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TITLE

Prevalence of Illicit Substance Use Among Patients Presenting to the Emergency Department with Acute Behavioural Disturbance: Rapid Point-of-Care Saliva Screening

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RUNNING TITLE

Illicit Substance Use in Behavioural Disturbance

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ABSTRACT AND KEY WORDS

Objective

To determine the prevalence of illicit substance use among patients presenting to one emergency department with acute behavioural disturbance using point-of-care saliva testing.

Methods

A prospective observational study was conducted. Acute behavioural disturbance was defined as any episode requiring a security response for unarmed threat (Code Grey). The setting was a single emergency department and tertiary referral centre located in metropolitan Australia. Participants were adults presenting to the emergency department requiring a Code Grey. Saliva was analysed for: meth/amphetamine, cannabis, cocaine, opiates using a rapid point-of-care test. Self-reported drug use was recorded at the time of saliva testing. Data collection occurred between August 2016 to March 2017.

Results

There were 229 valid saliva samples. Participants were, on average, 35 years (range 18 to 72) and male (168/229; 73%). Forty percent [95% confidence interval (CI) 34-47%] of samples tested positive, with 20% positive for two or more substances. Meth/amphetamines was detected in 92% of positive samples, 17% of samples tested positive for opiates, 8% for

cannabis, and 7% for cocaine. Among participants, 19% self-reported current substance use and 20% reported using illicit substances within the past 24 hours.

Conclusions

The prevalence of illicit substance use among this cohort was 40%. Self-reporting was unreliable. Point-of-care saliva testing is feasible. Early identification of harmful drug use may assist clinical decision making in selected or undifferentiated cases and provide an opportunity to implement harm minimisation strategies and make referrals.

Key words

Acute behavioural disturbance, point-of- care, saliva drug testing, emergency department, methamphetamine, illicit substance

INTRODUCTION

Epidemiological studies have identified emergency departments (EDs) as high-risk settings for violence [1]. There is a significant relationship between exposure to occupational violence and feelings of safety among ED staff [1]. The challenges associated with management of acute behavioural disturbance where there is, or suspected, concurrent illicit substance use are well documented in the literature [2-8]. In Australia, studies report 2- 4% of ED presentations are related to illicit substances [2, 7]. However, the rate of illicit drug use among individuals presenting with acute behavioural problems remains unknown.

Research has determined the prevalence of illicit substance use among individuals attending EDs using self-report and clinical judgement of staff. [2, 5, 7, 9]. A review of studies that examined the use of illicit substances in individuals presenting with injuries compared drug levels in blood and/or urine to self-report [10]. The prevalence of an illicit substance in blood and urine was 35 - 40%, and 1-5% for self-report [10]. This suggests significant under-reporting, thus objective biological measures may provide more reliable estimates of drug use.

For drug testing to have the greatest impact on patient management, it must be reliable, provide rapid turnaround, and identify true negatives and true positives. [11] In the setting of acute behavioral disturbance, urinalysis has a number of disadvantages over salivary testing. First, in many cases it is not practical to obtain a urine sample unless the patient is restrained and catheterised. This approach introduces an unnecessary procedure and increases the risk of complications. Second, the clinical question that is asked when a person presents with acute behavioural problems is whether this is drug related. Here, the short window of detection of salivary testing (<24 hours) with an earlier peak is more relevant than a positive urine result

which may indicate drug use up to 4 days earlier.[12] Third, while point of care urinalysis kits are available, in our practice samples are sent to the laboratory and results are not immediately available to staff. Additionally, given the nature of specimen acquisition, we believe obtaining a salivary sample in a patient who is unable to consent is more respectful of their autonomy than performing an invasive procedure. Salivary testing is more consistent with the ethical principles of beneficence (to do good in the interests of the patient) and non-maleficence: to do no harm [13].

Point-of-care (POC) saliva tests are quick, non-intrusive, and potentially easier to collect than urinalysis. The POC saliva drug tests have been investigated in roadside drug testing [14-17] and in nightlife settings [18-20]. There have been no studies of feasibility of POC saliva tests among individuals presenting to the ED with acute behavioural disturbance.

