

Division of Urology, Department of Surgery,
Princess Margaret Hospital & Tuen Mun Hospital

Clinical Research
Final Report

Research on Urological Sequelae of Ketamine Abuse

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Research grant:
Beat Drugs Fund Association

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Fig. 1a Photo of Tuen Mun Hospital clinical staff team



Fig 1b Photo of Princess Margaret Hospital clinical staff team

BACKGROUND

Since previous reporting in the Hong Kong Medical Journal¹ and British Journal of Urology International² by our group, “street ketamine”-associated bladder dysfunction is an emerging clinical problem that has gained much medical and mass media attention. Street ketamine abuse by inhaling ketamine powder is an important social problem of Hong Kong. In the first half of 2007, street ketamine accounts for 79.9% of abused drug among young abusers aged under 21 years, when compared to 73% in 2006. Patients with ketamine abuse presented with severe lower urinary tract symptoms of dysuria, frequency, urgency, urge incontinence, and painful hematuria. The functional bladder capacities decreased to 30 – 100ml only. There is documented detrusor overactivity in some of the patients and bladder mucosal biopsy yielded cystitis changes in the epithelium. In severe cases, there has been bilateral vesico-ureteric reflux, ureteric stricture causing renal function impairment. Its underlying pathophysiology and appropriate treatment regime is undetermined. Temporary symptomatic relief has been achieved with anticholinergic and treatment of superimposed urinary tract infection but the clinical outcome is sub-optimal.

There is no standard protocol now in Hospital Authority for management of ketamine abuser. Actually we receive the majority of patient load of Hong Kong, when compared to other public hospitals, since many ketamine abusers are from the lower social-economic class in Kowloon West and New Territories West. This group of patients reflects very well the high incidence of ketamine abuse in Hong Kong. There are also referrals from other territories of Hong Kong, the private practitioners and non-government organizations, and they account for one quarter of our patients. Longer follow-up is also essential to understand better the clinical course of this new disease entity and reveal other possible complications. With the aid of research grant obtained from the Beat Drugs Fund Association, the Security Bureau of the Hong Kong Government, we could establish a dedicated research team and clinical sessions for the investigations and procedures on these ketamine abusers. The objective of the current research is to assess the severity of urological symptoms associated with ketamine, and to evaluate the complications associated with ketamine abuse, including diminished bladder capacity, hydronephrosis, ureteric stricture, renal impairment and renal failure.

There are several questions in mind we would like to be addressed in the current research. We have to ascertain there is presence of ketamine/ ketamine metabolites in urinary tract of abusers, and no other impurity in 'street ketamine' that is known to cause similar clinical picture; symptoms of our patient are not caused by other concomitant disease like urinary tract infection. We would also investigate whether there is positive proportional relationship between ketamine dose and severity of disease; and whether the urological symptoms and complications will improve after cessation of ketamine.

RESEARCH OBJECTIVE AND PURPOSE

The objective of the current research is to assess the severity of urological symptoms in ketamine abusers, and to evaluate the subsequent health hazards associated with ketamine abuse, including diminished bladder capacity, hydronephrosis, ureteric stricture, renal impairment and renal failure. We postulate that the presence of ketamine/ ketamine metabolites in urine may be the underlying etiology for the urinary tract problems induced by ketamine.

The Beat Drugs Fund Association, the Security Bureau, Hong Kong Government has approved a research grant of \$ 1,330,000 HKD for the research project on 15th July 2008. The fund was used for establishment of two "Special Ketamine clinics" in Princess Margaret Hospital (PMH) and Tuen Mun Hospital (TMH), creation of a patient registry, hiring of a research assistant for data analysis, and publication of education pamphlets in order to promote drug quitting.

Targets and expected number of participants:

1) Patient group:

- street ketamine abuser with urinary problem
- exclusion criteria: patient with underlying psychiatric disease, other illicit drug abuser
- Targeted number of attendance: 100-110 patients
- Estimated number of patients included in research: 30-50 patients/ year, due to high default rate

2) Education group:

- general public, especially young people who are prone to drug abuse
- Estimated number of pamphlets: 10,000
- Pamphlets will be delivered in out-patient clinic, secondary schools in the local community

RESEARCH DESIGN

Research approval was obtained from the New Territories West Clinical Research Ethics Committee (NTW-CREC) and Kowloon West Cluster Clinical Research Ethics Committee (KWC-CREC) on 31st December 2008 and 16th December 2008 respectively. A Special Ketamine clinic with a team of dedicated medical doctors and nurses was established in the two hospitals to see ketamine abusers presenting with urinary tract symptoms on alternate Saturdays starting from January 2009 (Appendix 1a). Before consultation, they signed a written consent to the study (Appendix 1b), understanding that all the clinical information and personal details gathered were for research purpose solely and would be handled confidentially.

Clinical data obtained for each patient entering the study:

1. Medical history, voiding diary, and duration of ketamine use:
Templates for medical records were developed for objective and retrievable data entry (Appendix 1c-d)
2. Symptom severity quantification:
Pelvic pain and urgency/ frequency (PUF) symptom scale. This questionnaire, by C. Lowell Parsons, was developed in 2000 as a non-invasive diagnostic tool to quantify symptoms in patients with chronic pelvic pain or interstitial cystitis³, in which the presenting symptoms are similar in much to patients with "street-ketamine" associated cystitis. The Chinese version of PUF symptom scale was used for evaluation of symptoms and the degree of bother in these patients. The symptom scale consisted of two scores: symptom and bother scores. The symptom score comprised seven short questions on the issues of frequency, nocturia, urgency and its degree, bladder pain and its degree, and pain or symptoms during sex. The bother score comprised four questions on the degree of bother by nocturia, urgency, bladder pain and avoidance of sex because of pain or symptoms. The maximum total score was 35 (symptom score 23 + bother score 12). Adopting the PUF symptom scale in assessing ketamine abusers with urinary symptoms was first described by our group².
3. Urine tests:
Urine toxicology for testing of illicit drugs, presence of other illicit drug

abuse was documented

Urine culture to exclude urinary tract infection

Urine cytology to exclude malignancy

4. Blood tests:

Complete blood count (CBC), renal and liver function tests (R/LFT), calcium and phosphate levels (Ca,PO₄), erythrocyte sedimentation rate (ESR), c-reactive protein (CRP)

5. Radiological Investigations:

Bedside ultrasonography of the kidneys was performed to detect any hydronephrosis or abnormal renal lesions

Computed tomography of the urinary system or intravenous urography was arranged and performed if bedside ultrasound showed suspicious abnormalities

6. Urodynamic study:

Video cystometrogram (VCMG) was performed to evaluate the cystometric bladder capacity and to detect the presence of any detrusor instability, decreased bladder compliance or vesicoureteric reflux under fluoroscopic guidance

7. Endoscopic Investigation:

Flexible cystoscopy was performed for bladder mucosa evaluation, to document any cystitis changes, erythema or granulations.

Bladder biopsies were taken from suspicious sites for pathological examination



Fig. 2 a & b: A young ketamine abuse lady undergoing ultrasound of the kidneys during the clinic in TMH



Fig. 3 a-d Special ketamine clinic setting in PMH: consultation and counselling (a), ultrasound examination (b), urodynamic study (c) and flexible cystoscopy (d)

DATA PROCESSING

I. Building of a local patient registry:

A patient registry was developed with the assistance of information technology personnel in March 2009 and was installed into the two research project computer systems for prospective data input, enquiry and retrieval throughout the research period. This patient registry was coding-protected and restricted to use by authorized health-care personnel and research assistants only. It has formed the importance basis of information on the progress of every patient recruited in the study. Statistical work was then performed based on the data retrieved from the registry and for further analysis.



