Research report on

Acute Toxicity of Commonly Abused Psychotropic Drugs in Hong Kong

Submitted to

Beat Drug Fund Association

Submitted by

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Executive Summary

The objective of this research was to document the acute toxicity symptoms of psychotropic substances. Between June 2008 and May 2011, 145 substance abusers were recruited into the research project. Sixty-three participants visited the Accident and Emergency Department between June 2001 and May 2011, with 115 attendances in total. Drug overdose was the most common provisional diagnosis, followed by substance abuse. Urine drug tests were conducted on 44.3% of the participants and the most commonly detected substances were ketamine, methamphetamine, promethazine and zopiclone. The mean age of onset for psychotropic substance misuse was 21.6 years with a duration of 9 years. Acute physical and psychiatric intoxication symptoms were observed in 62.6% and 36.5% of participants, respectively. Neurological features such as collapse and loss of consciousness (41.7%), and urinary symptoms such as dysuria (13.0%) were the most common physical symptoms. Suicidal ideation (12.2%) and auditory hallucinations (11.3%) were the most common psychiatric symptoms.

行政撮要

是次研究的目的是記錄危害精神毒品的急性毒性。本研究於二零零八年六月至二零一一年五月共招募到 145 位危害精神毒品濫用者，當中包括 63 位曾於二零零一年六月至二零一一年五月期間到急症室求診。63 位參與者共有 115 次求診記錄，當中以用毒過量爲主，其次爲濫用藥物。在 115 次求診人次中有百分之四十四的人次被要求進行尿液測試，氯胺酮〔俗稱 k 仔〕是最常在尿液測試中被驗出陽性反應的危害精神毒品，其次爲甲基安非他命〔 Methamphetamines 〕，止咳藥物〔 promethazine 〕和安眠藥〔 zopiclone 〕。首次吸食毒品的平均年齡爲 21.6 歲，年期 9 年。急性中毒的徵狀中，生理徵狀佔百分之六十二點六，精神徵狀佔百分之三十六點五。在生理徵狀當中，最常見的中毒徵狀出現在神經功能 (41.7%)上，如虛脫和失去知覺，而尿道炎 (13.0%) 亦相當普遍。在精神徵狀方面，自殺念頭 (12.2%) 和聲音幻覺 (11.3%) 亦是最經常出現的徵狀。

Introduction

Substance abuse is a social problem in Hong Kong. The pattern of substance abuse has changed over the past decade. The number of reported substance abusers fluctuated between 17,966 and 11,469 between 2002 and 2011, with the highest point in 2008 and the lowest in 2011 (Narcotics Division & Security Bureau, 2002–2011). The improving situation may be due to success in combatting the drug problem, prevention education, and the increasing awareness of its chronic harmful influence in the past few years. However, the trend is unpredictable. Ketamine and cough mixture abuse increased by approximately 50% and methamphetamine ("Ice") abuse doubled between 2002 and 2011. Abuse of zopiclone slightly diminished overall, although it has remained the third most abused psychotropic drug in Hong Kong over the past 5 years (Narcotics Division & Security Bureau, 2002–2011).

Existing evidence indicates that psychotropic drug abuse is associated with different types of psychiatric comorbidities (Mahoney et al., 2008; Morgan et al., 2010; Urban et al., 2011) and chronic harmful complications. Cystitis and chronic abdominal pain are common physical complications in long-term ketamine users (Chan 2012; Chu et al., 2008). Apart from physical complications, cognitive dysfunction is also associated with the chronic abuse of drugs such as ketamine (Fu et al., 2005; Morgan et al., 2009), ecstasy (den Hollander et al., 2012; Verbaten, 2010) and methamphetamine (Hosak et al., 2012; Morgan et al., 2012).

