

JAMA Diagnostic Test Interpretation

Urine Drug Screens to Monitor Opioid Use for Managing Chronic Pain

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A 53-year-old woman presented for a prescription refill of hydrocodone/acetaminophen 10 mg/325 mg. She had chronic low back pain and partial paralysis from a thoracic spinal cord infarction, secondary to aortic dissection from prior cocaine use. Taking 2 to 3 tablets of hydrocodone/acetaminophen daily improved her back pain from 5 to 2 on a 10-point scale. She reported no recent illicit substance or drug use and stated her last dose of hydrocodone was that day. The patient had not achieved pain control with prior nonopioid pharmacologic pain management, including duloxetine and gabapentin. Although past cocaine use was a risk factor for opioid misuse, a trial of hydrocodone was initiated, after discussion of risks and benefits, with a plan for careful monitoring. The state prescription drug monitoring program showed no other prescribers of controlled substances. A urine immunoassay drug screen was ordered to evaluate for medication misuse and illicit use (Table).

Table. Urine Drug Screen Results

Component	Patient's Value	Reference Standard for Nonuse
Benzodiazepines	Negative	Negative
Cocaine	Positive	Negative
THC (marijuana)	Negative	Negative
MDMA	Negative	Negative
Methadone	Negative	Negative
Methamphetamine	Negative	Negative
Opiates	Negative	Negative
Phencyclidine	Negative	Negative

Abbreviations: MDMA, 3,4-methylenedioxy-methamphetamine; THC, tetrahydrocannabinol.

Answer

C. The patient may be using hydrocodone but is using cocaine.

Test Characteristics

The use of opioids for treating chronic noncancer pain has increased substantially, correlating with an increase in opioid use disorder and overdose.¹ The Centers for Disease Control and Prevention (CDC) guidelines for prescribing opioids for chronic pain suggest performing a urine drug screening before initiating treatment and considering screening at least annually.²

A urine drug screen is commonly performed using immunoassay panels that detect illicit drugs and frequently prescribed substances with potential for misuse. The drugs detected by these tests can vary, but a urine drug screen typically tests for opiates, opioids, cocaine, amphetamines, benzodiazepines, and cannabinoids. Different laboratories use different assays, and clinicians should be familiar with the drugs and metabolites measured by their laboratory and the associated detection thresholds and assay limitations.

Most opiate immunoassays are calibrated to detect morphine and codeine; they have varying performance to detect semisynthetic opioids (eg, hydrocodone and oxycodone) and do not detect synthetic opioids (eg, methadone and fentanyl) (Box).³ Immunoassays designed to detect semisynthetic and synthetic opioids have better diagnostic accuracy. Methadone immunoas-

HOW WOULD YOU INTERPRET THESE RESULTS?

- A.** The patient is not using hydrocodone but is using cocaine.
- B.** The patient is not using hydrocodone but may be using cocaine.
- C.** The patient may be using hydrocodone but is using cocaine.
- D.** The patient may be using both hydrocodone and cocaine.

says can have sensitivities greater than 95%.⁴ Hydrocodone is the most commonly prescribed opioid in the United States,⁵ yet some opiate screens are not sufficiently sensitive to detect it. For example, in one study, 72% (81/112) of urine specimens that had unexpected negative opiate immunoassay results were positive for hydrocodone or hydromorphone by gas chromatography mass spectrometry.⁶

Diagnostic accuracy of drug screens varies by drug class and assay manufacturer. Cocaine immunoassays have positive predictive values near 100%.^{4,7} The Medicare midpoint reimbursement for urine drug screening ranges from \$20.22 to \$107.85 based on the complexity of instrumentation used to read assay results.⁸ Immunoassays can be an inexpensive method for screening, although the limitations must be well understood.⁹

Application of Test Results to This Patient

CDC guidelines note that a urine drug screening may be clinically useful to determine whether patients are taking prescribed opioids, other substances with risk of misuse, or both.³ This patient's negative opiate screen may raise suspicion for nonadherence or diversion (giving or selling the medication to others). However, because the opiate screen used has limited cross-reactivity and a high cutoff (2000 ng/mL) for detecting hydrocodone,¹⁰ the negative result may be false. False-negative results may also occur when metabolite concentration is low. A test that improves

Box. Opioids by Type

Natural opioids (opiates)

Morphine

Codeine

Thebaine

Semisynthetic opioids

Heroin

Hydromorphone

Hydrocodone

Oxycodone

Fully synthetic opioids

Methadone

Fentanyl

Tramadol

Pethidine

Levorphanol

Dextropropoxyphene

Opioid antagonists and agonist/antagonists

Buprenorphine

Naloxone

overall diagnostic accuracy by increasing the sensitivity and specificity for hydrocodone and its metabolites would be necessary to confirm its absence. In contrast, the false-positive rate for a cocaine urine drug screening is near zero.

What Are Alternative Diagnostic Testing Approaches?

Assays using mass spectrometry can provide definitive drug and metabolite identification with improved sensitivity and specificity over

immunoassay methods; however, results may take longer, and cost is more than the widely available immunoassay screens. Medicare midpoint reimbursement for mass spectrometry-based drug tests ranges from \$158.98 to \$343.07, depending on the number of drug classes included.⁸

Patient Outcome

The patient restated that she had not used cocaine and was taking hydrocodone daily. The physician informed the patient that given the likelihood of cocaine use, she would no longer prescribe hydrocodone but wanted to continue caring for the patient. Naproxen and topical lidocaine were recommended, and the patient was referred to a pain management program. The patient canceled her next appointment. The state prescription drug monitoring program revealed new hydrocodone prescriptions from another clinician.

Clinical Bottom Line

- Centers for Disease Control and Prevention guidelines recommend obtaining a urine drug screening prior to the initiation of opioids for chronic pain and considering at least yearly screens thereafter.
- Clinicians must be familiar with the drugs and metabolites measured by a given urine drug screening and the associated detection thresholds and assay limitations.
- Opiate immunoassays may not detect semisynthetic opioids with adequate sensitivity and will not detect synthetic opioids.
- Patients should not be dismissed from care based on urine drug screening results. Unexpected results may require confirmation and should be used to modify the care plan, which may involve discontinuing opioids.

ARTICLE INFORMATION

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