ORIGINAL ARTICLE

Emergency department presentation of ketamine abusers in Hong Kong: a review of 233 cases

CME

SH Ng 伍時康
ML Tse 謝萬里
HW Ng 吳漢華
FL Lau 劉飛龍

Objectives To study the acute clinical presentations of ketamine abusers in Hong Kong.

Design Retrospective chart review.

Setting Fifteen accident and emergency departments in Hong Kong.

Patients Consultations associated with recent ketamine use either confirmed by history or urine test were searched for from the database of the Hospital Authority Hong Kong Poison Information Centre from 1 July 2005 to 30 June 2008. Their medical records and investigation results were analysed.

Results A total of 233 records of ketamine use were included for review. Patient ages ranged from 13 to 60, with a median of 22 years, and the male-to-female ratio being 2.1:1. The most common symptoms of ketamine misuse were impaired consciousness (45%), abdominal pain (21%), lower urinary tract symptoms (12%), and dizziness (12%). The most common abnormal physical findings were high blood pressure (40%), followed by tachycardia (39%), abdominal tenderness (18%), and white powder in the nostrils (17%).

Conclusion Most ketamine abusers presented acutely with transient central nervous system depression, abdominal pain, or lower urinary tract symptoms. Clinicians should be alert to the typical age-group, signs and symptoms of such abusers presenting in an acute medical setting.

Introduction

Ketamine hydrochloride, a structural analogue of phencyclidine, was a dissociative anaesthetic first introduced in the 1960s. It is a non-competitive N-methyl-D-aspartate (NMDA) receptor antagonist which interferes with the action of excitatory amino acids.[1] As an anaesthetic agent, ketamine can produce both anaesthetic and analgesic effects, and has a relatively stable cardiovascular profile. One of its adverse effects is psychological dissociation during emergence from anaesthesia, resulting in hallucinations and other phenomena, including out-of-the-body subjective experiences and states similar to the near-death experiences.[2,3] Its abuse potential was recognised soon after its introduction in anaesthesia.[4-6] Initially, it was more commonly abused by medical personnel[7] and later gained popularity as an agent in 'rave' parties and night clubs in different countries.[2,8-10]

In recent years, ketamine abuse has become more common among Hong Kong teenagers. Teenagers often used these drugs anywhere and everywhere; at home, in rave parties, in groups, or even in schools.[11] Moreover, they sometimes sniffed ketamine multiple times a day whenever they liked.[12] In Hong Kong, since 2005 it has become the commonest drug of abuse among persons aged 21 years or less; compared to the first three quarters of 2005, the number of ketamine abusers among teenagers has doubled in the first three quarters of 2008. In 2008 moreover, ketamine abuse constituted 85% of all kinds of drug abuse among persons aged below 21 years, compared to 61% in 2005.[13] The data collected by the Hospital Authority Hong Kong Poison Information Centre (HKPIC) also showed a marked increase in ketamine users. Ketamine abusers represented 16% of all drug abusers attending accident and emergency departments (AEDs) in the period of 1 July 2005 to 31 December 2005, and the proportion rose to 40% in the period of 1 January 2008 to 30 June 2008 (written communication, ML Tse, 2009).

There are recent reports of street ketamine–associated bladder dysfunction[14-25] as well as dilated common bile ducts and epigastric pain.[26,27] However, there were only a few reports describing the presenting symptoms and signs of ketamine abuse in acute medical

Key words
Adolescent; Adult; Ketamine; Substance-related disorders

Hong Kong Med J 2010;16:6-11

United Christian Hospital, Kwun Tong, Hong Kong:
Hong Kong Poison Information Centre
SH Ng, MB, BS, FHKAM (Emergency Medicine)
ML Tse, FRCS (Edin), FHKAM (Emergency Medicine)
FL Lau, FRCS (Edin), FHKAM (Emergency Medicine)
Accident and Emergency Department
HW Ng, MRCS(Ed), FHKAM (Emergency Medicine)

Correspondence to: Dr SH Ng
Email: szehong5@gmail.com

settings, which regrettably entailed small patient numbers and toxicological confirmation of exposure was often lacking. Previous reports showed that anxiety, palpitations, and chest pain were the most common presenting symptoms, whereas tachycardia, altered mental status, and slurred speech were the most common physical signs.[28,29] These features, however, are not consistent with observations in our locality. In order to assess the presentation of ketamine abusers attending acute medical care service in our locality, a retrospective study of these patients was therefore carried out.

