ORIGINAL ARTICLE

A Study Comparing Self-Reported Drugs and Results of An Immunoassay Test in Serum Samples in Patients Presenting to The Emergency Department with Acute Recreational Drug

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Abstract

Background: There is no consensus on the usefulness of toxicological analysis in the management of cases presenting to the Emergency Department (ED) with acute recreational toxicity. While in some centers urine samples are routinely analyzed, in others management is based on clinical interpretation and patient self-report on the drug(s) used. Most of the studies that investigated the role of toxicological analysis in this cohort have used urine for the drug testing. The aim of this study was to compare the drug(s) detected in blood samples analyzed by immunoassay (IA) with those self-reported by patients presenting to the ED with acute recreational drug toxicity.
Methods: The data were collected from self-reported drug(s) in patients presenting to the ED with acute recreational drug toxicity and compared to the results of a serum Immunoassay which includes 20 different tests.
Results: There was weak agreement (kappa 0.2 - 0.5) with significant disagreement between IA self-report for most of the drug assays, including cocaine, pregabalin, cannabis, and methadone. The poorest agreement was seen for synthetic cannabinoids (kappa 0.04) and benzodiazepines (kappa 0.13). The only exceptions with good agreement and insignificant disagreement between self-report and IA were methamphetamines (kappa = 0.65) and opiates (kappa = 0.60).
Conclusion: Poor agreement existed between the IA test results in blood and the self-reported data. Further studies comparing IA/self-report data to a gold-standard confirmatory mass spectrometry (MS)-based test are required to definitively address the role of analytical screening in the assessment of patients with acute recreational drug toxicity.

Keywords: Emergency Departments, Toxicity, Substance Use Disorders, Immunoassay, Drug Screening.

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INTRODUCTION

Recreational drug use is a common problem that is associated with significant morbidity and mortality . In 2018, nearly 35 million people worldwide were estimated to suffer from drug use disorders associated with drug dependence and/or requiring treatment [2]. In Europe, 29% of adults are estimated to have tried illicit drugs at some point in their lives, with 16.6% estimated to have used drugs in 2019 [3]. Acute recreational drug toxicity is a common reason for presentation to the Emergency Department (ED) [4, 5] and this has been increasing over the last two decades [6, 7]. In this regard, over 2800 overdose deaths related to illicit drugs were registered in England and Wales in 2019, which equates to 50.4 deaths per million population [8].

There is no consensus on the usefulness of analytical methods in the management of cases presenting to the ED with acute recreational drug /substance toxicity [9]. In many hospitals, the management of patients presenting to the ED with acute recreational drug toxicity is based on the clinical pattern of toxicity together with the drug(s) self-reported by the patient, without the routine use of toxicological screening to confirm the actual drug(s) involved in the presentation. However, the use of patients' self-reported data may be impacted by clinical factors (e.g., because the patient is intoxicated, confused or unconscious), or because the actual substance(s) used may not be known by the patient [10, 11]. Moreover, the clinicians' interpretation of the presentation is based on what they "believe" the drug(s) used were, and this may not be accurate [12].

The usefulness of analytical methods in the emergency setting hinges on the time to get the result (turnaround time), the extensiveness of the screening, and the accuracy of the results. Whilst comprehensive confirmatory toxicological screening can reliably confirm the drug(s) involved in presentations, these are generally limited by the long turn-around time. Rapid analytical tests using immunoassays [IA] may provide preliminary information about the substance(s)

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used. IAs are mainly based on the use of drug specific antibodies and the sample result is either positive or negative according to the presence or absence of the target drug above a certain cut-off concentration [13, 14]. The main advantages of these IA tests are that they are rapid and easy to perform, and that they can be used as point of care or near site tests because only minimal sample preparation is often needed [13]. However, immunoassay tests have some limitations. For example, testing for metabolites rather than or in addition to parent drug, and high false negative (due to poor sensitivity) and/or false positive (due to poor specificity or cross reactivity) rate which have limited their widespread use by most clinicians [14].