Fig. 4a Log-in window of the patient registry

Application Record System

Browse the Record File

| Case No. | HK ID Card No. | GENDER | AGE | DATE AT DIAGNOSIS | YEAR OF ABUSE | FREQ OF ABUSE | MONTH OF ABSTINENCE | ONSET(MTH) | FREQ | URGENCY | DYSURIA | NOCTURIA | HAEMATURIA |
|----------|----------------|----------|-----|-------------------|---------------|---------------|---------------------|------------|------|---------|---------|----------|------------|
| F | 24 | 21/02/09 | 5 | Daily | 0 | 18 | 0 | Yes | Yes | 4 | No | Yes | |
| F | 21 | 21/02/09 | 2 | Weekly | 0 | 12 | 1 | Yes | Yes | 4 | Yes | Yes | |
| F | 28 | 21/02/09 | 9 | Every few days | 0 | 24 | 1 | Yes | Yes | 2 | Yes | No | |
| M | 37 | 21/03/09 | 6 | Daily | 0 | 48 | 1 | Yes | Yes | 6 | Yes | Yes | |
| F | 25 | 18/04/09 | 3 | Daily | 0 | 12 | 0 | Yes | Yes | 4 | Yes | Yes | |
| M | 23 | 18/04/09 | 7 | Weekly | 12 | 24 | 1 | Yes | No | 1 | Yes | No | |
| F | 29 | 25/04/09 | 2 | Every few days | 1 | 12 | 1 | Yes | Yes | 3 | Yes | Yes | |
| F | 30 | 23/05/09 | 1 | NA | 24 | 12 | 0 | Yes | Yes | 2 | Yes | No | |
| M | 22 | 23/05/09 | 4 | Biweekly | 0 | 4 | 2 | Yes | Yes | 1 | Yes | No | |
| M | 25 | 23/05/09 | 3 | Every few days | 0 | 6 | 2 | Yes | Yes | 3 | Yes | No | |
| F | 22 | 30/05/09 | 3 | Daily | 3 | 34 | 0 | Yes | Yes | 8 | Yes | No | |
| M | 34 | 30/05/09 | 5 | Every few days | 18 | 36 | 1 | Yes | No | 7 | Yes | No | |
| M | 30 | 30/05/09 | 10 | Daily | 0 | 24 | 1 | Yes | Yes | 4 | Yes | Yes | |
| F | 23 | 30/05/09 | 3 | Every few days | 4 | 9 | 0 | Yes | Yes | 2 | Yes | No | |
| F | 18 | 13/06/09 | 3 | Every few days | 2 | 3 | 0 | Yes | Yes | 1 | Yes | Yes | |
| M | 39 | 13/06/09 | 1 | Every few days | 36 | 0 | 2 | No | Yes | 1 | Yes | No | |
| F | 34 | 13/06/09 | 5 | Every few days | 0 | 24 | 1 | Yes | Yes | 1 | Yes | Yes | |
| F | 23 | 20/06/09 | 5 | Daily | 0 | 24 | 0 | Yes | Yes | 10 | Yes | Yes | |
| M | 32 | 20/06/09 | 6 | NA | 0 | 12 | 2 | Yes | No | 4 | Yes | Yes | |
| M | 28 | 4/07/09 | 11 | NA | 3 | 6 | 1 | No | No | 0 | Yes | No | |
| F | 25 | 4/07/09 | 10 | Daily | 0 | 24 | 1 | Yes | Yes | 6 | Yes | Yes | |
| F | 27 | 4/07/09 | 5 | Daily | 4 | 12 | 1 | Yes | Yes | 3 | Yes | Yes | |
| M | 29 | 4/07/09 | 8 | Daily | 0 | 6 | 1 | Yes | Yes | 1 | Yes | No | |
| M | 23 | 11/07/09 | 4 | Daily | 0 | 8 | 0 | Yes | Yes | 2 | Yes | Yes | |
| M | 29 | 11/07/09 | 8 | Daily | 0 | 24 | 0 | Yes | Yes | 4 | Yes | Yes | |
| M | 24 | 19/09/09 | 7 | Daily | 0 | 12 | 1 | No | No | 3 | Yes | Yes | |
| M | 49 | 19/09/09 | 10 | NA | 0 | 48 | 0 | No | No | 2 | Yes | No | |
| M | 22 | 17/10/09 | 1 | NA | 36 | 84 | 3 | Yes | Yes | 1 | Yes | No | |
| F | 29 | 17/10/09 | 7 | Weekly | 0 | 24 | 1 | Yes | No | 3 | Yes | No | |
| F | 24 | 17/10/09 | 3 | Every few days | 0 | 12 | 0 | Yes | Yes | 5 | Yes | Yes | |
| F | 24 | 17/10/09 | 7 | Daily | 0 | 24 | 0 | Yes | Yes | 4 | Yes | Yes | |
| F | 28 | 31/10/09 | 3 | Every few days | 0 | 24 | 0 | Yes | Yes | 10 | Yes | Yes | |

View + Insert Change Delete Close Import From Xls Export to Xls

Record 12:47AM

Fig. 4b Patient registry overview panel

Record wordt gewijzigd

Internal Case NO: 02 Hospital: PMH TMH

Date at diagnosis: 21/02/09 ddm or ddmmyy

Name: HKID: Gender: Male Female

Date of Birth: Age: 21 (ddmmyy e.g. 310866)

Age at diagnosis: 20

YEAR OF ABUSE: 200

Frequency of Keatmine Abuse: Daily Biweekly Every few days Weekly Not Applicable

Period of abstinence: No Yes 0.00 (months) (Period)

Onset of urinary symptoms: 12 (months)

FREQUENCY: Once every 1 hours

URGENCY: Yes No DYSURIA: Yes No

NOCTURIA: 4 times HAEMATURIA: Yes No

PUF score: Symptom score 9 + Bother score 7 = 16

| FU Date | PUF SYMPTOM SCORE | PUF BOTHERSOME SCORE |
|----------|-------------------|----------------------|
| 21/02/09 | 9 | 7 |

Change

Blood results: CREATININE: 88 ALP: 62 ALT: 17 Bilirubin: 8 ESR: 0 CRP: 0

MSU: Positive Negative Not Available CYTOLOGY: Positive Negative Not Applicable

Urine Microscopy: WBC: + ++ +++ +++++ negative RBC: + ++ +++ +++++ negative

Urinetoxiology +ve/-ve for ketamine: Positive Negative Not Available other(s)

Bedside USG: NAD Rt.hydronephrosis Lt.hydronephrosis Bilhydronephrosis

VUD: date Urodynamic Finding: NAD detrusorinstability Rt. VUR Lt. VUR Poor compliance other defaulted

Cystometric bladder capacity: 0 ml VUD Reflux: R L Bil None

Radiological Exam Finding:

IvU Date: NAD Thickened bladderwall hydronephrosis Rt.hydronephrosis Lt.hydronephrosis Papillarynecrosis other

USG Date: NAD Thickened bladderwall hydronephrosis Rt.hydronephrosis Lt.hydronephrosis Papillarynecrosis other

CT Date: NAD Thickened bladderwall hydronephrosis Rt.hydronephrosis Lt.hydronephrosis Papillarynecrosis other

CYSTOSCOPY DATE: Finding: Cystitis other

BIOPSY: Inflamm other

MANAGEMENT: Antich Cystiste Augme

PU PUF score 9

Fig. 4c Individual patient profile

II. Statistics on Princess Margaret Hospital and Tuen Mun Hospital

Ila. Statistics on Princess Margaret Hospital section

First Special Ketamine clinic: 21 February 2009

Altogether 22 Special Ketamine clinic sessions involving endoscopic and urodynamic studies on recruited patients has been conducted in PMH until 10 April 2010. An extra clinic session of follow-up of a group of patients was held on 15 May 2010.

No. of patients managed under the project in PMH: 54

No. of consultants/ senior medical officers involved: 2

No. of medical officers involved: 2

No. of registered/enrolled nurses involved: 7

No. of research assistant involved: 1

Ilb. Statistics on Tuen Mun Hospital section

First Special Ketamine clinic: 24 January 2009

Altogether 30 Special Ketamine clinic sessions involving sonographic endoscopic and urodynamic studies on recruited patients has been conducted till 2 January 2010.

No. of patients managed under the project in TMH: 57

No. of consultants/ senior medical officers involved: 4

No. of medical officers involved: 7

No. of registered/enrolled nurses involved: 5

No. of research assistant involved: 2

III. Audit of clinical data

Data audited:

- patient demographic details
- duration of ketamine abuse
- symptomatology
- investigation results
- response to treatment
- abstinence period from ketamine

These data were reviewed in details after conduction of all Special Ketamine clinic sessions and filing of data into the patient registry. Our research assistant helped to perform relevant statistical analysis with the aid of statistic

program (SPSS®) installed in the computer system. Discussion of results among researchers was conducted and evaluation of the program was completed.

IV. Statistical tests used for the research

The statistical program used for the research was SPSS®. Paired samples T-test was used to find out the correlation between PUF scores and various continuous variables, while Pearson's correlation test and Spearman's Phi test was used to compare with non-numerical variables. A p-value of < 0.05 was taken to be statistically significant result.

RESULTS

I. Total number of patients enrolled and default rates

From the period of January 2009 to May 2010, a total of 111 ketamine abusers attended the Special Ketamine clinic (PMH: 54, TMH: 57). Altogether 52 Special Ketamine clinic sessions was completed. 7 patients have to be excluded from data analysis after reviewing the records: 3 experienced urinary symptoms before abusing ketamine, 2 was referred from social worker for check-up without any urinary symptoms, 2 had problems with the consent and refused further investigations after interview, and 1 had active psychiatric illness render him mentally not fit for interview. Therefore, 104 patients had completed the first clinic visits with clinical data available for analysis.

Many patients had only one clinic visit and defaulted subsequent follow-up visits. Phone-contacts were made to those defaulted follow-up but only a small number of patients returned for follow-up. Ultimately 46 patients had only one clinic visits (default follow-up rate = 41.4%). Among the 65 patients with more than one clinic visit, 39 (60.0%) admitted that they were still abusing ketamine at the time of follow-up, 19 (29.2%) had quitted ketamine while 7 (10.8%) had altering abuse status during subsequent follow-up visits. The mean duration of follow-up was 7.2 months (3-17 months).

