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Original Research Article

Urinary extract profiles of illegal substances at psychiatry and dependency clinics: three years report

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ABSTRACT

Background: Substance abuse is a serious problem all over the world. There are many studies report the illegal substance use profile but few studies present their toxicology laboratory analysis. This study reports a quantitative profile of (Urine Drug Screening)) for illegal substances in Sakarya-Turkey.
Methods: This study presents the urine analysis of all illegal substances which were made in the laboratory of Sakarya Training Research Hospital between March 2012 and February 2015. The results obtained from socio-demographic data and urine tests of patients were analyzed by examining their hospital record files. Urine drug screening was conducted with immunoassay quantitative analysis.
Results: People subjected to substance analysis (n=2948) ages vary between 12 and 76, their mean age was 28.30±9.46. 96.74% (n=2852) of them were males. Substance positivity was determined in 34.73% of all patients (n=1024/2948) and their ages varied between 14 and 70 and their mean age was 29.39±9.65. Distribution of the urine positivity of the substances contained: marijuana 79, 5% (n=814), amphetamine 30.17% (n=309), ecstasy 23.74% (n=199), benzodiazepine 9,1% (n=94), synthetic cannabinoid 4.9% (n=12/243); opioid 5.2% (n=54), cocaine 1.67% (n=14) and multiple substance 29.9% (n=308).
Conclusions: According to this study, marijuana is the most frequently used substance and multiple substance use is common. Synthetic cannabinoid seems to take place rapidly among the users. Updating the kits is important to reach the correct information in drug screening tests.

Keywords: Illegal, Probation, Substance, Urine drug screening

INTRODUCTION

Substance abuse is a serious problem all over the world. In the field of addiction, assessment of psychoactive substance use is a key element for diagnosis and medical management. But, studies about the substance use are mostly used the data obtained self-report of patients.[1] Nevertheless, this assessment is often difficult as self-reports underestimate the use of psychoactive substances.[2-6] Urine drug screenings (UDS) are used as supportive materials for diagnosis and follow up stages of substance use disorders.

UDS are based on immunoassay techniques and enable a qualitative and non-quantitative analysis with detection-based on designated thresholds. Urine drug screens in literature and Turkey are generally given in positive-negative manner so levels of extracts of substance in urine is not well known yet. It is essential to ensure their proposition of qualitative determination, in order to be able to interpret their significance. In addition, their limits need to be recognized to guarantee pertinent interpretation.[7] Whatever the method, caution is recommended for managers of clinical laboratories and good quality information is, therefore, required for clinicians in the field.[8]

In 2005, with the changes made to the Turkish Penal Code, substance abusers were no longer seen as criminals but rather as individuals in need of treatment. According to the program, carried out by the Ministry of Justice Penal and Detention Facilities Probation Directorate, the alternative of being treated was presented to substance abusers since 2006. In this way, individuals using substances would be able to be monitored in society and complete their treatment without being incarcerated. In Turkey, to purchase, accept, or possess sedative or stimulant drugs for the purpose of use is still a criminal act; however, the person using these drugs is sentenced with treatment and probation. If that person does not comply with the terms and requirements of the treatment and probation precautions, he or she is sentenced to 1 to 2 years of imprisonment.[9,10] Persons that are suspected to have use of illegal drugs are directed to psychiatry outpatient clinics by forensic units and they are evaluated about substance use with UDS tests as well as psychiatric examination.

In urine drug screenings, laboratories try to obtain the most accurate result due to its legal obligations and in order to conduct the diagnosis and treatment processes properly. However, new drugs are added to addictive substances day by day. The newly added and the most common drug is synthetic cannabinoid (SC) nowadays and its screening started in Sakarya University Training and Research Hospital (STRH) laboratory in October 2014. SCs are psychoactive substances which show agonistic effects via cannabinoid receptors and have similar effects of the active metabolite of cannabis, Δ9-tetrahydrocannabinol (THC).[11] More than 140 products were identified to contain SCs and such products do not only vary based on the type and amount of SCs, but also contain other psychoactive substances.[12-18] So it is difficult to determine all kinds of the SC products in urine analysis.