The available studies assessing the usefulness of toxicological analyses in the setting of acute recreational drug toxicity are few and their results are contradictory many limitations. Two opposing opinions exist, with a group of physicians finding that urine toxicological screening tests have limited or no value and so that they do not recommend it in the ED presentations [15-21], while the other group finds urine drug tests can be a useful diagnostic tool, because they provide confirmation and/or reassurance [22-29]. These studies have several limitations such as their retrospective nature, with many of them conducted on all patients presenting to the ED (either not focused on those with acute drug toxicity or not focused on recreational intake) and use of sometimes using subjective methods for evaluation (e.g. questionnaires about change in diagnosis or expert opinion).

A major limitation of previous studies is that most of them have evaluated the usefulness of urine drug screening in the emergency setting. The same is for the IA tests currently available for use in the ED in those centres that adopt the use of analytical methods, almost all of these methods that depend on urine analysis [9]. Moreover, it is worth noting that a key limitation to the use of urine in the setting of acute recreational toxicity is that drug presence in urine demonstrates drug use or exposure potentially outside the window of relevance to intoxication. It also does not necessarily indicate that the person is intoxicated or under the influence of the drug at or proximate to the time of sample collection. Moreover, there can be difficulties in obtaining a urine sample from someone who has acute drug toxicity and is likely to also be dehydrated with reduced urine output, or may be too drowsy or agitated to reliably give a urine sample. The detection of the drug(s) in blood can be more appropriate to reflect recent relevant drug use. In these settings, other biological matrices such as venous blood or finger prick blood/dried blood spot tests may be more feasible.

The aim of this study was to compare, in patients presenting to the emergency department with acute recreational drug toxicity, the drug(s) self-reported by the patient to those detected via the analysis of blood samples using an immunoassay analytical screening test.

METHODS

Study Type and Population

This is a cross-sectional study that was conducted in an inner-city, tertiary hospital in London, UK on adult patients aged ≥18 years, presenting to the Emergency Department [ED] with acute recreational drug toxicity who had a serum sample taken for electrolyte measurement as part of their routine clinical care in whom surplus serum was available for drug analysis. Acute recreational drug toxicity was defined when a patient had clinical features consistent with acute recreational drug toxicity and/or directly reported acute recreational drug use [30]. Detailed data on patients presenting to our ED with acute recreational drug is collected prospectively in a clinical toxicology database [30, 31]. For this study, we extracted from this database basic demographics (age, sex) and the drug(s) reported to have been used by the patient prior to presentation.

Procedures

For all patients in whom a serum sample was taken as part of routine clinical care and in whom there was surplus sample left, centrifuged samples were collected from the hospital pathology laboratory twice a week, anonymized and given a unique study code. The serum samples were then frozen at -20ºC for an approximate duration of 6-9 months, then the analyses were conducted. The analysis involved in this study used the Randox Evidence MultiSTAT Immnoanalyser (Drugs of Abuse - Blood array) [32].

The analytical methodology used by this blood array depends on competitive enzyme immunoassays that take place on the test biochip, a solid-state device with 20 discrete test regions (DTR) each containing immobilized antibodies specific to certain DOA compounds/classes. A competitive chemiluminescent immunoassay is employed, with the drug in the specimen and drug labelled with horseradish peroxidase (HRP) (added to the bioship in one of the automated steps) being in competition for the antibody binding sites on the biochip DTRs. Increased levels of drug in a specimen lead to reduced binding of drug labelled with HRP and thus a reduction in chemiluminescence being emitted. The light signal generated from each of the test regions on the biochip is detected using digital imaging technology and compared to that from the cut off material biochip. The classification of test result in a sample to "positive or negative" is determined according to the cut-off material.

The Randox DOA Blood Array Cartridges used in this study (Cat. No. EV4195) offered 20 tests (assays) to test for a range of the commonly abused drugs in each sample [33]. These tests included tests for stimulant drugs of abuse [3 assays; cocaine/benzoylecgonine (COC/BZG) assay, amphetamine assay, and methamphetamine assay] and numerous tests for opiates and opioids [7 tests; opiates assay, 6-monoacetylmorphine (6-MAM) assay, fentanyl assay, methadone assay, tramadol, buprenorphine, and oxycodone assay]. The presence of ethanol was tested by the ethyl glucuronide (EtG) assay and the presence of cannabis by the carboxy-tetrahydrocannabinol (COOH-THC) assay. Other tests included: benzodiazepines assay, pregabalin assay, tricyclic antidepressants, barbiturates assay, phencyclidine (PCP) assay, alpha-pyrrolidinopentiophenone (α-PVP) assay, and two assays for synthetic cannabinoids (AB-PINACA and AB-CHMINACA assays). The cut-off levels used for each of these analyses are available from the manufacturers [33].