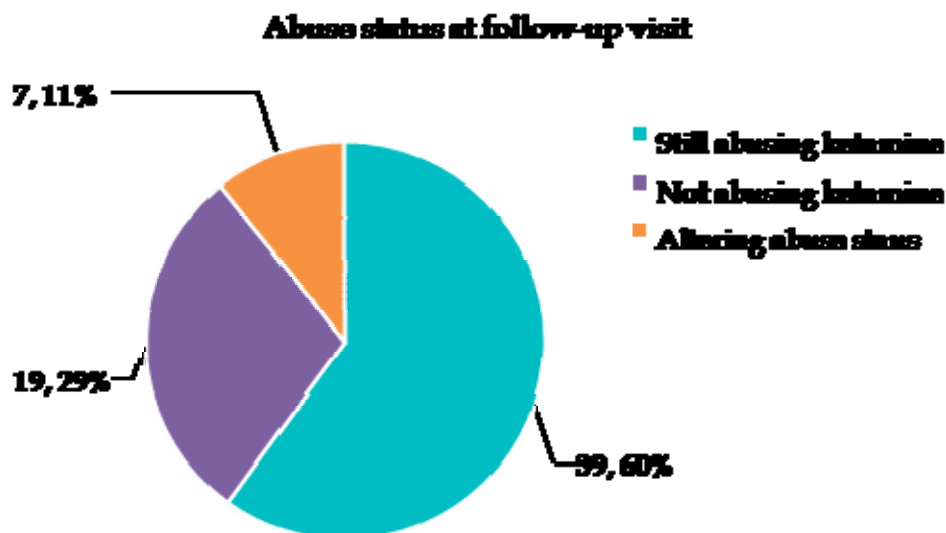


Fig. 5 Abuse status at follow-up visits (n = 65)

II. Basic demographic data of 104 eligible subjects

Among the 104 eligible ketamine abusers presenting with urinary symptoms, 54 were male and 50 were female. The mean age at diagnosis was 24.5 +/- 5.5 years, with the youngest patient being only 14 years old. The duration of ketamine abuse ranged from 2 months to 11 years, mean 4.6 years. The onset of urinary symptoms after ketamine abuse ranged from only 2 weeks to 48 months, mean 17 months. 26 patients confessed that they had abstained from ketamine at first clinic visit, ranging from 2 weeks to 36 months, mean 14.3 months. About 80% of patients on abstinence were accompanied by social workers or institutionalized in a drug rehabilitation centre.

| | Total No. of patients | Mean +/- 1 SD | Range |
|--|-----------------------|---------------|----------|
| Age at diagnosis | 104 | 24.5 +/- 5.5 | 14 - 48 |
| Duration of abuse (years) | 104 | 4.6 +/- 3.1 | 0.2 - 11 |
| Onset of urinary symptoms (months) | 104 | 17.0 +/- 16.7 | 0.5 - 48 |
| Duration of abstinence (if any) (months) | 26 | 14.3 +/- 17.2 | 0.5 - 36 |

Table 1 Basic demographic data of 104 patients

III. Ketamine abuse habit

Of 104 patients, 59 (57%) admitted that they were daily ketamine abusers. 21 (20%) abuse ketamine once every few days, while 8 (7.7%) and 6 (5.8%) were abusing ketamine weekly and bi-weekly respectively. 10 patients (9.6%) were unable to quantify their frequency of abuse as they had bouts of ketamine abuse during "rave parties" or gathering with friends. Nethertheless, the frequency of abuse may not be able to truly reflect the quantity of ketamine abused. The amount of ketamine powder sniffed each time varied among abusers and was difficult to have an universal quantification. Frequency of abuse, however, could be a way to reflect how addicted psychologically a patient was to ketamine. Correlation between frequency of abuse and the symptomatology were made and would be discussed in following sessions.

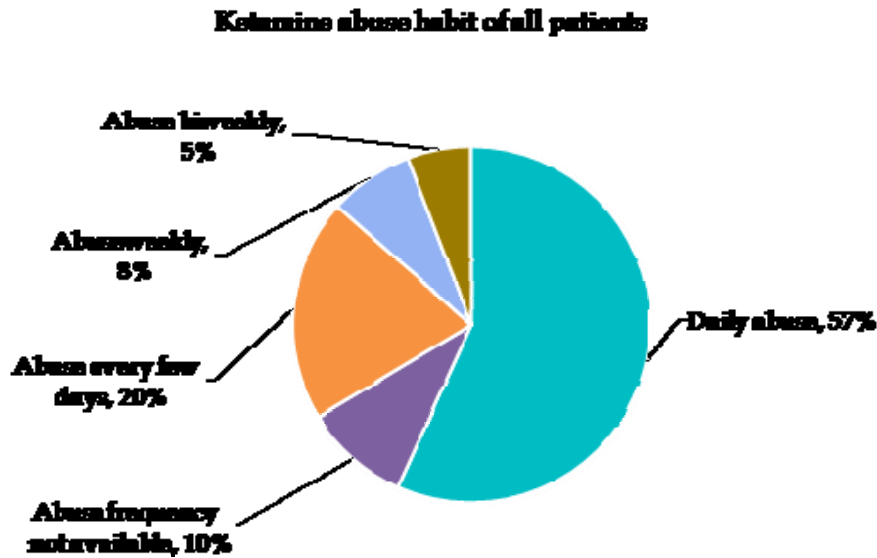


Fig 6 Ketamine abuse habit of 104 patients

IV. Presenting urinary symptoms

Most patients (99, 95.2%) presented with urinary frequency. The shortest interval between voids was 10 minutes, with a mean of 50 minutes. Nocturia, the need to wake up during the night to pass urine, was also present in 91 (87.5%) patients. The most severe patient suffered from nocturia of 20 times a night. 86 patients (82.7%) presented with urinary urgency, a sudden compelling desire to void which is difficult to defer. Other presenting symptoms include dysuria (painful urination) and hematuria (blood in urine) in 66 (63.5%) and 56 (53.8%) patients respectively.

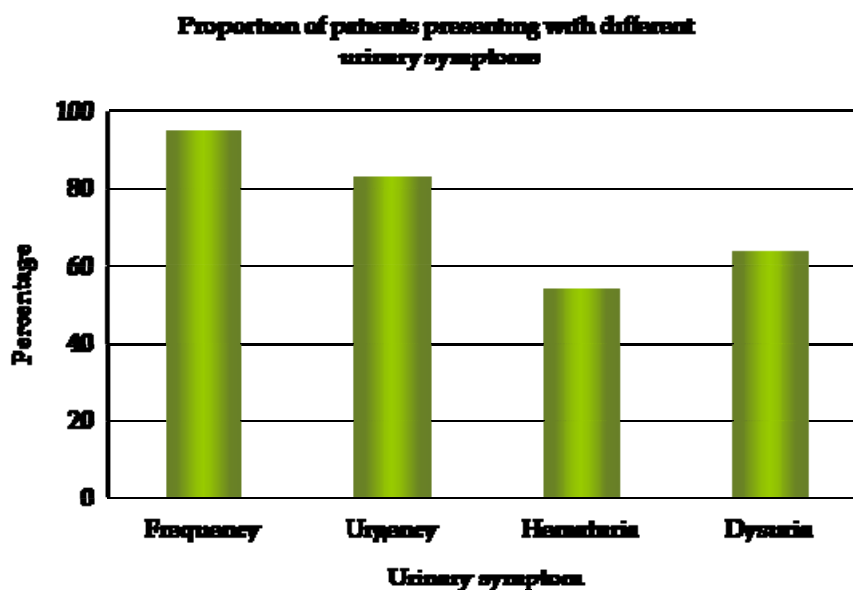


Fig. 7 Presenting urinary symptoms in 104 patients

| | Total No. of patients | Mean +/- 1 SD | Range |
|-------------------------|-----------------------|---------------|----------|
| Frequency (minutes) | 104 | 50.5 +/- 40.8 | 10 - 180 |
| Nocturia (no. of times) | 104 | 4.2 +/- 3.6 | 0 - 20 |
| PUF symptom score | 101 | 13.0 +/- 5.7 | 4 - 23 |
| PUF bother score | 101 | 7.0 +/- 3.5 | 0 - 12 |
| PUF total score | 101 | 20.0 +/- 8.9 | 6 - 35 |

Table 2 Urinary symptoms with data on frequency, nocturia and PUF scores

Quantification of the urinary symptoms was achieved by adopting the PUF scale, so that the severity of symptoms and degree of bother could be assessed and compared between patients. As suggested by Parsons⁴, a PUF score of ≥ 15 may indicate that one was suffering from chronic pelvic pain or interstitial cystitis. We consider a ketamine abuser with a PUF score ≥ 15 to be suffering from significant urinary symptoms.

PUF scale was not completed in three patients rendering 101 subjects eligible for analysis. The mean PUF score was 20 +/- 8.9. 67 patients (66.3%) had a significant PUF score of ≥ 15 . Among the 18 (17.8%) patients who had PUF score > 30 , 15 (83.3%) of them were daily ketamine abusers.

