An Explanation of “Lingering” Opiate Deaths?

Relative Concentration of Opiates in Medulla and Femoral Blood Following Lethal Intoxications.

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Introduction: Toxicologists and pathologists are sometimes confronted with difficult cases where the case history surrounding the deaths indicates an opiate overdose, but the postmortem blood levels measured are only in the therapeutic range. These cases are generally referred to as “Lingering Deaths” and the decedent is thought to have reached a lethal level of intoxication but remains alive sufficiently long enough to metabolize and eliminate the high level of opiate from blood down to therapeutic concentrations. Death from opiate intoxication is most often a result of respiratory and cardiac depression with resultant pulmonary pathology involving increased lung weights. Neurological control of respiration and cardiac rhythm resides in the medulla oblongata. Cases selected for this study were chosen based on the suspicion of overdose indicated in the case history.

Objectives: To uncover a possible explanation for lingering deaths, this study examined the relative concentration of opiates in femoral blood compared to brain samples in the medulla oblongata.

Methods: Specimens were collected during autopsy and kept refrigerated until processed for analysis. Extraction of drugs was accomplished using solid phase extraction (SPE) Clean Screen ZDIA/UDIA followed by derivatization with MUSTA (UCT). Analytes were separated, detected and quantitated by an Agilent (627) MS in the SIM mode using a Restek Rat-5sms capillary column and a previously published UCT method for opiates.

Results: As is shown in Table 1, the average opiate concentrations for morphine, codine and 6-acetylmorphine were higher in medulla than in blood.

Table 1: Distribution of Opiates in Blood and Brain (ng/mL):

<table>
<thead>
<tr>
<th>Opiate</th>
<th>Blood</th>
<th>Brain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>123</td>
<td>234</td>
</tr>
<tr>
<td>Codeine</td>
<td>123</td>
<td>234</td>
</tr>
<tr>
<td>6-AM</td>
<td>123</td>
<td>234</td>
</tr>
</tbody>
</table>

The preferential distribution of opiates to medulla (site of respiratory control) suggests that lingering opiate deaths may be explained, at least in part, because of higher relative concentrations of drug in brain, compared to femoral blood.

Keywords: opiates, medulla, lingering deaths

Conclusions: A person may die of an opiate overdose with non-lethal levels of drug being detected in postmortem samples.

One explanation for these “Lingering Deaths” may be that the relative concentration of the drug in the brain is sufficiently high to cause death.

Morphine concentrations were more concentrated in the medulla in 77% (34/41) of the cases examined (Table 2). The source of morphine in these cases was heroin. White and Irvine, 1999, suggested that heroin acts as a pro-drug and facilitates the entry of morphine into the brain.

A possible explanation for the lower morphine levels in the medulla may be that death occurred before heroin was completely distributed to the brain. Out of the 12 cases where morphine levels were higher in the blood, seven of the scenes contained drug paraphernalia, suggesting acute exposure.

Codeine and 6-AM were more concentrated in the medulla, compared to blood. Examination of the brain blood ratio for the three analytes demonstrated an increasing ratio from morphine, to codeine, to 6-AM, which directly corresponds to the relative lipophilicity of these analytes (Table 2).

These results suggest that elevated opiate levels in the medulla oblongata, compared to levels measured in blood, may at least in part, explain the “Lingering Death” phenomenon.

Another possible contributor to this phenomenon is sleep. Opiates as CNS depressants produce sleep. Sleep naturally decreases sensitivity of the medullary centers to CO2. The effect of opiates and sleep are additive.

It was noted in this study that the average lung weights of the decedents were in fact elevated: Right: 757g; Left: 671g (Combined: 1428g). A healthy, average lung weight for an adult is: Right: 450g; left: 375g (Combined: 825g).

No correlation was detected between lung weight and BMI. As height increased there was a slight increase in lung weight. Males tended to have higher lung weights.

No correlation was found between BMI and morphine, codeine or 6-AM concentrations and no correlation was found between combined lung weight and drug concentrations.

Additional Demographics:
- In this study there were 10 FEMALES and 31 MALES.
- The MANNER of death was ruled ACCIDENTAL in 31/41 cases.
- The CAUSE of DEATH (COD) was ruled ACUTE OVERTOXICITY for 34/41 of the cases. One case was ruled SUFFOCATION with a contributing factor of an OPIATE OVERTOXIC (the remaining six cases are still PENDING).
- Of the 35 cases that have been ruled on: 66% of COD rulings included Heroin + Other Drugs; 29% Heroin only; 5.7% Opiate intoxication.

References