K35 Postmortem Morphine Concentrations – Are They Meaningful?

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The goals of this presentation are to review factors influencing postmortem morphine concentrations and to compare concentrations in terminally ill patients to a varied population. The presentation will provide recommendations for interpretation of postmortem morphine concentrations, as well as, describe how these factors can influence the cause and manner of death.

Introduction: Morphine is a strong opioid agonist that has become the drug of choice for the treatment of moderate to severe pain associated with cancer and in palliative and terminal care. One of the most daunting tasks for forensic pathologists is interpretation of the toxicological findings. This is especially difficult in decedents with multiple medical problems who receive morphine and other opioids for comfort care in the terminal stages of disease, in which high concentrations may be suspicious for euthanasia. Many factors will alter postmortem morphine concentrations. Intrinsic factors include general health, disease processes, renal failure and hepatic function. Postmortem factors include the postmortem interval, site of specimen collection, and postmortem redistribution. Medication factors include dosing, frequency, duration of exposure to opioids and tolerance to opioids. Published therapeutic and toxic values of morphine are typically based on measures in living, nonchronic users, and postmortem data obtained from terminal patients receiving morphine for comfort measures is lacking.

Methods: We conducted a retrospective review of medical examiner cases with morphine identified in the toxicological evaluation. More than 50 cases from the District 5 Medical Examiners Office in Leesburg, Florida from the years 2001, 2002 and 2003 were identified. Included were deaths that occurred at home, with and without hospice care; in nursing homes and assisted living facilities, with and without hospice care; and deaths that occurred in a hospital, inpatient setting. Cases involving heroin use, those with incomplete medical records, or decedents who were embalmed were excluded from the study. Antemortem medical records were reviewed for age, general health status, and disease processes with special attention to evidence of renal and hepatic failure. In addition, medication schedules and dosing were reviewed, as well as, length of time receiving morphine and previous exposure to opioids. The autopsy files were reviewed for cause and manner of death, confirmation of disease processes, site of specimen collection and the time interval from death to acquisition of specimens (postmortem interval).Toxicological analyses were performed according to standard laboratory protocol using gas chromatography-mass spectrometry for identification and quantitation of morphine. Morphine concentrations in blood were measured as free and total morphine.

Results: Evaluation of the data revealed an age range from mid 40s to early 90s. Disease processes were highly varied including cancer, dementia, acute injury and chronic pain due to injury and other causes. The data showed a wide range of morphine concentrations from less than the defined therapeutic values to more than 20 times the therapeutic value (as compared to non-chronic users). The reported cause and manner of death varied from natural death resulting from end-stage disease processes to accidental deaths from injury and morphine toxicity. The results of our study mirror previous studies with elevated postmortem morphine concentrations in decedents with renal failure, chronic use of opioids and collection of specimens from central sites. Morphine concentrations were highly variable in decedents who were terminally ill and receiving morphine for comfort measures.

Conclusion: It is important for forensic pathologists to be aware of all factors that influence postmortem morphine concentrations before deciding how these values influence the determination of cause and manner of death. Postmortem morphine concentrations were elevated in decedents with renal failure because of a decreased ability to excrete the drug. Decedents with chronic illness, cancer, and liver failure had a decreased ability to metabolize the drug. Decedents with tolerance to opioids had higher postmortem concentrations beyond the defined therapeutic range. Specimen site must also be considered, as concentrations are higher when collected from a central site versus a peripheral site. Special attention to these variables is required when the decedent was terminally ill and receiving morphine for comfort measures, as the concentrations are highly variable. The significance of a prolonged postmortem interval in these cases is unknown.

In summary, when an elevated postmortem concentration of morphine is reported, an exhaustive search of the medical records must be conducted. Information obtained should include underlying disease processes, medication schedules and dosing and evidence of length of time on morphine, previous exposure to opioids and development of tolerance. Postmortem interval should be noted and communicated to the forensic toxicologist. This information, when considered, will be important when declaring the cause and manner of death.

Morphine, Postmortem, Interpretation

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