Journal of Food and Drug Analysis

Volume 26 | Issue 1 Article 36

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Original Article

Urine specimen validity test for drug abuse testing in workplace and court settings

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ARTICLE INFO

Article history:
Received 18 September 2015
Received in revised form
4 August 2016
Accepted 3 January 2017
Available online 14 February 2017

Keywords:
court
specimen validity test
urine drug test
workplace

ABSTRACT

In recent decades, urine drug testing in the workplace has become common in many countries in the world. There have been several studies concerning the use of the urine specimen validity test (SVT) for drug abuse testing administered in the workplace. However, very little data exists concerning the urine SVT on drug abuse tests from court specimens, including dilute, substituted, adulterated, and invalid tests. We investigated 21,696 submitted urine drug test samples for SVT from workplace and court settings in southern Taiwan over 5 years. All immunoassay screen-positive urine specimen drug tests were confirmed by gas chromatography/mass spectrometry. We found that the mean 5-year prevalence of tampering (dilute, substituted, or invalid tests) in urine specimens from the workplace and court settings were 1.09% and 3.81%, respectively. The mean 5-year percentage of dilute, substituted, and invalid urine specimens from the workplace were 89.2%, 6.8%, and 4.1%, respectively. The mean 5-year percentage of dilute, substituted, and invalid urine specimens from the court were 94.8%, 1.4%, and 3.8%, respectively. No adulterated cases were found among the workplace or court samples. The most common drug identified from the workplace specimens was amphetamine, followed by opiates. The most common drug identified from the court specimens was ketamine, followed by amphetamine. We suggest that all urine specimens taken for drug testing from both the workplace and court settings need to be tested for validity.

1. Introduction

Drug abuse has become one of the major public health issues in the world. In Taiwan, Lee et al [1] reported that methamphetamine was the most widely used illicit drug found in urine samples collected from suspects who were arrested for possessing and/or taking illicit drugs. They also showed that the number of ketamine seizures has been rising at an alarming pace. In Southeast Asia, crystal methamphetamine is

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http://dx.doi.org/10.1016/j.jfda.2017.01.001

the most commonly used drug, including in Brunei Darussalam, Japan, the Philippines, and the Republic of Korea [2]. The abuse trend of ketamine is also on the rise in Southeast Asia. In China (including Hong Kong), Malaysia, and Vietnam, ketamine use was also perceived to increase in 2010 [2].

Over the past few decades, employee drug testing has become a common business practice in the world workplace [3–8]. Workplace drug testing laboratories certified by the U.S. Department of Health and Human Services (HHS) are processing roughly 75,000 specimens each day. The 2004 Index from Quest Diagnostics Inc. (Madison, NJ, USA) reveals that the rate of positive drug tests has declined significantly since 1998, from nearly 14% to slightly greater than 4% [3].

In urine specimens for drug abuse testing administered for the correctional service in Canada, by checking the dilution rate only, Fraser and Zamecnik [9] reported that 6.7% of 38,431 urine specimens were dilute. To the best of our knowledge, there is no previous literature concerning further urine specimen validity tests (SVTs) for urine specimens taken in a court setting, including substituted, invalid, or adulterated modalities. For workplace drug testing of urine specimens, there have been several reports concerning urine SVT for drug abuse tests [10–15]. The aim of this study was to describe our findings from urine SVTs, including the rates of dilute, substituted, adulterated, and invalid samples, for drug abuse tests from court and workplace sources in southern Taiwan over 5 years.

2. Methods

2.1. Materials

Our laboratory is one of 13 urine drug abuse-testing laboratories certified by the Taiwan Food and Drug Administration (TFDA), Ministry of Health and Welfare in Taiwan. A total of 21,666 urine specimens from workplace and court settings for drug abuse testing were investigated by urine SVT during the period of April 1, 2009 to March 31, 2014. Of these urine specimens, 14,289 (65.9%) came from workplaces, and were mainly for random testing of safety security-sensitive personnel in southern Taiwan. The other 7,377 (34.1%) urine specimens came from courts, with 89.7% of these specimens coming from two juvenile courts for youths on probation in southern Taiwan. Urine specimen collection was guided by the Drug Abuse Urine Collection Guideline of the TFDA, which was implemented in August 1999. Urine donors were witnessed and placed in a room with no access to water. This study was approved by the Investigational Review Board of Kaohsiung Medical University Hospital (KMUH-IRB –EXEMPT -20140042).

