



URINE DRUG TESTS IN A PRIVATE CHRONIC PAIN PRACTICE

The likelihood of surprises leads to the recommendation that virtually all patients who receive chronic opioids should be tested initially, occasionally at random, as well as for cause.

By Jennifer Schneider, MD and Ashley Miller

Physicians who prescribe opioids for chronic pain are increasingly ordering urine drug tests (UDT) as part of the assessment and follow-up of such patients. The current recommendation is to do such screens initially and then subsequently on a random basis on all such patients. Those of us, like myself, who have been treating some chronic pain patients with opioids for many years have, in the past, obtained UDTs selectively on only those patients whose history or behavior raised some red flags for abuse or addiction potential. Yet physicians who do only selective UDTs may find unexpected results.

In 2007, Michna et al. reported on a retrospective analysis of data from 470 patients who had urine drug testing at a pain management program in an urban teaching hospital.¹ They found a 45% incidence of unexpected urine screens. Twenty percent had an illicit substance in their urine. Other abnormalities were the absence of a prescribed opioid or an adulterated urine sample. The only predictive variable for an abnormal UDS was younger age. They observed that common patient

descriptors and number, type, or dose of prescribed opioids were poor predictors of abnormal results.

To determine how likely it is that patients in a small private chronic pain practice would have abnormal urine drug tests, all patients on chronic opioids who were seen for routine appointments over a two-month period were asked to submit urine specimens in the office. This article describes the results obtained in this population of 188 patients.

Background

This is a private pain management practice in which medications are prescribed but no invasive procedures carried out. The physician has a background in internal medicine, addiction medicine, and pain management. Most patients are referred by other physicians. At the first visit, a history and physical exam is carried out, including a social and addiction history; procurement of old medical records; and photographing the patients. If patients are to be prescribed opioids, they sign an agreement that specifies the physician's expectations of the patients:

- They will not use illegal drugs,
- They will not change their dose without prior discussion with the physician,
- They will not obtain scheduled substances from another provider without notifying the pain physician,
- They will get their prescriptions filled at a single pharmacy (of their choosing),
- They will obtain consultations or go to physical therapy if asked to,
- They will not be given early refills if the medications are used up early or are lost or stolen, and
- They will give a urine specimen for drug testing if asked.

Breaches of the agreement are evaluated on a case-by-case basis.

The patients have a wide variety of chronic non-cancer pain with back pain being the most common diagnosis in the practice. Many of the patients have undergone surgery or other invasive procedures and are still in significant pain. They are informed early on that the physician will work with them if they have other issues such as addiction, but that lying to

the physician is likely to get them discharged. Stable patients are typically seen once every two months. Most patients on opioids are given both sustained-release and break-through pain medication.

Methods

In March and April of 2007, every patient coming in for a routine or urgent exam or consultation was asked to submit a urine specimen. Although all had given permission to do this as part of the opioid agreement they signed when first seen, many had not been tested in a long time and were not expecting it. Some long-term patients had not had an initial urine drug test (UDT). The patients were not observed urinating, but the medical assistant checked the temperature of the freshly voided urine as shown on a liquid crystal thermometer on the side of the cup, to assure it was within the range of 90 to 100 degrees Fahrenheit. Specific gravity measurements were not done. The patients were asked when they had last taken each of their opioid medications. The urine specimens were sent to a local laboratory where they were screened by enzyme immunoassay (EIA) using the lab's "routine" urine drug screen which included the usual drugs of abuse—alcohol, amphetamines, cannabinoids, cocaine, and phencyclidine—plus opiates, benzodiazepines, barbiturates, and propoxyphene, as well as whatever scheduled drugs the patient was being prescribed. Immunoassays have limitations regarding sensitivity and specificity. The immunoassay used by this laboratory employed an Olympus 2700 machine and Syva reagents, when available, along with Microgenics reagents for oxycodone and oxymorphone. Positive results were confirmed using a gas chromatography-mass spectrometry (GC/MS) test, which also provided a quantitative determination.

A total of 188 patients were screened. Their mean age was 53.8 years \pm 11.64, with an age range of 23 to 91. The results were classified as expected or unexpected. "Unexpected" results—found in 29 patients (15.4%)—were those in which the urine: (1) contained illicit substances, (2) contained another non-prescribed opioid, and/or (3) did not contain a prescribed opioid. Whenever an unexpected result was obtained, the patient was questioned for an explanation. For example, two patients had amphetamines in their urine because they were being prescribed

TABLE 1. Summary of Results of Initial Testing In This Practice (N = 188)

	Number	Percent (of 188)
Expected	159	84.6%
Unexpected	29	15.4%
Unexpected positive	26	13.8%
Any illicit drug	19	10.1%
Marijuana only	15	8.0%
Other illicit drugs	4	2.1%
Non-prescribed opioids	7	3.7%
Unexpected negative	3	1.6%

these drugs by a psychiatrist. In another case, a urine that screened positive for amphetamines was in fact negative on GC/MS. In yet another case, the patient had not taken a breakthrough pain medication in the past 12 hours but had mistakenly told us initially that she had taken both the long-acting and the short-acting that morning. If we were uncertain whether an unexpected result could reflect a metabolite of a prescribed drug, the laboratory was consulted.