Methods

This was a retrospective case note review of ketamine-related visits to the 15 AEDs in Hong Kong. The inclusion criteria were a history of ketamine use within 48 hours, or a urine test positive for ketamine.

The HKPIC maintains an electronic database for all telephone consultations from health care professionals largely from the 15 AEDs, as well as in the course of routine reporting of all poisoning cases from the six largest AEDs in Hong Kong. The database for the study period was searched using the key word "ketamine" as the poison name and urine toxicology fields. Respective AED case notes and any discharge summary, as well as any laboratory results, were retrieved. Patients were excluded if an alternative diagnosis could explain the clinical symptoms (eg surgical diagnosis for abdominal pain), presenting more than 48 hours after the last ketamine intake, not presenting to an AED, or urine toxicology analysis (if performed) revealing that no ketamine was present.

Patient demographic data including gender and age were included. Poisoning information—including duration of ketamine abuse, time, amount, and route of intake and any co-ingestion—was recorded. The presenting and associated symptoms, vital signs, any abnormal physical findings, electrocardiographic findings, blood test results (complete blood picture, renal and liver function test results, creatinine kinase level), patient outcomes and how they were followed up were also recorded. If available, confirmation of ketamine use by bedside urine immunoassay or toxicology tests was also recorded.

Results

During the study period, 282 records of ketamine-related visits were obtained. Forty-nine were excluded for various reasons (patient's urine not showing ketamine on toxicology analysis, alternative diagnosis, enquiries about ketamine not directly involving any patients). The remaining 233 patients had a median age of 22 (range, 13-60) years, and the male-to-female ratio was 2.1:1 (Fig). Most of these individuals took ketamine by insufflation for recreational purposes. It was used as a single agent by most patients, while the most commonly co-ingested agents were alcohol, methylenedioxy-N-methamphetamine (MDMA), methamphetamine, benzodiazepine, cocaine, and zopiclone (Table 1).

Impaired conscious level (45%), abdominal pain (21%), lower urinary tract symptoms (12%), and dizziness (12%) were by far the most common complaints (Table 2). High blood pressure (40%), followed by tachycardia (39%), abdominal tenderness (18%), white powder in the nostrils (17%), hyperthermia (14%) and decreased conscious level (13%) were the most common abnormal physical findings (Table 3).

Up to 46% of patients had a period of altered

到急症室求診的氯胺酮濫用者：回顧分析233個本地個案

目的 探討香港氯胺酮濫用者的急性臨床症狀。

設計 回顧性病歷分析。

安排 香港15間急症室部門。

患者 搜查醫院管理局香港中毒諮詢中心的資料庫內，於2005年7月1日至2008年6月30日期間，經病歷詢問或尿液測試證實曾服食氯胺酮而到急症室求診的病人，並分析病人的病歷紀錄及調查結果。

結果 研究個案共233個，病人年齡介乎13至60歲，中位數22歲；男女比例為2.1：1。氯胺酮濫用者的症狀普遍為神志不清（45%）、肚痛（21%）、出現下尿道症狀（12%）和暈眩（12%）。最普遍的異常體檢結果為高血壓（40%）、心跳過速（39%）、腹部壓痛（18%），以及鼻孔有白色粉末（17%）。

