CYPRUS JOURNAL OF MEDICAL SCIENCES

Original Article

DOI: 10.5152/cjms.2018.588

Utility of Bedside Urine Toxicology Screening Test in Emergency Department: A Retrospective Study

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Cite this article as: Pamukcu Gunaydin G, Kurtoglu Celik G, Ersen T, Sener A, Ozhasenekler A, Gokhan S. Utility of Bedside Urine Toxicology Screening Test in Emergency Department: A Retrospective Study. Cyprus J Med Sci 2018; 3: 98-102.

BACKGROUND/AIMS
In this retrospective study, our goal was to describe the use of urine toxicology screening (UTS) tests in patient management in an urban training and research hospital's Emergency Department (ED).

MATERIAL AND METHODS
This is a retrospective observational descriptive file review. All patients aged ≥16 who were admitted to the ED between March 2013 and March 2017 for any complaint and who were ordered a urine drug screening test were included in the study.

RESULTS
A total of 1866 patient files were included in the statistical analysis. The median age of 1866 included patients was 29 (16–99). 66.9% (n=1248) of patients were male. Of the 1866 patients, 26.7% (n=499) tested positive for at least one drug. There was no statistically significant difference between the ward hospitalization, intensive care unit hospitalization, and discharge or death rates among patients who tested positive for at least one drug and patients who tested negative for all drugs ($\chi 2$ p=0.097). Drug positivity was significantly higher in forensic cases, in patients who attempted suicide, and in patients who were in a rehabilitation program.

CONCLUSION
The UTS testing is a controversial subject in ED. Our results do not support its use with clinical curiosity being the only reason to order the test. The UTS testing may be more useful in targeted populations in ED.

Keywords: Emergency medicine, toxicology screening, urine

INTRODUCTION

Exposure to drugs, toxins, or ethanol is the major cause of emergency department (ED) visits (1). Even when not indicated in history, it is sometimes necessary to know if patient's condition can be explained by intoxication for an adequate diagnosis and treatment in ED (1). Therefore, a toxicological screening analysis of urine is performed if available in ED when a patient presents with various unexplained symptoms, has experienced unwitnessed trauma, has a history of drug ingestion, or if intoxication with illegal drugs or therapeutic drugs for any other reason is suspected (2). Screening urine for illegal drugs may guide choices of care in ED and shorten the length of stay (3, 4).

There are many on-site toxicology screening tests (these are also called point-of-care tests, near patient testing, and triage toxicology panels) for drugs of abuse and therapeutic drugs (5-7). Urine is by far the most widely used biological material for this purpose (2). Urine toxicology screening (UTS) tests that are currently available determine the presence of drugs qualitatively using a competitive binding immunoassay and are easy to perform. Turn-around times are generally within 5–15 min. Most of UTS tests have a multiple drug panel. When applied in a laboratory setting, many of these tests produce reliable results (2). UTS devices also have advantages regarding their cost and technical ease of use, as well as fast results (8).

This study was presented at the 20th National Congress of Clinical Toxicology, May 22-24, 2015, Ankara, Turkey.
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Received: 03.07.2018
Accepted: 18.07.2018

Urine toxicology screening tests are only the initial part of toxicological investigation; positive results may cause further investigation, but negative results are not always sufficient to exclude drug abuse or intoxication (9, 10). Another major limitation of UTS as argued by some authors is that sometimes, it may not have an impact on patient management (5).

In this study our goal is to describe the use of UTS testing in patient management retrospectively in an urban training and research hospital's ED.

MATERIAL and METHODS

Study Design

This study is a retrospective observational descriptive file review. Before the start of the study, the institutional ethical review board of Yıldırım Beyazıt University Faculty of Medicine approved the study protocol. In our ED, the same toxicology drug screen test has been in use since March 2013. The study was conducted in April 2017. The files of patients who presented to our ED between March 2013 and March 2017 were screened. Data were extracted from both the computer files and paper files of patients who were included in the study and were transferred to a Microsoft Excel worksheet and saved before the analysis. Since this was a retrospective chart review and no identity information was gathered or distributed, informed consent was not obtained from patients.