Clinicians who order urine drug tests need to understand the various types of urine tests and what they can or cannot do. Standard screening tests report only whether various classes of drugs are present or absent based on an *arbitrary cut-off level*. If a member of the drug class, (for example, opiates or benzodiazepines) is present in a quantity below the cut-off, the test is reported as negative. This is why it is a good idea to ask, at the time of testing, what time the patient last took any of the drugs being tested. The standard immunoassay reacts only with natural opiates (such as morphine, hydrocodone, hydromorphone, and codeine). This test is likely to miss semi-synthetic and synthetic opioids (such as fentanyl, oxycodone, and oxymorphone), although very high doses of semisynthetic opioids (e.g., oxycodone) may be picked up on the immunoassay. To identify specific drugs and their concentration in the urine, labs offer gas chromatography/mass spectrometry (GC/MS) or high-performance liquid chromatography (HPLC). Unexpected

positive and negative immunoassay results should be confirmed by one of these more specific techniques.

The clinician also needs to be familiar with various opioid metabolic pathways in order to correctly interpret the presence in the urine of prescription opioids that had not been prescribed for the particular patient. For example, codeine is metabolized to morphine, hydrocodone to hydromorphone, and oxycodone to oxymorphone.^{2,3} A patient prescribed codeine might appropriately have morphine in the urine. However, the reverse is not true—codeine should not be present in the urine of a patient prescribed morphine. Likewise for hydrocodone and oxycodone.^{4,5} Additionally, in some patients treated chronically with morphine, relatively small quantities of hydromorphone can appear in the urine as a result of a minor metabolic pathway.⁶

Whenever a non-prescribed opioid appeared in the urine and we were uncertain if it could be a metabolite of the prescribed opioid, the laboratory's toxicologist or other expert was consulted. Urine results were classified as unexpected only if no legitimate explanation for them could be obtained.

Because GC/MS testing was specified only for the prescribed opioids (e.g. oxycodone, fentanyl), we may have missed the presence of non-specified drugs obtained from other sources, and therefore might have underestimated the number of abnormal results. To address this deficiency, approximately four months after

the initial round of UDTs, we retested as many patients as possible, this time obtaining a broader range of confirmatory tests on every single patient, including fentanyl, oxycodone, oxymorphone, and hydromorphone, as well as to determine which opioids were present in specimens that tested positive for natural opiates (e.g. morphine, codeine, hydrocodone, hydromorphone). Whenever possible, the repeat tests were submitted to a national laboratories (Dominion Diagnostics) rather than to local labs.

Results

The results are summarized in Table 1. Of the 188 patients tested on the first round, 159 (84.6%) had expected results, and 29 (15.4%) had unexpected results. Of the latter, twenty-six patients (13.8% of the total) had an unexpected positive result—that is, they contained either a drug of abuse or a non-prescribed scheduled drug—and three (1.6%) did not contain a prescribed opioid. Of the 26 positives, 19 (10.1% of the total patients) showed illicit substances. Of these, 15 urines contained only cannabis (8.0% of the total), two had cocaine (one of which also had cannabis), and two had methamphetamine (the d-isomer, found in street methamphetamine). In addition, there were seven cases (3.7%) of non-prescribed scheduled substances in the urine.

One patient who had methamphetamine (on two drug screens a week apart) denied using it, and was told she would henceforth be treated only with non-opioids; she chose not to return to the practice. The other patient admitted using this drug, but denied regular use. He was counseled, and more regular urine testing was initiated to monitor compliance. One patient who had cocaine in the urine denied using it and was eventually discharged from the practice. The other patient admitted to occasional cocaine and cannabis use, was counseled, referred to therapy and a 12-step support group, and agreed to frequent random urine drug screens to monitor her compliance. The marijuana-using patients—several of whom complained that it helped their pain and that, after all, medical marijuana was legal in this state (Arizona)—were advised that the DEA frowns on cannabis use and that they would need to refrain from using it. A follow-up UDT (with a quantitative GC/MS test for cannabinoids) was obtained in each case to be sure

that the cannabinoid level was dropping or negative. One patient decided he preferred to seek pain management elsewhere rather than stop smoking marijuana.