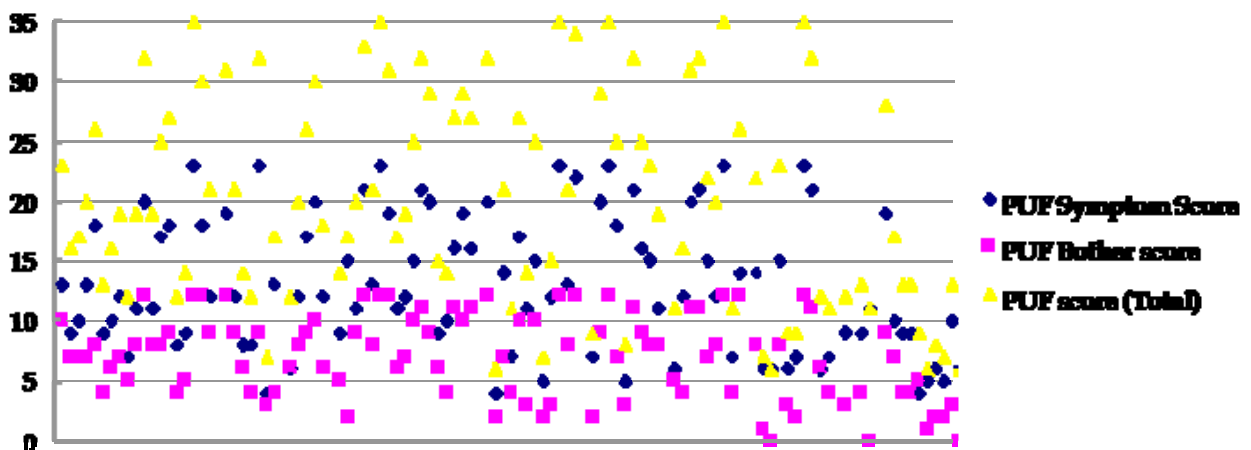


Fig. 8 Scatter plot showing the PUF symptom, bother and total scores of 101 ketamine abusers

V. Urine test results

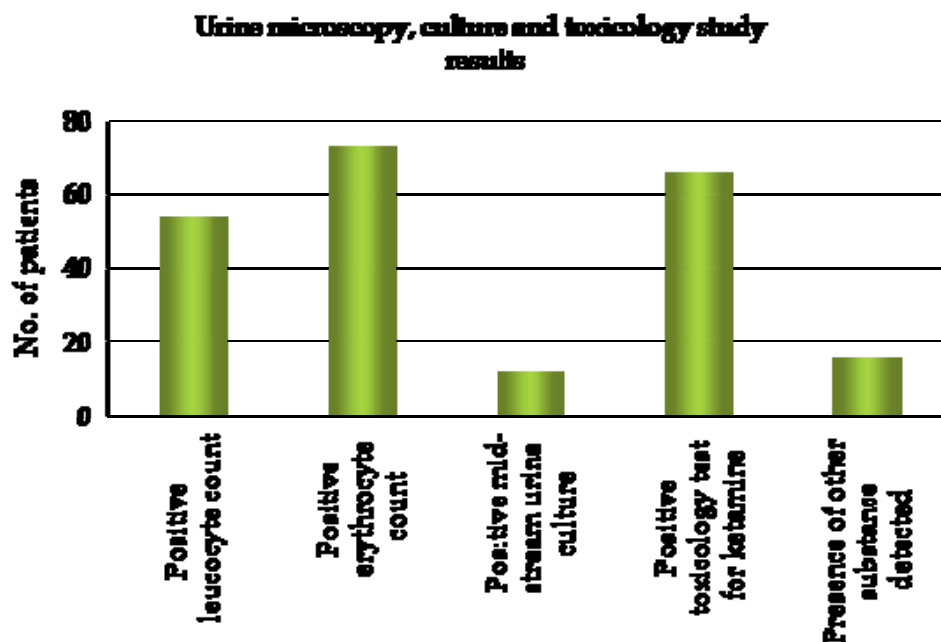


Fig. 9 Data on patients with abnormal urine tests results

54 (51.9%) and 73 (70.2%) patients had presence of leucocytes and erythrocytes in their urine microscopy examination respectively. However, only 12 (14.1%) out of 85 mid-stream urine culture tests were positive. This suggested most patients were having a form of non-bacterial cystitis and the inflammatory process was elicited by ketamine or its metabolites in urine. 66 (66%) out of 100 urine toxicology tests were positive for ketamine. Some patients were poly-drug abusers and 14 (14%) had substance other than ketamine detected in their urine samples: cocaine: 6, amphetamine: 2, cannabis: 1, opiate: 1, brompheniramine: 2, haloperidol: 1, codeine: 1. The diversity and limited kinds of other substances detected suggested that the hazard on the urinary tract was caused by ketamine and its metabolites rather than other substances. As ketamine has a short elimination half-life of 3-5 hours, a toxicology test for ketamine shall be positive if the patient had ketamine abuse within 2 days of saving urine sample. Thus toxicology test alone may not be able to prove that one has truly abstained from ketamine unless consecutive urine samples were all negative on follow-up tests.

VI. Blood test results

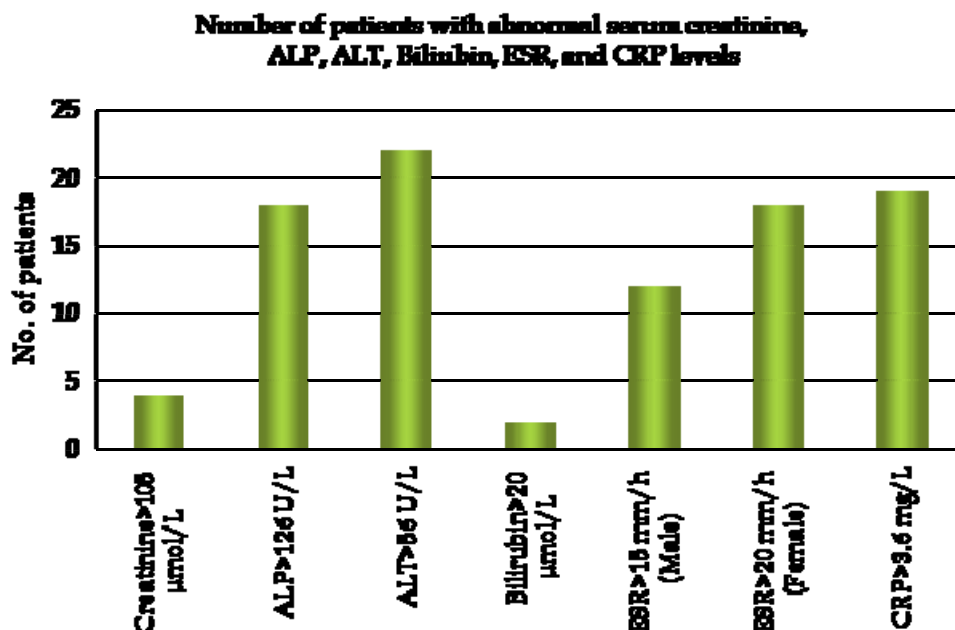


Fig. 10 Number of patients with abnormal blood test results

Mild grade renal impairment (Serum creatinine > 105 µmol/L) was detected in 4 patients (4.1%). The upper tract damage in the current series was not as overt as previously described^{1,2}. About 20 % of patients had liver enzyme derangement, accounted by the fact that ketamine is N-dealkylated in liver and then metabolized and > 90% excreted in urine. A significant portion of patients had elevated inflammatory markers (ESR and CRP). This reflects the nature of inflammatory process initiated after ketamine absorption.

| | No. of patients (%) | Range of abnormal values |
|-------------------------------|---------------------|--------------------------|
| Abnormal Creatinine (µmol/L) | 4/97 (4.1%) | 112.0 - 198.0 |
| Abnormal ALP (U/L) | 17/97 (18.6%) | 128.0 - 915.0 |
| Abnormal ALT (U/L) | 23/97 (22.7%) | 56.0 - 349.0 |
| Abnormal Bilirubin (µmol/L) | 2/97 (2.1%) | 28.0 (both) |
| Abnormal ESR in Male (mm/h) | 12/42 (28.6%) | 17.0 - 95.0 |
| Abnormal ESR in Female (mm/h) | 18/41 (43.9%) | 20.0 - 74.0 |
| Abnormal CRP (mg/L) | 19/48 (39.6%) | 3.8 - 45.2 |

Table 3 Range of abnormal values for different blood tests

VII. Radiological investigation results



Fig. 11a Ultrasonography image showing gross hydronephrosis in a patient with 5 years of ketamine abuse

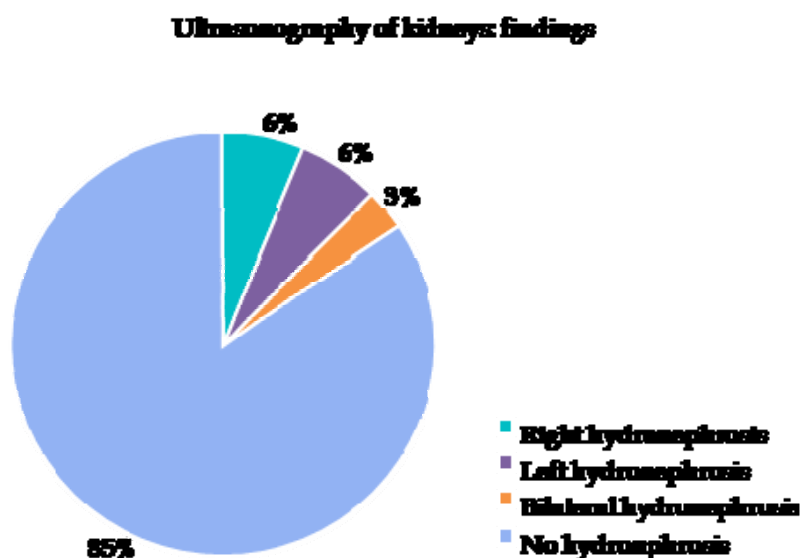


Fig 11b Pie-chart showing findings on ultrasonography of kidneys

Altogether 15% of patients presented with either unilateral or bilateral hydronephrosis on ultrasonography of kidneys. This suggested that with chronic ketamine abuse not only the bladder and lower urinary tract but also the upper tract was predisposed to significant damages. Among these patients, 12 had further imaging with intravenous urography (IVU) or computed tomography (CAT) performed. Common findings included a small, shrunken bladder with thickened wall, bilateral hydronephrosis and dilated upper ureters. Some patients had peri-ureteric wall thickening suggestive of inflammatory changes, while some had sites of ureteric narrowing suggestive of fibrotic strictures.

