite 6- monoacetylmorphine (6-MAM) in blood or urine. The poisoning deaths were identified from ICD-9 codes assigned by the medical examiner and then sorted according to whether these were mono-intoxications or poly drug users.

The mean (median) and upper 95<sup>th</sup> percentile concentration were 2.0 mg/L (1.5 mg/L) and 4.2 mg/L respectively for N = 36 mono- intoxications involving amphetamine. These findings compare with 1.6 mg/L (0.4 mg/L) and 4.3 mg/L, respectively for N = 383 poly-drug amphetamine-related deaths. The victims of amphetamine poisoning were mainly men (72-86%) and those in single-drug deaths were 13

years older than poly-drug deaths (48 y vs. 35 y). The median concentration of amphetamine in mono-intoxication deaths was four time higher than that of poly-drug users. The median concentration of amphetamine in blood of impaired drivers as the only drug was 0.9 mg/L compared with 0.6 mg/L in poly-drug DUID suspects. The DUID suspects had higher median B-amphetamine concentrations compared with medical examiner cases who were poly-drug users (0.4 mg/L). Regular use of amphetamine leads to tolerance although unusually high concentrations of this stimulant can be tolerated without a fatal outcome.

When forensic toxicologists report morphine in submitted blood- samples this is usually taken to mean abuse of heroin, arguably the most dangerous recreational drug. In this study the presence of 6-MAM in blood or urine was used as a biomarker for recent use of heroin. In the autopsy material, most victims of heroin-related deaths were men (88%) although there was no gender difference in their age (mean 35 y). In traffic cases, 91% of heroin users were men and they were on average two years younger than the women (33 y v 35 y). The use of heroin was identified using an analytical cut-off concentration for 6-MAM in blood of 0.005 mg/L the same as that for B-morphine. Both opiates were determined in blood and urine by isotope-dilution GC-MS.

In medical examiner cases (N = 766), the median B-morphine concentration in heroin-related deaths was 0.24 mg/L, which compares with a median of 0.15 mg/L (N = 124) in apprehended drivers with 6- MAM in blood. The concentration distributions of B-morphine in the living and the dead overlapped to a large extent. In medical examiner cases, 65% of the victims had a B-morphine concentration > 0.2 mg/L compared with 36% in the DUID cases. In traffic cases when 6-MAM was present in urine (N = 1950) but not in blood, the median B-morphine concentration was considerably lower (0.03 mg/L) and only 3.6 % had a concentration



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exceeding 0.2 mg/L. The presence of 6-MAM in urine but not in blood means that more time has elapsed after the last use of heroin and consequently the concentrations of morphine in blood decreases through metabolism. It was found that the concentrations of morphine in blood (median values) were remarkably similar in mono-intoxication deaths (0.25 mg/L, N = 63), poly-drug deaths (0.24 mg/L, N = 703), and in heroin overdose deaths (0.25 mg/L, N = 669); and also when the person died in some other way than drug poisoning (0.23 mg/L, N = 97).

Interpreting the concentrations of drugs in postmortem toxicology is complicated because the results do not reveal any information about the extent of prior exposure and the development of tolerance. When it comes to acute toxicity of opiates, the loss of tolerance is perhaps the most important determinant of an overdose death, especially when the drugs are administered intravenously. The results from this study show that the concentration of amphetamine and morphine in forensic blood samples cannot be used *per se* to conclude that death was the result of drug poisoning. Toxicology results should not be interpreted in a vacuum and the autopsy findings including histology, the police investigation, knowledge of the deceased person's drug habits, as well as witness statements all need to be considered when the cause and manner of death are assigned.

### **Amphetamine, Morphine, Blood**