結論 大部分氯胺酮濫用者到急症室求診時出現短暫的中樞神經系統性抑制、肚痛和下尿道症狀。醫生應對到急症室求診的某一年齡組別的病人及其病徵提高警覺。

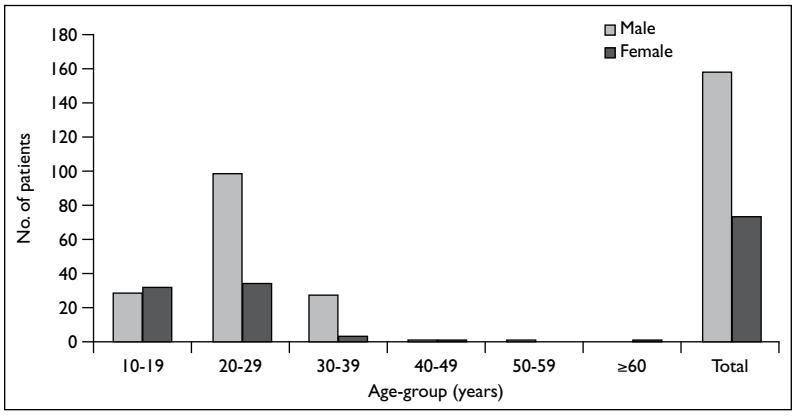

FIG. Sex and age distribution of patients

TABLE 1. Patient demographics and basic information about their ketamine use

Patient information	Data*
Demographics	
Male:female	159:74
Median age (range) [years]	22 (13-60)
Type of exposure	
Recreational	221 (95%)
Suicidal	8 (3%)
Non-accidental	1 (0.4%)
Others (eg suspected body stuffing†)	3 (1%)
Routes of ingestion	
Insufflation	204 (88%)
Oral	12 (5%)
Unknown	17 (7%)
Co-ingestion (according to history and/or urine toxicology)	
Alcohol	24 (10%)
MDMA‡	15 (6%)
Methamphetamine	14 (6%)
Benzodiazepine	10 (4%)
Cocaine	9 (4%)
Zopiclone	9 (4%)

* Data are shown as No. (%) of patients, unless otherwise stated
† Body stuffing refers to the ingestion of an illicit substance (usually poorly wrapped) in an expeditious manner, to conceal evidence from the authorities to avoid arrest or detection
‡ MDMA denotes methylenedioxy-N-methamphetamine

TABLE 2. Presenting symptoms

Specific symptoms in various systems	No. of patients
Neurological	
Impaired conscious level	106
Dizziness	28
Agitated/irritability	10
Hallucination/delusion	10
Muscle cramping	4
Seizure	2
Other neurological symptoms	7
Cardiovascular	
Chest pain/chest discomfort	13
Palpitations	12
Gastro-intestinal	
Abdominal pain	49
Nausea/vomiting	23
Urological	
Dysuria	20
Urgency/frequency	8
Other urological symptoms	4
Others	
Dyspnoea	17
Injury	7
Suspected body stuffing by police	2
Others	15
No active complaint	6

TABLE 3. Abnormal physical findings

Physical findings in various systems	No. of patients
Neurological	
GCS*≤8	3 (1%)
8<GCS≤14	31 (13%)
Cardiovascular	
Pulse <60 beats/min	7 (3%)
Pulse >100 beats/min	91 (39%)
Hypertension	93 (40%)
Gastro-intestinal	
Abdominal tenderness	41 (18%)
Others	
White powder in nostrils	40 (17%)
Hyperthermia	32 (14%)

* GCS denotes Glasgow Coma Scale score

consciousness some time after their ketamine use. This effect of ketamine was short-lived however; only 14% of the patients had Glasgow Coma Scale scores of less than 15 when examined in hospital.

Among patients who had blood tests performed, leukocytosis (in 36%) and raised creatinine kinase level (in 32%) were the most common abnormalities, whereas 16% had abnormal liver function test results and 3% had abnormal renal function test results (Table 4).

Regarding these 233 patients, 126 (54%) had toxicological confirmation of ketamine exposure, either by bedside urine immunoassay (11 cases) or formal urine toxicology analysis (115 cases) involving high-performance liquid chromatography. In 91 (72%) of these 126 patients, ketamine was found to be the only abused drug.

Initially, almost 20% of the patients did not provide a history of ketamine use. Their clinical presentation was appreciated to be due to ketamine only after their clinicians noted white powder in their nose (n=25) or urine analysis revealed ketamine (n=22).

In all, 35 (15%) of the patients had evaluation of their hepatobiliary or urological systems by ultrasound, computed tomography, or magnetic resonance imaging, some time after their presentation. Two patients were found to have dilated common bile ducts, whilst four had hydronephrosis.

