K15 The Transformation of Drug/Metabolite Ratios: An Objective Assessment of Toxicity

Oneka T. Cummings, PhD, Ameritox, LLC, 486 Gallimore Dairy Road, Greensboro, NC 27409; Frank Wallace, BA, Ameritox, LLC, 486 Gallimore Dairy Road, Greensboro, NC 27409; Erin C. Strickland, PhD, Ameritox, LLC, 486 Gallimore Dairy Road, Greensboro, NC 27409; Ronald C. Backer, PhD, 6815 S Highway A1A, Melbourne Beach, FL 32951; and Gregory L. McIntire, PhD, Ameritox, 486 Gallimore Dairy Road, Greensboro, NC 27409*

After attending this presentation, attendees will be aware of the use of a simple mathematical transformation of urine test results to afford an objective assessment of toxicity through the ratio of drug to metabolite (e.g., fentanyl to norfentanyl). Comparison of postmortem drug(s) to metabolite ratios from urine to a large database of such ratios from urine drug testing can help provide this objective assessment of toxicity.

This presentation will impact the forensic science community by demonstrating that the mathematical transformation described in this report can provide a tool to help with the assessment of toxicity in postmortem examinations. These data are necessarily from urine in which "normal" population data exists from pain medication testing. This will require a testing paradigm shift in postmortem samples in which often only the parent drug is tested in various bodily fluids.

Forensic assessment of toxicity is often subjective. For example, it is expected intuitively that fentanyl concentrations from postmortem samples are higher than corresponding therapeutic levels, whether in blood or urine. In fact, many forensic laboratories only test for fentanyl and not the metabolite, norfentanyl. Ruan et al. suggested that the absolute value of the ratio of norfentanyl to fentanyl could be related to the probability of "acute fentanyl toxicity."[1] This work reports that a simple logarithmic transformation of the ratio of parent drug concentrations to metabolite concentrations from a large body of therapeutic test results in urine can afford a stable database for comparison with forensic (postmortem) sample results treated the same way. The stable database for comparison is readily available from urine data obtained during pain medication monitoring testing.[2] Similar databases from blood testing are not available. While this approach can work for any number of potentially toxic drugs, the transformed ratios of fentanyl to norfentanyl in urine from several postmortem cases were compared with the "normal" therapeutic distribution of such transformed ratios to confirm this model/hypothesis. Urine fentanyl/norfentanyl data from overdose cases reported by Coopman et al., Peer et al., and Poklis et al. were similarly transformed to compare with the existing pain monitoring population (Figure 1).[3-5] There is some apparent overlap between the populations, but the overdose population is higher than the "normal" therapeutic results as predicted by Cummings et al.[6] Additional fentanyl/norfentanyl urine data from postmortem samples is expected to more clearly delineate that population of results in contrast to the therapeutic distribution. Thus, this simple transformation of the test results can provide an indicator of toxicity. Of course, the total setting of the death must be taken into consideration, but this approach could serve as an additional tool for forensic scientists in their investigations.

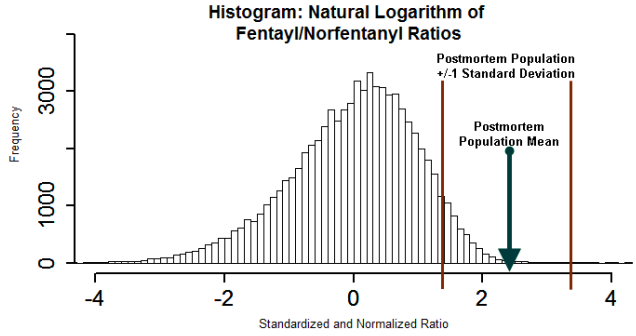

Figure 1.

Reference(s):

1. Ruan X., Chiravuri S., Kaye A. Fentanyl–Norfentanyl Concentrations During Transdermal Patch Application: LC–MS-MS Urine Analysis. *J. Anal. Tox.* 2017, 41(2), 163-164.
2. Oneka T. Cummings, Jeffrey R. Enders, Gregory L. McIntire, R. Backer, and A. Poklis. Fentanyl and Norfentanyl Concentrations During Application of Transdermal Patches: LC/MSMS Urine Analysis. *J. Anal. Tox.* 2016, 40(8), 595-600.
3. Coopman V. Cordonnier J, Pien K., Van Varenbergh D. LC-MS/MS Analysis of Fentanyl and Norfentanyl in a Fatality Due to Application of Multiple Durogesic® Transdermal Therapeutic Systems. *Forensic Science International.* 2007, 169, 223-227.
4. Peer C.J., Shakleya D.M., Younis I.R., Kraner J.C., and Callery P.S. Direct-Injection Mass Spectrometric Method for the Rapid Identification of Fentanyl and Norfentanyl in Postmortem Urine of Six Drug-Overdose Cases. *J. Anal. Tox.* 2007, 31, 515-521.
5. Poklis J., Poklis A., Wolf C., Mainland M., Hair L., Devers K., Chrostowski L., Arbefeville E., Merves M., and Pearson J. Postmortem Tissue Distribution of Acetyl Fentanyl, Fentanyl, and Their Respective Nor-Metabolites Analyzed by Ultrahigh Performance Liquid Chromatography with Tandem Mass Spectrometry. *Forensic Science International.* 2016, 257, 435-441.
6. Cummings O.T., Enders J., and McIntire G.L. Response to: Fentanyl-norfentanyl concentrations during transdermal patch application: LC-MS-MS Urine Analysis. *J. Anal. Tox.* 2017, 41(2), 165-166.

Fentanyl, Transformation, Postmortem

Copyright 2018 by the AAFS. Permission to reprint, publish, or otherwise reproduce such material in any form other than photocopying must be obtained by the AAFS.

*Presenting Author