Three patients had non-prescribed methadone in their urine, in addition to their prescribed opioids. One patient, who was referred for consultation by another physician who was prescribing morphine for her, vehemently denied using methadone, despite large quantities of methadone and methadone metabolite in the urine. This issue was referred back to the referring physician to sort out. The second patient had been prescribed methadone by me in the past and admitted having taken some that he had left over. He was counseled not to change his regimen without prior consultation. The third patient, surprisingly, admitted that he'd been going to a local methadone clinic for years (methadone clinics in this city often end up treating pain patients as well as addicted clients), that he took every opioid prescription I gave him to be reviewed by the methadone clinic staff, and that the combination of the two drugs was working very well for him. This physician was not happy having been kept in the dark by the methadone clinic but, understandably, they are very concerned about the privacy of their clients. The patient had not been asked for a urine drug screen when he first was seen, several years earlier, and at that time he did not volunteer information about his methadone prescription because, as he now explained, he was afraid he would not be accepted as a patient. He tearfully expressed great relief at no longer having this secret and living with the fear that he would be discharged from the practice. The patient was very functional, had never exhibited any aberrant drug-related behaviors, was very compliant, and there had never been any red flags for addictive disorders. The outcome of this case was that after discussion with the methadone clinic, I agreed to take over his methadone prescribing, thereby keeping him on the regimen that had worked well for him for a long time.

Four patients had other non-prescribed opioids: two cases of propoxyphene, one of morphine, and one of oxycodone. All admitted getting a pill from a relative or friend. They were informed that was, in fact, a felony and were admonished not to do it again.

Finally, three patients had urines negative for their prescribed drugs (sustained-release oxycodone in 2 cases, methadone in the third). On repeat questioning, all insisted that they were taking their drugs regularly, including on the morning of their urine drug test. No acceptable explanation could be found and the patients were informed that they would no longer be provided those medications.

Follow-up Study

Four months after the initial study, patients were asked to submit another urine specimen for UDT. Of the 159 patients whose first test was as expected, it was possible to retest 101 (63.5%). The samples were submitted to a national lab or local labs for broader testing, including GC/MS testing on a wider panel of opioids. The reasons for not testing the remaining patients included:

- had moved away,
- transferred care,
- were initially seen for a one-time consult (19 patients);
- hadn't yet returned for their next appointment (16);
- were unable to provide a sample because they were in a wheelchair, hospitalized, in hospice care, elderly and frail, bashful bladder (12),
- were self-pay and couldn't afford another UDT (6),
- had died in the interim (1), and
- refused to stay (1).

This last patient was generally very compliant, had never exhibited any aberrant drug-related behaviors, and was extremely involved with her own business, working perhaps 12 hours/day most days.

Of the 101 urine specimens from patients who had previously had good results on UDT, the new findings after testing for a wider array of opioids consisted of four cases where small amounts of hydromorphone were found. Hydromorphone is known to be a low-level metabolite of morphine. One patient, on high-dose morphine, had a small quantity of codeine (1.2%) in the urine; the lab informed us that in the production of morphine a small amount of codeine can sometimes be included. One patient had cocaine (and cocaine metabolite) on repeat testing, whereas the two prior urines had been clean. The patient initially denied having used cocaine, but later that day admitted it. It's common for a patient

when first confronted with evidence of illicit drug use to deny it, then later reconsider and come clean. When the initial discussion is unsatisfactory, I usually suggest to such a patient that if he (or she) reconsiders what he wants to tell me, he should phone and we would start all over talking about the abnormal UDT. In this case, the patient did phone, and we had a lengthy discussion about follow-up plans for preventing any further cocaine use.

Among the 29 patients whose initial urine tests detected abnormalities, 10 are no longer in the practice, and 13 submitted urines. Of these, four had abnormal results: three still contained cannabinoids, and one again had non-prescribed morphine. The patients who were still smoking marijuana have been counseled and warned; addiction treatment has been suggested, and additional UDTs will be obtained. The patient with non-prescribed morphine for the second time was referred for addiction counseling and was told her long-acting oxycodone would be tapered. She made the appointment for counseling, and then threw away her remaining oxycodone. The opioid agreement that patients sign specifically states they should not throw away their medications, but it is not uncommon for frustrated patients to impulsively do this, and then phone a day or two later, in withdrawal, asking for more opioids to alleviate their symptoms. When this patient phoned with such a request, she was told that the best that could be done would be to phone in a prescription for clonidine to help with withdrawal. She is now off all opioids and about to begin an addiction program.

In summary, on follow-up testing, one additional case of illicit drug use was uncovered, while 9 of 13 patients with previously abnormal results now had clean urines.