STRH has the unique laboratory that makes drug screening in quantitative manner thus it has the quantitative laboratory records of the city. Within our knowledge, there is not any study conducted in Turkey which shows the laboratory levels of the illegal substances. Kind and urine levels of illegal substances may differ according to the profile of users including economic, cultural, genetic, phamacodynamic factors determining the profile of substance users and levels of drugs may help to find a background for future social, politic, medical, legal solutions. This study presents laboratory derived data from Sakarya about substance use during the years 2012-2015 as the first report.

METHODS

This study presents the urine analysis of all illegal substances which were made in the laboratory of STRH between March 2012 and February 2015. Illegal substance screening is conducted in our hospital mainly within the scope of Probation Services and in addition to

this; drug screening is also made for diagnosis and follow-up. The results obtained from socio-demographic data and urine tests of 2948 patients were analyzed by examining their hospital record files.

Evaluation of socio-demographic data

Age and gender information of the patients screened were obtained from the database of the files according to their identity numbers.

Analysis of the urine tests

CEDIA (Cloned Enzyme Donor Immuno Assay) was used as the immunoassay method during the analysis of the urine tests. The multiplex CEDIA assay uses the genetically engineered enzyme fragments of enzyme donor (ED) and enzyme acceptor (EA) from ~-D-galactoside galactohydrolase (E. C. 3.2.1.23) or 13-galactosidase (~-gal) from E. *coli*. The generation of ED and EA, and the CEDIA homogeneous assay have been reported previously (15, U.S. Patent No. 4,708,929). The multiplex assay consists of multiple labels for the detection of amphetamine, benzodiazepine, barbiturate, opioids, MDMA (3,4-metilendioksi-N-metilamfetamin) (ecstasy), SCs, and THC drugs. In the assay, ED was covalently linked to each drug derivative in which each drug derivative is recognized by its specific antibody and the ED is capable of complementation with EA to form active [3-galactosidase enzyme. The enzyme substrate chlorophenolred-13-D-galactopyranoside (CPRG) is then cleaved by the active enzyme into galactose and CPR and CPR is measured by absorbency at wavelength 570 nm. The antibodies bind to ED conjugates and inhibit the enzyme formation. Calibrators or samples containing amphetamine, benzodiazepine, barbiturate, opioids, and ecstasy, SCs, and THC drugs compete with the conjugates for the antibodies. The amount of free conjugates in the assay system is proportional to the concentration of amphetamine, benzodiazepine, barbiturate, opioids, ecstasy, SCs, and THC drugs in the samples or calibrator.

The drugs which could be analyzed in 2012 are THC, opioid, amphetamine, benzodiazepine, cocaine and barbiturate. Screening of ecstasy and creatine levels started from 2013 while the screening of synthetic cannabinoids started within the last quarter of 2014. The rates are given for each drug based on the sampling screened

In urine drug analysis, any drug can be subjected to measurement and the measured values exceeding certain values are regarded as positive. The measurements above those values are included in the analysis based on their cut-off values.

We used the cut off levels in workplace drug testing are recognized values for groups of drugs to determine whether a sample is positive or negative for a group of

drugs. For the primary screen the cut off is for a group of drugs such as opioids, whereas confirmation testing is for a specific drug e.g. 6 acetyl morphine. Any result below the cut off is reported as negative, and results above the cut off are reported as either Non-negative (for screening tests) or Positive (for confirmed positive results).

The purpose of the screening test is to eliminate all negative samples quickly while highlighting samples that require further investigation. Screening test cut off levels are set at a point where there is a demonstrably high statistical probability that the drug will be detected if present. Results that fall below this are recorded as negative even though a more sensitive method would show the presence of the drug.

In order to quickly identify negative samples, screening tests are designed to react to any drug related to the target drug e.g. the amphetamine test will react to amphetamine and MDMA (ecstasy). It may also react with similar prescription or over the counter medicines. These results must therefore be confirmed by a method that can tell the difference between the different drugs within the group.

Cut off levels are; Cannabis 50 ng/ml, cocaine 300 ng/ml, opioid 300 ng/ml, amphetamine 500 ng/ml, benzodiazepine 200 ng/ml, barbiturate 200 ng/ml, buprenorphine 5 ng/ml, respectively.

