G47 Accidental Opioid-Induced Deaths: Modeling Relationships of Postmortem Opioid Levels to Co-Intoxicant Benzodiazepine, Alcohol Presence, and Selected Decedent Characteristics

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After attending this presentation, attendees will better understand the potential impact of co-intoxicant benzodiazepines, alcohol, and other decedent characteristics in opioid-induced deaths involving oxycodone, methadone, hydrocodone, or fentanyl.

This presentation will impact the forensic science community by providing research which can help medical examiners sort out toxicological complexity in opioid multi-drug deaths, which have increased in frequency.

Accidental poisoning is the second-highest cause of accidental death nationally, surpassing motor vehicle fatalities. Rural states, including the study population, have experienced unexpected increases in such deaths, which involve both prescribed and diverted drugs. The four most common opioids found in toxicology tend to be oxycodone, methadone, hydrocodone, and fentanyl, and the two most common benzodiazepines tend to be alprazolam or diazepam. Alcohol is also frequently involved. Despite the frequency of polydrug deaths with these drugs found in toxicology, there has been little research that addresses the complex relationships among them.

A Forensic Drug Database (FDD) was created to capture drug death data. A project funded as part of the West Virginia Injury Control Research Center's renewal grant from the Centers for Disease Control and Prevention (CDC) expands the FDD from West Virginia (WV) to the northern New England (NNE) states of Maine, New Hampshire, and Vermont. Decedent data collected in the medical examiner files is entered into the FDD, including demographic information, body condition, Body Mass Index (BMI), death certificate data, route of drug administration, whether a prescription was present for controlled substances identified, medical history, key autopsy findings, and toxicological analyses. The database utilized here contains information on WV drug-related deaths from January 2005 through most of 2010; data from NNE are being compiled.

Opioid-induced deaths in West Virginia were analyzed using medical examiner case files and a comprehensive forensic drug death database. This analysis is part of a larger study comparing opioid mortality and co-intoxication in four rural states. The focus of this presentation is on relationships between opioid levels and the presence of benzodiazepines and alcohol in West Virginia's decedent toxicology findings.

Due to significant deviations from the normal distribution in the opioid concentrations, natural logarithmic transformations were used, resulting in primary analysis of log-concentrations of each opioid. In order to examine associations between particular covariates of interest (age, BMI, gender, benzodiazepine presence, and alcohol presence) and opioid concentrations, multiple linear regression models on the log-concentrations were employed. Since the goal was to build the most parsimonious model (i.e., identify which covariates best predict opioid concentrations), backward model selection methods with an inclusion criterion of 0.1 were utilized.

Out of a total of 2,355 accidental drug deaths, 877 met the criteria for inclusion. These deaths had oxycodone, methadone, hydrocodone, or fentanyl as the only opioid present, with or without alprazolam or diazepam (but no other benzodiazepine), and with or without alcohol. This dataset included 135 deaths involving fentanyl, 135 involving hydrocodone, 337 involving methadone, and 270 involving oxycodone. Only those deaths with femoral or subclavian specimens were included.

The following significant relationships were found, accounting for covariates. Among deaths caused by oxycodone, alcohol is significantly associated with a decrease in the log-concentration of postmortem levels of oxycodone ($p=0.0011$). Among deaths caused by methadone, alcohol is significantly associated with a decrease ($p=0.0002$), benzodiazepine presence with a decrease ($p=0.0153$), and increasing age with an increase ($p=0.0420$) in the log-concentration of postmortem levels of methadone. Among deaths caused by hydrocodone, alcohol is significantly associated with a decrease ($p=0.0329$) and

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benzodiazepine presence with a decrease (p=0.0547) in the log-concentration of hydrocodone. Among fentanyl deaths, there were no significant relationships observed (p=0.77).

In conclusion, the four opioids in the model responded differently to the presence of alcohol, specific benzodiazepines, and age. Alcohol presence was significantly associated with decreased log-concentrations of oxycodone, methadone, and hydrocodone. Benzodiazepine presence was significantly associated with decreased log-concentrations of methadone and hydrocodone. Increasing age was only associated with an increase in one opioid, methadone. None of the variables were significantly associated with postmortem concentrations of fentanyl. BMI and gender were not significantly associated with concentrations of any of the four opioids.

Accidental Poisoning, Opioid, Postmortem Toxicology

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