Helping Physicians Interpret the Results of Opiate Urine Drug Tests

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Abstract

Opiates have been making headlines in the news over the past decade with their use and misuse. Opiates play a significant role in the management of pain. The opioid prescribing rate has been declining since 2012, but the amount of opioids in morphine milligram equivalents prescribed per person is still around three times higher than it was in 1999[1]. Physicians are under increased pressure to monitor compliance. One way for physicians to monitor compliance is in the form of signed contracts with patients who submit urine samples for proof of compliance. In order to monitor compliance, an understanding of the metabolism and half-life of opiates, the detection methods of opiates in urine, in this case enzyme immunoassay screens (EIA) and liquid chromatography-mass spectroscopy (LC-MS) confirmation testing is necessary. A literature review was conducted on the detection of opiates in the urine and a summary information sheet was created in order to help physicians in the interpretation of urine drug test results when assessing patient drug compliance. Opiates have a short half-life of 3-6 hours and are reduced into metabolites that can also have a pain-relieving effect. When the body metabolizes codeine, it becomes morphine, and then hydromorphine. A patient that takes codeine chronically will have high levels of morphine in their urine, which can be confusing to medical staff questioning compliance. The antibodies used in EIA drug screens can also cross-react with other drugs, resulting in false negatives or false positives. The short half-life of opiates results in challenges for their detection in urine specimens. Many patients take opiates as needed unless they submit a urine sample hours after taking the medication; there is no way to tell compliance. LC-MS is a more sensitive and specific method of detection. For this reason, some laboratories are now considering using confirmatory testing only. However, LC-MS also provides information about the drug metabolites found in the urine, which can result in incorrect interpretation of patient compliance. Sharing educational information with medical staff and patients regarding the interpretation of laboratory drug test results can help build a relationship of trust, which will benefit all individuals involved in a current opiate crisis.

Overview

Medical personnel can have difficulty with the interpretation of urine drug tests used to monitor compliance of pain management. In order to assist physicians and other medical personnel in the interpretation of opiate urine drug testing, a information sheet was developed explaining the metabolism of opiates, factors affecting urine drug concentration, detection windows for opiates in urine, and interpretation of urine drug testing.

Introduction

Opiate abuse has been making headlines over the past decade. Although the number of prescriptions written for opioids has been decreasing, the amount of opioids prescribed remains approximately three times as high as it was in 1999[1]. In the 2018 Annual Surveillance Report of Drug-Related Risks and Outcomes, the Center for Disease Control (CDC) reported that some states had more opiate prescriptions then the state had residents[2]. Physicians have been under increasing pressure to prescribe opiates for pain management by their patients, while simultaneously being under pressure by the CDC and Food and Drug Administration (FDA) to be held accountable for the prescriptions written to patients. In order to monitor compliance, many pain management centers have drafted a contract that states the patient must attend routine visits with submitted urine samples. If the contract is broken due to positive urine drug test for a non-prescribed opiate or lack of opiate prescribed, the patient is then taken off the therapy regiment[3].

Urine drug concentrations are dependent on several factors, including dosage, time of last dose, the patient's hydration status, and the patient's genotype for drug metabolism. If an EIA urine drug screen is performed, false negatives can be an issue due to their relatively short half-life (between 3-6 hours[4] depending on the parent compound), the time between dosing and sample collection, and the fact that some opiates, such as Oxycodone, are not detected very well by the antibodies used in the assay method. In order to combat this, some clinical laboratories are now directly using the confirmatory method of an LC-MS. The LC-MS is a more sensitive assay, able to both detect 50 ng/mL and to identify and quantify drug metabolites. This allows the laboratory to detect drugs and metabolites in the patient for a longer timeframe.

Confusion about patient compliance occurs when high amounts of the parent drug metabolites are seen, or when drugs are not detectable in the specimen. Opiates are metabolized by CYP450 enzymes in the first phase of metabolism, and in the second phase, conjugation occurs, making the metabolite more water-soluble[5]. Codeine, for example, is metabolized into morphine then into hydro-morphine. If the patient is taking codeine for chronic use, morphine levels will also be high in the sample due to its longer half-life[4]. Obtaining results that are misleading can cause medical staff to question if the patient is adhering to the pain management prescribed.