In contrast to these chronic effects, acute toxicity is a short-lasting aversive effect that arises from a single exposure or overdose of a substance. The effects vary from drug to drug and are tested in rats, for ethical reasons. The effects observed in rats or other animals may not be the same as in humans. Consequently, investigation of acute toxicity in humans is needed. According to the existing evidence, the acute toxicity effects of stimulants (ecstasy) are nausea and/or vomiting and chest pain (Goforth & Fernandez, 2012), whereas ketamine shows more neurologic and urinary symptoms, and MDMA presents with loss of appetite, insomnia and muscle tension (Kalant, 2001). Cannabis has an acute effect on the central nervous system that may induce, for example, visual and

auditory hallucinations (van der Linde et al., 1999). Although numerous studies have investigated the acute toxicity of specific substances, little is known about multi-psychotropic drug abuse. Thus, the objective of this study was to document the acute toxicity effects of multiple psychotropic drugs in substance abusers attending the Accident and Emergency Department (AED) between June 2001 and April 2011 in Hong Kong.

Study Objectives

(1) To document the acute toxicity symptoms of commonly abused psychotropic drugs in recreational substance abusers in Hong Kong between June 2001 and May 2011 in Hong Kong.

Study Methodology

Study Design

A retrospective chart review of a cohort of substance abusers from 1 June 2001 to 30 May 2011.

Recruitment of Participants

1. Participants were recruited from three substance abuse clinics run by the Hospital Authority, Hong Kong (Tuen Mun Substance Abuse Clinic (TMSAC), Prince of Wales Hospital Substance Abuse Clinic (PWHSAC) and North District Hospital Substance Abuse Clinic (NDHSAC)), and two counselling centres for psychotropic substance abusers (Hong Kong Lutheran Social Services – The Evergreen Lutheran Centre and Hong Kong Sheng Kung Hui Welfare Council Neo-Horizon).
2. Recruitment began in June 2008. Substance abusers were invited to participate in the study when they were admitted to the participating substance abuse clinics and counselling centres for psychotropic substance abusers.
3. The inclusion criteria were (a) presenting with a psychotropic substance-related problem (ketamine, MDMA, benzodiazepines/zopiclone, cannabis, cough medicine, methylamphetamine and cocaine); (b) presenting with a substance-related provisional diagnosis at an accident and emergency department (AED) between June 2001 and May 2011.

Data collection

AED record data, including provisional diagnosis, major toxic complications, and toxicological screening, were obtained from the Clinical Management System (CMS). Socio-demographic and clinical characteristics and drug use patterns were assessed when participants first attended the SACs or CCPSAs. Also, urine was collected at the first

assessment to detect the presence of specific substance use. In both of the toxicology screening and urine analysis, assays for opiates, methadone, ketamine, amphetamines and cocaine metabolite were carried out using homogenous enzyme immunoassay procedures and ultra-performance liquid chromatography (Kaufmann et al., 2007).

Statistical Analyses

The statistical analyses were performed using SPSS Version 17.0 (SPSS, Chicago, USA). Descriptive data are presented as means, medians or proportions as appropriate to categorise participants' demographic and clinical characteristics.

Results

General Characteristics

One hundred and forty-five recreational substance users were invited to participate. Only 63 of them had presented with a provisional substance-related diagnosis in the AED during the retrospective chart review period. The socio-demographic characteristics and referral patterns of the participants are depicted in Table 1. The mean age of the 63 participants was 28.7 $\pm$ 8.9 (range 16–59) and 60% were male. The average education level was 8.9 $\pm$ 2.7 years; 66.7% had never married; 61.9% were currently unemployed; and 55.6% had a criminal record. Of the 63 participants, 76.2% were referred by other HA facilities or by general practitioners, and 19.0% had been receiving social services from CCPSAs or other NGOs. The mean age of onset of substance abuse was 21.6 years and the average duration of substance misuse was 9.0 years. Lifetime drug treatment was found in 34.9% of participants and 26.9% had received a variety of drug treatments during the past two years, with a mean duration of 3.4 months [Table 1].