The user manual supplied by Randox stated that the benzoylecgonine/cocaine assay is sensitive to both parent cocaine and its metabolite benzoylecgonine. Amphetamine assay is sensitive to S(+)-amphetamine, MDA (the main metabolite of MDMA), PMA HCl (metabolite of PMMA), BDB and less sensitive to DL-amphetamine. Methamphetamine assay is sensitive to S(+)-methamphetamine, PMMA and MDMA. Opiate assay is mainly sensitive to morphine, 6-acetylmorphine, 6-acetylcodeine, heroin and less to codeine. The 6-MAM assay is only sensitive to 6-acetylmorphine [33]. Benzodiazepine assay in this array is sensitive to oxazepam, alprazolam, diazepam, midazolam, estazolam; while less sensitive to other benzodiazepines like chlordiazepoxide and bromazepam; and least sensitive to others as clonazepam, lorazepam, and flunitrazepam. The assay for pregabalin is declared to be only sensitive to pregabalin, not gabapentin or other related compounds.

Some recreational drugs are not tested by this system including most of the synthetic cannabinoids (SCs), Gamma-hydroxybutyrate (GHB) and its related analogue gamma-butyrolactone (GBL), ketamine, synthetic cathinones (for example mephedrone) and "Z" drugs (such as zopiclone and zaleplon).

Data Analysis and Statistics

Data were recorded in Microsoft Excel® and the statistical analyses were undertaken using IBM® SPSS® Statistics (V. 26). Descriptive statistics were used to describe the socio-demographic data (age and sex). The frequencies of analytically detected and self-reported recreational drugs were also calculated.

To assess the agreement and disagreement between immunoassay results and self-reports, contingency tables were constructed. From these tables, the agreement between immunoassay results and self-reports was assessed by calculating the percent agreement and Cohen's Kappa statistic. The disagreement was assessed using McNemar's test. The observed positive agreement was calculated as follow [= how many times the drug was self-reported and in the meantime positively detected by the IA / total times the drug was either reported or detected]. The observed total agreement was calculated using the formula [= the sum of (positive IA and self-reported + negative IA and not self-reported) / total]. Cohen's kappa was used as it adds the advantage of taking in consideration the expected agreement (a significant p value means that the agreement is significant, i.e. significantly higher than agreement expected by chance). Kappa statistic for inter-rater agreement can be interpreted as per Fleiss et al [34] or McHugh [35]. The Observed total disagreement was calculated as well [= sum of (positive IA while not self-reported + negative IA while self-reported) / total]. McNemar's test was used to assess the disagreement between self-reports and IA results. A significant p value for McNemar's test indicates significant disagreement.

When assessing the agreement/disagreement between self-reports and IA results, for each case if the drug was recorded to be self-reported by the patient this was considered as a 'positive' self-report, and when the drug was not recorded in the self-reports it was considered as a 'negative' self-report. The IA results for methamphetamine assay were compared to the self-reports of MDMA and/or methamphetamine. Opiate assay results were compared to self-reports of heroin or codeine, or to when "unknown opiate" was documented as the suspected drug used, but not for methadone, buprenorphine, tramadol, oxycodone or fentanyl (each of these drugs has a specific assay). Benzodiazepines were excluded in this comparison between self-reports and IA results because data were not collected on whether benzodiazepines had been administered as part of routine clinical care, and this would confound the comparison.

Research Ethics:

This study was approved by the UK National Research Ethics Committee (REC reference 14/YH/1293 (Amendment 5)). Informed consent was not required for this study, as no patient identifiable data was collected, the samples were sera (acellular samples), and we used the surplus of samples that were collected as a part of routine clinical care.

RESULTS

There were 1052 presentations with acute recreational drug toxicity during the study period, of which 287 presentations had sufficient residual serum to be included in this study. The mean (± SD) age of these patients was 33.9 (± 9.8) years old, and 244 (83%) were male.