The clinical course of these patients was rather

TABLE 4. Blood test results*

Test	Normal	Abnormal	Abnormality
Complete blood picture (n=174)	111 (64%)	63 (36%)	Leukocytosis (56 patients, 10.3-24.4 x 10^9/L; rr, 4.0-10.0 x 10^9/L) Thrombocytosis (9 patients, 385-634 x 10^9/L; rr, 152-358 x 10^9/L) Anaemia (4 patients, 42-109 g/L; rr, 116-155 g/L) Thrombocytopenia (1 patient, 104 x 10^9/L)
Renal function test (n=180)	175 (97%)	5 (3%)	Cr, 103-220 μmol/L (rr, 53-97 μmol/L)
Liver function test (n=178)	149 (84%)	29 (16%)	ALP (20, 100-508 IU/L; rr, 35-98 IU/L) ALT (16, 52-180 IU/L; reference level, <41 IU/L)
Creatinine kinase level (n=63)	43 (68%)	20 (32%)	225-13120 IU/L (rr, 38-174 IU/L)

* rr denotes reference range, Cr creatinine, ALP alkaline phosphatases, and ALT alanine aminotransferase

benign, in that none developed a major complication (eg myocardial infarction) after acute ketamine exposure. Most of these patients (197/233, 85%) developed no or only minor complaints; the majority (168/233, 72%) were safely managed in the AEDs with supportive measures, including intravenous fluid and benzodiazepines for agitation. The five patients managed in intensive care units had all co-ingested other drugs that could have contributed to their clinical status (Table 5[30]).

TABLE 5. Summary of patients who received intensive care unit care*

Sex/age (years)	Co-ingestion	Clinical features
F/19	Amitriptyline	GCS 10/15. Admitted to ICU for observation
M/24	MDMA	Suicidal ingestion of 40 tablets of ecstasy and ketamine. Frank sympathomimetic features required intubation and cooling
M/28	MDMA	Took 10 cans of beer with ketamine but ethanol level not detectable. GCS 7/15 on arrival. Intubated for airway protection. Urine toxicology showed ketamine and MDMA
M/30	Heroin	Collapsed with respiratory depression and GCS 7/15. Intubated for airway protection
F/23	Cocaine	Severe asthmatic attack after cocaine and ketamine. Admitted to ICU for treatment. Cocaine has previously been reported to cause bronchospasm[30]

* GCS denotes Glasgow Coma Scale score, ICU intensive care unit, and MDMA methylenedioxy-N-methamphetamine

Discussion

Our study provides the largest series of ketamine users presenting to an acute medical setting. The relatively low co-ingestion rate and high percentage of confirmed exposure makes these findings especially relevant to ketamine users in comparison to other studies.

Most ketamine abusers in our series were young (84% being 13-29 years old), male, and presented with impaired consciousness, abdominal pain, or dizziness. Co-abuse with other substances was uncommon; 72% whose urine was analysed showed that only ketamine was present.

In our series of ketamine users, abdominal pain and abnormal liver function test results were commonly encountered. Up to 21% had abdominal pain as one of their symptoms, and 16% had abnormal liver function test results. These findings are in agreement with previous reports in ketamine abusers[15] and recent observations that such patients may have dilated biliary tracts.[21,26,27] This symptom complex has not been described in the past, and we would therefore propose coining the term "ketamine-associated abdominal pain". The aetiology of this phenomenon is unknown and possibly multi-factorial, but may sometimes be related to injury to the hepato-biliary system. It has even been postulated that such biliary tree dilatation could be related to sphincter of Oddi dysfunction, but the exact pathophysiology remains unknown.[31]

Apart from gastro-intestinal symptoms, urological complaints (dysuria, urinary urgency or frequency) were present in 12% of our patients. Five of them had abnormal renal function test results (serum creatinine ranging from 103 to 220 μmol/L), and four had hydronephrosis revealed by ultrasonography or computed tomography. Since 2007, multiple case reports have described more than 40 patients with ketamine abuse–associated hydronephrosis.[14-25]

Cardiovascular symptoms were also reported in our series; 11% had chest discomfort and palpitations, 39% had tachycardia, and 40% had a high blood pressure on presentation to the AEDs. However, none of them had serious cardiovascular complications (myocardial infarction or significant arrhythmias).

