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Urine drug testing results and paired oral fluid comparison from patients enrolled in long-term medication-assisted treatment in Tennessee

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ABSTRACT

Urine drug testing is recommended for individuals receiving medication-assisted treatment. It provides objective information for practitioners to consider and may serve as a protective factor against drug-related mortality. The primary objective of our study was to describe urine drug testing results for patients undergoing long-term medication-assisted treatment (≥6 months). The secondary objective was to provide further evidence to establish oral fluid as a reliable alternative to urine. All subjects ($n = 639$) included in the study were enrolled in one of five treatment centers in the state of Tennessee, and all urine specimens were positive for either methadone or buprenorphine. Nicotine (87%), caffeine (70%), marijuana (15%), alcohol (14%) and gabapentin (10%) were the most prevalent substances identified through urine drug testing. The presence of non-maintenance opioids (prescription and/or heroin) may represent relapse; these drugs were present in 10% of specimens tested. Evidence of illicit drug use (cocaine, heroin, marijuana and/or methamphetamine) was detected in 19% specimens. For 126 of the 639 subjects included in the study, paired oral fluid and urine test results were compared for agreement. Of the total paired urine and oral fluid tests, approximately 7% were positive for a drug in both specimen types and 91% were negative in both, resulting in an overall agreement of 98%. The study demonstrates continued use of illicit and commercially available medications in a medication-assisted treatment population undergoing long-term treatment. The results affirm the reliability of oral fluid as an alternative specimen type for compliance testing in this population.

1. Introduction

According to the 2014 National Survey on Drug Use and Health, over 7 million individuals in the U.S. reported an illicit drug substance use disorder in the past year, of which 1.9 and 0.6 million were attributed to nonprescription opioids and heroin, respectively (Center for Behavioral Health Statistics and Quality, 2015). Opioid use disorder (OUD) is defined by the *Diagnostic and Statistical Manual of Mental Disorders*, *Fifth Edition* as "a problematic pattern of opioid use leading to clinically significant impairment or distress" with multiple signs such as ingestion of higher doses than prescribed, inability to decrease use, and interference of opioid use with personal and professional relationships and activities (American Psychiatric Association, 2013).

Opioid dependence increases an individual's mortality risk by nearly 15 times; however, this risk is lower for those actively engaged in a treatment program (Cousins et al., 2016; Degenhardt et al., 2011). Medication-assisted treatment (MAT), typically with buprenorphine or methadone, is a common treatment approach for OUD and has been shown to increase treatment retention, decrease infectious high-risk behaviors (e.g., intravenous drug use) and prevent accidental overdose in patients during active treatment (Connery, 2015).

The Substance Abuse and Mental Health Services Administration (SAMHSA) federal guidelines for opioid treatment programs (OTPs) mandate that programs administer adequate testing for drugs of abuse, including at least eight random drug tests yearly per patient in maintenance treatment (Substance Abuse and Mental Health Services Administration, 2015). Urine drug testing (UDT) in patients with OUD is also recommended by the American Society of Addiction Medicine during initial patient assessment and often during treatment (Kampman & Jarvis, 2015). UDT provides objective evidence of substance abuse and has been shown to have a protective effect against drug-related mortality in MAT patients (Cousins et al., 2011). A study

Abbreviations: GC–MS, gas chromatography–mass spectrometry; LC-MS-MS, liquid chromatography tandem mass spectrometry; LOQ, limit of quantitation; MAT, medication-assisted treatment; OTP, opioid treatment program; OUD, opioid use disorder; THC, tetrahydrocannabidiol; UDT, urine drug testing.

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of patients enrolled in MAT revealed that half of patients with positive opioid results denied use at least once during the study period. Patients were inconsistent in their denial; 34.9% would variably admit and deny opioid use at different times (Hilario et al., 2015). When interviewed, patients in long-term MAT acknowledged the importance of drug testing in remaining abstinent from drugs. One patient noted, "…it is difficult to stay clean without urine tests…" and "without urine tests everything would fall apart" (Lindgren, Eklund, Melin, & Graneheim, 2015, p. 966).

Due to its ability to be observed without creating an uncomfortable scenario for the patient and collector, oral fluid collection provides a reliable alternative to urine, especially in patients that cannot provide a urine sample or for whom adulteration or substitution is suspected. Advantages over blood collection for compliance testing include ease of collection and longer periods of detection for certain drugs. Alternative specimen types such as breath and hair are outside of the scope of this article as they are not recognized as preferred specimen types for medication compliance testing at this time. Despite anticipated differences due to specimen characteristics, two paired comparison studies between oral fluid and urine (one conducted in pain management and one in MAT) have shown substantial agreement between oral fluid and urine results (Heltsley et al., 2012; Vindenes et al., 2011). Furthermore, a recent study comparing overall positivity rates of oral fluid to urine testing in non-paired specimens of patients undergoing MAT showed higher positivity rates for oral fluid versus urine (Kunkel, Fey, Borg, Stripp, & Getto, 2015).