Immunoassay Results:

The frequencies of positive results for each assay are summarized in **Table 1.** The highest frequency for positive IA results was seen with the benzoylecgonine/cocaine assay followed by the ethyl glucuronide, then tetrahydrocannabinol and benzodiazepines assays. Assays that never reported positive results in this study sample were the oxycodone, fentanyl, AB-CHMINACA, α-PVP and PCP assays. The opiate assay showed a positive result in 48 samples, whilst the 6-MAM assay gave a positive result in only one sample. In the 20 samples that tested positive to the amphetamine assay, the methamphetamine assay was positive as well. However, in 47 samples, the methamphetamine assay tested positive whilst the amphetamine assay tested, while the amphetamine assay tested negative.

Table 1. The frequencies (n) of positive results detected by each of the 20 assays, in the 287 samples (total positive detections= 606).

Assay name	Positive results (n)	Analytes expected to be detected by the assay (according to the manufacturer)
BZG/COC*	124	Benzoylecgonine, cocaine
EtG**	107	EtG, methylethylglucuronide
THC	94	11-nor-9-carboxy-THC, and less to OH-THC and Δ9-THC

Table 1. Continued.

Assay name	Positive results (n)	Analytes expected to be detected by the assay (according to the manufacturer)
Benzodiazepine	87	Oxazepam, alprazolam, diazepam, midazolam, estazolam. less sensitive to others as chlordiazepoxide and bromazepam; least sensitive to clonazepam, lorazepam and flunitrazepam.
Methamphetamine	67	S(+)-methamphetamine, PMMA and MDMA.
Opiate	48	morphine, 6-acetylmorphine, 6-acetylcodeine, heroin and less sensitive to codeine.
Methadone	25	Methadone (not its metabolites).
Pregabalin	21	Pregabalin.
Amphetamine	20	S(+)-amphetamine, MDA, PMA HCl, BDB and less sensitive to DL-amphetamine
AB-PINACA	6	AB-PINACA, 5-fluro ADB-PINACA, 5-fluro AB-PINACA and metabolites.
Tramadol	2	Tramadol
Buprenorphine	2	Buprenorphine
6-MAM*	1	6-acetylmorphine.
TCA***	1	Nortriptyline, imipramine, and other TCAs.
Barbiturate	1	Phenobarbital, secobarbital, pentobarbital, butabarbital, and some other barbiturates.
Oxycodone, Fentanyl, AB-CHMINACA, α-PVP and PCP	0	Oxycodone, Fentanyl, AB-CHMINACA, α-PVP and PCP

* BZG= benzoylecgonine, COC= cocaine, **EtG= Ethyl glucuronide, THC= Tetrahydrocannabinol, 6-MAM= 6-monoacetylmorphine, ***TCA = Tricyclic antidepressants.

The immunoassay test gave negative results in 26 samples and in 21 samples, ethyl-glucuronide was the only positive assay. Table 2 shows the self-reported drugs in the 47 cases (16.4 %) when the IA test was totally negative for all the 19 assays for drugs of abuse (other than EtG assay). Some of these self-reported drugs were outside the scope of the immunoassay test used. They comprised GHB and related analogues, ketamine, mephedrone, poppers (the slang name for "volatile nitrites"), DMT, zopiclone, and LSD. In contrast, others drugs like cocaine, methamphetamine, MDMA, cannabis and heroin are within the scope of the immunoassay used (including cocaine, crystal methamphetamine, MDMA, cannabis and heroin).

Self-reported Recreational Drugs:

There were 439 recreational drugs/substances (excluding ethanol) reported to have been used in the 287 presentations (Table 3). The most common one was cocaine /crack cocaine followed by amphetamine-type stimulants and GHB. In 21 cases (7.4%) where there was a clinical diagnosis of acute recreational drug toxicity, the patients were not able to provide information about what recreational drug(s) they had used. The IA detections in these presentations is summarized in Table 4.

The Agreement/Disagreement between Self-reported Drug(s) Used and Immunoassay Results:

Figure 1 shows all the positive detections (either self-reports and /or IA) for the drug within the scope of the IA array used. Overall, this shows that there were three different categories in terms of IA/history concordance in this study:

- Moderate concordance (50.0-58.0%) was found for the three IA screens with large numbers (methamphetamines, cocaine, and opiates);
- Low concordance (15.4-31.8%) was found for cannabis, methadone and pregabalin; and

Very low concordance (3.9%) was found for synthetic cannabinoids.

