

Letters to the Editor

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THE TOXICOLOGY OF HEROIN-RELATED DEATH: ESTIMATING SURVIVAL TIMES

We read with interest the paper by Darke & Dufrou [1], published in *Addiction*. Darke & Dufrou examined the proportions of cases in which 6-monoacetyl morphine (6-AM) was present in the blood, and compared concentrations of secondary metabolites and circumstances of death by 6-AM status. They found that 6-AM was detected in 43% of cases. The median free morphine concentration of 6-AM-positive cases was more than twice that of 6-AM-negative cases. 6-AM-positive cases also had lower concentrations of the other major heroin metabolites: morphine-3-glucuronide (M3G) and morphine-6-glucuronide (M6G), with correspondingly lower M3G/morphine and M6G/morphine ratios. Darke & Dufrou conclude that in heroin-related deaths in their study sample, 6-AM was present in the blood in fewer than half of cases, suggesting that a minority of cases had survival times after overdose of less than 20–30 minutes. They believe that the toxicology of heroin metabolites and the circumstances of death were consistent with 6-AM as a proxy for a more rapid death [1].

We wonder if any urine 6-AM was tested in those decedents who tested negative for blood 6-AM or what percentage of 6-AM-positive blood also had positive urine 6-AM? If death occurred shortly after heroin intake, then very small or no 6-AM would be expected in the urine. If death occurred in a delayed fashion, one would expect a relatively high 6-AM concentration in the urine related to the concentrating effect of kidney [2]. The usually described window of time for 6-AM detection in urine is between 2 and 8 hours after injection of heroin, because the enzymatic hydrolysis of heroin is limited due to the lack of esterase [2]. We also wonder if the ratio of blood 6-AM concentration to urine 6-AM concentration may represent the proxy more clearly for a more rapid death? Further, urine 6-AM may help to define an estimate of survival time, as Darke & Dufrou have acknowledged that in their 6-AM-negative cases they could not predict accurately how long survival times were [1].

Finally, Darke & Dufrou emphasize that their toxicological data on morphine and its major metabolites supported 6-AM as a measure of survival times, i.e. cases in which 6-AM was present had higher free morphine

concentrations and lower concentrations of M3G and M6G, than other cases. Interestingly, Carroll and colleagues [3] conducted an investigation, prompted by a review of nine medical examiner cases that, on initial analysis 1–2 weeks after death, had only a trace amount or no free morphine detected in the blood but that, on re-examination 1.5–26 months later, found between 54 and 560 ng/ml free morphine in the re-analysed blood specimens. They hypothesized that the hydrolases might still be active in bacterially contaminated autopsy specimens, despite preservation and refrigeration. Carroll *et al.* have demonstrated further that the hydrolysis of M3G to free morphine *in vitro* occurs and may persist for months in antemortem and postmortem specimens under various conditions, despite using gray-top tubes for inhibition of bacterial growth. Therefore, did the bacterial hydrolysis of morphine metabolites confound the M3G and M6G/morphine ratios?

Declaration of interests

None.

Keywords 6-AM, free morphine, heroin, hydrolysis, monoacetyl morphine, morphine-3-glucuronide, morphine-6-glucuronide, survival times.

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