Statistical analysis

SPSS 20.0 program was used for the statistical analysis. Student's *t*-test and Mann-Whitney U test were used to compare the linear variables whereas chi square test was used to compare the cluster variables.

RESULTS

This study presents the urine analysis of all illegal substances which were made in the laboratory of STRH between March 2012 and February 2015.

General evaluation of the data

Two thousand eight hundred and fifty two (2852) 96.74% of 2948 people subjected to substance analysis are males, their ages vary between 12 and 76 and their mean age is 28.30±9.46.

Changing based on the years in this study, positivity was determined in 34.73 % of all patients subjected to urine analysis in our laboratory (n= 1024/2948), their ages vary between 14 and 70 and their mean age is 29.39±9.65. One thousand and five (n= 1005) 98.1% of the patients determined to have substance positivity are males.

Table 1: General evaluation of 3 year data (n: 2948 people, 2169 positive urine results).

Substance	Positive urine examination (person)		Number of positive examination (urine)	Mean urine level Mean ±SD, range
	n	%		
Marijuana	814	79.49	2186	138.78±87.85 (50-1500)
Opioid	54	5.2	114	2494.03±1567 (301-7552)
Amphetamine	309	30.17	442	3601.67±1958.93 (500-10000)
Benzodiazepine	94	9.1	232	1931.94±1212.59 (201-5000)
Cocaine*	14	1.67	30	2264.07±1383.96 (311-5000)
Ecstasy*	199	23.74	315	1478±826.60 (501.17-4124)
Multiple substance**	308	29.9		
Total	1024	100		

* Data of 2013 and 2014. ** Since screening of synthetic cannabinoid 6 acetyl morphine started later, it was not included in this table.

Table 2: Socio-demographic data of the people (n: 186) who had substance positivity in urine tests (n= 596) in 2012 and their characteristics with regard to substance use.

	Positive urine test person		Age		Gender	
Substance	N %		Mean±SS, Min-Max		N %	
Marijuana	151	81.1	31.27±10.72	16-70	147 Men 4 Women	97.40 2.60
Opioid	6	3.22	32.83±8.49	22-44	6 Men	100
Amphetamine	63	33.8	28.71±8.40	18-54	62 Men 1 Woman	98.41 1.59
Benzodiazepine	17	9.13	32.82±8.68	20-46	17 Men	100
Multiple Substance	44	23.6	31.15±10.41	17-56	43 Men 1 Woman	97.72 2.28
Total Substance Positivity	186	31.20	31.20±10.37	16-70	182 Men 4 Women	97.8 2.2

Distribution of the urine positivity of the substances contain marijuana 79, 5 % (n= 814), amphetamine 30.17% (n= 309), ecstasy 23.74% (n= 199), benzodiazepine 9, 1% (n= 94), SC 4.9% (n= 12/243); opioid 5.2 % (n= 54), cocaine 1.67% (n = 14) and multiple substance 29.9 % (n = 308). Information about the drug distribution is given in Table 1. The average substance levels of the patients who were determined to have substance positivity in urine are 138.78±78.85; 2494.03±1567 and 3601.67±1957.93 for marijuana, opioid and amphetamine, respectively (Table 1).

Data of 2012

UDS analyses of 596 people were made in 2012 during the evaluation of the data. Mean age of the subjects corresponds to 30.21±10.11, the age range is 13-70 and

97.5% of them are males. One hundred eighty six (186) (31.20%) of them were determined to have substance positivity while multiple substance positivity was detected in 44 of 186 people (23.7%). Among the users of multiple substances, the number of the people who use two drugs, three drugs and four drugs simultaneously corresponded to 39 (88.6%), 3 (6.8%) and 2 (4.5%), respectively. Barbiturate and cocaine could not be detected in the urine tests. The number, rate and mean age of the people determined to have substance positivity in urine are shown in Table 2.

One thousand nighty and twelve 1912 package analyses were conducted for all patients in total. The number of examinations per person was detected as 1912/596 = 3.20. 514 of 1912 urine samples were found to have substance positivity and their substance-based distribution is given in Table 3.

Table 3: Analysis of the urine samples (n: 514) determined to have any substance positivity during the urine drug screenings (n: 1912) in 2012.