Setting

This monocentric study was conducted in the ED of an urban training and research hospital with 150,000 ED patient visits per year. In our ED, UTS is not ordered at the time of triage. Emergency physicians order the test after history completion and a physical exam. Emergency physicians are free to order the test for any patient who they think may benefit from a toxicology screen, such as but not limited to people with altered mental status, unwitnessed trauma, first-time seizure, first psychotic episode, symptoms suggesting a toxidrome, people with unexplained symptoms, or suspected intoxication. In our ED, emergency medicine residents are supervised by an attending emergency medicine specialist 24 hours a day, 7 days a week, and diagnostic tests decisions are always discussed with the attending physician. No clinical rules apart from clinical judgment are used to order UTS.

TABLE I. Threshold Values for Each Drug in Triage-TOX Drug Screen

Drug Name	Threshold Values
Acetaminophen (APAP)	5 µg/mL
Amphetamines (AMP)	1000 ng/mL
Methamphetamines (mAMP)	1000 ng/mL
Barbiturates (BAR)	300 ng/mL
Benzodiazepines (BZO)	300 ng/mL
Cocaine (COC)	300 ng/mL
Methadone (MTD)	300 ng/mL
Opiates (OPI)	300 ng/mL
Phencyclidine (PCP)	25 ng/mL
Tetrahydrocannabinol (THC)	50 ng/mL
Tricyclic antidepressant (TCA)	1000 ng/mL

In our ED, Alere Triage®-TOX Drug Screen Panel is used for urine toxicology screening. This test can measure 11 substances in urine quantitatively. During the study period, Triage-TOX Drug Screen was performed in the ED laboratory by biochemistry technicians. The ED laboratory is located in the department.

Data needed for the study and the UTS results were obtained from our hospital's registry system.

Participants

All patients aged ≥16 who were admitted to the ED between March 2013 and March 2017 with any complaint and who were ordered a urine drug screen were included in the study. Patient files were included in the study if an emergency physician thought the patient could benefit from a UTS test, and the test was ordered in ED according to patient files.

If any of the UTS test result data or study outcome measures data were missing from both the paper and digital files of a patient, that patient's file was excluded from the study.

Measurements

Demographic data (age, sex), the patients' time of presentation, major complaint and Glasgow Coma Scale scores at the time of presentation, the UTS test results, and the outcome of the patient visit (hospitalization, ICU hospitalization, mortality) were recorded on a Microsoft Excel worksheet. To ensure anonymity, patients' names were replaced by a research number, and age was entered instead of the date of birth.

The on-site UTS device, Alere Triage-TOX Drug Screen Panel (Alere Inc., San Diego, CA, USA), uses competitive fluorescence immunoassay, and it gives qualitative results for determination of parent drugs or drug metabolites in urine through a one-step process after analyzing the sample in an automatic analyzer, ensuring objectivity by instrumental colorimetric calibration, followed by the printing of positive/negative results, independent of the operator (8). The substances that are investigated by the test and the positive result threshold values for each parameter are presented in Table I. If a urinary catheter was present at the time when the test was ordered, the urinary sample was obtained from the catheter; otherwise, the patients gave samples by urinating in a disposable plastic container. Samples were than carried immediately to the ED laboratory, and testing was performed as soon as possible. No further confirmatory testing was done.

Statistical Analysis

Data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 16.0 (SPSS Inc.; Chicago, IL, USA). They were grouped for analysis, and the mean±standard deviation, median, minimum, maximum, and percentages were calculated. The Kolmogorov–Smirnov test was used to test the normality of the data distribution. The chi-squared test and Mann-Whitney U test were used for statistical comparison, and a $p<0.05$ was considered to be statistically significant.

