AN OVERVIEW OF URINE DRUG TEST AND ROLE OF PHARMACIST TOGETHER WITH LABORATORY

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Abstract:
Urine drug monitoring, often known as UDM, is an essential instrument for screening patients who are receiving opioid medication for adherence and identifying potential instances of misuse and abuse. The necessity of UDM as a standard of care is emphasized several times across the various guidelines for opioid therapy. It is suggested that all patients who are receiving long-term opioid therapy undergo routine and random monitoring prior to the beginning of treatment and even while they are receiving treatment. The recommended frequency of UDM varies from person to person and is determined by clinical judgment and individual risk assessment. As is the case with any other diagnostic or monitoring test, the objective of UDM should be to direct treatment and enhance the quality of care provided to patients. Inappropriate interpretation of the results and inability to arrange definitive testing when it is necessary can have a negative impact on patient care. It is essential for pharmacists to be able to determine the right dosage and excretion of various medications in this section together.

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Introduction:

The conventional methods of drug testing in clinical medicine have traditionally depended on the methods that were initially established for use in the workplace. In spite of the fact that this study will concentrate on opioids, testing of a similar nature can be carried out for a wide variety of chemicals. The traditional testing method has two different levels of testing in its testing methodology. It is the goal of the first tier to screen a large number of specimens for opioids in a short amount of time. In most cases, the second level of testing is carried out by employing highly specific techniques, such as gas chromatography or liquid chromatography with mass spectrometry, which are used to validate the screening result. Confirmatory testing is required in both the forensic and workplace settings, with the latter setting adhering to the testing recommendations established by the Substance Abuse and Mental Health Services Administration (SAMHSA) [1]. It is possible that hospital laboratories that do urine drug testing primarily for clinical purposes do not commonly perform this second tier of testing [2]. This is due to the fact that confirming data are not typically available on the same day, and as a result, they are less likely to impact clinical decision making.

Regardless of the testing scheme, the initial screening stage is a very important component. When it comes to workplace opioid testing, the goal is to identify individuals who are using illegal drugs in a community that has a relatively low rate of opioid usage [3]. Due to the fact that individuals are pre-selected for screening in clinical settings based on clinical suspicion of drug exposure or prescription of opioid drugs, the prevalence of drug exposure is significantly greater in clinical settings [4]. In the clinical setting, where the goal is frequently to detect nonuse of a prescribed opioid medicine, which may imply drug diversion, where drug diversion is a key contributor to the current crisis of prescription opioid drugs, the purpose of testing may also be different. There is a significant influence that these variations in prevalence and testing purpose have on the utility of testing [5]. The effectiveness of the test can theoretically be increased in the clinical context by making adjustments to the concentration cutoff that is used to determine a positive or negative test. Most clinical laboratories still use the 300 ng/mL of morphine as the cutoff concentration for a positive opioid screen; however, the effectiveness of this cutoff concentration in the detection of intoxication or aberrant opioid use has not been rigorously evaluated in many clinical settings in which it is generally used. It is possible that this threshold is not suitable for children since they generate urine that is less concentrated [6]. This threshold was also created in adult populations. It has been suggested that lower thresholds should be used in the field of pain medicine. The level of 2,000 ng/mL that is established by the federal government and utilized in occupational testing (which will be discussed further below) is probably not acceptable in the majority of clinical settings.

Within the context of the workplace, the cutoff concentration has received a great deal more attention than it traditionally has. Because of the potential medical and legal repercussions of testing in the workplace, there is a significant emphasis placed on the ability to control false positive results. In several opiate immunoassays, it has been noted that commonly administered medications, such as fluoroquinolone antibiotics, might produce false positive results [7]. It is possible to correct for these false positive immunoassay results through the use of confirmatory testing; however, this comes at a large cost because, in contrast to automated immunoassay testing, confirmatory testing is a process that requires great amounts of manual labor. Consequently, it is of the utmost importance to reduce the number of false positive outcomes. Prior to the year 1998, the SAMHSA threshold value for confirmatory testing was a morphine concentration of 300 ng/mL [7]. This standard was imposed by the federal government. The federal occupational testing standards increased the confirmatory morphine concentration threshold to 2,000 ng/mL [7]. This was done in order to address the issue of natural morphine and codeine in poppy seed containing products, which can result in a "false" positive test for the usage of illegal drugs. This change in cutoff concentration was predicted to significantly improve the positive predictive value (i.e., reduce the number of false positive tests) of screening without having an impact on the negative predictive value of screening [8]. This was in the context of heroin being the opioid drug that was abused the most during the 1980s and 1990s. On the other hand, the epidemiology of opioid misuse has shifted, and it is highly likely that testing standards will need to be revised as well in order to improve the detection of prescription opioids, which are now more commonly abused than heroin [8].