Table 2. The self-reported drugs in the 47 cases in which the IA was totally negative (or only positive to EtG).

Drug	Frequency of self-reports
GHB* (and related analogues)	11
spice	11
cocaine	7
methamphetamine	4
MDMA**/ecstasy	3
ketamine	3
mephedrone	2
poppers***	2
cannabis	2
heroin	1
DMT****	1
zopiclone	1
LSD*****	1

* gamma (γ)-hydroxybutyrate,
** 3,4-methylenedioxymetamfetamine
*** the slang name for "volatile nitrites".
****Dimethyltryptamine
***** lysergic acid diethylamide

Table 3. The frequencies of self-reported recreational drugs in the 287 presentations.

Self-reported Recreational Drug	Frequency of reporting (cases)	Details
A) *Drugs within the scope of the IA test used in the study: (total n = 342)**		
Cocaine / crack cocaine	106	67 cocaine, 39 crack cocaine
Amphetamine-type stimulants	72	49 crystal methamphetamine alone, 13 MDMA** alone, 6 Ecstasy, 2 both methamphetamine and MDMA together.
Opiates (heroin, morphine, codeine)	48	46 heroin, 2 codeine,
Synthetic Cannabinoids (Spice)	47	
Cannabis / marijuana	30	
Benzodiazepines	21	16 diazepam, 4 alprazolam, 1 clonazepam
Opioids (Methadone, Tramadol, Buprenorphine)	10	5 Methadone, 1 Tramadol, 1 Buprenorphine, 3 reported as unknown opiate/opioid
Pregabalin	8	
B) *Drugs only self-reported and not within the scope of the IA test: (total n = 97)*		
GHB*** (and related analogues)	68	64 GHB, 2 GBL, and 2 reported as G drug.
Ketamine	13	
Z drugs	5	5 zopiclone
LSD****	4	
Others (poppers, magic mushroom, Dimethyltryptamine (DMT))	4	2 poppers, 1 magic mushroom, 1 DMT.
Mephedrone / methedrone	3	

* In this table, the frequencies mentioned did not include the self-reported ethanol use,
** MDMA: 3,4-methylenedioxymetamfetamine,
*** GHB: gamma-hydroxybutyrate GBL: gamma-butyrolactone,
**** LSD: lysergic acid diethylamide.