Substance	Positive urine		Interval of the measurable values	Number of measurable urine samples (over the value)	Corrected Substance Level (Mean± SD)
	N	%			
Marijuana	378	73.5	50 -300	166	208.98 ±96.10
Opioid	12	0.23	300-2000	6	1341.45±702.02
Amphetamine	91	17.7	500-5000	49	3059.99±2100.32
Benzodiazepine	33	0.64	200-1000	6	553.20±269.09

Table 4: Substance usage characteristics of the patients applying in 2013 (n: 985).

Substance	Positive urine test person		Age		Gender	
	N	%	Mean ±SS , min-max		N	%
Marijuana	293	80.9	29.83±9.62	14-69	286 Men 5 Women	97.61 2.39
Opioid	22	6.1	31.40± 10.96	21-60	Men	100
Amphetamine	129	64.4	28.69±9.71	14-69	126 Men 3 Women	97.72.3
Benzodiazepine	17	4.7	29.88±8.98	16-53	Men	100
Cocaine	4	1.1	34.75±10.27	24-47	Men	100
Ecstasy	74	20.4	28.31±9.47	14-69	72 Men 2 Women	97.32.7
Multiple Substance	115	31.8	28.86±9.60	15-60	111 Men 4 Women	96 3.5
Total Substance Positivity	362	36.75	29.49±9.60	14-69	354 Men 8 Women	97.8 2.2

Data of 2013

UDS analyses of 985 people were made in 2013 during the evaluation of the data. Mean age of the subjects corresponds to 28.91±9.61; the age range is 12-76. Nine hundred and fifty four (954) (96.8 %) of them are males. Three hundred and sixty two (362) (36.75 %) of them were determined to have substance positivity in 2013

while multiple substance positivity was detected in 115 of 362 people (36.75 %). Among the users of multiple substances, the number of the people who use two drugs, three drugs and four drugs simultaneously corresponded to 54 (47.0 %), 55 (47.8 %) and 6 (5.2 %) respectively. The number, rate and mean age of the people determined to have substance positivity in urine are shown in Table 4. In 2013, 3324 urine analyses were conducted in total. The number of examinations per person was detected as

3.37. One thousand two hundred and fifteen (1215) of 3324 urine samples were found to have substance positivity and their substance-based distribution is given in Table 5.

Data of 2014

UDS analyses of 1367 people were made in 2014 during the evaluation of the data. Mean age of the subjects corresponds to 27.04±9.08, the age range is 12-64. One thousand three hundred and seventeen (1317) (96.3 %) of them are males. Four hundred and seventy six (476) (34.82 %) of them were determined to have substance positivity while multiple substance positivity was detected in 149 of 476 people (31.3%). Among the users of multiple substances, the number of the people who use two drugs, three drugs, four drugs and five drugs simultaneously corresponded to 69 (46.3%), 66 (44.2%), 10 (6.7%) and 4 (2.7%) respectively.

Table 5: Analysis of the positive (n=1215) results obtained from urine drug screenings (n: 3324) in 2013.

Substance	Positive Urine		Interval of the Measurable Values	Number of Measurable Urine Samples (over the value)	Corrected Substance Level (Mean± SD)
	N	%			
Marijuana	845	69.54	50 -300	156	157.88±84.18
Opioid	40	3.29	300-5000	15	2692.64±1902.50
Amphetamine	184	15.14	500-5000	116	3615.96±1890.17
Benzodiazepine	22	1.81	200-5000	2	1826.69±1401.09
Cocaine	8	0.65	300-5000	3	3153.78±1671.80
Ecstasy	116	9.54	500-2000	-	1071,75±258,42

Table 6: Socio-demographic data of the patients (n: 1367) applying in 2014 and their characteristics with regard to substance use.