The aim of this study was to determine the prevalence of illicit substance use among patients presenting to the ED with acute behavioural disturbance using a rapid POC saliva test.

METHODS

Research Design

A prospective observational study.

Setting

An adult ED within a metropolitan tertiary referral hospital in Victoria, Australia. More than 70,000 visits occur annually.

Participants

All patients aged 18 years or more, who presented to the ED and required a Code Grey were eligible to be enrolled within four hours of arrival. The Code Grey team is comprised of medical and nursing and security staff. The decision to enroll a person into the study was at the discretion of the attending clinical staff based on an assessment of safety.

Outcome Measures

Prevalence of cannabis, opiates, cocaine, meth/amphetamines was estimated using POC saliva testing and self-report.

Sample

A convenience sample of patients between August 2016 and March 2017 was recruited. Sample size was calculated with a power of 0.8 and alpha of 0.05. A meta-analysis of toxicologically proven amphetamine presentations to ED by high-risk patient populations report a positive test rate of 22.8% (95%CI: 15.4-32.5) [21]. To detect a proportion outside this confidence interval would require at least 171 patients.

Instruments

Participants were screened using the Securetec DrugWipe® 5S, an immunological rapid screening test for the detection of cannabis, meth/amphetamines (including MDMA, ecstasy), cocaine and opiates. DrugWipe® was chosen because of high reliability, short collection time, and small volume of saliva (20µL) required [14-20, 22]. Sensitivity is reported at: 94% for

cannabis, 100% for meth/amphetamine, cocaine, and opiates. Specificity is reported at: 98% for cocaine, 99% for meth/amphetamine, and 100% for cannabis and opiates[23]. This test was found to have good performance in studies conducted in both nightlife and roadside screening [21] [16].

Procedure

All nursing staff were trained to perform the test and interpret the results. Once individuals were deemed suitable and safe to be tested, staff would ask if they were willing to undergo a swab for the presence of drugs (analogous to a breathalyser test). This approach to drug screening is established as routine practice among trained members of the emergency mental health teams at the study site and was extended to the ED for the purpose of this study. Unconscious patients who met inclusion criteria were tested. Results were recorded on the data collection sheet.

The test was conducted by wiping the saliva from the tongue using the sample collector. Test results are visible within 3-8 minutes and remain valid for 10 minutes. Result were interpreted and documented by trained staff on the designated case report form. Information on substance use within the last 24 hours was requested from all participants before they left the ED.

Participant demographics and presentation characteristics were extracted from medical records by investigators retrospectively. No identifying information was retained.

Data Analysis

Demographics and baseline characteristics were analysed descriptively and reported as frequencies and percentages. Categorical variables were compared using the chi-square test or Fisher exact test. Pre-selected variables (age, gender, triage category) were tested for association with the saliva drug screening using univariate logistic regression and odds ratios (ORs) with 95% confidence intervals (CIs) were reported. Variables with P values less than 0.1 were then entered into a multiple logistic regression model and adjusted ORs with 95% CI. Cohen's κ was used to measure agreement between self-reported drug use and results from the saliva drug test. Analyses were performed using IBM SPSS® Statistics, Version 23.0 (IBM Corp, 2015). Level of significance was 0.05.

Ethical Considerations

Human Research Ethics Committee at the Melbourne Health reviewed the study in accordance the ethical standards outlined by the National Statement on Ethical Conduct in Human Research[24]. All conscious patients who were eligible received a verbal explanation of the study. The test procedure and samples were collected only with their verbal consent.

A waiver of consent was approved for unconscious patients on the basis that screening for illicit substances was already part of routine assessment by emergency mental health clinicians approved by the organisation.

RESULTS

During the study period, 32% of the 752 eligible individuals were identified by the Code Grey response team as suitable for inclusion (n=239). Of the identified samples, 229 (95.8%) people provided saliva samples that yielded a result. Of the remainder, five (2%) tests were deemed invalid due to operator error and five (2%) individuals were excluded due to

incomplete documentation (Figure 1). Participants providing a valid sample were, on average, 35 years (range 18 to 72) and male (168/229; 73%).

