

BACKGROUND

Urine drug testing (UDT)

- Used to monitor adherence[1]
- Reduces potential for abuse of controlled prescription drugs.
- Ensures that patients receive appropriate treatment for their medical conditions.

This case presents a unique opportunity to illustrate:

- The potential for UDT to yield false-positive results due to cross-reactivity with other substances.
- The complexities involved in accurately interpreting UDT results, which can often be misleading.

CASE DESCRIPTION

Patient profile:

- 70-year-old female patient w/ hx of rheumatoid arthritis, hip osteoarthritis, lumbar spondylosis, and long-standing methadone use for pain management presented to our interdisciplinary pain clinic seeking to establish care after her previous provider relocated.

Management:

UDT ordered during onboarding for methadone weaning plan

- Urine Drug screening (UDS)results:
 - Consistent with methadone use
 - False-positive for buprenorphine
- Patient denied buprenorphine use
- CURES (Controlled Substance Utilization Review and Evaluation System)database supported patient's claim
- Methadone not refilled during visit
- Repeat UDS yielded negative results for buprenorphine

DISCUSSION

- Cross-reactivity between methadone and buprenorphine in immunoassay-based UDS is a recognized phenomenon that can complicate interpretation[2]
- The **CEDIA® Buprenorphine II Assay** (Thermo Scientific) is used to detect buprenorphine and its major metabolites.

FIGURES/TABLES				
Buprenorphine Spike Concentration (ng/mL)	% of Cutoff (10 ng/mL)	(10 ng/mL) LC-MS/MS (ng/mL)	Number of Determinations	Immunoassay Results (Negative/Positive)
0	-100%	0	80	80/0
2.5	-75%	2.99	80	80/0
5	-50%	5.31	80	80/0
7.5	-25%	7.63	80	80/0
10	100%	10.99	80	27/53
12.5	+25%	12.97	80	0/80
15	+50%	15.05	80	0/80
17.5	+75%	18.92	80	0/80
20	+100%	20.38	80	0/80

Table 1: The 10 ng/mL calibrator is used as a cutoff reference for distinguishing ‘positive’ from ‘negative’ samples. A sample that exhibits a change in absorbance values (Δ A) equal to or greater than that obtained with the cutoff calibrator is considered as positive. A sample that exhibits a change in absorbance value (Δ A) lower than that obtained with the cutoff calibrator is considered as negative. Samples were prepared by spiking Buprenorphine into drug free urine at the cutoff, 25%, 50%, 75% & 100% above and below the cutoff and tested using a Clinical Laboratory and Standards Institute (CLSI) protocol. Results presented below were generated by testing all samples in replicates of 2, twice per day for 20 days, total n=80. Representative data is presented below. **(Total precision= 80)**

Cross-reactivity of commonly used opiates and related drugs	Tested Concentration (ng/mL)	Positive / Negative	% Cross-Reactivity
Codeine	100,000	Negative	<0.01
Dextromethorphan	100,000	Negative	<0.01
Fentanyl	100,000	Negative	<0.01
Hydrocodone	100,000	Negative	<0.01
Hydromorphone	100,000	Negative	<0.01
Methadone	100,000	Negative	<0.01
Meperidine	100,000	Negative	<0.01
Morphine	100,000	Negative	<0.01
Naloxone	100,000	Negative	<0.01
Naltrexone	100,000	Negative	<0.01
Oxycodone	100,000	Negative	<0.01
Tramadol	100,000	Negative	<0.01

Table 2 : The cross-reactivity of Buprenorphine was evaluated by adding known amounts of each analyte to drug free urine (at 10 ng/mL cutoff) with CEDIA® Buprenorphine II Assay

DISCUSSION (cont.)

- This assay Identifies methadone as possible cross-reactant due to structural similarities and shared metabolites [5]
- Negative screening cut off at 100,000 ng/mL
- Previous studies indicate that methadone concentrations exceeding 320,000 ng/mL, can occur in individuals with chronic use, may lead to significant cross-reactivity [3]

Cutoff level importance:

- Manufacturer (**CEDIA® Buprenorphine II Assay**) cutoff: 10 ng/mL
 - Many labs (including ours) use 5 ng/mL; increasing chances of false-positive
 - Increasing the cutoff from 5 ng/mL to 10 ng/mL enhances the specificity of the assay

Implications of false-positive results:

- Impact on patient care and provider-patient relationship [4]
- Potential for unwarranted suspicion of non-adherence or illicit drug use
- Risk of punitive measures or loss of trust

CONCLUSION

The possibility for a UDT to yield false-positive results due to cross reactivity between medications highlight the importance of awareness amongst providers regarding inherent limitations of testing, as false-positive results can significantly impact patient care in addition to the provider-patient relationship

REFERENCES

1.Christo, Paul J., et al. "Urine drug testing in chronic pain." *Pain physician* 14.2 (2011): 123.

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3. Böttcher M, Beck O. Evaluation of buprenorphine CEDIA assay versus GC-MS and ELISA using urine samples from patients in substitution treatment. *J Anal Toxicol.* 2005;29(8):769-776.

4. McMillin GA, Slawson MH, Marin SJ, Johnson-Davis KL. Demystifying analytical approaches for urine drug testing to evaluate medication adherence in chronic pain management. *J Pain Palliat Care Pharmacother.* 2013;27(4):322-339.

5. Reisfield GM, Goldberger BA, Bertholf RL. 'False-positive' and 'false-negative' test results in clinical urine drug testing. *Bioanalysis.* 2009;1(5):937-952.