Discussion

The experience of obtaining a urine drug screen on every patient was very educational for this physician. First, it was gratifying that there were not too many surprises. Probably the biggest one was the number of patients who were using marijuana, some for its medical benefits and others undoubtedly for recreation. The patient who chose to seek another pain doctor rather than quit smoking marijuana was certainly addicted but is in strong denial about this; addiction issues are also

being addressed with the patients who continue to smoke despite admonition to stop. The marijuana issue is a big one in states, such as Arizona, which have passed statutes legalizing the medical use of marijuana. Some patients on opioids truly find that marijuana is more effective than prescribed anti-emetics to treat their nausea. Others appreciate its pain-relieving effect. Recent studies have shown that cannabinoids alleviate multiple sclerosis-related pain⁷ and other neuropathic pain⁸ and have an opioid-sparing effect in pain relief.⁹ In Canada and the UK, a plant-derived cannabinoid nasal spray (Sativex) is approved for the pain and spasticity of multiple sclerosis. Nonetheless, as long as marijuana cannot be purchased legally in the U.S, people who use it are likely to have access to the street drug scene, and therefore potentially could be more knowledgeable than nonusers on how to sell their prescribed opioids. For this reason—and because the DEA disapproves of prescribing opioids to marijuana-using patients—it seems prudent to counsel such patients that they will need to stop using marijuana if they want to be prescribed opioids.

The three cases of nonprescribed methadone use were also a surprise, as this is an unlikely drug of abuse, especially in patients who are already being prescribed opioids. In such cases, the physician needs to address the meaning of the behavior. The patient who used a few pills left over from last year was not a serious problem; his behavior was on a par with the other patients who had occasionally used a family member or friend's oxycodone or propoxyphene. While in this prescriber's judgment this did not establish grounds for stopping opioids, these patients will be observed closely and understand that further "borrowing" of medications from others may become grounds for opioid cessation. Counseling against using non-prescribed opioids or against changing one's regimen usually suffices.

The patient who repeatedly denied methadone use in the face of a positive urine is a more serious issue. It is possible to work with patients who admit to illicit or nonprescribed drug use, to sort out the reasons, to distinguish pseudoaddiction (undertreated pain) from addiction or to recognize naivete or ignorance, and to deal with each accordingly. But it is more problematic to work with a patient who lies. For this reason, patients who re-

peatedly lie are usually dismissed from the practice.

On the other hand, the patient who had been going to the methadone clinic daily for years as well as the pain management practice benefited greatly from the consequences of the urine drug screen. He was unaware that a regular physician, working outside a methadone clinic, could prescribe methadone for chronic pain, and was overwhelmed with gratitude that this was possible and with regret that he'd been carrying the secret for so long when a simple solution was available. More than any other, it was this one patient's case that made me realize how valuable it is to obtain a urine drug screen on every patient initially, as well as occasionally at follow-up.

The three cases of negative urine drug screens in patients on sustained-release opioids or methadone who insisted they were taking them regularly suggests the possibility of diversion. In such cases, it is advisable to confirm with the patient the exact time they took the last dose and discuss issues of dosage, cutoffs, and lab error with the lab's toxicologist in search of a legitimate explanation for the negative result. If none are found, then it is reasonable to discontinue prescribing those drugs. These patients were not continued on the opioids that were found missing in the urine. Again, the issue of the patients' truthfulness was paramount in the physician's decision.

Compared to Michna et al. findings of 45% unexpected urine results in their population of chronic pain patients at an urban university hospital pain clinic,¹ the present finding of 14.8% unexpected results suggests that these two settings may have a different patient population. In the Michna study, the mean age of the patients was 47.0 ± 10.4 years, with an age range of 21 to 85. In the present study, the patients were, on the average, six years older, with a mean age of 53.8 ± 11.6 years, and an age range of 23 to 91. Older patients may be less likely to demonstrate aberrant behaviors. Perhaps the two populations differed in their socioeconomic status. Another difference between these two settings is that at a teaching hospital patients are likely to see a parade of different health-care providers so that there is less continuity of care. Moreover, it is unclear whether in such a setting patients are evaluated routinely regarding any prior use of illicit drugs, personal and

family history of addiction, and their work and family life. This is more likely to be done in a private pain and addiction practice. In addition, when the same physician in an office setting sees the patient for months and years, this may make the patient feel more accountable to the physician, can build a positive ongoing relationship between physician and patient, and may make it more likely for the physician to recognize red flags for abuse, psychosocial issues that interfere with compliance, etc.

Conclusion

This study confirmed the utility of obtaining initial urine drug screens on patients being considered for opioid treatment and occasionally, at random, during follow-up. My management of several cases improved as a result of having obtained these tests. The lower percentage of unexpected results in a private practice compared with a university teaching hospital pain clinic suggests that an ongoing relationship between patient and practitioner can be one element in increasing the

accountability that patients feel and in decreasing potential aberrant behaviors. While there are some clinicians who consider urine drug testing should be part of every visit for patients on chronic opioids, I believe it makes more clinical sense to test every opioid-receiving patient occasionally, at random, rather than on every visit. What we can all agree on is that routine urine drug tests increase patients' accountability and are highly recommended to monitor patient compliance and potential diversion. ■

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