to confirm either LSD or its metabolite 2-oxo-3-hydroxy LSD by liquid chromatography–mass spectrometry (LC-MS).

The case involved a 31-year-old male with severe end-stage cardiomyopathy secondary to rheumatic heart disease and crack cocaine abuse. He called emergency medical services from home with complaints of shortness of breath. He was subsequently diagnosed with cardiogenic shock secondary to sepsis and cardiomyopathy. He was intubated and admitted to the coronary care unit for hemodynamic support including intraaortic balloon pump. His initial urine drug screen on admission was negative.

The patient was treated for sepsis and gradually weaned from ventilatory and pressor support. The patient’s condition steadily improved. While in the unit, the patient had frequent visits from his girlfriend, whose behavior was noted to be inappropriate and included lying on top of the patient. After one such visit, the patient’s mentation deteriorated, and he became incoherent and questionably began hallucinating. A second urine drug screen was performed and was presumptively positive for LSD by immunoassay (CEDIA, Microgenics Corporation; Emit II, SYVA Company). LC screening of the urine (Remedi HS, Bio-Rad Laboratories) showed only ranitidine and lidocaine. A third urine drug screen obtained 3.5 h later was also presumptively positive for LSD. These findings raised the strong suspicion that the patient’s girlfriend had given him LSD. All three urine specimens (one negative and two presumptively positive for LSD) were analyzed next by LC-MS for confirmatory analyses (2). All results were negative for both LSD and its major metabolite 2-oxo-3-hydroxy LSD.

To further investigate the potential cause of the false-positive LSD immunoassay screens, both immunoassay package inserts were reviewed to determine what drugs may lead to substantial cross-reactivity, but none was initially identified as causal. The concentration of lidocaine in the patient’s urine, 0.8 μg/L, was too low.

References
to be responsible for a false-positive LSD screen because the CEDIA package insert shows no cross-reactivity at 500 μg/L.

Review of the package insert from Microgenics (CEDIA) for potentially interfering drugs for their LSD immunoassay identified only fentanyl as having any potential cross-reactivity, with a concentration >40 μg/L listed as a cross-reactant. Quantification of fentanyl by gas chromatography–MS in both urine specimens that tested positive for LSD gave concentrations of 0.67 and 0.7 μg/L, respectively. However, metabolites of fentanyl, such as norfentanyl, hydroxyfentanyl, or despropionylfentanyl, were not quantified; nor was information available for possible cross-reactivity in any manufacturer package insert.

Review of the physician orders in the medical record in our case revealed that fentanyl was administered within 24 h before each false-positive LSD urine drug screen. Screening by the Remedi LC assay was negative for fentanyl and norfentanyl because the limits of detection by this assay are ≥100 and ≥20 μg/L, respectively. Other concomitant medications given were not likely sources of a potential false-positive LSD screen, as per information from package inserts.

For further validation, we sampled the urine of two random surgical patients who were receiving fentanyl epidurally by patch. Of the long list of medications these patients were medicated with, fentanyl was determined to be negative for LSD by this methodology. The package insert for the Coat-A-Count assay reports no cross-reactivity with fentanyl or metabolites at concentrations of at least 100 000 μg/L.

It is not unusual that positive LSD urine screens by immunoassay are not confirmed by MS analysis when only the parent LSD compound is screened. LSD is rapidly and extensively metabolized, with only 1% LSD appearing in the urine (3). A recent study now shows that the 2-oxo-3-hydroxy LSD metabolite is eliminated in urine at 16- to 43-fold higher concentrations than the parent drug (2). Several reports have identified multiple drugs, such as sertraline, haloperidal, and diethylamine, that cause false-positive urine screens for LSD (4–7). None of the individuals who tested positive by the Emit and CEDIA assays in this study was medicated with fentanyl or its metabolites, a fact confirmed in this study.

Supplementing a negative LSD control urine sample with fentanyl and norfentanyl confirmed that at 40 μg/L, fentanyl, but not norfentanyl (testing negative for LSD up to 100 μg/L) gave a false-positive urine LSD result, confirming the manufacturer’s (CEDIA) claim. Thus, we conclude that patients receiving fentanyl, without exposure to LSD, may be prone to false-positive urine screens by either the CEDIA and Emit II assays.

These findings have retrospectively assisted in the final disposition of a medical examiner’s case in which urine from a 24-year-old male, suspected of an overdose, was screened positive for both fentanyl (after having used his mother’s fentanyl patch) and LSD. There was no associated history of LSD exposure. LC-MS analysis for LSD failed to confirm the positive immunoassay LSD urine screen, and the final report now reflects that this was a false-positive result.

Other prescribed medications, such as mirtazapine, metoprolol, clonazepam, and midrin, were all unlikely candidates for cross-reactivity, according to the manufacturer. Subsequently, the two false-positive urine specimens were analyzed by RIA (Coat-A-Count; Diagnostic Products Corporation) and determined to be negative for LSD by this methodology. The package insert for the Coat-A-Count assay reports no cross-reactivity with fentanyl or metabolites at concentrations of at least 100 000 μg/L.

We conclude that patients medicated with fentanyl by either the SYVA Emit II LSD or the CEDIA LSD immunoassay, may likely be attributable to fentanyl metabolites not measured in this study because all measured urine fentanyl concentrations were <40 μg/L. However, we cannot definitively rule out another unidentified medication causing the false-positive findings. Furthermore, our findings suggest that a presumptively positive LSD immunoassay screen should be interpreted with caution, especially after fentanyl medication is administered.

References


Angelique Gagajewski1
Gershwin K. Davis1
Julie Kloss3
Gregory K. Poch2
Cynthia J. Anderson2
Fred S. Apple7

1 Hennepin County Medical Center
Clinical Laboratories MC 812
701 Park Ave.
Minneapolis, MN 55415

2 Navy Drug Screening Laboratory
San Diego, CA 92134

*Author for correspondence. Fax 612-904-4229; e-mail fred.apple@co.hennepin.mn.us.