2.2. Specimen validity test

For urine SVT criteria, we used a mildly modified version of the 2008 Mandatory Guidelines for Federal Workplace Drug Testing Program of the United States [10]. We used a Food and Drug Administration-cleared immunoassay test that assayed amphetamine, 3,4-methylenedioxymethamphetamine (MDMA) using Microgenics (Microgenics Corporation, Fremont, CA, USA), other opiates, phencyclidine (PCP), marijuana, and benzodiazepines using Diagnostic Reagents Inc. (DRI) reagent. Ketamine was also assayed using DRI reagent as the initial screen test on each urine specimen [10]. If the immunoassay test result was below the cutoff, the specimen was reported as negative. If the immunoassay result was positive, we further established the identity of the drug or drug metabolite definitively by using gas chromatography/mass spectrometry (GC/MS) (Agilent, 6890/5973N, Hewlett-Packard, Palo Alto, CA, USA). The cutoff levels of each drug in urine for immunoassay screening and GC/MS confirmation were guided by the TFDA (Table 1).

For every sealed urine specimen submitted for a drug abuse test from the court or workplace, the collection process was under the chain of custody principle and then the samples were sent to our laboratory. For every specimen that underwent urine SVT, we: (1) determined the creatinine concentration with a Hitachi 7170 (Diamond Diagnostics, Holliston, MA, USA) based on the colorimetric Yaffe method; (2) determined the specific gravity using a UG-alpha refractometer (Atago, Tokyo, Japan) if the urine creatinine concentration was less than 20 mg/dL; and (3) determined the pH using pH paper (Adventec; Toyo Rash Karisha, Tokyo, Japan).

We first used pH paper with the detection range of pH 5–8; if the pH was outside this range, we then used pH paper ranging from 0–14. Of all the urine specimens, >99% were in the range of pH 5–8 and none of the specimens had pH <3 or >10.

Results for specimens reported using SVT were categorized as follows [10]. (1) A urine specimen was reported as dilute when the creatinine concentration was ≥2 mg/dL but <20 mg/dL, and the specific gravity was >1.0010 but <1.0030 on a single aliquot. A dilute specimen is a urine specimen with creatinine and specific gravity values lower than expected for human urine. (2) A urine specimen was reported as substituted when the creatinine concentration was <2 mg/dL on both the initial and confirmatory creatinine test, and the specific gravity was

Table 1 – Taiwan Food and Drug Administration guidelines.

Screen items	Screen cutoff (ng/mL)	Confirmation items	Confirmation cutoff (ng/mL)
Amphetamine	500	Amphetamine	500
		Methamphetamine	500 and amphetamine > 100
		MDMA	500 or MDMA + MDA ≥ 500
		MDA	500
Opiate	300	Morphine	300
		Codeine	300
Marijuana	50	Marijuana	15
Cocaine	300	Cocaine	300
Ketamine	100	Ketamine	100 or K + NK ≥ 100
		Norketamine	100
PCP	25	PCP	25
Benzodiazepines	200	Benzodiazepines	≥ LOD

K = ketamine; LOD = limit of detection; MDMA = 3,4-methylenedioxymethamphetamine; MDA = 3,4-methylenedioxyamphetamine; NK = norketamine, PCP = phencyclidine.

<1.0010 or >1.0200 on both the initial and confirmatory specific gravity tests using a refractometer on two separate aliquots. A substituted specimen is a urine specimen with creatinine and specific gravity values that are so diminished or divergent that they are not consistent with normal human urine. (3) A urine specimen was reported as adulterated if the pH was <3 or >11. An adulterated specimen is a urine specimen containing a substance that is not a normal constituent of urine or containing an endogenous substance not present at a normal physiological concentration. (4) A urine specimen that did not meet any of the above criteria (dilute, substituted, or adulterated) but was clearly not normal was reported as invalid.

The drug test items for the urine specimens from the workplace and court settings were examined according to the government requirements in Taiwan. For workplace specimens, basic drug test items were amphetamine and morphine, and other tests were enrolled as necessary. The majority of the urine specimens from the courts were tested for amphetamine, MDMA, and ketamine.

Table 2 – Dilute, substituted, and invalid samples in workplace urine specimens.

Year	1	2	3	4	5	Total
Dilute	28 (100)	29 (85.3)	23 (85.2)	30 (85.7)	22 (91.7)	132 (89.2)
Substituted	0 (0)	2 (5.9)	3 (11.1)	5 (14.3)	0 (0)	10 (6.8)
Invalid	0 (0)	3 (8.8)	1 (3.7)	0 (0)	2 (8.3)	6 (4.1)
Total	28 (100)	34 (100)	27 (100)	35 (100)	24 (100)	148 (100)

Data are presented as *n* (%).

