Clinical Research
Final Report

Research on Urological Sequelae of Ketamine Abuse

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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 Journal\textsuperscript{1} and British Journal of Urology International\textsuperscript{2} 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 cystitis\(^3\), 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 score12). Adopting the PUF symptom scale in assessing ketamine abusers with urinary symptoms was first described by our group\(^2\).

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 groemerulations.
   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), urodynmaic 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
### Fig. 4b  Patient registry overview panel

<table>
<thead>
<tr>
<th>Patient ID</th>
<th>Gender</th>
<th>Date of Birth</th>
<th>Age</th>
<th>Year of Diagnosis</th>
<th>Frequency of Urination</th>
<th>Frequency of Diarrhea</th>
<th>Frequency of Vomiting</th>
<th>Frequency of Headache</th>
<th>Frequency of Pain</th>
<th>Frequency of sweats</th>
<th>Frequency of dizziness</th>
<th>Frequency of fatigue</th>
<th>Frequency of dysuria</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>01/01/2000</td>
<td>3</td>
<td>2015</td>
<td>Every day</td>
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<td>Every other day</td>
<td>Every other day</td>
<td>Every other day</td>
<td>Every other day</td>
<td>Every other day</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>01/01/2000</td>
<td>3</td>
<td>2015</td>
<td>Every day</td>
<td>Every other day</td>
<td>Every other day</td>
<td>Every other day</td>
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<td>Every other day</td>
<td>Every other day</td>
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<td>3</td>
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<td>01/01/2000</td>
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<td>2015</td>
<td>Every day</td>
<td>Every other day</td>
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<td>Every other day</td>
<td>Every other day</td>
<td>Every other day</td>
<td>Every other day</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

### Fig. 4c  Individual patient profile
II. Statistics on Princess Margaret Hospital and Tuen Mun Hospital

IIa. 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

IIb. 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 Pho 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).

![Abuse status at follow-up visit](image)

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.

<table>
<thead>
<tr>
<th>Total No. of patients</th>
<th>Mean +/- 1 SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at diagnosis</td>
<td>104</td>
<td>24.5 +/- 5.5</td>
</tr>
<tr>
<td>Duration of abuse (years)</td>
<td>104</td>
<td>4.6 +/- 3.1</td>
</tr>
<tr>
<td>Onset of urinary symptoms (months)</td>
<td>104</td>
<td>17.0 +/- 16.7</td>
</tr>
<tr>
<td>Duration of abstinence (if any) (months)</td>
<td>26</td>
<td>14.3 +/- 17.2</td>
</tr>
</tbody>
</table>

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

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

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 Parsons\(^5\), 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

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, brompheniramoine: 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\textsuperscript{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.

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

Table 3  Range of abnormal values for different blood tests
VII. Radiological investigation results

![Image](image_url)

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

![Pie-chart](image_url)

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.
The functional status of the bladder and voiding pattern of patients was assessed by video cystometry (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+/−142mL (range 11-497 mL), with 26 (41.3%) had bladder capacity reduced to < 100 mL. 11 (15.7%) had significantly reduced bladder capacity of ≤ 50mL. 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.

<table>
<thead>
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<th>Paired Samples Correlations</th>
<th>N</th>
<th>Correlation</th>
<th>P value</th>
<th>Sig</th>
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<td>PUF Symptom Score &amp; Age at Dx</td>
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<td>.124</td>
<td>.218</td>
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<td>.030</td>
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<td>PUF Symptom Score &amp; Onset of urinary symptoms (months)</td>
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<td>.120</td>
<td>.230</td>
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<td>PUF Symptom Score &amp; Nocturia (times)</td>
<td>101</td>
<td>.549</td>
<td>.000</td>
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<td>PUF Symptom Score &amp; Bladder capacity (ml)</td>
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<td>-.565</td>
<td>.000</td>
<td>Yes</td>
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<td>PUF Bother score &amp; Age at Dx</td>
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<td>.124</td>
<td>.217</td>
<td>No</td>
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<td>PUF Bother score &amp; Years of Abuse</td>
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<td>.118</td>
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<td>PUF Bother score &amp; Onset of urinary symptoms (months)</td>
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<td>.532</td>
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<td>63</td>
<td>-.609</td>
<td>.000</td>
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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.
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.

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

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:

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

<sup>#</sup> Estimated part-time hourly pay scale according to Hospital Authority

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

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

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:

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

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
REFERENCES


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

Most of the patients recruited for the clinics are referrals from either the Accident and Emergency Department of various hospitals, general practitioners or psychiatry or other departments.

Upon receiving the referral letters, patients will be contacted by phone to confirm their attendance.