RESULTS

A total number of patients who presented to our ED was 565,754, and the UTS test was ordered for 0.004% (N=2436) of these patients during the study period. In 469 of the files, test results were not recorded in the computer file of the patient (the patient either did not give a sample, the sample was lost, or the test was not performed for any other reason, such as device failure, for example). Remaining 1967 files had test results available, but 101 of these patient files were missing paper files, thus were missing data and were excluded from the statistical analysis. The remaining 1866 patient files were included in the statistical analysis.

The median age of 1866 included patients was 29 (16–99). 66.9% (n=1248) of the patients were male, and 33.1% (n=618) of the patients were female.

TABLE 2. Number of Drugs Tested Positively in Patients Who Tested Positive for at Least One Drug

Number of Drugs	n	%
0	1367	73.3
1	331	17.7
2	100	5.4
3	52	2.8
4	14	0.8
5	2	0.1
TOTAL	1866	100.0

TABLE 3. Distribution of the Number of Positive Tests for Each Drug That Was Tested

Name of Drug	n	Percentage
Benzodiazepines	159	21.1
Opiates	98	13
Tetrahydrocannabinol	96	12.7
Methamphetamines	87	11.5
Methadone	85	11.3
Tricyclic antidepressant	72	9.6
Barbiturates	42	5.6
Cocaine	23	3
Phencyclidine	20	2.7
Amphetamines	18	2.4
Acetaminophen	53	7
Total	753	100

Of those 1866 patients, 26.7 % (n=499) were found to be positive for at least one drug. The number of drugs tested positively in these subjects is shown in Table 2. The distribution of the number of positive tests is shown in Table 3.

Divided into age groups, 64.8% (n=1209) of the patients were between the age of 16 and 35, 18.3% (n=341) of the patients were between 36 and 50, 8.9% (n=167) of the patients were between 51 and 65, and the remaining 8.0% (n=149) of the patients were older than 65. The rate of patients who tested positive for at least one drug was significantly lower in the patients who were older than 65 (18.8%, n=28) compared to patients who were 65 or younger (27.4%, n=471, χ^2 p=0.022).

When examined the time frame of presentation, we observed that 31% (n=578) of patients presented to ED between 8 and 16, 37.4% (n=698) between 16 and 24, and 31.6% (n=590) of patients presented between 24 and 8. The rate of patients who tested positive for at least one drug did not differ significantly between these three time frames (χ^2 p=0.492).

We found that 12.7% (n=237) of patients were hospitalized in wards, 2.7% (n=51) were hospitalized in the intensive care unit, 83.5% (n=1558) were discharged from the ED, and 1.1% (n=20) of the patients died during their hospital visit so the test was ordered. There was no statistically significant difference between the ward hospitalization, intensive care unit hospitalization, and discharge or death rates among the patients who tested positive for at least one drug and patients who tested negative for all drugs (χ^2 p=0.097).

The median observation period for patients who were discharged from the ED was 5 hours (range from 1 to 96). There was no statistically significant difference in terms of the observation period between patients tested positive for at least one drug (median 5, range 1 to 96) and patients who tested negative for all drugs (median 6, range 1 to 96; Mann-Whitney U test, p=0.075).

The final diagnosis was trauma (traffic accident, fall from heights, assault, firearm injury, hanging, simple falls, lacerations, electrical injuries) in 18.1% (n=338) of the cases; suicidal or accidental intoxication (drugs, carbon monoxide, mushrooms, plants, ethanol, lithium, digoxin, hydrocarbons) consisted 23.5% (n=439) of the cases; neurologic disorders (ischemic–hemorrhagic cerebrovascular disease, epileptic seizure, neurologic syncope) were observed in 20.4% (n=380) of the cases; metabolic, infectious, oncologic, and cardiac problems (pneumonia, meningitis, encephalitis, urinary tract infection, sepsis, electrolyte abnormalities, type 2 respiratory failure, acute renal failure, malignancies, acute coronary syndrome, dysrhythmia, cardiac syncope, cardiac arrest, congestive heart failure) were observed in 16% (n=299); and psychiatric conditions (acute psychosis, anxiety,

