

DETECTION OF SOME SUBSTANCES OF ABUSE DURING DAILY PRACTICE IN EMERGENCY HOSPITAL, MANSOURA UNIVERSITY

BY

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ABSTRACT

Illicit drug abuse represents a worldwide problem. Urine drug screening is an effective tool for monitoring illicit drug consumption. However, true clinical utility of toxicology screens is still controversial. Diagnosis of substance abuse may be challenging and some clinicians believe that just sending a urine sample to the lab will give conclusive results. This study aimed to evaluate laboratory based toxicological analysis of urine and to identify its clinical utility in detecting the prevalence of substance abuse among a group of overdosed patients presented to Mansoura Toxicology Unit. A total of 390 urine samples were collected. All samples were subjected to preliminary screening by Enzyme Multiplied Immunoassay Technique (EMIT). The study revealed that the overall prevalence of positive drug screen using EMIT was (65.12%). GC-MS confirmation showed that incidence of drug abuse is 43.83%. It is concluded that good communication between the physicians and laboratory can minimize lab errors and provide a clearer picture of possible problematic drug use. It is emphasized that diagnosis of substance abuse needs thorough history and clinical assessment integrated with judicious ordering of urine screen, accurate knowledge of its advantages and possible pitfalls with careful interpretation of toxicological results.

Keywords: Drug abuse, Screening, EMIT, GC-MS

INTRODUCTION

Substance abuse indicates improper unlawful use of illegal substances, drugs and / or prescription medications with potential harmful consequences to the individual and society. This may fail to meet criteria of dependence which include: compulsion, tolerance to the drug where greater doses are required to produce an effect, withdrawal symptoms and multiple unsuccessful attempts to control substance

use (Saunders, 2006; Butler et al., 2007).

The prevalence of prescription drug use and /or other substance use disorders should continue to be monitored, due to the observed increases among certain subpopulations along different periods. Drug abusers have a great tendency to keep their drug abuse secret with their liability to lie and to give imprecise history. Thus, results of questionnaire-based interview are inaccurate with high false negative

rates. Urine toxicology analysis is a valuable, yet underutilized, tool to monitor patterns of medication use and potential use of illicit drugs to evaluate their effects on health outcomes (McCabe et al., 2008; Mordal et al., 2008).

Patients visiting the emergency departments (ED) have been important sources for monitoring the trends of illicit drug use (Joranson et al., 2000). One of the most frequently performed toxicologic tests is the urine drug immunoassay screening. It can evaluate broad populations and provide rapid results. Yet, it should be confirmed by another different method as Gas Chromatography-Mass Spectrometry (GC-MS) that has a greater specificity with fewer false positives and additional information about the quantity of substance involved (McKay, 2005; Jaffee et al., 2007). However, the true clinical utility of toxicology screens is still controversial. Diagnosis of substance abuse may be challenging and some clinicians believe that just sending a urine sample to the lab will give conclusive results (Eldridge, 2007).

The purpose of this study was to evaluate results of laboratory based toxicological analysis of urine and to identify its clinical utility in detecting the prevalence of some substances of abuse among a group of overdosed patients presented to Mansoura Toxicology Unit.

SUBJECTS AND METHODS

(1) Subjects:

This study was conducted on 390 patients aged 15-50 years presented to Toxicology Unit in Mansoura Emergency Hospital with acute drug abuse overdose in the period between November 2001 and April 2005.

(2) Material:

A) Kits:

- Emit® d.a.u. TM (drug of abuse in urine) Opiate Assay: for qualitative analysis of opiates in human urine.
- Emit® d.a.u. TM Benzodiazepine Assay: for qualitative analysis of benzodiazepines in human urine.
- Emit® d.a.u. TM Barbiturate Assay: for qualitative analysis of barbiturates in human urine.
- Emit® d.a.u. TM Cannabis Assay: for qualitative analysis of cannabis in human urine.
- Emit® d.a.u. TM Ethanol in Serum (ETS) Plus Ethyl Alcohol Assay: for diagnostic use in the quantitative analysis of ethanol in human urine and serum. It should be used to detect ethyl alcohol exclusively and not other alcohols such as isopropanol or methanol. Reactivity with compounds structurally unrelated to ethyl alcohol has not been observed (Behring Diagnostics Inc., 1996). So, it is considered specific.

B) Instruments:

- Syva, Solaris S/N 1076 Version 3.00L. Using Emit® d.a.u. Assay.
- GC-MS (Hewlett Packard, 6890 series):

It separates the chemicals by retention time into constituent components. Mass spectrometry identifies and counts the relevant components.