Insert Figure 1 here

Prevalence of illicit substance use

Of the 229 saliva tests included in the analysis, 40.2% [95% confidence interval (CI) 34-47%] of samples returned a positive result, with 18/92 (20%; 95% CI 13-29%) positive for two or more substances. Of the 92 positive samples, meth/amphetamines was most commonly detected [92% (85/92); 95% CI 85-96%]. A further 17% (16/92; 95%CI 11-26%) of samples tested positive for opiates, 8% (7/92; 95% CI 4-15%) for cannabis, and 7% (6/92; 95% CI 3-14%) for cocaine.

Twenty percent (47/229; 95% CI 16-26%) of those people tested admitted using illicit substances within the 24 hours prior to presentation. The highest self-reported prevalence of illicit substance use was for meth/amphetamines. Other illicit substances that have been self-reported infrequently included gamma hydroxybutyrate [6/229, 2.6% (95% CI 1.2-5.6%), phencyclidine [1/229, 0.4% (95% CI 0.08-2.4%)], and ketamine [1/229, 0.4% (95% CI 0.08-2.4%)].

The clinical characteristics and management for the 229 individuals who provided samples based on test outcomes (negative or positive for meth/amphetamine, cannabis, cocaine, and opiates) is shown in Table 1. Over two thirds (73%) of the eligible patients were male, with a mean age of 35 years (range 18 to 72).

Insert Table 1 here

Age and other presentation characteristics differed significantly between those identified for screening and those who were not. The outcomes of the multivariable analysis that explored associations between patient characteristics and saliva drug screening is shown in Table 2. These analyses found that time to first activation of a Code Grey was independently associated with saliva testing for illicit substances. Other individual characteristics independently associated with saliva testing for illicit substance use included younger age (51 years or younger), arrival between 7am and 1pm, presentation during weekends, and transport to ED by police.

Insert Table 2 here

Overall, there was only slight agreement between self-reported drug use, and saliva test result [Cohen's $\kappa = 0.18$, (95% CI 0.06-0.29), p=0.002]. Of 92 people who tested positive for any substance, 28 (30%, 95% CI 22-41%) reported having used illicit substances during the previous 24 hours. Of patients who tested negative for any substances, 14% (19/137; 95% CI 9-21%) reported that they had used illicit substances during the last 24 hours. Nineteen self-reported taking meth/amphetamine and 14 tested positive.

Agitation was the most commonly observed sign in all of those who tested positive. Hallucinations, delusions, repetitive movements, skin picking and agitation were observed in 92% of people who tested positive for an illicit substance. Bruxism was the only sign

particular to those testing positive to meth/amphetamines. A range of other clinical signs were observed such as rapid speech, confusion, erratic behaviour, diaphoresis, altered conscious state, blurred vision, seizure and elevated mood where reported by the nurses in almost one third of patients testing positive for meth/amphetamines (32.9%) and opiates (31.3%). Clinical characteristics of substance intoxication at the time of saliva testing are shown in Table 3.

Insert Table 3 here

DISCUSSION

To our knowledge this is the first study to use POC saliva drug tests to detect substance use among individuals with acute behavioural disturbance presenting to the ED. The prevalence of substance among this cohort was found to be 40% with meth/amphetamines present in most of the positive saliva samples (92%).

We have demonstrated that it is feasible to screen people who present to the ED with acute behavioural disturbance for illicit substance use using the DrugWipe® 5S device. This method was found to be superior to self-report, which was, in most cases, unreliable.

In terms of prevalence, the finding that meth/amphetamines was the most common substance detected is consistent with previous research that confirms meth/amphetamine-related agitation is a common clinical problem in EDs worldwide [2, 3, 5, 25, 26].