Review:

Absorption, distribution, metabolism, and elimination are the four components that are used to quantify pharmacokinetics, which refers to the movement of the medication through the body. The pharmacokinetics of a medicine or its metabolites ultimately dictates how much of the drug or

metabolite is found in the urine and how quickly it is found there. In order to correctly interpret the results of UDM by chromatography, it is essential to have a solid understanding of pharmacokinetics. This is because the data that are provided comprise both parent medicines and metabolites [9].

The patient might be misled into believing that they are taking a medicine that was not prescribed to them if they are exposed to certain metabolites of commercially available pharmaceuticals. For instance, hydromorphone is a metabolite of hydrocodone, and oxymorphone is a metabolite of oxycodone. Both of these metabolites are available for purchase as stand-alone prescriptions on the commercial market. Similarly, oxazepam and temazepam are both metabolites of diazepam, and both of these substances are available for purchase in the market. Additionally, it is essential to take into account the patient's body habitus, since this has an impact on the volume of distribution. This means that a greater quantity of the medication is stored in the periphery, which may result in a longer detection window. Patients who have renal and/or hepatic impairment may experience a decrease in the removal of the drugs from their bodies [9].

Due to the fact that polymorphisms might have an effect on the outcomes, it is equally vital to take into consideration the function that pharmacogenetic polymorphism can play in UDM. Consider the case of a patient who is taking 30 milligrams of extended-release oxycodone twice a day like this. Cytochrome P450 enzyme 3A4 is responsible for the conversion of oxycodone into noroxycodone, whereas CYP2D6 is responsible for the conversion of oxymorphone, but to a considerably smaller level. In this particular scenario, the urine level of oxycodone in the patient should be higher than the amount of either of the metabolites, as determined by chromatography. More precisely, the level of noroxycodone in the patient's urine should be higher than the level of oxymorphone and vice versa. There are two possible explanations for the presence of only concentrations of oxycodone in the urine, if there are no metabolites present. The first possibility is that the patient dissolved oxycodone into the urine sample without ingesting it. The second possibility is that the patient may have poor activity of CYP2D6 and CYP3A4 isoenzymes, the latter of which can be confirmed by pharmacogenetic testing. On the other hand, interactions between drugs that inhibit CYP can also result in the same consequence [10].

The use of chromatography is often reserved for testing that is either confirmatory or definitive in the event that the first results of the UDM by IA are unexpected.1. Chromatography, in contrast to immunoassay, has the ability to identify the presence of particular medicines and/or metabolites. Chromatography and mass spectrometry (GC/MS), liquid chromatography tandem mass spectrometry (LC/MS/MS), and high-performance liquid chromatography are all examples of several types of chromatography testing. Depending on the particular test, chromatography may make use of either a gas or a liquid carrier medium in order to separate the substances that are present in the urine sample based on the molecular interactions that they have with the carrier medium (mostly due to differences in polarity). As part of this separation procedure, each of the separate compounds is introduced into a mass spectrometer. The mass spectrometer ionizes the compounds and identifies fragments by utilizing the mass-to-charge ratios of the compounds. The identification of various substances can be accomplished through the use of this approach by utilizing their molecular fingerprints [11].

Confirmatory testing has traditionally been performed using gas chromatography/mass spectrometry as the normative method. On the other hand, it is essential to point out that LC/MS/MS has been increasing popularity in comparison to GC/MS. As a result of the fact that the LC/MS/MS method requires a smaller volume of urine to carry out an analysis and that the analysis itself includes a second analytical separation phase, it is anticipated that it will have a lesser susceptibility to erroneous results that are brought about by the concurrent use of other medications [12].

When compared to IA, quantitative confirmation using chromatography offers a number of advantages, regardless of the test media being taken into consideration. The fact that it can identify even minute concentrations of particular medications and verify their presence in urine makes it a more accurate method.8. Furthermore, although there are still cutoff limitations connected with chromatography, the specific cutoffs found in chromatography are far lower in value compared to those found in IA testing. In conclusion, a study that was carried out in 2010 by Pesce and colleagues discovered that IA testing was related with different rates of false-negative results when compared to the results obtained by LC-MS/MS and other methods. To be more specific, the

percentages of false-negative results linked with IA were discovered to be 22%, 50%, and 23.4% for benzodiazepines, cocaine, and propoxyphene, respectively. It is unfortunate that the procedures of chromatography testing take longer to give results and are more expensive when compared to those of imaging analysis. The use of chromatographic testing procedures is therefore often reserved for situations in which the IA delivers results that are unexpected. In contrast, IA can be performed at the point of care using readable cups or strips that are located within the clinic, or it can be sent out for a turnaround time that ranges from 24 to 48 hours [13].

