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Drug screening during pregnancy: Urine dip cups measure up

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ABSTRACT

Background: Substance use during pregnancy is a major medical and public health concern. Determination of the most appropriate screening protocol remains a clinical conundrum. Interviews and/or laboratory drug screens may be costly, inaccurate, and are frequently inadequate to identify patterns of substance use for a given population or geographic area. We compared commercially available urine "dip cup" toxicology screens obtained in the clinic to university hospital drug toxicology results.

Methods: 267 observed urine samples were collected from pregnant women with known substance use disorders enrolled in a specialized treatment program that included access to buprenorphine medication-assisted treatment. Each urine sample was tested by commercial dip cup with temperature confirmation and then sent to the university hospital laboratory for analyses. The number of substances detected and cost for each screening method were compared.

Results: Uniformly, the dip cup had comparable detection of amphetamines, barbiturates, cocaine, methadone, opiates, and tetrahydrocannabinol to the university hospital laboratory with the exception of benzodiazepines. In addition, the dip cup detected use of buprenorphine (a commonly misused opiate receptor ligand not included in the hospital screen) and was significantly less expensive.

Conclusions: Commercially available urine dip cups are cost-effective, equally comparable to hospital based screening, and provide 'real time' results germane to clinical care and treatment planning.

1. Introduction

Substance use during pregnancy is a prevalent public health concern. In a 2016 national survey, 20% of pregnant women reported use of illicit drugs, tobacco, or alcohol with 6.3% reporting illicit drug use (Center for Behavioral Health Statistics and Quality, 2017). Fetal exposure to substances has been associated with poor obstetrical and neonatal outcomes and may impair child developmental trajectories (for review, see Forray, 2016; Viteri et al., 2014). The American Medical Association (AMA; American Medical Association, 2017), the American Psychiatric Association (APA; Council on Addiction Psychiatry, 2016), and the American College of Obstetricians and Gynecologists (ACOG; American College of Obstetricians and Gynecologists, 2011) have issued official statements supporting screening for substance use as part of routine prenatal care to facilitate early intervention and improve outcomes.

The best practices for substance use screening are unclear. ACOG recommends routine universal screening using tools such as the 4 Ps (Chasnoff et al., 2005) and National Institute on Drug Abuse (NIDA) Quick Screen (National Institute on Drug Abuse, 2012). Studies have demonstrated that women underreport substance use (including nicotine and alcohol) and may not disclose prescription exposure (Dietz et al., 2010; Garg et al., 2016; Shipton et al., 2009). Thus, self-report screening tools likely underestimate the prevalence of substance use during pregnancy. Screening questionnaires validated for use during pregnancy are typically validated through comparison to other self-report measures rather than toxicology screens. Yonkers compared self-report of illicit substance use to urine toxicology results and found 78% of women with a positive toxicology screen for marijuana and 86% of women with a positive screen for cocaine had reported use in the past 28 days (Yonkers et al., 2011). The first study comparing and validating three existing substance-use screeners for pregnancy against biologic

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screening measures is ongoing (Coleman-Cowger et al., 2018).

Urine drug screens can be used as an adjunctive or potentially alternative measure for substance use screening, but are also limited. Urine screening tests typically involve an immunoassay panel with common panels based on the "SAMHSA-5" ("5-Panel Drug Test"), a standard panel established in the 1980s under the Drug-Free Workplace Act which tests for amphetamines, tetrahydrocannabinol (THC), cocaine metabolites, opiates (excluding synthetic opioids such as oxycodone, hydrocodone, fentanyl, buprenorphine, or methadone), and phencyclidine (PCP) (Dupont et al., 2013). Variants on this panel offered by laboratories often include benzodiazepines, barbiturates, and specific synthetic opiates; however, there is no standardized protocol for additional substance inclusion. Substances included in urine drug screens vary greatly across university hospitals and commercial laboratories and do not account for geographic and population-specific distribution of misused substances. Testing for additional substances beyond the standard panel offered by an institution or company typically incurs an increase in cost. Results are delayed secondary to laboratory turnaround time. Hospital laboratories often cite a 1–2 hour turnaround time for emergency departments and inpatients, while commercial laboratories report anywhere from 24 to 72 hours later. Furthermore, these panels do not address non-illicit substances, such as nicotine and alcohol. The consideration of quicker, more comprehensive options for screening is important in facilitating treatment planning and optimizing clinical care.

