The HKU Scholars Hub   The University of Hong Kong   香港大學學術庫

Title	**The Chinese version of the pelvic pain and urgency / frequency symptom scale: a useful assessment tool for street-ketamine abusers with lower urinary tract symptoms**
Author(s)	**Ng, CM; Ma, WK; To, KC; Yiu, MK**
Citation	**Hong Kong Medical Journal, 2012, v. 18 n. 2, p. 123-130**
Issued Date	**2012**
URL	**http://hdl.handle.net/10722/149158**
Rights	**Hong Kong Medical Journal. Copyright © Hong Kong Academy of Medicine Press.**

The Chinese version of the pelvic pain and urgency/ frequency symptom scale: a useful assessment tool for street-ketamine abusers with lower urinary tract symptoms

CM Ng 吳志文
WK Ma 馬偉傑
KC To 杜劍聰
MK Yiu 姚銘廣

Objective To investigate the use of a translated Chinese version of the pelvic pain and urgency/frequency symptom scale as an assessment and prognostic tool to evaluate the severity of street-ketamine–associated lower urinary tract symptoms and their reversibility after abstinence.

Design Cross-sectional study.

Setting A special designated out-patient clinic in a regional hospital in Hong Kong.

Participants There were 50 patients with street-ketamine–associated lower urinary tract symptoms and 20 healthy individuals.

Main outcome measures Reliability and validity of the questionnaire; frequency of individual lower urinary tract symptoms, cystoscopic, urodynamic and radiological abnormalities, and their correlation with pelvic pain and the urgency/frequency score.

Results The test-retest reliability coefficient was 0.755 (P<0.001). Cronbach's alpha was 0.974. Mann-Whitney U test proved the discriminatory ability of the questionnaire (P<0.001). Patients with specific lower urinary tract symptoms had a higher mean pelvic pain and urgency/frequency total score compared to those without them: frequency (23.8 vs 17.3), nocturia (22.4 vs 14.0), urgency (22.5 vs 15.1), dysuria (22.7 vs 13.3), and haematuria (24.8 vs 16.2). The number of daytime voids and nocturia episodes correlated well with pelvic pain and urgency/frequency scores. With an increasing score, the likelihood of having cystitis changes, urodynamic abnormalities and hydronephrosis increased, while the cystometrically determined bladder capacity decreased. None of the patients with a score of 16 or below had urodynamic abnormality or hydronephrosis. The mean score change in the abstinence group was -4.33, versus +3.33 in their counterparts.

Conclusions The Chinese version of the pelvic pain and urgency/frequency questionnaire is reliable and valid for assessment in patients with street-ketamine–associated lower urinary tract symptoms. The pelvic pain and urgency/frequency score correlates well with symptom severity as well as endoscopic, urodynamic and radiological abnormalities in patients with street-ketamine–associated lower urinary tract symptoms. A cut-off total pelvic pain and urgency/frequency score of 17 may suggest more serious urological sequelae from ketamine abuse. Abstinence from ketamine reduced lower urinary tract symptoms, but the extent of reversibility of urinary tract damage is yet to be evaluated.

Division of Urology, Department of Surgery, Princess Margaret Hospital, Laichikok, Kowloon, Hong Kong
CM Ng, MB, BS, MRCS (Edin)
WK Ma, FRCS (Urology) (Edin), FHKAM (Surgery)
KC To, FRCS (Urology) (Edin), FHKAM (Surgery)
Division of Urology, Department of Surgery, Queen Mary Hospital, Pokfulam, Hong Kong
MK Yiu, FRCS (Urology) (Edin), FHKAM (Surgery)

Correspondence to: Dr WK Ma
Email: mwk054@ha.org.hk

New knowledge added by this study

* With an increasing pelvic pain and urgency/frequency (PUF) symptom score of above 16 in patients with lower urinary tract symptoms after ketamine abuse, the urological sequelae are more serious, with increasing likelihood of having cystitis changes, urodynamic abnormalities and hydronephrosis, while the cystometrically determined bladder capacity decreases.

Implications for clinical practice or policy

* The Chinese version of the PUF patient symptom scale can be adopted as an assessment tool in patients with lower urinary tract symptoms after ketamine abuse. This tool can be used by social workers, teachers, and medical personnel. Those with a score of 17 or above warrant more in-depth urological care.

盆腔疼痛及尿急／頻尿症狀測量表（中文版）作為偵測街頭氯氨酮濫用者下尿道症狀的一個有效工具

目的 探討使用盆腔疼痛及尿急／頻尿症狀測量表（中文版）作為氯氨酮濫用者下尿道症狀的一個偵測工具是否有效。當他們停止濫藥後，這測量表又是否可以作為一個預後的工具檢測其逆轉情況？

