The toxicology of heroin-related death: estimating survival times

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We read with interest the article by Darke and Duflou [1] published in *Addiction*. Darke and Duflou 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 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 and Duflou conclude that in heroin-related deaths in their study sample, 6-AM was present in the blood in under half of cases, suggesting that a minority of cases had survival times after overdose of under 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 blood 6-AM positive 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 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 h after injection of heroin, because the enzymatic hydrolysis of heroin is limited due to the lack of esterase [2]. We wonder if the ratio of blood 6-AM concentration to urine 6-AM concentration may better represent the proxy for a more rapid death? Further, urine 6-AM may help define an estimate of survival time as Darke and Duflou have acknowledged that in their 6-AM negative cases, they could not accurately predict how long survival times were [1].

Finally, Darke and Duflou 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 review of nine medical examiner cases that, on initial analysis 1 to 2 weeks after death, had only a trace amount or no free morphine detected in the blood but that, on re-examination 1.5 to 26 months later, found between 54 and 560 ng/ml free morphine in the reanalyzed blood specimens. They hypothesized that the hydrolases might still be active in bacterially contaminated autopsy specimens, despite preservation and refrigeration. Carroll et al. further have demonstrated 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?

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References:

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