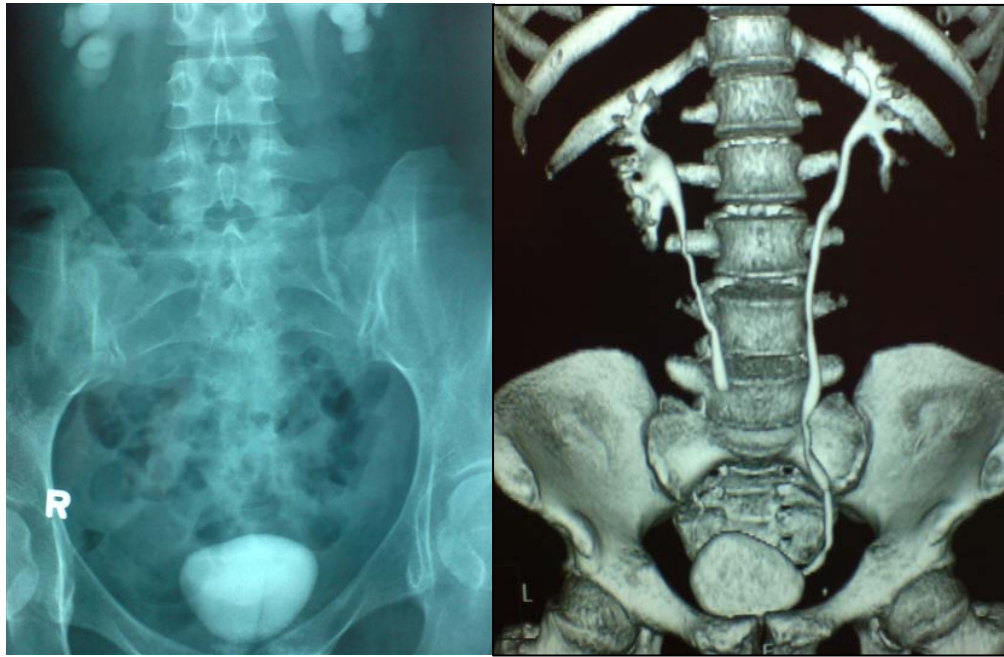


Fig. 12 Intravenous urogram (left) and computed tomography (right) of a two ketamine abusers showing small bladder and prominent bilateral upper tracts.

VIII. Urodynamic study results

The functional status of the bladder and voiding pattern of patients was assessed by video cystometrography (VCMG), which was performed in 70 patients. 17 (24.8%) patients had detrusor instability (unstable bladder muscle contractions), 15 (21.4%) had poor bladder compliance (reduced distensibility of the bladder when filled) and 7 (10.0 %) had bilateral vesicoureteric reflux on fluoroscopy. 4 patients (5.7%) had contracted bladder that were virtually unable to fill up. The mean cystometric bladder capacity were 171 ± 142 mL (range 11-497 mL), with 26 (41.3%) had bladder capacity reduced to < 100 mL. 11 (15.7%) had significantly reduced bladder capacity of ≤ 50 mL. This finding correlated well with the symptoms of these patients, in that both the functional and cystometric bladder capacities were markedly decreased, causing them to have very frequent small voids. Furthermore, the high intra-vesical pressure resulted from the detrusor instability or reduced bladder compliance increased the risk of irreversible upper tract damage.

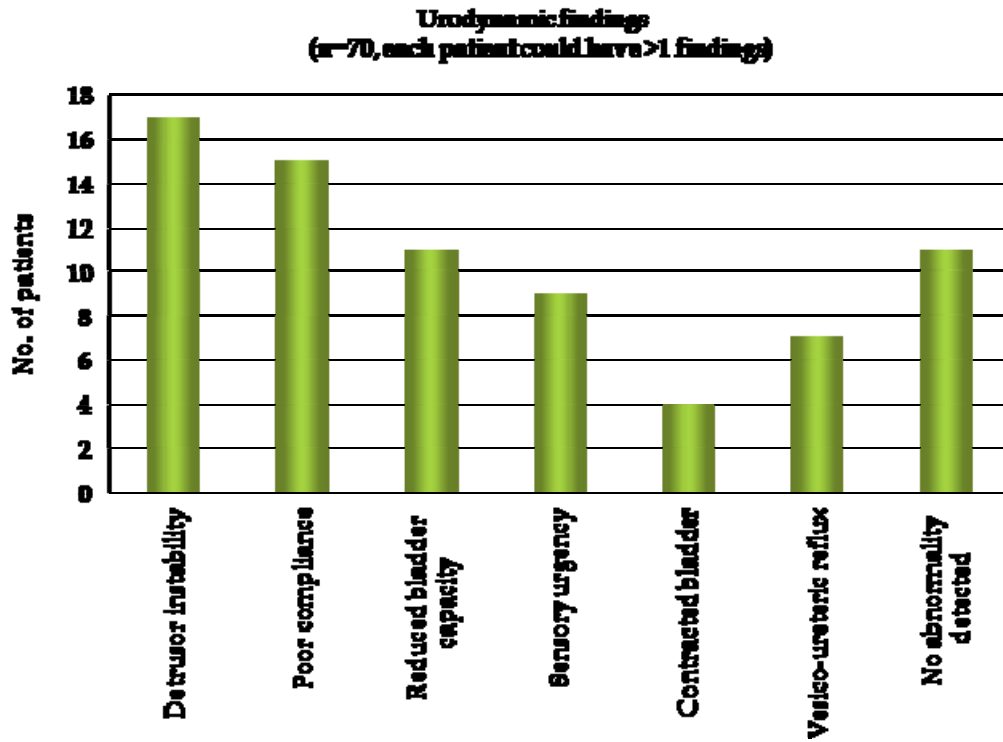


Fig. 13a Urodynamic findings in 70 patients with VCMG performed

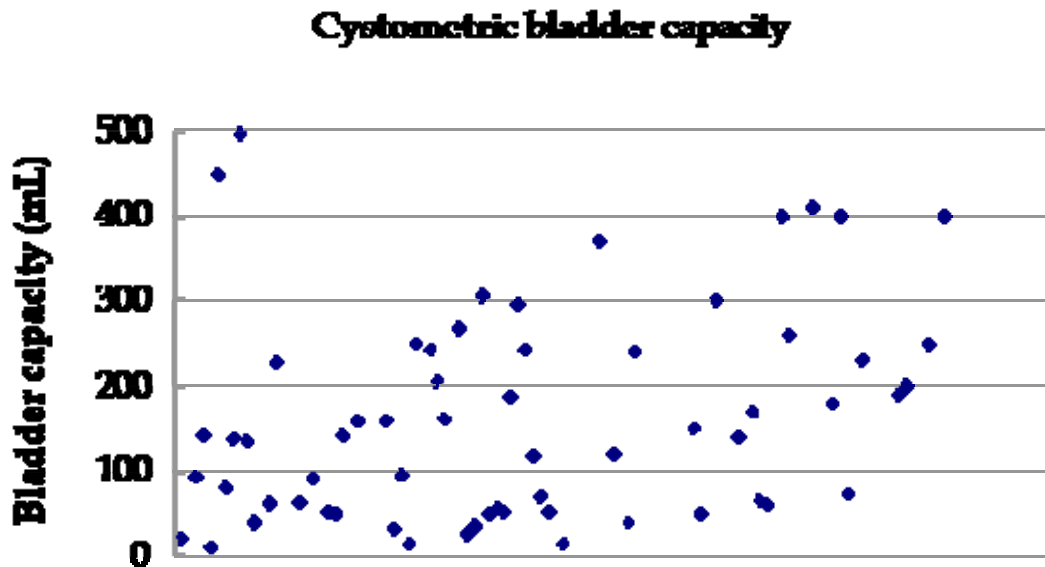


Fig. 13b Scatter plot showing the cystometric bladder capacity

IX. Cystoscopy results

66 patients underwent cystoscopy examination and bladder biopsy was performed in 7 patients. All patients showed various degrees of cystitis changes in bladder. Severe cases showed petechial haemorrhages, diffuse erythematous and raised mucosa, with some showing glomerulations as classically described in patients with interstitial cystitis. Pathological examination of bladder biopsy revealed that bladder mucosa was denuded with focal presence of reactive urothelium. The lamina propria showed granulation tissue and congested vessels with lymphocytic and eosinophilic infiltration. Patients often required analgesic or sedation before cystoscopy examination.