There is increasing evidence that methadone and buprenorphine, medications utilized in medication-assisted treatment for opioid use disorder, are commonly misused. In fact, buprenorphine-related ED visits involving nonmedical use of buprenorphine increased 255% (i.e., 4,440 to 15,778 visits) from 2004 to 2010 (Substance Abuse and Mental Health Services Administration, 2013). Opiate use disorder at delivery quadrupled between 1999–2014 (Haight et al., 2018). A parallel increase in neonatal abstinence syndrome (NAS) has also been observed (Patrick et al., 2015). Objective methods of measuring misuse are necessary to facilitate prevention and intervention efforts as well as decrease diversion. Laboratory drug screens often exclude common opioid medication-assisted therapies as a consequence of the Americans with Disabilities Act, which ensures confidentiality for patients entering substance use treatment programs. These regulations "impose restrictions upon the disclosure and use of alcohol and drug patient records which are maintained in connection with the performance of any federally assisted alcohol and drug abuse program" (42 CFR § 2.3(a)), and apply to any information disclosed by a substance use treatment program which "would identify a patient as an alcohol or drug" user (42 CFR §2.12(a) (1)). With the increasing misuse of methadone and buprenorphine, it may be prudent to include these medications in a drug screen for screening purposes.

Due to current legislation and bias, screening during pregnancy has become synonymous in some settings with potential legal consequences. Current legislation varies across the United States and is often at odds with the official recommendations issued by professional societies. According to the Guttmacher Institute, 23 states and the District of Columbia consider substance use during pregnancy to be a form of child maltreatment, and 3 states (Minnesota, South Dakota, Wisconsin) consider it grounds for civil commitment (Guttmacher Institute, 2018). Less than half of states have funded drug programs specifically for pregnant women or provide priority access to treatment programs for pregnant women (Guttmacher Institute, 2018). Practitioners may be unwilling to screen for substance use in order to protect patients from legal repercussion or due to a lack of local treatment programs.

1.1. Objectives of the current study

Substance use during pregnancy has potential negative impacts on the developing fetus, and prompt identification and treatment of mothers is necessary. The present study directly compares urine cup screening to standard urine drug screening (immunoassay confirmed by gas-chromatography- mass spectrometry) at a university laboratory in a high-risk pregnant population with substance use disorders in order to characterize and compare effectiveness between the two urine drug screening methods with respect to 1) total cost and 2) sensitivity to potential exposures.

2. Material and methods

2.1. Participants

The Women's Mental Health Program (WMHP) at the University of Arkansas for Medical Sciences (UAMS) provides treatment, including medication-assisted treatment with buprenorphine, for pregnant women with a history of substance use disorders. Treatment involved an initial evaluation and drug screen followed by weekly appointments with a psychiatrist, weekly group therapy, and weekly drug screens. All women were diagnosed with opioid use disorder. Urine samples were collected at each clinic visit for the purpose of substance use screening. With consecutive negative drug screens, women were transitioned into less frequent visits. Multiple samples may have been collected from the same participant throughout the course of treatment. The number of individual women providing samples for this analysis is unknown to protect the anonymity of the samples. The purpose of the study was to examine substances captured by the different screening methods, so multiple samples from one individual would not affect the findings. A total of 267 witnessed urine samples were de-identified, and assay results were entered into a database. All urine samples were included in the present analyses.