設計 橫斷面研究。

安排 香港一所分區醫院的指定特別門診。

參與者 出現與濫用街頭氯氨酮有關的下尿道症狀的50名病人，以及20名健康狀況良好的參與者。

主要結果測量 測量表的信度和效度。出現下尿道症狀的頻率；膀胱鏡、尿動力學及影像學檢查的異常情況；以及與上述有關的盆腔疼痛及尿急／頻尿症狀測量表得分。

結果 重測信度為0.755（P<0.001），Cronbach's alpha係數為0.974。曼・惠特尼U檢定證明測量表具辨別力（P<0.001）。與健康狀況良好的一組比較，出現下尿道症狀的氯氨酮濫用者均在以下幾方面有較高的盆腔疼痛及尿急／頻尿症狀測量表總得分：頻率（23.8比17.3）、夜尿（22.4比14.0）、尿急（22.5比15.1）、排尿困難（22.7比13.3）及血尿（24.8比16.2）。白天排尿和夜尿的次數與測量表得分相關。測量表得分越高，患者膀胱炎的變化、尿動力學異常結果及腎積水的可能性便越高，而經膀胱壓力流率測試的膀胱容量則減少。測量表得分為16分或以下的患者均沒有尿動力學異常或腎積水的情況。已停止服食氯氨酮的患者，其測量表得分與之前比較為-4.33。相比之下，繼續服食氯氨酮的患者，其測量表得分與之前比較為+3.33。

結論 盆腔疼痛及尿急／頻尿症狀測量表（中文版）作為偵測街頭氯氨酮濫用者下尿道症狀的一個工具是可靠及有效的。測量表得分與濫用者下尿道症狀的嚴重程度，以及內鏡、尿動力學及影像學異常情況呈正相關。研究發現測量表總分為17分的截取值可以顯示氯氨酮濫用者有較為嚴重的泌尿後遺症。停止服食氯氨酮可以減少下尿道症狀；至於是否可以逆轉氯氨酮對尿道的傷害，則有待進一步評估。

Introduction

Ketamine is a N-methyl-D-aspartate receptor antagonist developed in 1962 as an anaesthetic agent.[1] It is less potent and shorter-acting than phencyclidine and is used as a dissociative anaesthetic.[2] However, it has been increasingly used as a recreational drug by youngsters in clubs and parties, including raves. This global phenomenon involves countries/regions like China (including Hong Kong), Taiwan, Indonesia, Malaysia, Japan, Korea, the United Kingdom, Netherlands, Belgium, Russia, Canada, and the United States.[3,4] A significant proportion of street ketamine abusers develop lower urinary tract symptoms (LUTS), which have been reported in many different countries.[5-14] This new clinical entity, first termed ketamine-associated ulcerative cystitis,[5] or 'street-ketamine' associated bladder dysfunction,[6] is characterised by symptoms of lower urinary tract irritation related to ketamine use among young adults.[7-9] With more studies of this entity, it is now known that not only the bladder is involved, since it actually comprises a spectrum of urinary tract damage ranging from mild cystitis changes on endoscopy[10] to obstructive uropathy and kidney injury.[11] This condition is considered to be a classical LUTS syndrome (frequency, urgency, nocturia, dysuria and/or haematuria) with cystitis and contracted bladder that is associated with ketamine abuse, which ensues without other known causes (bacterial infection, stone disease, or neurogenic problem). Cystoscopic or pathological evidence of cystitis is not a prerequisite for diagnosing this syndrome.

The pathophysiology of this syndrome is not clear. A previous study by our group has examined urinary bladder biopsies in these patients, which yielded inflammatory changes (polymorph and eosinophil infiltration in the urothelium, and presence of granulation tissue and congested vessels in the lamina propria).[15] Under electron microscopy, querciphylloid muscle cells with vacuoles at the periphery of muscle cells were identified, mimicking those in interstitial cystitis.[14,15] These bladder biopsy features are, therefore, not solely pathognomonic of ketamine-associated cystitis.[4]

Currently, there is no established diagnostic tool to assess LUTS severity in ketamine-induced cystitis. In view of its clinical and pathological consistency with interstitial cystitis, existing symptom scales for assessing interstitial cystitis may be adopted for that purpose. There are several assessment tools available for interstitial cystitis, including the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) criteria,[16] the University of Wisconsin Symptom Instrument (UWI), the O'Leary-Sant instrument (OSI),[17] and the pelvic pain and urgency/frequency (PUF) patient symptom scale.[18] Among these, the PUF patient symptom scale is a more efficient screening tool for interstitial cystitis.[19,20] Developed by Parsons et al, the PUF score comprises eight questions giving rise to two scores, the symptom score and the bother score, with a maximum total score of 35.[21] It was proven to be an accurate method for detecting interstitial cystitis, and was validated by intravesical potassium sensitivity testing in more than 5000 patients.[21] We proposed adoption of the PUF score as a useful non-invasive diagnostic tool to assess ketamine-induced cystitis patients.

In this study, we translated and validated the Chinese version of the PUF symptom scale (Fig

1) and investigated the feasibility of using it as an assessment and prognostic tool to evaluate the severity of ketamine-associated cystitis. Anticipating good correlation between the PUF score and the symptomatology, a cut-off value suggestive of more serious urological sequelae was also looked for. Furthermore, the reversibility of the symptomatology of ketamine-associated cystitis after abstinence from ketamine was evaluated.