Table 3 – Dilute, substituted, and invalid samples in court urine specimens.

Year	1	2	3	4	5	Total
Dilute	41 (93.2)	70 (94.6)	62 (96.9)	78 (96.3)	26 (88.5)	274 (94.8)
Substituted	2 (4.5)	2 (2.7)	0 (0)	0 (0)	0 (0)	4 (1.4)
Invalid	1 (2.3)	2 (2.7)	2 (3.1)	3 (3.7)	3 (11.5)	11 (3.8)
Total	44 (100)	74 (100)	64 (100)	81 (100)	26 (100)	289 (100)

Data are presented as *n* (%).

3. Results

Figure 1 shows the prevalence of dilute, substituted, and invalid urine samples from the workplace and court settings over 5 years. The mean 5-year prevalence of dilute, substituted, or invalid urine specimens from the workplace was 1.09%, lower than that of the court specimens, which was 3.81%. As shown in Table 2, of the urine specimens from the workplace that failed the SVT, the 5-year mean percentages of dilute, substituted, and invalid urine specimens were 86.2%, 5.8%, and 4.1%, respectively. Dilution was the predominant method of tampering in the workplace urine specimens. Of the urine specimens received from the court, the prevalence of dilute, substituted, and invalid urine specimens are shown in Table 3. Of the urine specimens from the court that failed the SVT, the 5-year mean percentages of dilute, substituted, and invalid urine specimens were 94.8%, 1.4%, and 3.8%, respectively. These data reveal that dilution (94.8%) was also the predominant method of tampering in the court urine specimens. There existed a trend in increasing percentage of invalid urine specimens. There were no adulterated urine specimens, from either the workplace or court setting. Among all of our urine specimens, <0.1% had a pH value outside the range of 5–8. None of the submitted urine specimens had a pH value <3 or >10.

With confirmation by GC/MS, the mean 5-year urine drug positive rates were 1.26% and 15.7% for the workplace and court settings, respectively. The most common drug identified from the workplace specimens was amphetamine (40.8%), followed by opiates, including morphine and codeine (32.2%). The most common drug identified from the court specimens was ketamine (51.2%), followed by amphetamine (32.2%). No specimens from either the workplace or court setting were positive for marijuana.

4. Discussion

In Canada, Fraser [16] reported that the greatest proportion of analyzed urine specimens for drug testing came from offenders on conditional release in the community. Fraser and Zamecnik

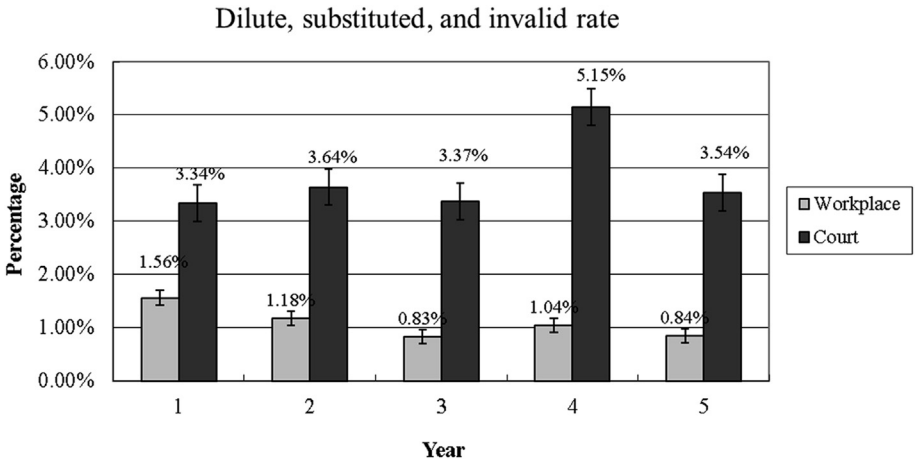

Figure 1 – Prevalence of dilute, substituted, and invalid urine specimens from workplace and court urine tests.

[9] also observed that 6.8% of specimens from the correctional service were dilute. In a toxicology laboratory in the United States, 4.94% of 4227 specimens were dilute [17]. In this study, the rate of dilute specimens was 3.81% from a court setting; this may be owing to most of our specimens coming from youth on probation in two juvenile courts. These youth probably do not have to dilute their urine as there is only a mild penalty in Taiwan for abusing the most common class III ketamine.