Upon arrival to the clinic, nurses on duty will confirm with the patient the correct identity.

They will be seen by a medical officer/ associate consultant/ consultant of the urology team of respective hospitals.

Informed consent had to be obtained before proceeding with history taking and physical examination and necessary procedure (Appendix 1a)

The details of the patients’ history will be asked according to Appendix 1b & 1c

Bedside ultrasound tests with or without flexible cystoscopy or video urodynamic study will be performed for the patients

patient will be discharged and given an appointment to follow up in two weeks’

Pamphlets of different non government organizations with availability of social workers were distributed to the patient

Referral letter to substance abuse clinic of different hospital authority hospitals may be issued

Upon follow up two weeks later, the patients were informed of the results of the initial work up and were counseled on the potential detrimental effect of ketamine on their urinary system (Appendix 1d).
Appendix 1b  Chinese version of patient consent to the study

醫院管理局

瑪嘉烈醫院

對“凝固”氣管阻塞的尿道插管研究病人同意書

瑪嘉烈醫院及屯門泌尿外科正進行對“凝固”氣管阻塞有關的尿道插管研究，針對氣管阻塞引起的腎臟、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損害程度，並提供日後更多研究的基礎。

治療計劃

計劃為在為曾發生“凝固”氣管阻塞及後出現尿道阻塞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。之後再為有需要者安排排尿流動力學檢查，腦部掃描及膀胱內窺鏡，以作進一步檢查。患者需定期覆診以跟進病情及治療進展。

腦部尿流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適感，因為這會導致起時的加重惡化，瞳孔及尿急。

研究之中需以膀胱尿細胞抽取膀胱內壁組織以作病理化驗。

膀胱鏡檢查一般都是安全的，而且大多數副作用都是暫時性的。接受膀胱鏡檢查後，你可能會稍有不適，但數小時內便會復原。抽尿時可能會感到灼痛，尿液帶血是正常的（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，但尿道感染和發炎時有發生，須以藥物治療。檢查也曾經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、研究人員及有關責任人仕使用，絕不外洩。

您可自由決定是否參加此項研究。如果您同意參加，您需要簽署此份同意書，但您仍可隨時退出而無需給原因，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問題，可致電24885941，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： __________________________
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

<table>
<thead>
<tr>
<th>Still abusing K: +/-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any period of abstinence: ____ mths</td>
</tr>
<tr>
<td>Frequency: _______times per day/week/month</td>
</tr>
<tr>
<td>Amount each time: ______________</td>
</tr>
<tr>
<td>Money spent: HK$________ per month</td>
</tr>
<tr>
<td>Co-ingestion Y/N</td>
</tr>
</tbody>
</table>

| 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：____________________

塲腔痛楚 及 尿急/尿频

病人症狀尺度

<table>
<thead>
<tr>
<th>項目</th>
<th>症狀分數</th>
<th>困擾分數</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

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？
      - 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. 你有沒有關於排尿或塲腔、陰道、陰蒂、陰阜、會陰、睾丸、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. 這些症狀困擾你嗎？
      - 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. 你有獲得性的行為嗎？
   - 有
   - 無

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：

1. 護理措施：
   a. 預防感染
   b. 輔助排尿
   c. 保持身體衛生

2. 藥物治療：
   a. 抗生素
   b. 利尿劑
   c. 保護膜

戒毒治療和康復服務：

香港精神健康中心
治療號：8720 8269
電話：2483 2000

香港戒毒服務處 PS33
治療號：8720 8269
電話：2483 2000

香港愛康復康復中心
治療號：8720 8269
電話：2483 2000

康復號：8720 8269
電話：2483 2000

康復號：8720 8269
電話：2483 2000

如何防止氣細菌？

氣細菌（Ketamine）是一種強效的興奮劑，會影響腦部功能，導致腦意識障礙。對氣細菌的治療包括治療和康復服務。康復號：8720 8269

表狀：

氣細菌的治療包括：

1. 抗生素治療
2. 保護膜
3. 保護膜

吸食氣細菌的特別危險：

1. 氣細菌療程中，須嚴格遵守治療計劃和康復服務。
2. 嚼食療程中，須注意飲食和覆蓋，以免引起破傷。
3. 保護膜
4. 保護膜

治療細菌治療中，須注意飲食和覆蓋，以免引起破傷。

吸食氣細菌的特別危險：

1. 氣細菌療程中，須遵守治療計劃和康復服務。
2. 嚼食療程中，須注意飲食和覆蓋，以免引起破傷。
3. 保護膜
4. 保護膜

治療細菌治療中，須遵守治療計劃和康復服務。