2.2. Procedures

Urine samples were collected for examination using both the University hospital's laboratory method and a urine dip cup (American Screening Corporation, LLC, 9742 St Vincent Ave. Ste 100. Shreveport, LA 71105. Discover 8 Panel Cup). The hospital's laboratory method included immunoassay, and if the sample tested positive, samples could be confirmed using gas-chromatography-mass spectrometry per physician order. Confirmatory testing was completed for all hospital-based samples utilized in this study. The hospital's laboratory tested for amphetamine/methamphetamine, barbiturate, benzodiazepine, THC, cocaine, methadone, opiates and PCP. The opiate screen included the following substances: morphine, codeine, dihydrocodeine, hydrocodone, hydromorphone, levorphanol, morphine-3-glucuronide, norcodeine, and oxycodone. The dip cup contained a built-in temperature strip and tested for amphetamine/methamphetamine, barbiturate, benzodiazepine, THC, cocaine, methadone, opiates, oxycodone, PCP, and buprenorphine. The frequencies of positive identification for a particular substance were compared between the dip cup and the hospital laboratory.

3. Results

Frequencies of identified substances are depicted in Table 1. The dip cup identified more samples positive for amphetamines (+29 samples), THC (+2), methadone (+2), and opiates (+38). Detected methadone samples represent illicit use as methadone was not prescribed through this treatment program. The hospital laboratory identified more samples positive for barbiturates (+1) and benzodiazepines (+8). The dip cup and hospital laboratory identified the same number of samples positive for cocaine.

Buprenorphine was not included in the standard university hospital screening assay. The urine dip cup identified 29 samples negative for buprenorphine that should have been positive (prescribed buprenorphine); and 10 samples were positive for buprenorphine that should

Table 1
Substances detected in urine drug screens, by number of samples.

	Hospital Lab[a]	Dip Cup[b]
Amphetamines	40	69
Barbiturates	2	1
Benzodiazepines	86	78
THC	51	53
Cocaine	5	5
Methadone	15	17
Opiates	59	97
Buprenorphine	NA	178

[a] Hospital Lab = University of Arkansas for Medical Sciences laboratory.
[b] Dip cup = American Screening.

have been negative (not prescribed buprenorphine).

The cost of each urine dip cup test was $3.87 (total = $1,033.29). The cost of the university laboratory screen ranges between $50-112 (total range = $13,350 – $29,904), depending on additional substances tested for beyond the standard panel (information provided by UAMS).

4. Discussion

Fetal exposure to substances negatively impacts fetal development and child outcomes highlighting the need for prevention and early intervention efforts among pregnant women (Forray, 2016). The results of this study underscore the importance of revisiting screening procedures for drug exposures in pregnancy, particularly in light of increasing misuse of buprenorphine, and emphasize specific areas for improvement.

Results indicated that a curated urine dip cup test detected amphetamines more frequently than the hospital laboratory, while other substances were detected at a similar rate. Through the addition of buprenorphine to the screening panel, the dip cup detected 10 samples in which buprenorphine was detectable but had not been prescribed, indicating possible illicit use. Equally important were the 29 samples that were negative despite prescriptions for buprenorphine maintenance treatment – suggesting possible diversion. If the hospital laboratory results alone had been used, clinical management would have relied solely on verbal report, and these instances may not have been addressed.

The results highlight the importance of providing clinicians the flexibility to screen for substances relevant to the population. In an effort to protect the developing fetus, comprehensiveness and relevancy of testing should be prioritized to maximize the physician's ability to intervene quickly and monitor treatment response effectively. Furthermore, the disadvantages of interview have been explored by others when compared to biological screening methods, stating that maternal interview is a "time-consuming test of low sensitivity" (Ostrea et al., 2001). Urine dip cups offer an option that could be utilized in combination with interview or self-report measures in an effort to improve clinical evaluation and treatment.