Intercommunication between medical staff and laboratory professionals for correct interpretation of drug testing can aid in the correction of any misinterpretation of the urine drug test results. Understanding the metabolites and detection limits are critical for proper patient treatment and preventing inappropriate removal of patients from pain management plans. This project details the development of a information sheet to aid in the interpretation of laboratory drug testing for medical personnel involved in pain management for patients taking opiate medication.

Methods

A literature review was performed looking at the opiate metabolism and detection limits using EIA and LC-MS as the drug testing methodologies. Information obtained described how opiate metabolism, dosage, time from dosing, patient hydration status, and genotype makeup can affect testing results that are used to determine compliance with pain management. Drugs like tramadol or fentanyl were not included because these pain-relieving drugs are not routinely tested.

Results

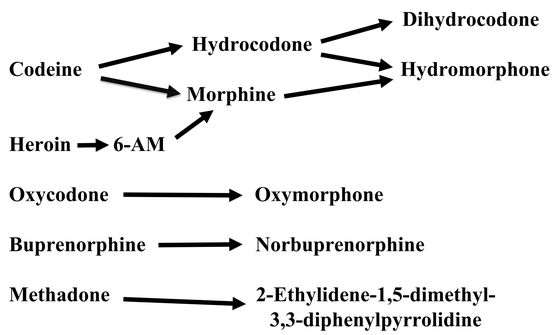

Figure 1. Opiates share common drug metabolites, such as morphine and hydromorphone, which can affect how the results are interpreted.

DRUG	HALF-LIFE	DETECTION LIMITS
Heroin	0.1 – 0.25 Hours	<1 Day
Codeine	1.9 – 3.9 Hours	1 – 3 Days
Morphine	1.3 – 6.7 Hours	1 – 3 Days
Hydromorphine	1.5 – 3.8 Hours	1 – 3 Days
Oxycodone	3.0 – 6.0 Hours	1 – 3 Days
Oxymorphine	7.5 – 9.5 Hours	1 – 3 Days
Buprenorphine	24 - 42 Hours	3 – 4 Days
Methadone	8.0 - 50 Hours	7 days

Table 1. This table represents the drug, the half life of the opiate in plasma, and the length of time in which the opioid can still be detected in the urine[6,7].

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Discussion

Physicians have difficulty detecting single-use or low dose opiates due to their short half-life. In many situations, after 24 hours, the parent drug has been metabolized, and is no longer detectable. The drug metabolites may still be detectable for what may be an additional few hours to a few days. Codeine, for example, takes 1-3 days to metabolize into morphine (between 5-10%), and to a lesser extent, hydrocodone. The morphine then takes an additional 1-3 days to break down into hydromorphone. If codeine is the drug the patient is using, then morphine is most likely to be seen a few days after the codeine prescription has been ingested. Hydrocodone is the opioid found in Vicodin. If morphine and or hydrocodone are detected in the patient's urine after using codeine as a prescribed drug, the physician may incorrectly assume the patient has been using heroin, morphine or Vicodin, which could result in the patient being removed from a drug treatment program.

EIA is used to screen out negative results. However, the antibodies used in the kit can be too specific for particular opiates, leading to false negatives in the detection of other forms of opiates and their metabolites. Liquid chromatography is more sensitive, and is able to detect the metabolites of the drug. If there are any opiates in the urine sample, the LC-MS is more likely to detect them. For this reason, many clinical laboratories are omitting the immunoassay drug screening test, and starting directly with a confirmatory LC-MS test.

Many factors can affect drug screening. These factors are unique for each patient and can interact with one another. Gathering a full history on each patient can minimize how individual patient factors can mislead the test being performed.

This information sheet should serve as a quick reference as to how complex drug testing can be. Results can be misleading if they are not interpreted keeping the drug metabolism, clearance rates, and other factors in mind. This information sheet can serve as a communication point between medical staff and the medical laboratory. Further research is needed to determine if creating this education information will help the relationship between patient and provider.

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