Table 1. Demographic characteristics of all participants, N=63

Variables	**mean $\pm$ s.d/n (%)**
Age (years)	28.7 $\pm$ 8.9
Age range (years)	
<21	12 (19.0)
21-30	27 (42.9)
31-40	19 (30.2)
41-50	3 (4.8)
>51	2 (3.2)
Sex (male)	38 (60.3)
Education (years)	8.9 $\pm$ 2.7
Marital status	
Never married	42 (66.7)
Married	13 (20.6)
Separated/Divorced	8 (12.7)
Occupation	

Variables	**mean ± s.d/n (%)**
Employed/Student	24 (38.1)
Unemployed	39 (61.9)
Criminal record (yes)	35 (55.6)
Source of referral	
HA facilities or general practitioners	48 (76.2)
Social services (CCPSA/other social services)	12 (19.0)
Others	2 (3.2)
Justice system	1(1.6)
Age of onset of substance misuse (years)	21.6 ± 6.8
Duration of substance misuse (years)	9.0 ± 8.0
Treatment history (lifetime)	29 (46.0)
Treatment type in the past 2 years	22 (34.9)
HA (IP/OP)	18 (28.6)
Residential detox facilities	1 (1.6)
Other	2 (3.2)
Methadone	1 (1.6)
Treatment duration in the past 2 years (months)	3.4 ± 7.0

CCPSA = Counselling centre for psychotropic substance abusers

HA = hospital authority

IP = inpatient

OP = outpatient

Drug Abuse Patterns

According to participants' self-reports, the most common lifetime abused drug was ketamine, followed by benzodiazepines and amphetamine/ice. The duration of ketamine use was 4.79 ± 3.19 years; 67.6% of ketamine users had used the drug in the past 30 days. The durations of other substance use ranged from 2.27 – 20.00 years [Table 2].

Table 2. Participants' patterns of alcohol/drug use, N=63

Type of drug	Lifetime use N (%)	Lifetime (years) mean ± s.d	Used in the past 30 days* N (%)	Past 30 days (days) mean ± s.d
Ketamine	37(58.7)	4.8 ± 3.2	25 (67.6)	14.4 ± 11.9
Benzodiazepines and non-benzodiazepine hypnotics	21(33.3)	6.6 ± 4.9	14 (66.7)	21.9 ± 12.8
Amphetamine/Ice	21(33.3)	2.3 ± 2.2	10 (47.6)	11.5 ± 12.2
Cough medicine	13(20.6)	6.9 ± 5.1	7 (53.8)	22.9 ± 12.2
Heroin	11(17.5)	8.52 ± 11.26	3 (27.3)	8.3 ± 2.9
Cocaine	10(15.9)	1.8 ± 2.0	3 (30.0)	3.0 ± 2.0
Cannabis	8(12.7)	4.2 ± 4.7	2 (25.0)	3.5 ± 2.1
Ecstasy	7(11.1)	3.5 ± 3.2	1 (14.3)	20.0
Other Opiates/ Analgesics/ Tramadol/Panadol	2(3.2)	12.5 ± 10.6	1 (50.0)	30.0
Methadone	1(1.6)	20.0	0	0
Barbiturates	1(1.6)	5.0	1 (100)	2.0

* Percentage refers to the proportion of lifetime users who had used the drug in the past 30 days.

According to the results of the urine analysis at the first assessment, the three most commonly used drugs in the previous month were ketamine (30.2%), cough medicine (23.8%) and opiates (17.5%). Fifteen point nine percent reported no drug use in the previous month. Barbiturates and MDMA were the least-abused drugs [Table 3].