In the absence of a collateral history, meth/amphetamine-induced psychosis is almost indistinguishable from acute schizophrenia, [27] making a diagnosis based on presenting signs

and symptoms challenging. In our study we found that the ED nurses frequently reported signs and symptoms of agitation in most of the people who tested positive for any substance. Additionally, nurses documented a wide range of non-specific clinical signs and symptoms including suicidality, psychosis, sympathomimetic effects, as well as outward signs of abuse such as bruxism and repetitive movements.

Early screening for meth/amphetamine use, in individuals presenting to the ED with acute behavioural disturbance may be clinically useful. In practice, a negative POC saliva test confirms acute behavioural signs and symptoms are unlikely to be due to meth/amphetamine use in the last 24 hours. These results need to be interpreted with caution as a positive POC saliva result does not rule out other physical and psychological factors influencing behavior [28]. We found a sizable proportion of people with a final diagnosis of mental illness tested positive for meth/amphetamines. However, testing positive or negative for an illicit substance does not reliably rule out mental health or underlying medical conditions.

A small number of patients who reported meth/amphetamine use tested negative when the sample was collected (5/19 cases). This finding may be related to the person taking the substance outside the windows of detection or to the composition of substance taken.

Our study results indicate that under-reporting of illicit substance use is common among those presenting with acute behavioural disturbance. We observed positive saliva drug tests at a rate approximately double that of self-reported drug use.

Further research is required to examine the influence of POC saliva testing on clinical decision making and safety and quality of care. Here consideration must be given to clinical cost implications associated with routine POC saliva drug testing in the ED.

During the study planning, concerns were raised regarding the possibility of obtaining a saliva sample where a person was acutely agitated, however we found nursing staff willingly took part in training sessions to learn to use the test. Staff were able to collect samples from one third of all eligible individuals and were able to use their clinical judgement to determine when it was safe to obtain a test. This suggests that this test is acceptable to many staff and at least a third of all individuals who present to the ED with acute behavioural disturbance.

LIMITATIONS

This study is based on a sample of convenience, which may have introduced selection bias. Obtaining a saliva sample from individuals with agitation is challenging and the risks and benefits were considered. In practical terms clinical judgement needed to exclude individuals where behaviour may have deteriorated if asked to submit to the test.

Our report of prevalence is limited in that we only able to screen one-third of all eligible individuals. The multivariable analysis suggests that other factors influenced the decisions to conduct a test. For example, time from arrival to Code Grey was the strongest factor associated a saliva drug test.

The single hospital setting is a limitation to generalisability. The availability of various types of substances such as meth/amphetamine varies considerably by geographic region [26].

Our analysis was presented by individual types of substances thus the same people in the study may be included on more than one occasion due to polysubstance use. However, as there were only 19 patients self-reported or tested positive for polysubstance use, the degree of overlap is unlikely to change the reported findings.

Finally, we only tested for four types of substances where the windows of detection in saliva are up to 24 for meth/amphetamine. This test will not detect other substances with psychoactive properties.

CONCLUSIONS

Meth/amphetamines have the highest prevalence in our study of individuals presenting to ED with acute behavioral disturbance. We have shown that POC saliva drug testing is feasible in the ED. Self-report often does not correlate with POC testing. Further studies are needed to investigate the role of POC saliva drug testing in identifying individuals in need of substance abuse assessment and treatment in the ED alongside risk reduction policies for healthcare workers.

Table 1 Patient characteristics and management outcomes (N= 229)