(3) Methods:

- a. Thorough history taking was done to evaluate some socio-demographic data of the patients and pattern of drug overdose. This was conducted by senior clinical toxicology staff in Mansoura Emergency Hospital.
- b. Complete medical examination was performed to determine pattern of drug abuse according to the clinical manifestations of the patients.
- c. Urine sampling: after having informed consent, forty ml urine was obtained from each patient at time of admission and prior to giving any treatment. Each sample was collected in a dry, labeled container (serial number, age, gender of the patient, clinical provisional diagnosis and date of taking the sample).
- d. Toxicological analysis:
 - Preliminary drug screen test by EMIT system: Each urine sample was screened for cannabinoids, opiates,

benzodiazepines, barbiturates and ethyl alcohol.

- Confirmatory testing of positive results by GC-MS.

- Drug cut-off levels:

Sensitivity of the method is the ability to detect a drug when it exists at or above cut-off levels which are listed in table (1). Screening methods generally use higher detection cut-offs than do testing methods to reduce the incidence of false negative results (Jaffee et al., 2007).

e. Statistical analysis:

Quantitative data were presented as mean \pm standard deviation and qualitative data were presented as number and percentage.

RESULTS

All samples were subjected to screening by EMIT and only positive samples were then confirmed by GC-MS.

I- Age and gender characteristics of patients included in the study (Table 2):

Age of patients ranged between 15-50 years with a mean age 25.72 ± 7.05 . More than half of these patients (56.41%) were encountered in the age group 20-30 years. Regarding gender, men accounted for 92.8% of the studied group with 7.2% only for women. (Men: women ratio is 12.9:1).

II- Pattern of substance abuse in relation to age of the studied group (Table 3):

The present work showed that cannabinoid abuse was the most common (37.69%) followed by opiates (27.18%), benzodiazepines and barbiturates (13.59% each) and finally ethyl alcohol (7.95%). These results were based upon history taking and clinical examination. The most common age for substance use was 20-30 years (220 patients: 56.41%).

III- Pattern of substance abuse in relation to gender of the studied group (Table 4):

History and clinical examination revealed that women were more likely to abuse benzodiazepines (57.14%) while cannabis was the commonest substance of abuse among men (39.23%).

IV- Toxicological screening data of patients included in the study (Figure 1):

a. Enzyme Multiplied Immunoassay Technique (EMIT):

This study revealed that the percentages of positive urine samples using EMIT were (27.18%, 14.87%, 11.54%, 9.74% and 1.79%) for cannabinoids, opiates, benzodiazepines, barbiturates and ethyl alcohol respectively.

b. Gas Chromatography-Mass Spectrometry (GC-MS):

Positive results obtained by EMIT

were confirmed by GC/MS which revealed that the prevalence rates were as follows: cannabinoids (16.15%), benzodiazepines (10.25%), opiates (8.46%) and barbiturates (8.97%).

DISCUSSION

The aim of this study was to evaluate results of laboratory based toxicological analysis of urine by two different methods and assessing their actual role in detecting the prevalence and use pattern of some substances of abuse among 390 overdosed patients presented to Mansoura Toxicology Unit.

Our results revealed that the mean age of patients was 25.72 ± 7.05 . More than half of these patients (56.41%) were encountered in the age group 20-30 years as illustrated in table (2).

These findings support many reports which stated that substance abuse by young people had increased in the past decade. It was found that illicit drug use is a youth phenomenon. The rate of consumption is higher among 18-24 year old males. Also, the risk of illicit drug initiation increased steadily from ages 12-21 years (Elekes and Kovacs, 2002; Guo et al., 2002).

This could be explained by the fact that young people usually want to live sense of

happiness and self confidence. Also, this is the period of active life, work and responsibilities with more liability for facing problems, emotional difficulties, exposure to stress, and fear of failure. There is a false belief that drug use can help them to establish their individuality, independence, their ways of living, and to show their rejection of social standards (Çirakoglu and Isin, 2005).

Also, experimentation with new experiences is normal and necessary aspect of youth development. The initiation of illicit substance often starts as a form of experimentation for recreational purposes, for thrill seeking or as a way to bond with peers. Experimentation may be followed by more frequent drug use that may progress to more serious abuse problems (Kaul and Coupey, 2002).

Regarding gender, our study showed that men accounted for 92.8% of the studied group with 7.2% only for women (Men: women ratio is 12.9:1) as shown in table (2).

Our findings confirm previous epidemiological data reported by Rodham et al. (2005); Bloor (2006) and Fergusson et al. (2008) who determined higher prevalence of substance abuse among men.