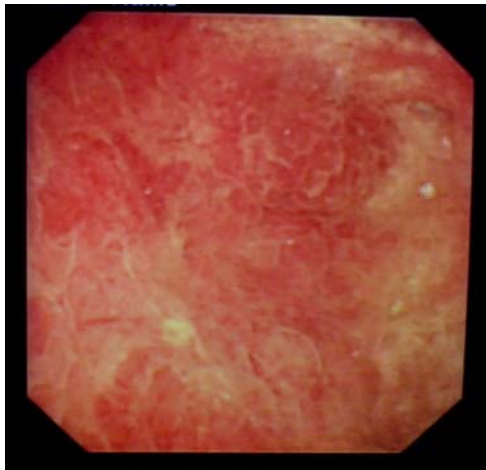


Fig. 14 Clinical photo showing cystoscopic view of a ketamine abuser with severe cystitis changes.

X. Correlation studies

Paired Samples T-test is used to find out the correlations between

- PUF symptoms score and Age at diagnosis, Years of abuse, Onset of urinary symptoms, Nocturia, and Bladder capacity
- PUF bother score and Age at diagnosis, Years of abuse, Onset of urinary symptoms, Nocturia, and Bladder capacity
- PUF score (total) and Age at diagnosis, Years of abuse, Onset of urinary symptoms, Nocturia, and Bladder capacity

Pearson's correlation to compare the PUF scores status of with or without abstinence, urinary frequency (< 1 hour vs >1 hour), with or without hydronephrosis, and with or without abnormal urodynamic findings.

Paired Samples Correlations

| | N | Correlation | P value | Sig |
|--|-----|-------------|---------|-----|
| PUF Symptom Score & Age at Dx | 101 | .124 | .218 | No |
| PUF Symptom Score & Years of Abuse | 101 | .216 | .030 | Yes |
| PUF Symptom Score & Onset of urinary symptoms (months) | 101 | .120 | .230 | No |
| PUF Symptom Score & Nocturia (times) | 101 | .549 | .000 | Yes |
| PUF Symptom Score & Bladder capacity (ml) | 63 | -.565 | .000 | Yes |
| PUF Bother score & Age at Dx | 101 | .124 | .217 | No |
| PUF Bother score & Years of Abuse | 101 | .157 | .118 | No |
| PUF Bother score & Onset of urinary symptoms (months) | 101 | .077 | .444 | No |
| PUF Bother score & Nocturia (times) | 101 | .532 | .000 | Yes |
| PUF Bother score & Bladder capacity (ml) | 63 | -.603 | .000 | Yes |
| PUF score (Total) & Age at Dx | 101 | .128 | .201 | No |
| PUF score (Total) & Years of Abuse | 101 | .200 | .045 | Yes |
| PUF score (Total) & Onset of urinary symptoms (months) | 101 | .108 | .284 | No |
| PUF score (Total) & Nocturia (times) | 101 | .563 | .000 | Yes |
| PUF score (Total) & Bladder capacity (ml) | 63 | -.609 | .000 | Yes |

Table 4 Paired Sample T-test showing correlation between PUF scores and various clinical issues

Results from the paired sampled correlations:

- PUF Symptom score is correlated with years of abuse, nocturia, and bladder capacity
- PUF Bother score is correlated with nocturia and bladder capacity
- PUF total score is correlated with years of abuse, nocturia, and bladder capacity

It is suggested that the the PUF symptom score (objective finding) and bother score (subjective finding) both correlate with nocturia and bladder capacity. PUF symptoms score and PUF total score are correlated with the years of abuse. However, the PUF scores are not correlated with the age at diagnosis and the onset of urinary symptoms.

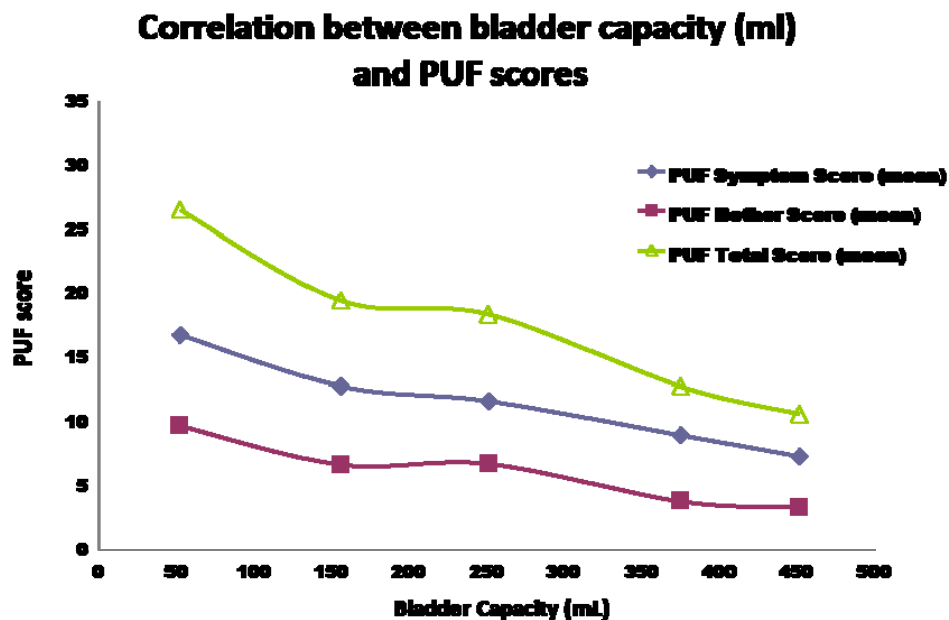


Fig. 15 Correlation curves between bladder capacity and PUF score

It is demonstrated that the PUF score correlates well with the cystometric bladder capacity and is consistent for both symptom and bother scores within subjects. Our results suggested that PUF scale is a representative and useful screening tool to predict the cystometric capacity in ketamine abusers.

Attempts in establishing the correlation between change in PUF score on follow-up visits with abstinence from ketamine or not has been made with independent t-test. 21 patients who were still abusing ketamine with follow-up PUF scores were compared with 26 patients who abstained from

ketamine. The results, however, failed to demonstrate the correlation with statistical significance ($p = 0.509$ for symptoms score, $p = 0.978$ for bother score and $p = 0.679$ for total score). A reason for this is that patients symptoms might have been partially relieved with the medications and treatments from our clinic, and some might continue ketamine abuse but with altered frequency and dosage, so that these confounding factors have affected the PUF score in subsequent follow-up visits. However, the importance of quitting ketamine abuse in order to prevent worsening of symptoms and irreversible upper tract damages have to be emphasized.

EDUCATION OF HEALTH CARE STAFF AND THE PUBLIC

I. Lecture to health care staff

A lecture titled "Street Ketamine-associated Urinary Tract Problems" was delivered by Dr MA Wai Kit in Tuen Mun Hospital on 26th September 2008. 22 nurses attended the lecture. The information provided in the lecture included current trend of ketamine abuse, the adverse effects of ketamine abuse on the urinary system, and how patients were assessed and managed clinically. This lecture helped the frontier health care professionals in understanding the clinical entity and equipped them with the necessary knowledge in caring these patients. Participants had active response in the lecture and rated the lecture helpful and relevant to their clinical practice.



Fig 16a Ms Grace Chiu and Dr WK Ma in the lecture



Fig 16b Dr Ma explaining to the audience the current trend of ketamine abuse

II. Education to the public

10000 education pamphlets on the adverse effects of ketamine abuse was designed and published as an important tool to educate the public why ketamine abuse is detrimental to health (Appendix 2). Information on drug abstinence programs and rehabilitation institutes is also included in the pamphlets so that abusers interested in drug quitting are provided with contact methods to these institutes. These pamphlets will be distributed in various hospitals of the Hospital Authority, local community centres and schools as an anti-drug abuse education tool.

| Hospital | Ward | Pamphlets distributed |
|--|--------------------|------------------------------|
| Caritas Medical Center | 7B | 100 |
| North District Hospital | 3B | 100 |
| Princess Margaret Hospital | BLG2 | 600 |
| Prince of Wales Hospital | Lithotripsy Centre | 100 |
| Pok Oi Hospital | Day Ward | 100 |
| Pok Oi Hospital | 6S | 100 |
| Pamela Youde Nethesole Eastern Hospital | Urology ward | 100 |
| Tseung Kwan O Hospital | 6B | 100 |
| Tuen Mun Hospital | A4 | 100 |
| Tuen Mun Hospital | B4 | 100 |
| Tuen Mun Hospital | C4 | 100 |
| Tuen Mun Hospital | D4 | 100 |
| Queen Elizabeth Hospital | G4 | 100 |
| Queen Mary Hospital | B5 | 100 |
| Tuen Mun Hospital | A&E | 100 |
| Beat Drugs Fund | | 50 |
| Caritas Hugs Centre | | 100 |
| Hong Kong Jockey Club Drug Info Centre, Narcotics Division | | 1100 |
| The Hong Kong Federation of youth groups | | 100 |
| Hong Kong Medical Council (to general practitioners) | | 100 |
| | Total | 3450 |