Table 3. Participants' urine analysis at first assessment, N=61*

Type of drug	N (%)
Ketamine	19 (30.2)
Cough medicine	15 (23.8)
Opiates	11 (17.5)
Benzodiazepines	11 (17.5)
None	10 (15.9)
Amphetamines	8 (12.7)
Methadone	2 (3.2)
Cocaine	2 (3.2)
Analgesics	2 (3.2)
Barbiturates	2 (3.2)
MDMA	1 (1.6)

* Two participants had missing data

Acute Toxicity

One hundred and forty-five recreational substance abusers were invited to participate in the study. Of these, 63 had presented with substance-related problems in the AED between June 2001 and May 2011, with a total of 115 attendances; 44.3% were assigned to urinalysis. Ketamine, methamphetamine, promethazine and zopiclone were the most commonly abused drugs in the past 30 days for each AED attendance. Of the 115 attendances, 47.8% involved a diagnosis of drug overdose, 43.5% substance abuse, 5%) and 8.7% ketamine-associated problems. Of he observed complications, physical symptoms accounted for 62.6% and psychiatric symptoms for 36.5%. Of the physical complaints, neurological symptoms (41.7%) (e.g., collapse and loss of consciousness) were the most common, followed by urinary symptoms (13.0%) (e.g., dysuria), gastrointestinal symptoms (12.2%) and cardiovascular symptoms (5.2%). Suicidal ideation (12.2%) and auditory hallucinations (11.3%) were the most common complaints among the psychiatric cases [Table 4].

Table 4. Clinical characteristics of patients attending the AED (acute toxicity), N= 115

	N (%)
Number of drug-related attendances at AED	115 (100)
Provisional Diagnosis	
Drug overdose	55 (47.8)
Substance abuse	50 (43.5)
Ketamine-associated cystitis	5 (4.3)
Ketamine-associated abdominal pain	2 (1.7)
Ketamine-associated dysuria	2 (1.7)
Ketamine-associated lower urinary tract symptoms	1 (0.9)
Complaints/Symptoms	
Physical symptoms	72 (62.6)
Urinary symptoms	15 (13.0)
Dysuria	15 (13.0)
Lower urinary tract symptoms	1 (0.9)
Urinary symptoms	4 (3.5)
Gastrointestinal symptoms	14 (12.2)

Abdominal pain	13 (11.3)
Diarrhea	3 (2.6)
Vomiting	2 (1.7)
Cardiovascular symptoms	6 (5.2)
Shortness of breath	4 (3.5)
Chest pain	3 (2.6)
Neurological symptoms	48 (41.7)
Collapse	21 (18.3)
Loss of consciousness	9 (7.8)
Head injury	7 (6.1)
Confusion	6 (5.2)
Dizziness	5 (4.3)
Drowsiness	5 (4.3)
Headache	2 (1.7)
Others	8 (7.0)
Fever	8 (7.0)
Psychiatric symptoms	42 (36.5)
Suicidal ideation	14 (12.2)
Auditory hallucinations	13 (11.3)
Depressive mood	6 (5.2)
Suicidal intention	6 (5.2)
Dull	5 (4.3)
Emotional unstable	5 (4.3)
Paranoia	4 (3.5)
Violent behaviour	4 (3.5)
Abnormal behaviour	3 (2.6)
Aggressive behaviour	3 (2.6)
Delusions	2 (1.7)
Anxiety	1 (0.9)
Insomnia	1 (0.9)
Memory problems	1 (0.9)

Of those who attended the AED, only 44.3% were assigned and agreed to toxicological screening. Ketamine was detected in 20.9% and methamphetamine in 8.7% [Table 5].