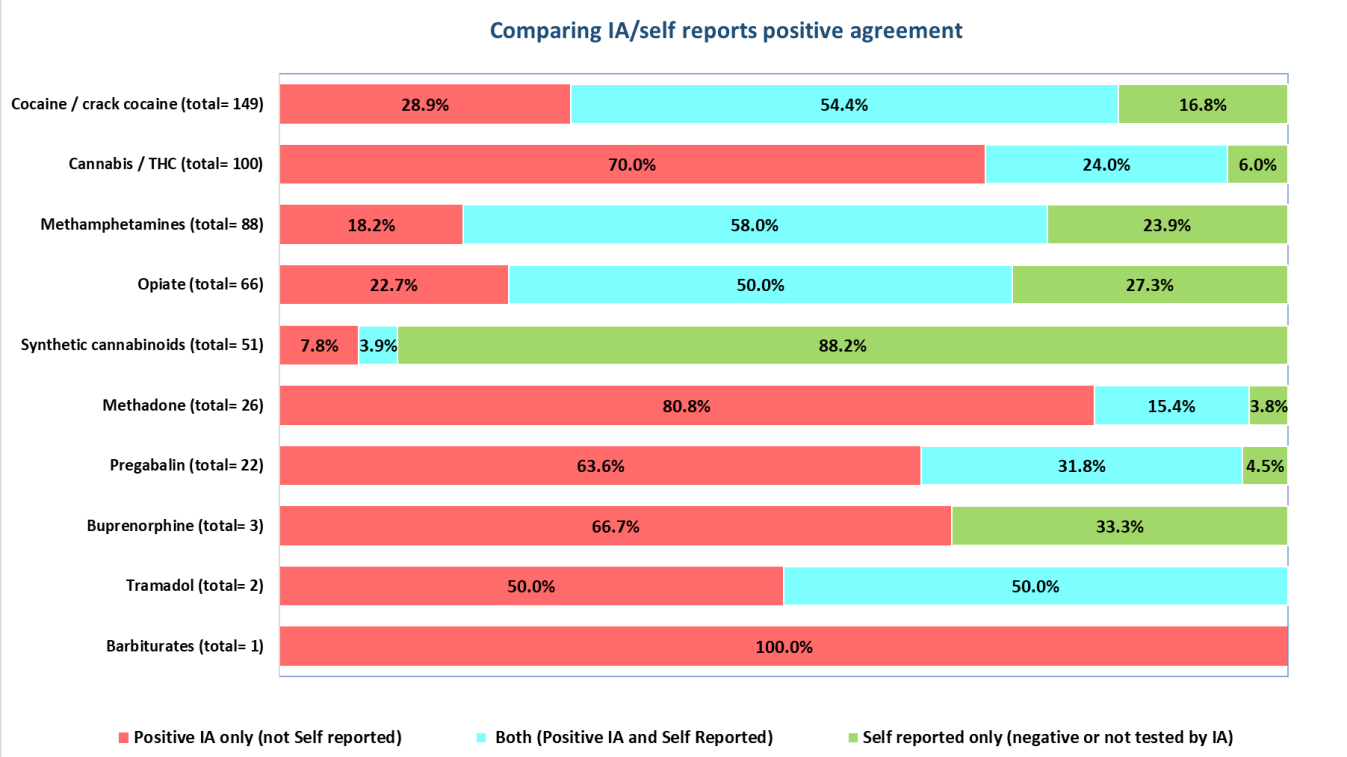

Figure 1. Positive detections and positive agreement (%) between Immunoassay (IA) results and self-reports.

Table 4. The IA positive detections where the patients were unable to provide information on the drug(s) used.

IA test	Frequency of positive results
BZG/COC assay	9
EtG (ethylglucuronide) assay	9
THC assay	7
Benzodiazepines assay	6
Methamphetamine assay	4
Opiate assay	3
Methadone assay	2
Pregabalin assay	2

Table 5 illustrates the observed agreement (positive and total) and the observed disagreement between IA results and the self-reported data. It shows that good agreement and insignificant disagreement (insignificant p value with McNemar test) were only observed between IA results and self-reported data for methamphetamines [total agreement = 87 %, positive agreement = 58 %, and kappa = 0.65] and opiates [88.5 %, 50%, and 0.60], as highlighted in yellow.

Fair to poor agreement [kappa = 0.25 - 0.51] with significant disagreement [significant p value with McNemar's test] between IA results and self-reports was observed for cocaine, pregabalin, cannabis and methadone, while no agreement [kappa < 0.20] with significant disagreement was found for benzodiazepines and synthetic cannabinoids.

DISCUSSION

The usefulness of toxicological screening in informing the management of patients presenting to the ED with acute recreational drug toxicity has not been established. There is a variation in practice around the world considering this issue. In the UK and many countries in Europe, toxicological screening is not routinely performed in patients with acute recreational drug toxicity [9], whilst in other countries such as the United States [36], Australia [37], [37], Japan [38], and the Netherlands [39], analytical methods are undertaken more widely. The aim of this study was to assess the use of an IA test in the ED setting, and explore the agreement and disagreement between self-reports and IA test results in patients presenting with acute recreational drug toxicity.

This study was conducted to compare the drug(s) self-reported by the patients presenting to the emergency department with acute recreational drug toxicity and those detected on their blood analysis via immunoassay analytical screening test. The immunoassay test used in our study was the Randox MultiSTAT analyzer using the Randox – Drug of Abuse – Blood Array which includes 20 different drug/drug group-tests.

There was generally fair/weak agreement (kappa 0.2 - 0.5) with significant disagreement (tested by McNemar's test) between the immunoassay screening test results and the self-reported data for most of the drug assays, including cocaine, pregabalin, cannabis, and methadone. The weak agreement for the cocaine (COC/BZG) and cannabis (THC) assays were due to large numbers of IA positive samples for COC/BZG or THC not associated with self-reported use. The COC assay in the IA used in the current study has a low cut-off to read positive (25 ng/mL for BZG and 18.8 ng/mL for COC), so that it can be expected that this IA will continue to be positive for one or two days after cocaine use. Hence, it is likely therefore that a significant proportion of these false-positive

Table 5. Assessment of the agreement and disagreement between self-reports and IA results.