Men are liable to become drug abusers as they are financially able to pay for get-

ting the abused substance. On the other hand, women are more protected by the family than men. Moreover, friendly relations, criminal and aggressive behavior associated with substance abuse play an important role making it easier for men to be involved in drug abuse (Emara, 1998). Brady and Randall (1999) attributed the predominance of drug abuse among men due to the fact that substance abuse is more stigmatized in women who also experience more social disapproval of drug use.

The present work showed that the percentages of positive urine samples using EMIT were (27.18%, 14.87%, 11.54%, 9.74% and 1.79%) for cannabinoids, opiates, benzodiazepines, barbiturates and ethyl alcohol respectively.

Drug screening techniques use immunoassay technologies that lack specificity, and are subject to false-positive and false-negative test results (Substance Abuse and Mental Health Services Administration, 2007). Therefore, all specimens identified as positive on screening test should undergo confirmatory analysis. Gas chromatography/mass spectrometry (GC/MS) is generally accepted by the scientific community for the confirmed identification of drugs of abuse (Macario and Pergolizzi, 2005).

Hence, positive results obtained by EMIT were confirmed by GC/MS which

revealed that the incidence rates for substance abuse were as follows : cannabinoids (16.15%), benzodiazepines (10.25%), opiates (8.46%) and barbiturates (8.97%).

In our locality, cannabis is the most popular substance of abuse as it is relatively of low price, can be easily obtained and cultivated illegally in many areas in Egypt with no special arrangement for its use (Ewida et al., 1996). In addition, survey data show that increasing numbers of young people are using marijuana as they become less concerned about its dangers. Its abuse among teenagers has increased as the perceived harmfulness of regular use has decreased and the perception of peer acceptance has increased (Committee on substance abuse, 2004).

Similarly, Bonomo and Proimos (2005) found that cannabis is the most common substance of abuse. Its use usually starts at about 16-17 years old. In addition, 67% of young men aged 18-30 years use marijuana on a regular basis in Emergency department injured patients (Rich and Grey, 2005).

Our study showed that benzodiazepines and opiates were also common drugs of abuse. Several studies have reported recent increases in prescriptions for opioid medications in the general population (Zacny et al., 2003). Moreover, the

number of emergency room visits associated with the use of sedative /hypnotics in 2005 was 34% of the total visits involving non medical use of prescription drugs (Substance abuse and Mental Health Services Administration, 2007). More strikingly, the number of benzodiazepine-related emergency department visits was not only comparable to those involving misuse of prescription opiates (approximately 29% of sedative / hypnotic visits), but they had increased 19% since 2004. So, abuse of these drugs especially benzodiazepines is on the rise and a cause for concern (Licata and Rowlett, 2008).

Reasons for a negative urine result include taking less medication than prescribed owing to reduced need, taking medication on an irregular schedule (i.e., bingeing), adulterating the urine sample so as to hide illicit drug use (Macario and Pergolizzi, 2005). The duration of detection times for all drugs depends to a great extent on the volume, dose, and duration of drug use. Despite the benefits provided by urine toxicology analysis, there are numerous limitations to the interpretation of the findings that can result in inconclusive or misinterpreted results. Specimen collection, cross-contamination, and laboratory errors do occur, most often resulting in false-negative results. Such errors include: mislabeling of specimen, bacterial contamination of sample or equipment, operator error, contamination with adulterants or

cleansers such as bleach, or strong oxidizing agents (Compton, 2007).

False-negative opiate test results do occur and can be challenging to interpret. Studies suggest that between 11% and 21% of samples test negative on confirmatory GC/MS analysis (Katz et al., 2003). If the patient is taking a prescribed opioid at irregular intervals, an opiate may be present in urine but at levels below the laboratory's identification threshold. Alternatively, hepatic metabolism of opiates is highly dependent on P450 enzyme systems; thus, the patient (either by nature or owing to concomitant medication use) may be a rapid metabolizer of opioids and present with low opioid blood levels (Stamer et al., 2005).

Interpretation of opiate results requires special consideration. Certain opiates metabolize to other opiates, so both-or only the metabolite may appear in urine sample. In addition, the half-life of these drugs and the time from the last dose of the drug affect results. If the prescribed analgesic is a synthetic or semi-synthetic opioid, it will not be detected with standard opioid screens; immunoassay is fairly sensitive for morphine and codeine, but patients using other opioids will likely test negative for urine opiates (Heit and Gourlay, 2004; Macario and Pergolizzi, 2005).