Substance	Substance positivity		Age Mean ±SD and n-max		Gender	
	N	%				
Marijuana	370	77.70	28,12±8,67	(15-67)	364 Men 6 Women	%98.4 %1.6
Opioid	26	5.50	31.50±9.18	(16-63)	All Men	
Amphetamine	117	24.06	26.80±7.13	(15-49)	115 Men 2 Women	%98.3 %1.7
Benzodiazepine	60	12.60	33.48±11.74	(16-62)	57 Men 3 Women	%95.0 %5.0
Cocaine	10	2.1	38.70±9.10	(25-52)	All Men	
Ecstasy	125	26.30	26.78±7.48	(15-49)	12 Men 2 Women	%98.4 %1.6
Synthetic cannabinoid*	12	4.9	25.83±3.63	(21-33)	11 Men 1 Women	%91.7 %8.3
6 acetyl morphine *	3	1.2	35.66±4.04	(31-38)	All Men	
Multiple Substance	149	31.30	27.17±7.64	(15-56)	147 Men 2 Women	%98.7 %1.3
Total Substance Positivity	476	34.82	28.61±9.32	(15-67)	469 Men 7 Women	%98.5 %1.5

*This data belongs to the last quarter of 2014 and gives the rate of 243 people determined to have positivity after screening. Screening was conducted.

Table 7: Analysis of the urine samples (n=1195) of the patients determined to have substance positivity.

Substance	Threshold value	n	Cut off/above upper limit	CPSL* Mean± SD	CPSL*Interval
Marijuana	50	963	none	93.06±37.67	(51-412)
Opioid	300	62	4	2589.01±1360.06	(425-5000)
Amphetamine	500	167	118	3881,09±1903,84	(509-5000)
Benzodiazepine	200	177	110	2202,08±1118,61	(203-3000)
Cocaine	300	22	11	1940,54±1141,11	(311-3000)
Ecstasy	500	199	155	1714,80±944,32	(549-3000)
SC**	20	22	none	31,03±5,08	(22,24-41,73)

After the urine drug screenings in 2014 (n=5201); *Corrected positive substance levels ** Synthetic Cannabinoid (n=1715)

It was found that at most 5 drugs are used simultaneously. The number, rate and mean age of the people determined to have substance positivity in urine are shown in Table 6.

In 2014, 5201 urine analyses were conducted in total. The number of examinations per person was detected as 3.80. 1195 of 5201 urine samples were found to have substance positivity and their substance-based distribution is given in Table 7.

Comparison between the groups according to years

The rates of determining substance positivity were compared according to years among the subjects of drug screening. 31.20 %, 36.75 % and 34.82 % of the people who applied in 2012, 2013 and 2014, respectively had substance positivity. When the groups are compared through chi square test, the difference between the groups was significant (chi square p = 0.000) and the rate of the drug users was significantly high in 2013. 38.94 % (243/624) and 31.35 % (233/743) of the people who were subjected to UDSin the last quarter of 2014 and within the first 9 months of 2014, respectively had substance positivity (p > 0.05). The number of the people using the detected drug and distribution of the positive urine analyses according to years are given in Table 8.

Table 8: Distribution of the data obtained from urine analyses according to years.

	2012	2013	2014
Number of the people subjected to substance screening	596	985	1367
Number of the substance users identified	186 (31.20 of the applicants)	362 (36.75 of the applicants)	476 (34.82 of the applicants)
Total number of the package process	1912	3324	5201
Number of the urine samples determined to have substance positivity	514	1215	1195
Age group (Substance positivity) Mean ±SD (min-max)	31.20±10.37 (16-70)	29.49±9.60 (14-69)	28.61±9.32 (15-67)

DISCUSSION

In this study ages of substance users (positive urine test) were about 29.39±9.65. The youngest age determined was 14, and the oldest one is 70. Mean age of the people subjected to UDS was determined as 28.30±9.46 and 12 and 76 are the minimum and maximum ages, respectively. This results is similar to other studies conducted in Turkey.[19,20] However, the information could not be matched with the toxicological analyses in those studies. In another study conducted in Turkey, the mean age of the people subjected to substance analysis was reported as 33±11.6 (18-69).[21]

This study presents males for the huge amount of substance use positive urine test with the ranges over 98.1% for all substances. 96.74% of the people subjected to urine substance analysis are males. This rate corresponded to 98.5%, 99.5% and 95.7% in the studies in Turkey respectively.[19,22,23] In the addiction unit of Ege University, the rate of males was found as 98.2% which is similar to our results.[21] Although the substance use disorders increase in women in the world, they are seen more commonly in men.[24] But it is thought that higher rates of men in these studies arise from mainly the probation cases.