	287 cases: Immunoassay / Self report Agreement							Immunoassay / Self report Disagreements		
Drug	Positive Agreement % (count)	Observed Total Agreement % (count)	Expected Agreement	Cohen's Kappa	Interpretation of Cohen's Kappa		p value for Cohen's Kappa	Observed Disagreement % (count)	McNemar's p value	Interpretation
					Fleiss et al, 2003**	McHugh, 2012				
Methamphetamines	58 % (51)	87 % (250)	63 %	0.65	Good	Moderate	0.000*	13 % (37)	0.511	Insignificant disagreement
Opiates	50 % (33)	88.5 % (254)	71 %	0.60	Good	Moderate	0.000*	11.5 % (33)	0.728	Insignificant disagreement
Cocaine	54.4% (81)	76 % (219)	52 %	0.51	Fair	Weak	0.000*	24 % (68)	0.038*	Significant disagreement
Pregabalin	31.8 % (7)	94.8 % (272)	90.3 %	0.46	Fair	Weak	0.000*	5.2 % (15)	0.001*	Significant disagreement
Cannabis (THC)	24 % (24)	73.5 % (211)	63.6 %	0.27	Poor	Minimal	0.000*	26.5 % (76)	0.000*	Significant disagreement
Methadone	15.4 % (4)	92 % (265)	89.9 %	0.25	Poor	Minimal	0.000*	8 % (22)	0.000*	Significant disagreement
Synthetic cannabinoids	3.9 % (2)	83 % (238)	82 %	0.04	No agreement	None	0.257	17 % (49)	0.000*	Significant disagreement

* Significant agreement
** Fleiss et al 2003, classify the agreement according to Cohen's Kappa value to poor beyond chance, fair to good beyond chance, or excellent agreement beyond chance.

IA results represent previous cocaine use not directly associated with the index presentation. The same is for COOH-THC, that can remain detected in blood for 2-7 days [40] and up to weeks in chronic users. Pregabalin and methadone were more likely to be detected by IA than self-reported. This could either be due to unreported recreational use or be related to the IA detecting therapeutic use of these drugs.

The only exceptions, where good agreement and insignificant disagreement were found between the self-reported data and the IA results, were for methamphetamines (kappa = 0.65) and opiates (kappa = 0.60), indicating the likelihood of lower true false positives and false negatives; however this needs to be corroborated with a confirmatory assay such as liquid chromatography-mass spectrometry (LC-MS).

The poorest agreement was observed for synthetic cannabinoids (kappa 0.04 with insignificant p value) and benzodiazepines (kappa 0.13). This lack of agreement between IA and self-report for synthetic cannabinoids was likely to be due to the IA only including a small number of synthetic cannabinoids whilst the lack of agreement for benzodiazepines may at least in part relate to benzodiazepines given for management of the patients, which is common in this group of patients for example to treat agitation or seizures; data were not collected in this study on drugs administered within the ED or pre-hospital.

In the current study, the IA test was totally negative for recreational drugs in 47 cases (16.4%). This may relate to either true negative samples or could be due to the presence of other recreational drugs that are outside the scope of the IA test or false negative results. On the other hand, in 21 cases (7.4%) with a clinical diagnosis of acute recreational drug toxicity, the patients were not able to provide information about what recreational drug(s) they had used - the true findings in these IA negative samples / unknown self-report cases can only be known if a confirmatory assay such as LC-MS is used.

Reviewing the literature, the studies that have assessed the potential usefulness of toxicological screening methods have used different methodologies and ended in contradictory findings and many limitations [41]. Some studies have examined the utility of toxicological screening tools in emergency settings; either in cases of suspected intoxication [18], or in patients with reported recreational drug toxicity [9], or in the setting of acute psychiatric presentations when recreational drug use is assessed [21, 42]. Nevertheless, other studies have assessed toxicology screening tools in other clinical settings such as in patients with chronic pain [43, 44] or those on rehabilitation programs [45].