Patient variable	Test Positive (n=92)	Test Negative (n=137)	p value
Age, years, mean (95%CI)	34 (32-36)	35 (33-37)	0.465
Age range, years	*18-54*	*18-72*	
Male, n (%)	60 (65.2)	108 (78.8)	0.022
Status under Mental Health Act on arrival, n (%)			0.286
Not under treatment order	32 (34.8)	34 (24.8)	
Section 351	51 (55.4)	80 (58.4)	
Assessment order	6 (6.5)	18 (13.1)	
Varied treatment order	0 (0.0)	1 (0.7)	
Apprehension order	1 (1.1)	3 (2.2)	
Treatment order	2 (2.2)	1 (0.7)	
Self-report substance use	28 (30.4)	19 (13.9)	0.002
Co-ingestion at time of presentation, n (%)			
Alcohol	18 (19.6)	44 (32.1)	0.036
Polysubstance use	16 (17.4)	7 (5.1)	0.002
ATS category, n (%)			0.065
1 (to be seen immediately)	5 (5.4)	2 (1.5)	
2 (to be seen within 10 minutes)	34 (37.0)	36 (26.3)	
3 (to be seen within 30 minutes)	48 (52.2)	93 (67.9)	
4 (to be seen within 60 minutes)	5 (5.4)	6 (4.4)	
Mode of arrival, n (%)			0.216
Ambulance	63 (68.5)	83 (60.6)	
Police	20 (21.7)	44 (32.1)	
Self-present	10 (7.3)	9 (9.8)	
Weekend arrival (Friday, Sat, Sun), n (%)	43 (46.7)	68 (49.6)	0.667
ED visit in the past 12 months, n (%)			0.054
No previous visit	16 (17.4)	40 (29.2)	
1-4 visits	66 (71.7)	77 (56.2)	
>4 visits	10 (10.9)	20 (14.6)	
Restraint			

Mechanical, n (%)	40 (43.5)	83 (60.6)	0.011
Chemical, n (%)	44 (47.8)	76 (55.5)	0.256
Referral made to emergency mental health services, n (%)	45 (48.9)	96 (70.1)	0.001
Final diagnosis, n (%)			0.001
Mental illness	33 (35.9)	84 (61.3)	
Intoxication (drugs and/or alcohol)	40 (43.5)	33 (24.1)	
Organic illness	19 (20.7)	20 (14.6)	
Disposition, n (%)			0.617
Home	24 (26.1)	29 (21.2)	
ED short stay	38 (41.3)	49 (35.8)	
Psychiatric admissions	15 (16.3)	30 (21.9)	
Medical admission	13 (14.1)	26 (19.0)	
Correctional facilities	2 (2.2)	3 (2.2)	
ED length of stay, hours, median, IQR	5.7 (3.7-11.4)	6.2 (3.6-12.1)	0.662

Table 2 Associations between patient characteristics and saliva drug screening

Patient variable	No. (%) tested for illicit substances (n=239)	Odds ratio (95% confidence interval)	Adjusted odd ratios (95 % confidence interval)
Age, years			
≤ 30	95 (39.7)	3.1 (1.8-5.2)	2.6 (1.4-4.7)
31-50	123 (51.5)	2.6 (1.5-4.3)	2.2 (1.3-3.9)
≥ 51	21 (8.8)	#	#
ATS category, n (%)			
1 (to be seen immediately)	7 (2.9)	0.8 (0.3-1.9)	0.5 (0.2-1.3)
2 (to be seen within 10 mins)	72 (30.1)	1.6 (1.1-2.3)	1.3 (0.8-1.9)
3 (to be seen within 30 mins)	148 (61.9)	#	#
4 (to be seen within 60 mins)	11 (4.6)	0.3 (0.2-0.6)	0.7 (0.1-6.2)
5 (to be seen within 120 mins)	1 (0.4)	0.4 (0.1-3.7)	0.4 (0.2-0.9)
Weekend arrival (Friday-Sunday)	118 (49.4)	1.4 (1.0-1.9)	1.4 (1.0-2.0)
Time of Triage, n (%)			
00:00-06:59	63 (26.4)	1.5 (1.0-2.3)	1.2 (0.8-1.9)
07:00-12:59	56 (17.8)	1.8 (1.2-2.8)	2.0 (1.2-3.2)
13:00-18:59	74 (31.0)	#	#
19:00-23:59	46 (19.2)	0.8 (0.5-1.2)	0.7 (0.4-1.1)
Mode of arrival, n (%)			
Ambulance	152 (63.6)	#	#
Police	67 (28.0)	2.2 (1.5-3.3)	1.9 (1.3-3.0)