Although the presence of an illicit drug

in urine shows that the patient has used this drug in the recent past, it should not be concluded that a substance use disorder (abuse or addiction) is present. Urine toxicology provides objective confirmation of medication use which may not be obvious in patient appearance/behavior or self-report. However, diagnosis of addiction should never be based on the results of urine toxicology alone and should be considered within the context of aberrant medication use, drug-seeking behaviors, and unimproved or declining function (Compton and Athanasos, 2003; Jaffee et al., 2007).

Therefore, clinicians must not follow the results blindly and should avoid over-interpretation of positive results or providing false reassurance with negative tests. Successful urine toxicology testing depends on a good working relationship with the laboratory personnel who will perform the analyses. It is helpful to mention with the request that a specific opiate or over-the-counter medication may cause a positive result.

The present work provides several important guidelines for future research. First, the prevalence and pattern of substance abuse should continue to be monitored, due to the observed increases among certain subpopulations (such as men and adolescents). Second, urine toxicology analysis should never be used in

isolation to identify abuse or addiction, and that medication use, patient's functionality and behavior should always be evaluated. Third, drug testing in urine is an important popular solution in many

settings. Fourth, good communication between the physicians and laboratory can minimize the occurrence of lab errors and can provide a clearer picture of possible problematic drug use.

Table (1) : Cut-off levels in ng/ml for substances tested in this study.

Substance	Cut- off levels (ng/ml)	
	EMIT	GC-MS
Opiates	300	300
Barbiturates	200	200
Benzodiazepines	200	200
Cannabinoids	50	15
Ethyl alcohol	15	15

Table (2) : Age and gender of patients presented with drug overdose (n=390).

Age groups (in years)	Men (362)		Women (28)		Total (390)	
	No	%	No	%	No	%
15- < 20	42	11.6	-	-	42	10.77
20- < 30	205	56.63	15	53.57	220	56.41
30- < 40	90	24.86	13	46.43	103	26.41
40-50	25	6.91	-	-	25	6.41
Total	362	92.8	28	7.2		
Mean± SD	27.57±7.56		23.87±6.54		25.72±7.05	
Men: Women ratio= 362:28 = 12.9:1						

Table (3) : Prevalence rates for pattern of substances of abuse in relation to age groups (n=390).

Type of substance abuse	Age groups (in years)								Total	
	15- < 20		20- < 30		30- < 40		40-50			
	No	%	No	%	No	%	No	%	No	%
Cannabinoids	15	36	84	38.2	34	33	14	56.7	147	37.69
Opiates	11	24.9	65	29.6	25	23.7	5	21.3	106	27.18
Benzodiazepines	9	21.3	18	8.2	23	22.1	3	10	53	13.59
Barbiturates	5	12.9	36	16.5	12	11.6	-	-	53	13.59
Ethyl alcohol	2	4.9	17	7.5	9	9.6	3	12	31	7.95
Total	42	100	220	100	103	100	25	100	390	100

Table (4) : Pattern of substance abuse in relation to gender of the studied group (n=390).

Type of substance abuse	Men (362)		Women (28)		Total (390)	
	No	%	No	%	No	%
Cannabinoids	142	39.23	5	17.86	147	37.69
Opiates	104	28.73	2	7.14	106	27.18
Benzodiazepines	37	10.22	16	57.14	53	13.59
Barbiturates	48	13.26	5	17.86	53	13.59
Ethyl alcohol	31	8.56	-	-	31	7.95