To assess the potential usefulness of toxicology screening tests in the ED setting, some studies assessed the toxicology screening methods compared to self-reported data [9, 22, 42], some studies assessed the performance and the diagnostic accuracy of variable immunoassay screening tests against MS method [18, 46], while others used some subjective tools (e.g. questionnaires about change in diagnosis or expert opinion) [17, 21, 39].

The population assessed in the current study were adult patients (≥18 years) who presented to the ED in an inner-city, tertiary hospital in London, in whom acute recreational drug / NPS toxicity was either reported or diagnosed/ suspected based on clinical or circumstantial evidence. This is an important difference from other studies in which dissimilar population has been examined, including von Mack et al. who performed their study on patients with ED presentations caused by any acute intoxication including self-poisoning with pharmaceutical drugs [18], Skelton et al. whose study was carried out on patients admitted with suspected self-harm [47] or Fortu et al. and Kyle et al. who assessed the use of urine toxicology screens in paediatric patients [48, 49].

Low concordance between urine drug screen and self-report has been observed in a previous study that had assessed the EMIT urine screening test (testing for amphetamines, barbiturates, benzodiazepines, cocaine, ethanol, methadone, methaqualone, opioids, phencyclidine, propoxyphene, and THC) against self-reports in ED patients who needed or requested psychiatric consultation for suspected recreational drug use[42]. The highest agreement between the urine screen results and the self-reports was identified for cocaine (kappa 0.78), while the lowest agreement was for alcohol (kappa 0.07) [42]. However, this study assessed the patients' history for any drugs that had been taken over the 3 days prior to hospital admission and compared this to the urine screens at the time of admission. The presence of the cocaine metabolite benzoylecgonine in urine for up to 48-72 hours can explain the highest concordance found for cocaine [42].

In a Euro-DEN Plus Project study in 2018 [9], Liakoni et al. retrospectively investigated the concordance between self-reported data on recreational drug use and analytical results using a variety of different analytical methods (either IA or MS methods) in a population similar to the current study that is ED presentations with acute recreational drug/NPS toxicity. There was good concordance between self-reported data and analytical results for heroin and cocaine. Similar to our study, pregabalin and methadone were more commonly detected by IA than self-reported - this could either be due to unreported recreational use, or relate to the IA detecting therapeutic use of these drugs. Inhalants, poppers, magic mushrooms, GHB, LSD, NPS, and methylphenidate were mainly self-reported but not analytically detected. The findings of Liakoni et al. are comparable to our study in the sense that the self-reported data added more to the diagnosis of recreational drugs outside the scope of the IA test, including most of the synthetic cannabinoids, GHB, ketamine, cathinones, z drugs, LSD, poppers, magic mushrooms and DMT.

LIMITATIONS

The current study suffered from some limitations. One of the limitations was that the study was only conducted on the patients from whom a serum sample was taken for routine clinical care and there was surplus sample available for the project, which has a causing potential of selection bias. Although the sample collection in the current study was prospective, samples were frozen (approximate duration of

6-9 months at -20°C) and the analyses were conducted in batches. There is the potential that this storage could have impacted on drug stability [50-52].

Additionaly, a limitation for the IA positive results is that some of these could relate to therapeutic use of the drugs, or drugs administered to the patient. Data were not collected on drugs administered in ED/pre-hospital, or on the patient's normal therapeutic drug history. Finally, the absence of confirmatory analysis (e.g. GC-MS or LC-MSMS) did not make it possible to evaluate the reliability of IA results or to detect the potential false positive and false negative IA results.

CONCLUSION

In conclusion, this study revealed that using the Randox MultiSTAT immunoanalyzer for analyzing serum samples, there was only good agreement between the immunoassay results and self-reports for methamphetamine and opiates, while poor agreement was found for other drugs commonly involved in acute recreational drug toxicity presentations including cocaine and cannabis. Methadone and pregabalin were more analytically detected than self-reported. The IA screen did not include GHB and most synthetic cannabinoids. This study represents a primary step towards assessing the potential utility of serum immunoassay in emergency department. Further studies comparing IA/self-report data to a gold-standard confirmatory mass spectrometry (MS)-based test are still required to definitively address the role of analytical screening in the assessment of patients with acute recreational drug toxicity.

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