Self-present	20 (8.4)	0.6 (0.3-0.9)	0.9 (0.5-1.6)
Arrival to first Code Grey, mins			
≤ 60	160 (66.9)	5.5 (3.7-8.2)	5.0 (3.3-7.7)
61-120	24 (10.0)	2.0 (1.1-3.5)	2.2 (1.2-4.0)
121-179	15 (6.3)	1.5 (0.8-2.9)	1.7 (0.9-3.4)
≥ 180	40 (16.7)	#	#

ATS=Australasian Triage Scale[29]
# Reference category

Table 3 Clinical characteristics of substance intoxication (n=229)

Clinical characteristics, n (%)	**Meth (n=85)**	**Opiates (n=16)**	**Cannabis (n=7)**	**Cocaine (n=6)**
Hallucinations	7 (8.2)	1 (6.3)	1 (14.3)	0 (0.0)
Delusions	27 (31.8)	2 (12.5)	2 (28.6)	0 (0.0)
Repetitive movements	21 (24.7)	5 (31.3)	2 (28.6)	3 (50.0)
Skin picking	6 (7.1)	2 (12.5)	0 (0.0)	0 (0.0)
Bruxism	10 (11.8)	0 (0.0)	0 (0.0)	0 (0.0)
Agitation	75 (88.2)	15 (93.8)	7 (100.0)	6 (100.0)
Others	28 (32.9)	5 (31.3)	1 (14.3)	0 (0.0)

**others clinical characteristics including suicidal, rapid speech, confusion, erratic behaviour, self-harm, diaphoretic, altered conscious state, flight of ideas, blurred vision, seizure, elevated mood, etc.*

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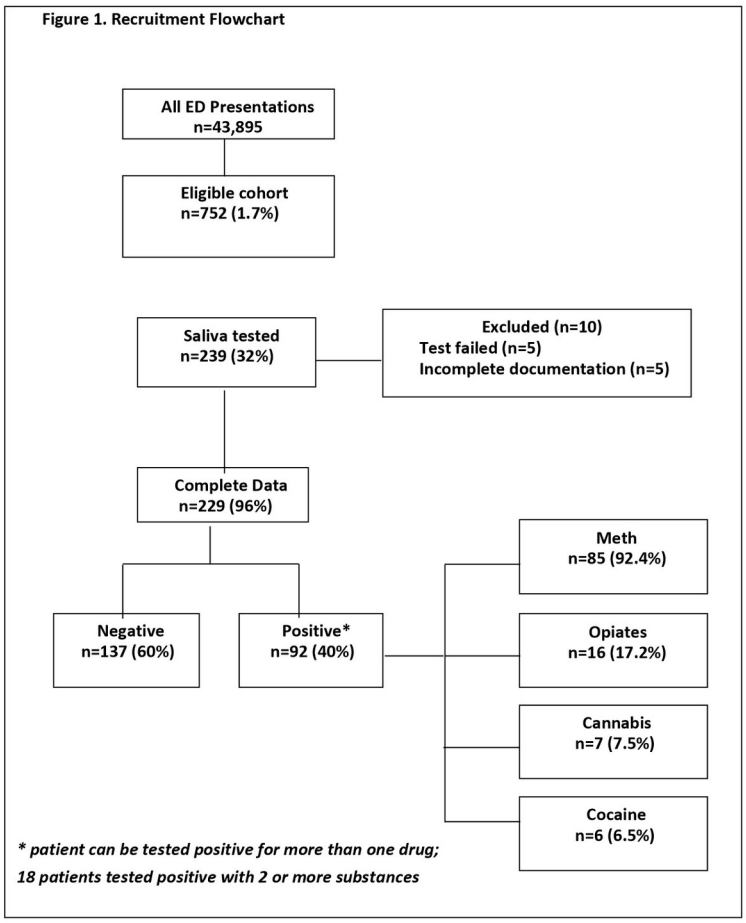
Figure 1 Recruitment Flowchart



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TITLE
Prevalence of Illicit Substance Use Among Patients Presenting to the Emergency Department with Acute Behavioural Disturbance: Rapid Point-of-Care Saliva Screening

RUNNING TITLE
Illicit Substance Use in Behavioural Disturbance

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