In this study, the urine tampering (dilute, substituted, and invalid) prevalence from the workplace for the 1st to the 5th year was 1.56%, 1.18%, 0.83%, 1.04%, and 0.84%, respectively. In the United States, there were almost 6,800,000 federal and federally regulated specimens tested in the HHS-certified urine drug testing laboratories in 1 year. Of these specimens, about 2.1% were drug-positive, and about 0.15% were found to be adulterated, substituted, or invalid [10]. For the workplace urine specimens in this study, 16 (0.11%) were found to be substituted or invalid, similar to the 0.15% described in the report of Bush [10]. Our lower drug positive rate (1.26%) in workplace specimens compared to that from the United States (2.1%) [10] was probably owing to differing abuse problems in different countries or the limited, selected drug items required by the government for workplaces in Taiwan.

In this study, dilution was the most common cause of tampering of urine specimens from both workplace and court settings. Diluting urine is usually the simplest way to make an otherwise positive drug test result negative [11]. Beck et al [18] reported that 11% of all urine specimens submitted to their laboratory for drug abuse testing were dilute (creatinine <4 mmol/L). Fraser and Zamecnik [19] suggested urine screening and confirmation method with a lower threshold to avoid false negative rates for drug abuse testing. They found that 26% of all dilute specimens screened positive for one or more drugs. So far, the Substance Abuse and Mental Health Services Administration program does not allow analysis of dilute urine specimens at lower screening and confirmation cutoffs [11].

Cook et al [12] observed that urine pH is not useful in determining the dilute status of urine and suggested that measurement of pH is a valuable test for assessing chemical adulteration. Because the kidneys are limited to producing urine within the pH range of 4.5–8, pH values beyond this range are highly suspicious for adulteration. The use of pH paper relies on the ability of hydrogen ion levels in the solution to cause a color change in an indicator dye. Because no indicator dye will cover the entire normal urinary pH range, most reagent strips utilize two indicators, methyl red and bromothymol blue, to provide a reportable range of 2–8. Urine pH cutoff values of <3 and >11 have been established to classify a urine specimen as adulterated [6]. Burrows et al [13] also described that urine should be reported as adulterated if the pH was <3 or >11. In addition, a urine specimen is reported as invalid when the urine pH is ≥3 and <4.5 or ≥9 and <11 [20].

In this study, no adulterated cases were found. Jaffe et al [21] reported that many research protocols operate under the assumption that adulteration does not occur (due to few consequences). They also found that, in a healthy volunteer, the specific gravity of a urine specimen is expected to be ≥1.003 and have a pH between 3 and 11; thus, a pH or specific gravity outside of this range may suggest chemical adulteration [21]. All of the urine pH values in our study ranged between 3 and 10.

Several *in vitro* household adulterants were previously reported to mask marijuana [21–26], but marijuana is very rarely identified in drug abuse tests, and there is little marijuana abuse in Taiwan [according to TFDA statistics, in 2014, only 9 out of 258,295 urine specimens for drug testing were positive for marijuana (0.003%), while 31.6% were positive for ketamine and 16.0% were positive for amphetamine]. In this study, there were only 564 urine specimens from the workplace and 2009 specimens from the court setting for marijuana testing. None of these specimens were positive for marijuana.

The most common drug identified from the court specimens in our study was ketamine. Concerning drug abuse problems in Asia, Bart [27] observed that though opiate use appears to have stabilized throughout Asia, there has been an increase in methamphetamine use and the use of new psychoactive substances (ketamine et al.). Hsu et al [2] also reported that ketamine has gained popularity among young people in Taiwan and has become the most commonly abused drug of choice for recreation in pubs.

The limitation of the study is that for urine adulteration detection, we used pH value only without a test for oxidizing adulterants [10]. Dasgupta [11] described that most adulterants can be detected by a routine specimen integrity test, such as pH, creatinine, and specific gravity, with the exception of eye drops [23], Klear [28], Whizzies [11], Urine Luck [29], and Stealth [30]. They also mention that eye drops and other adulterants that are oxidizing agents, such as Klear, Urine Luck, and Stealth, cause false negative results in the immunoassay used for screening drugs by directly destroying Tetrahydrocannabinol (THC) metabolites [11].

In conclusion, for the court urine specimens, we reported our experience in urine SVT including dilute, substituted, and invalid prevalence in Taiwan. For the workplace urine specimens, we reported SVT prevalence, including dilute, substituted, and invalid urine drug tests. The mean 5-year urine tampering (dilute, substituted, or invalid) prevalence from the workplace and court specimens was 1.09% and 3.81%, respectively, in our study. We suggest that all urine specimens for drug abuse testing from the workplace and court setting undergo a specimen validity test.

Conflicts of interest

All authors declare no conflicts of interest.

Acknowledgments

This work was supported by the Department of Laboratory Medicine, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan.

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