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Recommendations for Specimen Collection for NBOMe Analysis in Clinical Toxicology

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To The Editor

Since 2012, dimethoxyphenyl-N-[(2-methoxyphenyl) methyl]ethanamine (NBOMe) derivatives, a new class of designer hallucinogens, have become a threat to public health and safety (1,2). The most commonly reported drugs are para-halogenated derivatives on the 2,5-dimethoxy-phenethylamine portion of the NBOMe molecule, referred to as 25I-NBOMe, 25B-NBOMe, and 25C-NBOMe (3). Over the past four years, our laboratory has developed and applied validated HPLC/MS/MS methods to identify and quantify NBOMe drugs in serum and urine specimens from intoxicated patients, as well as postmortem fluid and tissue specimens from Medical Examiners' cases from across the United States and around the world. Based on this experience, we present some recommendations for clinical toxicologists on the collection and utility of clinical specimens for NBOMe testing.

When testing one series of serums from an alleged NBOMe intoxication we observed dramatically different concentrations between specimens collected contemporaneously, but in two different blood collection tubes. Specimens collected at admission to the Emergency Department (ED) yielded the following 25B-NBOMe serum results: Red Top, 1.2 ng/mL and Gold Top, 0.32 ng/mL. Similarly, specimens collected four hours post-admission yielded these 25B-NBOMe results: Red Top, 0.51 ng/mL and Gold Top, 0.20 ng/mL. This decrease of 73% and 61% in 25B-NBOMe values between Red Top and Gold Top tubes is likely due to the sequestration of the NBOMe by the Gold Top serum separator gel, a mechanism well documented for many therapeutic drugs (4). We then conducted a small

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Declaration of interest

The authors report no declarations of interest. The authors alone are responsible for the content and writing of the paper.

study over 72 hr in five types of BD Vacutainer® collection tubes; Red Top; Purple Top containing EDTA; Gray Top containing EDTA and sodium fluoride; Green Top containing spray-coated lithium heparin and a gel for plasma separation; and Gold Top containing clot activator and gel for serum separation. After 1 hour, no significant loss of drug was observed. At 24 hours, recovery of added 25B-NBOMe was only 70% in both Green Top and Gold Top tubes. By 72 hours significant amounts of all NBOMe drugs were apparently sequestered in the separator gel in both the Green and Gold Top tubes with recoveries at 70%. If initial serum concentrations are very low, NBOMe sequestration may reduce the concentration below the assay's lower limit of detection (25pg/mL), resulting in a false negative. Therefore, blood collection tubes with serum/plasma separator gels are not recommended if NBOMe derivatives are to be tested. However, if blood is collected in a serum/plasma separator gel tube, the serum should be poured off from the gel within one hour and refrigerated to prevent loss of NBOMe drugs.

We have found parent NBOMe may be a reliable urine biomarker, particularly in scenarios following recent drug use as in ED toxicological testing. However, it should be noted that in one case we did not detect 25I-NBOMe in urine from an intoxicated patient collected 13 hours post-admission. Four O-desmethyl metabolites were the only 25I-NBOMe analogs detected (5). With the exception of 2CT-NBOMe, 2-[2,5 dimethoxy-4-(methylthio) phenyl]-N-(2-methoxybenzyl)ethanamine, which is unstable in urine at room temperature, we have found NBOMe derivatives are stable in urine at room temperature for 3 days and frozen for at least one month (6).

When specimens are being shipped to an off-site laboratory for analysis, we recommend tightly sealing the capped blood/serum tubes and/or urine containers with "parafilm" to prevent leakage, double bagging sample containers in zip lock bags in the event of leakage, and shipping them overnight with "cold packs." While NBOMe concentrations may have minimal effect on patient management, the accurate detection and identification of NBOMe derivatives corroborates or disproves drug histories, supports accurate diagnosis and adds to the understanding of the effects of these intoxicants.

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