Fig N. Distribution of pamphlets to different centres and hospitals dated 25/1/2011

FINANCIAL REPORT

Based on estimated information from target number of patients, number of clinic sessions during study period, cost of investigation tests and staff emolument from the hospital finance department, the financial budget was written and approved by the Beat Drugs Fund Association at the start of the research. Each patient required a total of approximately 6 hours' medical attention by a senior medical consultant, a medical officer and a registered nurse. The following table shows the budget breakdown for the two hospitals:

| | TMH (HKD) | PMH (HKD) |
|---|--------------|------------|
| 1. Personal emolument [#] | | |
| - 4 part-time doctors (Cons/ SMO/ AC/ MO/ Resident) | \$ 181,000 | \$ 181,000 |
| - 4 part-time nurses (APN/ RN/EN) | \$ 72,500 | \$ 72,500 |
| - 2 part-time supporting staff | \$ 18,800 | \$ 18,800 |
| - 2 part-time radiographers | \$ 34,200 | \$ 34,200 |
| - 2 part-time research assistants | \$ 65,300 | \$ 65,300 |
| Sub-total | \$371,800 | \$ 371,800 |
| 2. Computer system with statistics program | \$ 30,000 | \$ 30,000 |
| 3. Urodynamic and cystoscopy study cost | \$ 54,950 | \$ 54,950 |
| 4. Pathology tests | \$ 128,250 | \$ 128,250 |
| 5. Auditing* | \$ 60,000 | -- |
| 6. Pamphlet publication | \$ 100,000 | -- |
| Total | \$ 745,000 | \$ 585,000 |
| Grand total | \$ 1,330,000 | |

Cons = Consultant, SMO = Senior medical officer, AC = Associate consultant, MO = Medical officer, APN = Advanced practise nurse, RN = Registered nursed, EN = Enrolled nurse

[#] Estimated part-time hourly pay scale according to Hospital Authority

Consultant HKD \$ 573

Medical officer HKD \$ 293

Registered nurse HKD \$ 100

Staff emolument has included expense on Mandatory Provident Fund (MPF)

*Estimated auditing cost \$20,000/year, total 3 financial years (Jul 2008 – Mar 2009, Apr 2009 – Mar 2010, Apr 2010 – Jun 2010)

The final expense of the research project was substantially lower than the budget. A total of HKD \$ 582,466.43 was the grand total expense. Within this expense, the target number of patients managed was achieved and the education purpose of the project, including the pamphlet publication and education to health care staff was successfully conducted. The following table shows the expense breakdown for the two hospitals:

| | TMH (HKD) | PMH (HKD) |
|---|---------------|---------------|
| 1. Personal emolument | | |
| - 4 part-time doctors (Cons/ SMO/ AC/ MO/ Resident) | \$ 107,129.60 | \$ 35,085.08 |
| - 4 part-time nurses (APN/ RN/EN) | \$ 44,395.56 | \$ 22,798.00 |
| - 2 part-time supporting staff | \$ 9,906.48 | \$ 3,354.20 |
| - 2 part-time radiographers | \$ 17,024.56 | \$ 27,169.72 |
| - 2 part-time research assistants | \$ 24,049.20 | \$ 3114.03 |
| Sub-total | \$202,505.40 | \$ 91,521.03 |
| 2. Computer system with statistics program | \$ 30,818.00 | \$ 30,243 |
| 3. Urodynamic and cystoscopy study cost | \$22,612.00 | \$ 52,967.00 |
| 4. Pathology tests | \$ 87,000.00 | -- |
| 5. Auditing | \$ 59,000.00 | -- |
| 6. Pamphlet publication | \$ 5,800.00 | -- |
| Total | \$407,735.40 | \$ 174,731.03 |
| Grand total | \$ 582,466.43 | |

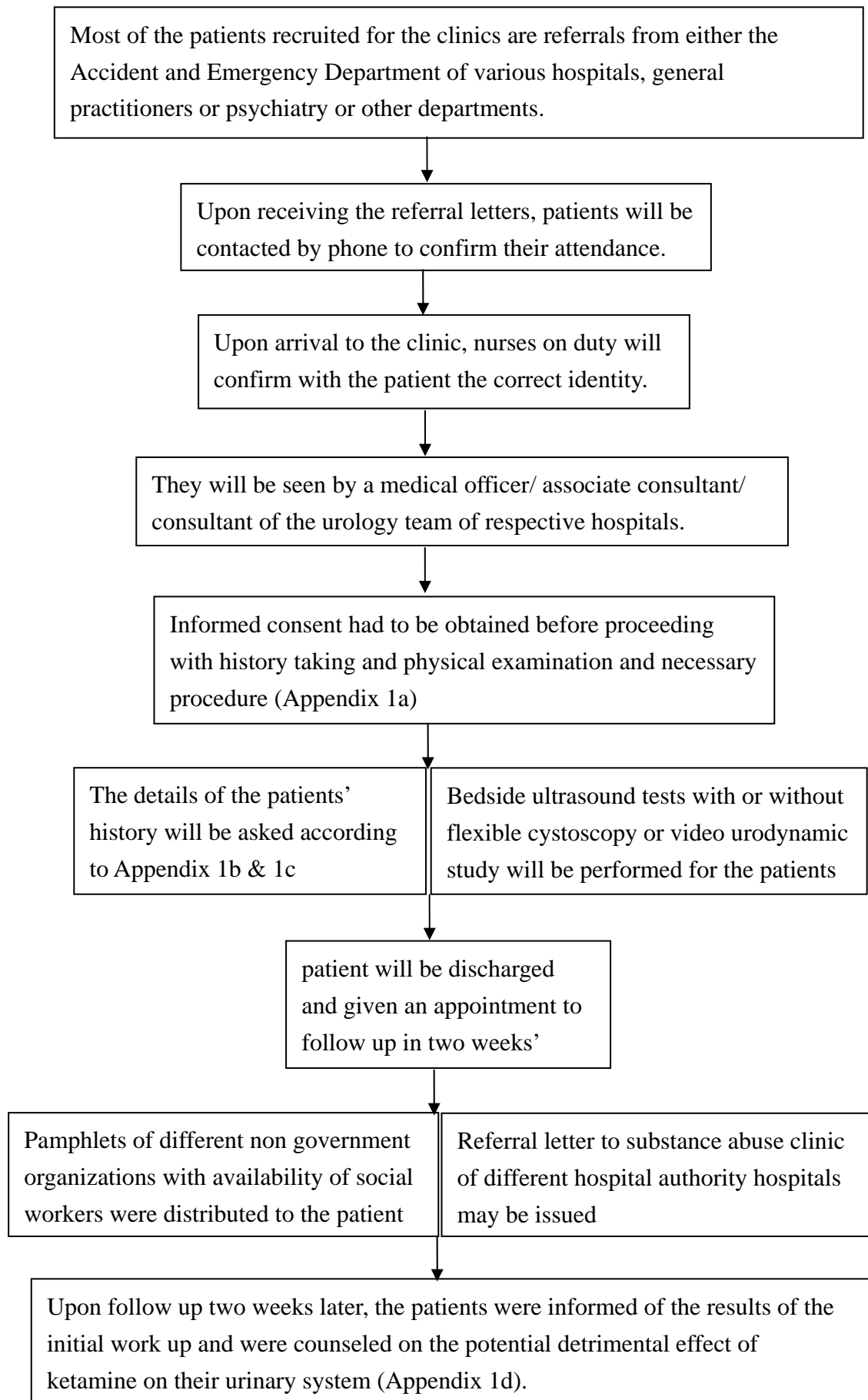
There are several factors for the low expense for the project:

- high rate of defaulted follow-up visits from the ketamine abusers, reducing the total hours spent on each patient
- expense for pathology tests in PMH was not separated from the hospital laboratory expense for logistic reason
- lower expense for auditing required
- lower expense for pamphlet publication as the design and drawing of the pamphlet was performed by volunteer

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Appendix 1a. Flow chart of patient attending the ketamine abuse clinic



Appendix 1b Chinese version of patient consent to the study

醫院管理局

瑪嘉烈醫院/屯門醫院泌尿外科

對"街頭"氯胺酮有關的尿道徵狀研究病人同意書

瑪嘉烈醫院及屯門泌尿外科正進行對"街頭"氯胺酮有關的尿道徵狀研究，針對氯胺酮引起的膀胱、尿道及腎臟損害而作出資料蒐集及病人跟進，期望更多了解患者的排尿症狀和膀胱/上尿道受損程度，並提供日後更多研究的基楚。

治療計劃

計劃為在為曾經吸食"街頭"氯胺酮及後出現排尿症狀的患者提供一連串的檢查及徵狀評估，包括：抽血，小便化驗，超聲波檢查，徵狀問卷等，作為初步評估。之後再為有需要病者安排膀胱尿動力學檢查，電腦掃描及膀胱內窺鏡，以作進一步檢查。病者需定期覆診以跟進病情及治療果較。