The objective of this study is to describe UDT results in patients receiving long-term MAT. A secondary objective of the study is to provide further evidence to establish oral fluid testing as a valuable alternative to urine.

2. Materials and methods

2.1. Study design

This prospective, observational study included two rural and three urban OTPs in Tennessee. All subjects provided informed consent to be drug tested as part of their treatment program. The study was approved by the Tennessee Department of Mental Health and Substance Abuse Services Institutional Review Board. Inclusion criteria were treatment for at least 6 months, age ≥ 18 years, and a visit to one of the clinics between August 1 and September 12, 2014. Specimens were excluded if urine volume collected was <30 mL or if oral fluid specimens had insufficient volume to complete all testing. Subjects were prescribed either methadone or buprenorphine for OUD, with the overwhelming majority prescribed methadone. Most patients received MAT under onsite observation. Counseling, medical services, HIV and hepatitis risk education, and a comprehensive range of rehabilitation services were available to each subject depending on the individualized care plan.

One urine specimen per eligible subject was collected for inclusion in the study. Additionally, simultaneous oral fluid collections were planned for the first 30 patients per site, for a total of 150 specimens.

2.2. Collection procedures and laboratory analysis

Written instructions regarding proper specimen collection procedures were provided to ensure consistency among the sites. Specimens were collected onsite prior to medication administration and shipped same day to Aegis Sciences Corporation. Since refrigeration was not universally available at all sites, programs were instructed to send specimens within one day. Urine and oral fluid specimens were tested for multiple drugs of abuse. The analytes tested for each drug varied slightly by specimen type due to differences in drug distribution. Refer to Table 1 for a list of drugs/metabolites tested by specimen type and the limit of quantitation (LOQ) utilized for testing of each.

Table 1
Drugs and metabolites tested.

Drug or metabolite	Urine LOQ (ng/mL)	Oral fluid LOQ (ng/mL)
Alcohol metabolite (ethyl glucuronide)	500	NT[a]
Alcohol metabolite (ethyl sulfate)	500	NT
Alprazolam	50	0.5
Alpha-hydroxyalprazolam	50	NT
Amphetamine	80	5
Buprenorphine	1	0.5
Norbuprenorphine	2.5	2
Butalbital	50	25
Caffeine	0.5 (mcg/mL)	NT
Carisoprodol	100	10
Clonazepam	NT	1
7-Aminoclonazepam	50	NT
Cocaine	50	2
Benzoylecgonine	50	2
Diazepam	50	1
Nordiazepam	50	2
Dihydrocodeine	50	1
Eszopiclone/zopiclone	4	NT
N-desmethylzopiclone	10	NT
Fentanyl	5	0.1
Norfentanyl	5	0.5
Flurazepam	NT	1
2-Hydroxy-ethyl flurazepam	50	NT
Gabapentin	2.5 (mcg/mL)	NT
Heroin	4	NT
6-Monoacetylmorphine	4	NT
Hydrocodone	50	1
Norhydrocodone	50	1
Hydromorphone	50	1
Lorazepam	50	1
MDA[b]	80	8
MDEA[c]	80	NT
MDMA[d]	80	8
Meperidine	50	NT
Normeperidine	50	NT
Meprobamate	100	10
Methadone	50	2
EDDP[e]	50	1
Methamphetamine	80	8
Nicotine metabolite (cotinine)	125	NT
Oxycodone	50	1
Noroxycodone	50	1
Oxymorphone	50	1
Pentobarbital	125	NT
Phenobarbital	125	NT
Phentermine	125	NT
PMA[f]	125	NT
Pregabalin	2.5 (mcg/mL)	NT
Secobarbital	100	NT
Synthetic cannabinoids[g]	2	NT
Synthetic cathinones[h]	25	NT
Temazepam	50	0.5
THC[i]	NT	2
Carboxy-THC	2	2
Tapentadol	50	0.5
Nortapentadol	50	0.5
Tramadol	50	20
O-desmethyltramadol	50	20
N-desmethyltramadol	50	20
Zaleplon	4	NT
5-Oxozaleplon	10	NT
Zolpidem	4	NT
Zolpidem metabolite	4	NT

[a] Not tested.
[b] Methylenedioxyamphetamine.
[c] Methylenedioxyethylamphetamine.
[d] Methylenedioxymethamphetamine.
[e] 2-Ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine.
[f] Paramethoxyamphetamine.
[g] Synthetic cannabinoid testing included 4-OH-butyl-JWH-073, 4-OH-pentyl-AM-2201, 4-OH-pentyl-JWH-018, 4-OH-pentyl-JWH-122, 4-OH-pentyl-JWH-210, 4-OH-pentyl-JWH-250, 4-OH-pentyl-UR-144, 5-COOH-pentyl-JWH-210, 5-COOH-pentyl-JWH-250, 5-OH-pentyl-JWH-018, 5-OH-pentyl-JWH-081, 5-OH-pentyl-JWH-122, 5-OH-pentyl-JWH-210, 5-OH-pentyl-JWH-250, 5-OH-pentyl-JWH-398, 5-OH-pentyl-UR-144,

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