TABLE 4. Patients Tested Positive for Benzodiazepine, Methadone, and Tricyclic Antidepressants

	Male (n=1248)		Female (n=618)		χ2
	n	%	n	%	p
Benzodiazepine positive	91	7.3	68	11.0	0.007
Methadone positive	66	5.3	19	3.1	0.031
Tricyclic antidepressants positive	38	3.0	34	5.5	0.010

bipolar mood disorders) were observed in 22% (n=410) of the cases. In 60 (12%) of the 499 patients who tested positive for at least one drug, the final diagnosis was not intoxication.

The percentage of patients who tested positive for at least one drug was 29.6% (n=183) in females and 25.3% (n=316) in males. A statistically significant difference was observed between genders in terms of being positive for at least one drug (χ^2 p=0.049). The percentage of patients who tested positive for acetaminophen, amphetamines, methamphetamines, barbiturates, cocaine, opiates, phencyclidine, and tetrahydrocannabinol were not significantly different between genders. The percentage of patients who tested positive for benzodiazepines and tricyclic antidepressants were significantly higher in females. The percentage of patients who tested positive for methadone was significantly higher in males (Table 4).

According to files, all patients were also ordered a blood ethanol level test. Test was considered positive if the serum ethanol level exceeded 10 mg/dL. 8.6% (n=161) of the ordered blood ethanol level tests were positive. 18% of the patients who were tested positive for ethanol also tested positive for at least one drug.

We observed that 33.3% (n=622) of the patients were forensic cases. 35% (n=218) of the forensic cases tested positive for at least one drug compared to 22.6% (n=281) of non-forensic cases who were tested positive for at least one drug, and the difference was statistically significant (χ^2 p<0.001).

We found that 13.9% (n=260) of the patients presented with attempted suicide. 47.3% (n=123) of patients with attempted suicide were tested positive for at least one drug, compared to 23.4% (n=376) of patients who presented with symptoms other than suicide attempt, and the difference was statistically significant (χ^2 p<0.001).

Whereas 1.3% (n=25) of patients stated that they were in a rehabilitation program for drug addiction. 48% (n=12) of these patients were tested positive for at least one drug in UTS compared to 26.5% (n=487) of patients who did not point out to be in a rehabilitation program, and the difference was statistically significant (χ^2 p=0.016).

DISCUSSION

Differential diagnosis of patients presenting with altered mental status in ED includes intoxications with illegal drugs or commercial drugs. A full history and investigation of the environment by close ones, witnesses, and paramedics are mandatory, but the reliability of information in intoxicated ED patients is often limited (11). The main goal of drug testing in ED patients should be for diagnostic and treatment purposes (1). In contrast to legally required drug testing, the standards for UTS are different from forensic toxicology, and the results of unconfirmed UTS should be used only to assist patient management decisions (1).

Patient self-reporting of intoxication is not always accurate, and it is sometimes not possible because of the fear of legal persecution (3, 12). Especially in psychiatric patients, self-reported drug use may be unreliable and with a high false-negative rate, reaching up to 25%–66% (12). Many doctors would like to know if their patient is somewhat intoxicated. A point-of-care testing device is a good choice for initial toxicology screening in ED because it is rapid and accurate (3). Some authors have found urine drug screening to be a valuable tool because it provides information useful in decision making and increases the confidence of the physicians in the treatment choice (2, 11). UTS tests in ED may result in a decrease of the undesirable use of naloxone or flumazenil as diagnostic antidotes for opiates and benzodiazepines (2).

However, the ED UTS are questioned by many authors because they test for a small number of drugs, and new drugs are invented every day. These authors also claim that the results do not change the management of the patient because most abused drugs do not have an antidote, and therapy in ED is usually focused on the symptoms management (3, 2, 13). Some also argue that UTS tests are inappropriately used for diagnostic but not screening purposes in ED, and this is the fundamental reason for UTS poor clinical utility in ED (13).

