K36 Investigation of Cocaine Metabolite Concentrations in Postmortem Cases

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Attendees will learn the cocaine metabolic pathway; understand the methodologies used for quantitatively measuring cocaine and 13 cocaine metabolites in postmortem blood and urine; and acquire information concerning cocaine metabolite concentrations in postmortem specimens.

This presentation will impact the forensic community and/or humanity by providing preliminary data to suggest that analysis of minor cocaine metabolites may aid in the differentiation of cocaine from noncocaine related deaths.

Toxicological testing of apparent cocaine-related deaths typically involves identification, confirmation, and quantification of the parent analyte (cocaine) and a selection of cocaine metabolites, for example: cocaine (COC), benzoylecgonine (BE), cocaethylene (CE), and ecgonine methyl ester (EME). CE is produced if cocaine is used with ethanol. Other analytes that may be measured include anhydroecgonine methyl ester (AEME), a pyrolysis product, and norcocaine (NCOC). A previous study of 13 cases [Jenkins and Goldberger, *J. Forensic Sci.* 42(5): 824-827, (1997)] found no relationship between cause of death and concentrations of cocaine, BE, EME, and/or CE. However, it is not known if these analytes in addition to other cocaine metabolite concentrations could be useful in understanding cocaine related deaths.

This study examined a total of 13 cocaine metabolites from 103 cases, containing both cocaine and non-cocaine related deaths in postmortem blood and urine. The analytes of interest included AEME, EME, ecgonine ethyl ester (EEE), NCOC, norcocaethylene (NCE), *o,m,p*-hydroxycocaine (*o,m,p*-HOCOC), CE, norbenzoylecgonine (BNE), and *o,m,p*-hydroxybenzoylecgonine (*o,m,p*-HOBE). The COC and BE findings for 100 of these cases have been previously reported [Jenkins, Levine, Titus, and Smialek, Forensic Sci. Int. 101:17-25 (1999)] and will not be discussed in this report.

Heart blood and urine specimens from postmortem cases were analyzed according to a previously published method [Cone, Hillsgrove and Darwin, Clin. Chem. 40 (7): 1299-1305 (1994)]. Briefly, buffered specimens were extracted with calibrators and controls using deuterated internal standards by solid phase extraction followed by gas chromatographic/ mass spectrometric analysis of the silyl derivatives.

Cases were divided into 2 groups for evaluation: those cases in which “cocaine intoxication” was listed as the cause of death were classified as cocaine related; and those for which cocaine intoxication was not listed in the cause of death were classified as non-cocaine related deaths. This latter group included gunshot wounds, drowning, asphyxia, blunt force injuries, as well as deaths determined to be due to other drugs (narcotics, alcohol, N=15).

There were 34 cocaine related deaths. Metabolites were grouped according to the prevalence in which they were found positive in the various cases. Other than BE (previously reported) the two most common metabolites detected were EME (N=33 for blood, N=34 for urine), followed by *m*-HOBE (N=29 for blood, N=34 for urine). The concentration ranges (mean +/- SD) of EME in blood and urine specimens were 16-6413 ng/ml (835.8 +/- 14.9 ng/ml) and 6-179524 ng/ml (11183.7 +/- 309.3 ng/ml), respectively and for *m*-HOBE, the concentration ranges were 4-563 ng/ml (72.9 +/- 14.7) and 5-166804 ng/ml (5190.4 +/- 281.7), respectively. In the blood specimens, other analytes were found in the following order, from most common to least common: *p*-HOBE (N=29); EEE, CE, and *o*HOBE (N=25); *p*-HOCOC (N=21); *m*-HOCOC (N=18); AEME (N=14); BNE (N=13); NCOC (N=12); *o*-HOCOC (N=9); NCE (N=2). However, the urine specimens demonstrated a slightly different prevalence: NCOC (N=33); *m*-HOCOC, CE, *p*-HOBE (N=32); EEE (N=31); *p*-HOCOC (N=29); BNE (N=28); NCE (N=27); *o*-HOBE (N=15); *o*-HOCOC (N=9).

There were 69 non-cocaine related deaths. In these cases, apart from BE, the same two common metabolites in cocaine-related deaths were most prevalent: EME (N=68 for blood, N=69 for urine) and *m*-HOBE (N=52 for blood, N=69 for urine). The concentration ranges (mean +/- SD) of EME in blood and urine were 2-717 ng/ml (155.6 +/- 16.4) and 28-54939 ng/ml (6112.9 +/- 108.7) respectively and for *m*-HOBE, the ranges and mean concentrations were 1-1171 ng/ml (43.7 +/- 15.0) and 7-62751 ng/ml (3284.4 +/- 110.8) respectively. In the blood specimens, other analytes appeared in the following order, from most common to least common: *p*-HOBE (N=49); CE (N=46); *o*-HOBE (N=43); *p*-HOCOC (N=40); EEE (N=33); *m*-HOCOC (N=32); AEME (N=15); BNE (N=10); *o*-HOCOC (N=8); NCOC (N=7); NCE (N=6). For the urine specimens prevalence was as follows: NCOC (N=69); *m*-HOCOC, *p*-HOBE (N=68); CE (N=67); EEE (N=65); *p*-HOCOC, BNE (N=58); NCE (N=53); AEME (N=51); *o*-HOBE (N=39); *o*-HOCOC (N=24).

Minor metabolites of cocaine are readily detectable in postmortem specimens. It appears the most prevalent minor metabolites detected in both cocaine and non-cocaine related deaths were *m*-HOBE and *p*-

HOBE. However, there were some differences between the two groups. In blood, AEME, EEE, *o*-OHCOC, and BNE were more than twice as likely to be present in cocaine related deaths and NCOC was more than three times as likely to be present than in non-cocaine deaths. More variability was observed with the urine data. The data demonstrated that the mean concentrations of the majority of metabolites in blood and urine were lower in the non-cocaine deaths than the cocaine-related deaths, except for NCE and EEE. This study has provided preliminary data to suggest that analysis of minor cocaine metabolites may aid in the differentiation of cocaine from non-cocaine related deaths.

Forensic Science, Toxicology, Cocaine Metabolites

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