膀胱尿動力學檢查的副作用很小，只侷限於剛開始的導管插入時的不舒適，因為這會導致起初的加重惡化諸如頻尿及尿急。

研究之中需以膀胱內窺鏡抽取膀胱內壁組織以作病理化驗。

膀胱鏡檢查一般都很安全，而且大多數副作用都是暫時性的。接受膀胱鏡檢查後，你可能會稍感不適，但數小時內便會復元。排尿時可能會感到灼痛，尿裏帶血是正常的（尤其是拿取了活組織後）。但這些徵狀應會在 48 小時內消失。其他併發症比較罕見，但尿道感染和發炎偶有發生，須以藥物治療。檢查也可能會弄損或刺穿尿道或膀胱，引致出血和感染，須以藥物或手術治療。在你同意接受治療及清楚明白程序的情況下，醫生才會進行膀胱鏡，病理化驗組織也只作學術研究用途，資料及病人紀錄僅供醫生、研究人員及有關專責人仕使用，絕不外洩。

您可自由決定是否參加這項研究，如果你同意參加，你需要簽署此份同意書，但您仍可隨時退出而無需給與原因，這不會影響您接受的標準治療。

如果您有任何關於此研究的詢問，您可致電 24685941 朱秀群 醫生 (屯門醫院) 或 29901960 馬偉傑 醫生 (瑪嘉烈醫院) 聯絡。

本人理解並同意參與上述同意書所指之研究。

病人簽署： _____

日期： _____

Appendix 1c

Ketamine associated cystitis Clinic first visit questionnaires

Duration of K abuse: ____ month/years

Frequency of K abuse: ____times per day/week/month* (*average in past 12 months)

Amount each time: _____

Money Spent: HK\$ _____ per month

Co-ingestion: Y/N Drug group: _____

Any period of abstinence: ____ mths

Onset of urinary symptoms: ____ mths/ years

Frequency +/- Q ____min ; nocturia ____ times

Urgency +/-

Hematuria +/-

Dysuria +/-

Napkins +/- _____per day

PUF score: symptom score ____ + bother score ____ = ____

Bedside USG: R / L/ bilateral / No hydronephrosis

Plan of management:

Urine and blood for toxicology

ESR, CRP, CBP, R/LFT

MSU R/M C/ST

Bedside USG kidney and bladder

Cystoscopy + bladder biopsy LA

Book Video UD 4/52 in Saturday Clinic

Book CTU+ CT abdomen + CT pelvis +/- USG urinary tract if there is abnormality detected in Bedside USG

+/- ditropan 5mg tds

FU Ketamine Clinic

Appendix 1d

Ketamine associated cystitis follow-up clinic 2nd/3rd visit

Still abusing K: +/-

Any period of abstinence: ___ mths

Frequency: _____times per day/week/month

Amount each time: _____

Money spent: HK\$ _____per month

Co-ingestion Y/N Drug group _____

Frequency +/- Q ___ min ; nocturia ___ times

Urgency +/-

Hematuria +/-

PUF score today:

symptom score ___ + bother score ___ = ___

Bedside USG: R / L/ bilateral / No hydronephrosis

Results of first visit

Cr ____, ALP ____, ALT ____, Bili ____

ESR ____

MSU RBC _____

WBC _____

Culture _____

Cystoscopy findings:

Bladder biopsy results:

CTU results(if done):

Video UD cystometric bladder capacity ___ ml

Detrusor overactivity +/-

Decrease bladder compliance +/-

FU plan:

Check blood and urine toxicology in final visit

+/- ditropan, pyridium, dologesic/ponstan + triact

+/- Elmiron (self-purchase)

FU Ketamine Clinic 3/12 (for 2nd visit)

Appendix 1 e Chinese version of PUF score questionnaire

姓名: _____ 日期: _____

**盆腔痛楚及尿急/尿頻
病人症狀尺度**

| | | 0 | 1 | 2 | 3 | 4 | 症狀分數 | 困擾分數 |
|---|-------------------------------------|------|------|-------|-------|-----|------|------|
| 1 | 你在日間上廁所多少次? | 3-6 | 7-10 | 11-14 | 15-19 | 20+ | | |
| 2 | a.你在夜間上廁所多少次? | 0 | 1 | 2 | 3 | 4+ | | |
| | b.若你在夜間起床排尿,這情況困擾你嗎? | 從不 | 間中 | 時常 | 經常 | | | |
| 3 | a.你現在/以往曾否在性行為時或之後感到痛楚/不適? | 從不 | 間中 | 時常 | 經常 | | | |
| | b.你曾否因為痛楚或尿急/不適而避免性行為? | 從不 | 間中 | 時常 | 經常 | | | |
| 4 | 你有沒有膀胱或盆腔(陰道、陰唇、下腹、會陰、睪丸、或陰囊位置)的痛楚? | 從不 | 間中 | 時常 | 經常 | | | |
| 5 | a.若你有此痛楚,程度是: | | 輕微 | 中度 | 嚴重 | | | |
| | b.這些痛楚困擾你嗎? | 從不 | 間中 | 時常 | 經常 | | | |
| 6 | 你排尿後還有尿急的感覺嗎? | 從不 | 間中 | 時常 | 經常 | | | |
| 7 | a.你有尿急嗎?若有,程度是: | | 輕微 | 中度 | 嚴重 | | | |
| | b.尿急的情況困擾你嗎? | 從不 | 間中 | 時常 | 經常 | | | |
| 8 | 你有恆常的性行為嗎? | 有/沒有 | | | | | | |

困擾分數 (1, 2a, 3a, 4, 5a, 6, 7a) = _____

症狀分數 (2b, 3b, 5b, 7b) = _____

總分 (困擾分數 + 症狀分數) = _____

治療方法：

醫生對吸食者進行詳細檢查，並按其膀胱容量及對泌尿系統損害的嚴重程度提供適當治療；包括 (i) 藥物治療；(ii) 止痛療法，較嚴重個案或需進行腎穿刺引流及膀胱擴張手術。直至現時，最有效的方法是**應即時停止吸食氯胺酮**。

藏有氯胺酮的法律責任：

藏有或吸食氯胺酮即屬違法，可被判處入獄。
氯胺酮已於2000年12月被列入“危險藥物條例”，販運及非法製造氯胺酮，最高可被判處終身監禁及罰款五百萬港元。



戒毒治療和康復服務：

香港路德會社會服務處

路德會青怡中心
服務範圍：九龍東
聯絡電話：2712 0097

香港路德會社會服務處

路德會青欣中心
服務範圍：新界東
聯絡電話：2660 0400

東華三院越峰成長中心

服務範圍：香港島
聯絡電話：2884 0282

香港基督教服務處 PS33

服務範圍：九龍西
聯絡電話：2368 8269

香港明愛愛容園中心

服務範圍：新界西
聯絡電話：2453 7030

製作：香港泌尿外科學會泌尿外科護士分會
香港泌尿外科護理學院
屯門及瑪嘉烈醫院外科泌尿外科組
鳴謝：屯門醫院急症部
贊助機構：保安局禁毒處禁毒基金



K仔毒害你一生



何謂氯胺酮：

氯胺酮(ketamine)，俗稱K粉、K他命、克他命或K仔，是一種很危險的精神科藥物，它屬於非鴉片系麻醉科藥物。日常所見的氯胺酮產品的主要成份是鹽酸氯胺酮(Ketamine hydrochloride)，通常為獸醫採用作麻醉用途。

表狀：

氯胺酮的製成品，通常是液體，不過常見的吸食方式是嗅吸氯胺酮粉劑，或服食含有氯胺酮的丸劑。



吸食氯胺酮有? 後果

對腦部及心肺功能的影響：

- 它會引起一種“分離”幻覺，令人感到靈魂出竅，有種“high”的感覺。切勿以為“high”完無事，即使濫用一次，身心亦嚴重受創。甚至有人因受K仔影響而自殘身體。
- 對氯胺酮有依賴。
- 記憶力及智力衰退。
- 說話含糊、口齒不清。
- 情緒不穩定。
- 行動機能受損，步履不穩。
- 呼吸/心臟機能受損。

對泌尿系統功能的影響：

1. 小便時感到刺痛，膀胱容量減少、尿频，每十五分鐘如廁一次，甚而要用尿片。



2. 部份病人可能因為膀胱體積太小及劇痛，失去功能，而要割除膀胱。病人割除膀胱後，可能長期需要佩帶尿袋。



3. 部份病人腎功能嚴重衰退：
 - ① 需經皮膚穿刺造瘻術以緩解腎盂積水。



- ii) 腹膜透析
吸食氯胺酮會引致腎衰竭，需依賴腹膜透析。



- ii) 腎衰竭後，需進行血液透析及長期定期覆診及抽血檢查。



吸食氯胺酮的特有危險：

根據香港於2005年所作的一項有關青少年濫用氯胺酮的研究顯示，長期吸食氯胺酮會對腦部造成永久損害。



一名36歲，因吸食危害精神毒品導致腦部受創，造成四肢癱瘓，終生需要使用輪椅，並需永久配戴導尿管。