Most of the patients were managed in the AEDs (72%) and 85% had no or only minor complaints. In our patients there were no deaths, which is in agreement with multiple case series in which few deaths were caused by intoxication exclusively due to ketamine.[32,33]

For patients reaching hospitals, supportive treatment was needed. Profoundly obtunded patients may require airway support, intravenous fluids, and titrated benzodiazepine therapy if they are agitated,

hyperthermic, or show overt sympathomimetic signs. Complications (such as injuries and rhabdomyolysis) warrant appropriate therapy to ensure satisfactory clinical outcomes.

Limitations

Ours was a retrospective study that included patients presenting to multiple institutions, and complaints related to multiple disciplines, for whom there was no consistent investigation or management protocol. Thus, information on the duration of ketamine use and detailed physical examination findings (eg presence of mydriasis or nystagmus) were not always available.

Being a retrospective study and data collection dependent on voluntary reporting, the breakdown of presenting symptoms and signs may not reflect the true picture. While the possibility of missing the diagnosis of ketamine abuse in young persons with impaired consciousness was low, patients presenting with abdominal pain and lower urinary tract symptoms might not be readily recognised and reported, especially if such diagnoses are not entertained early on by doctors working in the AEDs.

The patients presenting with the most severe bodily disruptions (multiple trauma victims in road traffic accident or head injury) may be missed, because in-charge physicians may not be able to obtain a history of or suspect ketamine abuse. There is a possibility that patients with incidental complaints (epistaxis or minor injuries) associated with ketamine use may also remain undetected.

Some of these patient's symptoms, signs, and laboratory abnormalities may have been contributed by co-ingestants. Although 54% of our patients had confirmed ketamine exposure according to urine tests, there may have been false-positive results, particularly with bedside urine immunoassay. High-performance liquid chromatography (used in most of our cases) is a more accurate method than bedside immunoassay for confirming ketamine exposure.

Conclusion

Although our study may have missed some patients with acute presentations associated with ketamine abuse, it is the largest cohort ever published. The typical ketamine abuser was young and presented with impaired consciousness, abdominal pain, lower urinary tract symptoms, or dizziness, together with unexplained high blood pressure or tachycardia. Patients in at-risk age-groups presenting with these complaints could well be ketamine users. The presence of white powder in nostrils is another important tell-tale sign. Notably, many patients denied a ketamine abuse, but confessed only after the clinicians found white powder (ketamine) in their nostrils.

Acknowledgements

The authors would like to thank Ms Bonnie Leung, Ms Jen Ng, and Mr MH Wong for clerical and technical support in the collection and organisation of data.

References

1. Corssen Co-G. Clinical use of CI-581. Acta anaesthesiologica Scandinavica Supplementum 1966;25:416-8.
2. Jansen KL. Non-medical use of ketamine. BMJ 1993;306:601-2.
3. Fine J, Finestone SC. Sensory disturbances following ketamine anesthesia: recurrent hallucinations. Anesth Analg 1973;52:428-30.
4. Reier CE. Ketamine—"dissociative agent" or hallucinogen? N Engl J Med 1971;284:791-2.
5. Collier BB. Ketamine and the conscious mind. Anaesthesia 1972;27:120-34.
6. Ketamine abuse. FDA Drug Bull 1979;9:24.
7. Ahmed SN, Petchkovsky L. Abuse of ketamine. Br J Psychiatry 1980;137:303.
8. Dotson JW, Ackerman DL, West LJ. Ketamine abuse. J Drug Issues 1995;25:751-7.
9. Awuonda M. Swedes alarmed at ketamine misuse. Lancet 1996;348:122.
10. Lua AC, Lin HR, Tseng YT, Hu AR, Yeh PC. Profiles of urine samples from participants at rave party in Taiwan: prevalence of ketamine and MDMA abuse. Forensic Sci Int 2003;136:47-51.
11. Drug checks urged for schoolkids. The Standard 2007 Jul 4. Available from: http://www.thestandard.com.hk/news_detail.asp?pp_cat=11&art_id=48260&sid=14337067&con_type=1&d_str=20070704&sear_year=2007. Accessed 22 Aug 2009.
12. Muetzelfeldt L, Kamboj SK, Rees H, Taylor J, Morgan CJ, Curran HV. Journey through the K-hole: phenomenological aspects of ketamine use. Drug Alcohol Depend 2008;95:219-29.
13. Central Registry of Drug Abuse, Narcotics Division, Security Bureau, HKSAR Government. Available from: http://www.nd.gov.hk/statistics_list/doc/en/t3.pdf. Accessed 22 Aug 2009.
14. Shahani R, Streutker C, Dickson B, Stewart RJ. Ketamine-associated ulcerative cystitis: a new clinical entity. Urology 2007;69:810-2.
15. Chu PS, Kwok SC, Lam KM, et al. 'Street ketamine'–associated bladder dysfunction: a report of ten cases. Hong Kong Med J 2007;13:311-3.
16. Cottrell AM, Ayres R, Weinstock P, Warren K, Gillatt D. Urinary tract disease associated with chronic ketamine use. BMJ 2008;336:973.
17. Chu PS, Ma WK, Wong SC, et al. The destruction of the lower urinary tract by ketamine abuse: a new syndrome? BJU Int 2008;102:1616-22.
18. Cottrell A, Warren K, Ayres R, Weinstock P, Kumar V, Gillatt D. The destruction of the lower urinary tract by ketamine