Although the rates vary according to years, the mean rate of substance positivity was detected as 34.73% and marijuana was found in 79.5% of the subjects having substance positivity. The other substances found included amphetamine 30.17%, ecstasy 23.74%, benzodiazepine 9.1%, SC 4.9%; opioid 5.2% and cocaine 1.67% whereas the rate of multiple substances was determined as 29.9%. In urine analyses of 116 people conducted in Ege University, 56 (48.2%) people were found to have substance positivity and the use of marijuana, cocaine, amphetamine, opioid and multiple substance corresponded to 50 (89.2%), 2 (3.5%), 2 (3.5%), 1 (1.7 %) and 1(%1.7), respectively.[21] The drugs seized by urine test in a one study(n=115) in Turkey for substance abusers among the probationers were marijuana in 98 (85.2%) cases, heroin in 3 (2.6%) cases, ecstasy in 10 (8.7%) cases, and cocaine in 4 (3.5%) cases.[25] The studies conducted in Turkey are generally based on self-reports and UDS has become widespread due to probation cases. In one study from Turkey which published its all toxicological analyses before, marijuana was found to be the most frequently used substance after 201 cases (47.2%) who were chosen among 425 cases and sent due to substance addiction were evaluated.[19] Since the people detected to have positivity in urine tests are included in the addiction program as required by the regulations of probation, it can be considered that substance positivity was detected in 201 cases, but their toxicological analyses were not published in the relevant article.[26] These findings are higher than the rates of substance positivity found in this study and similarly, the most common used substance is marijuana. In the same study, results of the urine analyses of 47 patients sent to forensic

medicine institute show that only 13 patients and 1 patients used marijuana and amphetamine - marijuana, respectively.[19] In another study which was conducted in Eastern Black Sea region based on the probation cases, 196 cases were detected to use mostly marijuana and only 10% of them had substance positivity, because the cases included mainly the first applicants and the addictive patients were sent to Alcohol-Drug research, treatment and training center.[20] Results of this study are compatible with the publications and probation data showing that the most commonly used illegal substance is marijuana in our country and the world.[27-29] However, most of the multiple substance use was not specified in the study, its rate found in another study is quite lower than the rate in our study (1.7%-29.9%) and the number of the subjects in other studies is lower than the relevant number in our study, so it causes us to think that multiple substance use is more common in essence and goes unnoticed.[30]

It is investigated that how many of the admissions to psychiatry outpatient clinics has substance positive urine results and how it changes year by year. Results of this study determined that the most positive proportion in urine screening test for use of illegal drugs belongs to year 2013. In 2013, 36.75 % of persons who admitted for UDS had positive results. And it was also over 31 % in 2012 and 34 % 2014 too.

In this study, lower substance use in 2014 compared to the data of 2013 may cause an optimist estimation asserting that the rates of substance use are decreasing. However, it is also possible that some of the substances used may be the drugs which cannot be detected in urine. SC is the most known substance among them. SC is a substance which the users in Turkey have started to find and use recently.[31,32] In fact, SC took place in the screening which was made in the last quarter of 2014 and the first month of 2015, with a positivity of 4.9% (12/243). The substance users know which substances can be detected in the judicial screenings and it can be thought that they keep using their preferences when the alternative of using a non-detectable substance is eliminated. After the urine screening of SC started, the number of the positive urine samples increased significantly (38.94%-31.35%). This data underlines the importance of renewing the analyses of the UDS based on the current substances.

In this study, the mean substance levels of the patients having substance positivity are 138.78±78.85, 2494.03±1567 and 3601.67±1957.93 for marijuana, opioid and amphetamine, respectively.

Within our knowledge, it is the first study which presents a substance profile in urine with the substance levels by making quantitative analysis in the natural sampling. The data obtained from the other countries and provinces may help us to compare the urine levels of the substances. Thus, it can be possible to reach the information about the usage amounts of the substances according to regions or excretion-distribution of the individuals having different genotypes. It is anticipated that this study can trigger the pharmacoeconomic, pharmacocultural and pharmacogenetic studies in this field.

CONCLUSION

According to the study conducted in STRH laboratory, 34.73% of the patients subjected to illegal substance analyses in urine between 2012 and 2015 were found to have substance positivity. The most found substance is marijuana and multiple substance use is common. Updating the laboratory kits in order to detect new illegal substances is important.

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