Urine toxicology screening (UTS) tests may give false-positive results due to cross-reactions with chemicals having similar structures as the target drugs of abuse or false-negative results due to their relatively high cutoff levels for the target substances, which may lead to misdiagnosis (14). The panels of UTS manufactured by different companies use different cutoff values to determine a positive test result. They also differ in drugs and drug metabolites that may produce false-positive results (4). It should be remembered that UTS tests only provide a preliminary analytical test result, and a more specific alternative analytical method must be used to confirm the result, especially in the presence of inconsistency between the result of UTS and the patient's clinical condition (5, 2). Because the UTS results will be used immediately for diagnosis and treatment of the patient, and test results will arrive later, confirmation is not practical in ED (2).

Another factor that may limit the reliability of UTS is the operator's ability to execute and interpret a bedside test if a clinical laboratory worker does not perform the test (2, 3, 5). In our ED, the test was performed in the ED laboratory by experienced laboratory technicians.

The median age (29, age range 16–99) of our patients and the gender distribution (66.9% male) in our study were similar to literature (7, 11).

Different rates of UTS positivity were detected in different ED studies reaching up to 78%. Lower rates were observed with unselected ED patient populations, and higher rates were observed in studies where testing was limited to certain patients (5, 11). In our study, the percentage of patients who were positive for drugs was lower because no restriction for test use was applied, except attending physicians' judgment for test need. The difference may also be related to local drug habits.

In our study, no statistically significant difference was observed between the ward hospitalization, intensive care unit hospitalization, discharge or death rates, observation period, and among patients who tested positive for at least one drug and patients who tested negative for all drugs. The UTS testing does

not seem to affect hospitalization decisions or predict mortality. In 60 (12%) of the 499 patients who tested positive for at least one drug, the final diagnosis was not intoxication.

In our study, drug positivity was significantly higher in forensic cases, in cases of attempted suicide, and in patients who were in a rehabilitation program. These may be the target populations for UTS in ED.

The UTS testing is a controversial subject in ED. Our results do not support its use, with clinical curiosity being the only reason to order the test. The UTS testing may be more useful in targeted populations in ED.

The study has a retrospective design. An important part (17%) of urine sample results was lost in the logistics of samples reaching the laboratory, or the samples being tested.

The study was conducted in a single center. Unfortunately, the UTS test available in our department does not screen drugs that are presently popular. No confirmatory laboratory tests are done in the ED laboratory.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Yıldırım Beyazıt University School of Medicine (Approval Date: January 6th, 2015; Approval Number: 10/06/2015-129)

Informed Consent: N/A

Peer-review: Externally peer-reviewed.

Author contributions: Concept – G.P.G., G.K.Ç., T.E., A.Ş., A.Ö., Ş.G.; Design - G.P.G., G.K.Ç., T.E., A.Ş., A.Ö., Ş.G.; Supervision - G.P.G., G.K.Ç., T.E., A.Ş., A.Ö., Ş.G.; Resource - G.P.G., G.K.Ç., T.E., A.Ş., A.Ö., Ş.G.; Materials - G.P.G., G.K.Ç., T.E., A.Ş., A.Ö., Ş.G.; Data Collection and/or Processing - G.P.G., G.K.Ç., T.E., A.Ş., A.Ö., Ş.G.; Analysis and/or Interpretation - G.P.G., G.K.Ç., T.E., A.Ş., A.Ö., Ş.G.; Literature Search - G.P.G., G.K.Ç., T.E., A.Ş., A.Ö., Ş.G.; Writing - G.P.G., G.K.Ç., T.E., A.Ş., A.Ö., Ş.G.; Critical Reviews - G.P.G., G.K.Ç., T.E., A.Ş., A.Ö., Ş.G.

Conflict of Interest: The authors have no conflicts of interest to declare.

Financial Disclosure: The author declared that this study has received no financial support.

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