The dip cup utilized in the current study cost $3.87, which clearly offers a cost-saving advantage to hospital laboratory screenings. It proved to detect similar frequencies of substances and offered the advantage of screening for buprenorphine at a low cost. The timeliness of results and the temperature monitor were additional potential benefits to the clinic setting. This low-cost alternative to hospital-based laboratory screenings and interviews could be a welcome solution to concerns regarding the cost and accuracy of previous methods.

Several limitations of the current work should be noted. Samples and toxicology results were obtained as part of a specialized clinic for substance use treatment during pregnancy and were identified by sample rather than subject, so multiple samples from a single individual are included. However, the purpose of the study was to examine the reliability of each screening method, and both labs had the opportunity to test each sample. As such, repeated samples from a single woman would not affect the results. Dip cup assays were completed with knowledge of current medications, though these would not be expected to influence the comparability of the results. Furthermore, neither screening option included commonly used substances in pregnancy, such as alcohol and nicotine, that can adversely impact fetal outcomes, which is noted to be a general limitation of typical UDS methods. A comparison to confirmatory mass spectrometry for all urine samples would have provided a more accurate comparison; however, confirmatory mass spectrometry results were not available for dip cup samples.

Screening for substances during pregnancy is the first step toward providing comprehensive psychiatric and behavioral health care. Through a systematic process, providers can offer education, expedite treatment referrals, and continue to monitor use for maternal and fetal safety. The results indicated that urine dip cup examination, when compared to a hospital-based protocol, is similar in detection rates, comprehensive, cost-effective, and efficient. Further, the dip cup offers a temperature strip to assess validity. As such, consideration should be given to this methodology as a readily available, time-effective adjunct to interviews and alternative to traditional laboratory protocols.

5. Conclusions

This study presented a comparison of a university hospital protocol to a commercially available urine dip cup screening protocol in terms of sensitivity and cost-effectiveness. The dip cup provided an inexpensive, rapid, and comprehensive assessment supporting clinical decision-making in a population of pregnant women with substance use disorders. The results accentuate the need for a reconsideration of methodology for drug screening during pregnancy in order to have increased knowledge of substance use that may impact the developing fetus, facilitate treatment planning, and provide cost savings for patients and health systems.

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Contributors

Drs. Kroska and Meller wrote the first draft of the manuscript and revised the manuscript with feedback from all authors. Ms. Doyle aggregated data and provided feedback on the manuscript. Drs. Coker and Ray-Griffith helped collect the data and provided feedback on the manuscript. Ms. Knight helped with data collection and study execution, as well as provided feedback on the manuscript. Dr. Nembhard provided feedback on the manuscript and conceptualization of the findings. Dr. Stowe conceptualized the study, collected the data, and provided extensive feedback on the manuscript. All authors reviewed the final manuscript and were provided ample opportunity to make changes or suggestions

Declaration of Competing Interest

Dr. Kroska: No conflicts declared.
Ms. Meller: No conflicts declared.
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Dr. Coker: financial support from the National Institute for Drug Abuse 92T32DA022981-06) and the Arkansas Children's Research Institute. She has served as a physician (un-compensated) on clinical trials sponsored by SAGE, Janssen, and Boerhinger Ingelheim Pharmaceuticals. She has never served as a consultant to any biomedical or pharmaceutical corporation. Neither she nor family members have ever held equity positions in biomedical or pharmaceutical corporations.

Ms. Knight: received research support from NIH, Bristol-Myers Squibb, Cyberonics, Eli Lilly, Forest, Janssen, Novartis, and Wyeth; and her adult, nondependent son is employed by and holds stock options for GlaxoSmithKline.

Dr. Ray-Griffith: currently receives clinical trial support from Neuronetics and has received clinical trial support from Sage Therapeutics. She has never served as a consultant to any biomedical or pharmaceutical corporation. Neither she nor family members have ever held equity positions in biomedical or pharmaceutical corporations.

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