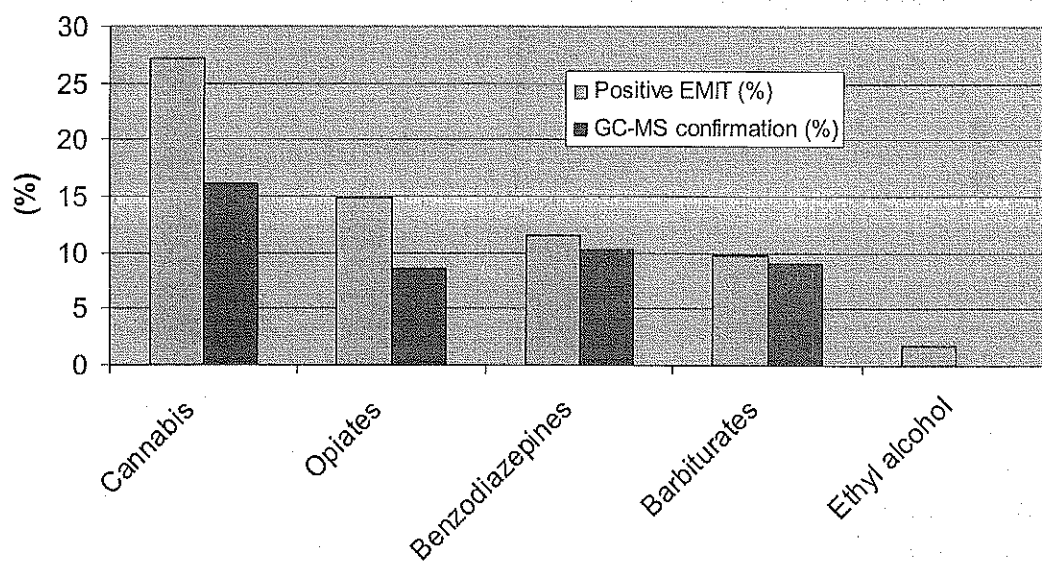


Figure (1) : Prevalence rates for pattern of substances of abuse screened by both EMIT and GC/MS

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الكشف المعملي اليومي عن بعض عقاقير الإدمان في مرضى وحدة السموم بمستشفى الطوارئ - جامعة المنصورة

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إن مشكلة تعاطي الأدوية والمخدرات مشكلة عالمية ولا تختلف في خطرها من دولة إلى أخرى سواء كانت هذه الدولة متقدمة أو نامية لأنها تؤثر على القوة البشرية، وهناك تصور خاطيء أن مجرد الاعتماد التام على الكشف عن تلك الأدوية عن طريق تحليل عينات البول وتقرير النتائج المرسل من المعمل هو دليل قاطع على تعاطي تلك العقاقير من عدمه مما يسفر عن أخطاء تشخيصية من جانب الأطباء خاصة غير المتخصصين في علم السموم الإكلينيكية، وقد استهدف البحث تقييم النتائج المعملية لأنماط تعاطي بعض الأدوية وعقاقير الإدمان وتجري مدى أهميتها الإكلينيكية، وقد أجريت الدراسة على مجموعة من المرضى (٣٩٠ مريض) تم إدخالهم وحدة السموم بمستشفى الطوارئ نتيجة تناولهم جرعة زائدة من تلك العقاقير مع أخذ التاريخ المرضي التفصيلي للحالات وعمل فحص إكلينيكي شامل وتم أخذ ٤٠ مللى بول من كل مريض عند الدخول وقبل تلقي أى علاج للكشف النوعى عن مخلفات الأيض لبعض المواد المؤثرة نفسياً، وقد تم الكشف عن العقاقير باستخدام جهاز المناعة الإنزيمية (EMIT) وجهاز كروماتوجرافيا الغاز مع مقياس طيف الكتلة لتأكيد النتائج.

وقد أسفرت الدراسة عن النتائج الآتية : أكثر من نصف المرضى (٥٦٤١٪) كانوا في المرحلة العمرية من ٢٠-٣٠ سنة ونسبة الذكور إلى الإناث (١٢٩ : ١). واتضح أن عينات البول الإيجابية من خلال إستخدام جهاز المناعة الإنزيمية (EMIT) كانت على النحو التالي : مادة الحشيش بنسبة (٢٧١٨٪)، الأفيون (١٤٨٧٪)، البنزوديازيبين (١١٥٤٪)، الباريتيبورات (٩٧٤٪)، والكحول (١٧٩٪) ولتأكيد النتائج باستخدام جهاز كروماتوجرافيا الغاز مع مقياس طيف الكتلة فقد تبين أن نسب إنتشار هذه العقاقير كانت كالآتى مادة الحشيش (١٦١٥٪)، البنزوديازيبين (١٠٢٥٪)، الباريتيبورات (٨٩٧٪)، والأفيون (٨٤٦٪). كما أثبت البحث أن مادة الحشيش كانت الأكثر شيوعاً واستخداماً فى الذكور والإناث (٣٧٦٩٪) يليها الأفيون (٢٧١٨٪) وكان عقار البيزنوديازيبين الأكثر إستخداماً بين المرضى الإناث (٥٧١٤٪)، وعلى ضوء هذه النتائج يوصى بضرورة وجود علاقة تعاونية متكاملة بين الأطباء المنوطين بتشخيص حالات تعاطي المخدرات والإدمان وفنى المعمل القائم على عمل التحاليل والدراسة الشاملة بكيفية إرسال العينات على أن تكون مصحوبة بتقرير وافى من الطبيب

المختص وتوخى الحرص التام فى تفسير النتائج المعملية مع الإلمام بالأخطاء التى يمكن أن تحدث عند أخذ العينة أو أثناء تحليلها مع التأكيد بأن التاريخ المرضى الكامل للحالة والفحص الإكلينيكى الدقيق يمثلان العامل الأساسى والأهم فى الوصول للتشخيص السليم والكشف المعملى هو وسيلة إضافية مساعدة لتأكيد ذلك التشخيص.