Table 5. Toxicological screening, N=115

	N (%)
Assigned and agreed to urinalysis	51 (44.3)
Ketamine	24 (20.9)
Methamphetamine	10 (8.7)
Promethazine	8 (7.0)
Zopiclone	8 (7.0)
Ephedrine	6 (5.2)
Chlorpheniramine	5 (4.3)
Caffeine	4 (3.5)
Chlorpromazine	4 (3.5)
Dextromethorphan	4 (3.5)
Fluoxetine	4 (3.5)
Amitriptyline/nortriptyline	3 (2.6)
Amphetamine	3 (2.6)
Benzhexol	3 (2.6)
Benzodiazepine	3 (2.6)
Tramadol	3 (2.6)
Cocaine	2 (1.7)
Opiates	2 (1.7)
Propoxyphene	2 (1.7)
Atropine	1 (0.9)
Brompheniramine	1 (0.9)
Cetirizine	1 (0.9)
Cimetidine	1 (0.9)
Codeine	1 (0.9)
Ibuprofen	1 (0.9)
Lidocaine	1 (0.9)
Lorazepam	1 (0.9)
Methylephedrine	1 (0.9)
Phenaopyridine	1 (0.9)
Phenylpropanolamine	1 (0.9)
Sulpiride	1 (0.9)
Trazodone	1 (0.9)
Trifluoperazine	1 (0.9)
Venlafaxine	1 (0.9)
Zolpidem	1 (0.9)

Discussion

General Characteristics

The findings are in accordance with the CRDA, which reports that the most common age of first exposure to drugs is between 16 and 25 (Narcotics Division & Security Bureau, 2002-2011). The level of self-reported drug abuse is close to that of the overall trend for commonly abused drugs in Hong Kong (Tang et al., 2011). However, the self-reported pattern was slightly different from the urinalysis. Detection of the use of cough medicine was more frequent than the use of zopiclone and amphetamine/ice. The positive rates for cough medicine, benzodiazepines, and opiates were also much higher than for self-reported lifetime use. One explanation for this is that participants who abuse cough medicine, benzodiazepines and opiates might tend to deny the use of drugs.

Acute Toxicity

The urine screening by the AED suggests that the acute effects of drug overdose can be largely attributed to the administration of ketamine, methamphetamine, promethazine and zopiclone. The current finding appears to be generally consistent with those of previous studies (Chan 2012; Greene et al., 2008; Lan et al., 1998). Neurological, gastrointestinal and cardiovascular features are found in ketamine and methamphetamine acute intoxication (Chan 2012; Greene et al., 2008; Lan et al., 1998). Although ketamine abusers are usually found to have fewer psychiatric complications (Chan 2012), it was the second-most common complaint in the current study sample. This suggests that other psychotropic substances, such as benzodiazepines (zopiclone) might play a crucial part (Ruedy, 1973; Stein et al., 1993). However, the clinical profile of drug intoxication varies with dosage and the poly-drug repertoire; more dangerous toxic combinations may be present in acute cases.

The acute and chronic toxicity of psychotropic drugs may differ. Ketamine-associated cystitis, abdominal pain, dysuria and lower urinary tract symptoms are also likely to be due to chronic toxicity in participants (Chan 2012; Nomiya et al., 2011; Wood et al., 2011). Urinary complications, rather than neurological complications, are the most common symptoms in long-term ketamine use (Chan 2012). In addition, according to the existing evidence, neurological complications are not reported in chronic intoxication (Chan 2012).

Conclusion

In conclusion, neurological and psychiatric presentations were the most common intoxication symptoms in this sample, in which ketamine, methamphetamine, promethazine, and zipiclone were the most abused substances. The findings suggest that psychotropic substance use not only leads to chronic harmful effects, but also to acute intoxication.

Limitations

The study has four major limitations. First, the sample size was relatively small. Second, there was a selection bias in the study sample as participation was on a voluntary basis, thus the results may not be generalisable to the substance abuse population. Third, as only 44.3% were assigned for urinalysis, the abused substances of the other half of the sample are unknown. Further, the toxic complications could not be narrowed down to one specific psychotropic drug, because only 43.4% of the urinalyses detected positive for only one drug. Finally, although the current study documented acute toxicity in humans, the dosages of the substances that resulted in the adverse health effects remain unclear. Further studies of acute toxicity should obtain a larger sample size and conduct on-site research in the AED, with all attendees presenting with acute substance-related problems invited to participate.

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