abuse: a new syndrome? BJU Int 2008;102:1178-9; author reply 1179.
19. Dhillon BS, Nuttall MC, Coull N, O'Brien TS. Minerva. BMJ 2008;336:898.
20. Colebunders B, Van Erps P. Cystitis due to the use of ketamine as a recreational drug: a case report. J Med Case Reports 2008;2:219.
21. Selby NM, Anderson J, Bungay P, Chesterton LJ, Kolhe NV. Obstructive nephropathy and kidney injury associated with ketamine abuse. NDT Plus 2008;1:310-2.
22. Chen KT, Foo NP, Lin HJ. Frequent visits with urinary symptoms: subtle signs of ketamine abuse. Am J Emerg Med 2008;26:1061-2.
23. Tsai JH, Tsai KB, Jang MY. Ulcerative cystitis associated with ketamine. Am J Addict 2008;17:453.
24. Huang Y, Jeng C, Cheng T. Ketamine-associated ulcerative cystitis. Tzu Chi Med J 2008;20:144-6.
25. Grégoire MC, MacLellan DL, Finley GA. A pediatric case of ketamine-associated cystitis (Letter-to-the-Editor RE: Shahani R, Streutker C, Dickson B, et al: Ketamine-associated ulcerative cystitis: a new clinical entity. Urology 69: 810-812, 2007). Urology 2008;71:1232-3.
26. Wong SW, Lee KF, Wong J, Ng WW, Cheung YS, Lai PB. Dilated common bile ducts mimicking choledochal cysts in ketamine abusers. Hong Kong Med J 2009;15:53-6.
27. Ng SH, Lee HK, Chan YC, Lau FL. Dilated common bile ducts in ketamine abusers. Hong Kong Med J 2009;15:157; author reply 157.
28. Weiner AL, Vieira L, McKay CA, Bayer MJ. Ketamine abusers presenting to the emergency department: a case series. J Emerg Med 2000;18:447-51.
29. Dalgarno PJ, Shewan D. Illicit use of ketamine in Scotland. J Psychoactive Drugs 1996;28:191-9.
30. Wilson KC, Saukkonen JJ. Acute respiratory failure from abused substances. J Intensive Care Med 2004;19:183-93.
31. Thune A, Jivegård L, Polland P, Moreau J, Schwartz JC, Svanvik J. Location of enkephalinase and functional effects of [Leu5]enkephalin and inhibition of enkephalinase in the feline main pancreatic and bile duct sphincters. Clin Sci (Lond) 1992;82:169-73.
32. Gill JR, Stajic M. Ketamine in non-hospital and hospital deaths in New York City. J Forensic Sci 2000;45:655-8.
33. Schifano F, Corkery J, Oyefeso A, Tonia T, Ghodse AH. Trapped in the "K-hole": overview of deaths associated with ketamine misuse in the UK (1993-2006). J Clin Psychopharmacol 2008;28:114-6.