A screening for alcohol abuse, which can undermine the safe use of opioids, could also be something that health care practitioners could do. The term "dose dumping" refers to the phenomenon that occurs when alcohol speeds up the release of some sustained-release formulations. On top of that, drinking alcohol can further raise the probability of experiencing respiratory depression brought on by opioids. There are numerous laboratories that contain ethanol, which is then assessed through an enzymatic reaction and is often detectable twelve hours after the consumption of alcohol. When it comes to determining alcohol use, urinary ethanol is not the best marker to employ. There are two minor metabolites of ethanol that are produced by the enzyme UDP-glucuronosyltransferase. These metabolites are ethyl glucuronide (EtG) and ethyl sulfate (EtS). Following the use of alcohol, these indicators can be identified for a period of up to eighty hours. Some of the indicators that indicate extended and/or heavy drinking are phosphatidylethanol, γ-glutamyltransferase, and carbohydrate-deficient transferrin [14]. However, these indicators are not the only ones that may be used.

Because nordiazepam, oxazepam, and temazepam are all metabolites of diazepam, benzodiazepine immunoassays are frequently developed to detect these three psychoactive substances. Benzodiazepine independent assays, on the other hand, are also able to identify additional substances that share a structural similarity with benzodiazepines. In other words, the ability of benzodiazepines to cross-react with the IA test is what allows them to be distinguished from other drugs. While clonazepam and lorazepam have a modest level of cross-reactivity, they are typically not identified on benzodiazepine immunoassay procedures. Because of this, it is not unusual for patients who are taking lorazepam or clonazepam to have a negative result for benzodiazepines when they are tested using this IA. If these patients do test positive at modest dosages, it may be a cause for concern that they are taking a different benzodiazepine in place of or in addition to the drug that was prescribed to them [15].

Due to the fact that both amphetamines and methamphetamine are extremely basic compounds, it is challenging to create specific antibodies against them. As a result, they have a high rate of false-positive results when tested with IA. Due to the fact that methylphenidate is not an amphetamine, the amphetamine IA does not detect it. This is an essential fact to keep in mind. There is no cross-reactivity between the IA for cocaine and benzoylecgonine, which is a metabolite that is exclusive to cocaine and does not have any other metabolites. False positives are quite common using IA because of the lack of specificity of UDM. The only exception to this is when cocaine is being tested. It is imperative that clinicians acquire a complete medication history of the patient, which should include information on herbal remedies, vitamins, and over-the-counter drugs [15].

Conclusion:

Urine drug monitoring is an important method for determining whether or not a substance is being misused or abused, also known as adhering to the prescribed regimen. As a result of its low cost and rapid results, the UDM by IA test is the one that is utilized the most frequently. It does, however, come with a wide variety of outcomes that are both false positives and false negatives. Before making any adjustments that could potentially affect patient care, clinicians should first go through the process of obtaining conclusive results through confirmatory testing. Additionally, all of the data should be discussed with the patient. It is generally accepted that clinical pharmacy specialists are a good resource that is frequently underutilized for the purpose of providing guidance for the interpretation of chromatographic and immunoassay testing. They have a comprehensive understanding of drug metabolites and interactions that may increase or decrease drug concentrations, which may account for possible false positives and false negatives, and they are able to assist in the interpretation of unexpected results. Clinical pharmacy specialists have an excellent understanding of the physical and medicinal chemistry properties of laboratory testing. Laboratory medicine, on the other hand, is a field that is both complicated and constantly evolving, with new analytical methods and instruments being produced on a regular basis. In light of this, techniques differ significantly from one laboratory

to another, and even from one laboratory to another, even on occasion within the same laboratory. It is essential to implement quality control methods in order to guarantee accurate and dependable results. Clinical laboratories are staffed by medical technologists who have received extensive training in their respective fields. When it comes to the interpretation of laboratory tests and the limitations of those tests, pharmacists should seek the advice of medical technologists as consultants. In a similar vein, the pharmacist can act as a consultant to the laboratory in a variety of areas, including therapeutic medication monitoring, amongst many others. A better understanding of the clinical laboratory will be beneficial to pharmacists who are active in patient care. In addition, these pharmacists may discover new prospects for clinical pharmacy practice and the opportunity to communicate with other experts in the health care industry.

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