Methods

This study consisted of two components: (1) the validation of a Chinese version of PUF symptom scale, and (2) the investigation of its use as an assessment and prognostic tool in evaluating the severity of street-ketamine–associated LUTS as well as symptom reversibility after abstinence.

The Chinese version of the pelvic pain and urgency/frequency scale

Although health care professionals can use the original English version of the PUF scale for assessment of patients, we developed the Chinese version with a view to popularise the use of the questionnaire by local paramedics, domestic researchers, social workers, and even ketamine abusers themselves. The translation and linguistic validation process was similar to that of the Korean version of the PUF scale, with evaluated face and content validity.[22] It involved (1) forward translation by bilingual urologists (two of the authors), (2) reconciliation of the two versions into one after detailed discussion, (3) back-translation of the reconciled Chinese version to English by an independent nurse with a bachelor's degree in translation, (4) debriefing and cognitive debriefing

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						

症狀分數 (1, 2a, 3a, 4, 5a, 6, 7a) = _____

困擾分數 (2b, 3b, 5b, 7b) = _____

總分（症狀分數＋困擾分數）= _____

FIG 1. Chinese version of the pelvic pain and urgency/frequency symptom scale

involving five ketamine-associated cystitis patients and five healthy individuals expressing feedback to the questions, and (5) formulation of the finalised Chinese version of PUF scale (Fig 1). The test-retest reliability of the questionnaire was tested on health care workers with a negative history of ketamine use. The translated Chinese version of the questionnaire was filled in by them twice with a 2-week interval and the test-retest reliability was analysed. Further analysis of results from questionnaires filled in by both health care workers and patients with street-ketamine–associated LUTS attending our institution before January 2009 was then carried out. This entailed split-half reliability and internal consistency by Cronbach's alpha, which aimed to evaluate the construct validity of the questionnaire. The

discriminatory ability of the questionnaire was then evaluated by the Mann-Whitney U test of the scores of the healthy individuals and the patients.

Patient assessment

In Princess Margaret Hospital, a special 'ketamine clinic' was launched dedicated to evaluating street-ketamine abusers presenting with LUTS from February 2009 to May 2010. All the patients attended the clinic were recruited into the study. Exclusion criteria were LUTS before starting ketamine use, other known causes of LUTS (bacterial cystitis with positive urine culture), use of urological/neurological medications like anti-cholinergic or antipsychotic medications, and neurological disorders that might result in voiding dysfunction and recent instrumentation of the urinary tract.

Data on the duration and amount of ketamine abuse, monthly expenditure on ketamine, LUTS (in terms of frequency, nocturia, urgency, dysuria, and haematuria according to the 2002 International Continence Society definition) were prospectively collected. Each patient also completed the PUF symptom scale questionnaire during every clinic visit. Investigations including blood tests (routine renal and liver function tests), urine tests (culture and toxicology), renal ultrasonography, flexible cystoscopy, and video urodynamic study were performed. All patients were assessed, counselled, and followed up by urologists from the centre.

Data analyses

Mean PUF scores of patients with or without certain symptoms were compared. A correlation analysis of quantitative parameters and PUF scores was performed. Significance was defined at a P value of less than 0.05. Mean PUF scores of patients with positive investigation results were compared to those without such results. Investigation results of patients with different PUF total scores were compared and analysed to identify the best cut-off value. Correlation analysis between bladder capacity and PUF score was also performed. Patients with ketamine abstinence on follow-up were selected and the change in their PUF scores with time was reviewed. All the data analyses were performed with the Statistical Package for the Social Sciences (Windows version 17.0; SPSS Inc, Chicago [IL], US), except the use of MedCalc (version 11.6.1.0; MedCalc software, Mariakerke, Belgium) for identifying the best cut-off PUF score.

Results

Validation of the Chinese version of pelvic pain and urgency/frequency scale score

Twenty health care workers with a negative history

TABLE 1. (a) Reliability and (b) internal consistency of the pelvic pain and urgency/frequency questionnaire

(a) Reliability statistics

Item	Data
Cronbach's alpha	
Part 1	
Value	0.936
No. of items	6*
Part 2	
Value	0.966
No. of items	6†
Total N of items	12
Correlation between forms	0.949
Spearman-Brown coefficient	
Equal length	0.974
Unequal length	0.974
Guttman split-half coefficient	0.972

* The items are: Q1, Q2a, Q2b, Q3a, Q3b, Q4
† The items are: Q5a, Q5b, Q6, Q7a, Q7b, Q8

(b) Item-total statistics

	Scale mean if item deleted	Scale variance if item deleted	Corrected item-total correlation	Squared multiple correlation	Cronbach's alpha if item deleted
Q1	12.3939	154.871	0.849	0.872	0.972
Q2a	11.7576	146.502	0.905	0.899	0.972
Q2b	12.3030	158.030	0.888	0.928	0.971
Q3a	13.0303	170.218	0.680	0.658	0.975
Q3b	12.7879	162.860	0.817	0.871	0.973
Q4	12.5758	161.127	0.897	0.913	0.971
Q5a	12.4545	157.631	0.964	0.959	0.969
Q5b	12.5152	157.945	0.948	0.968	0.969
Q6	12.5455	160.631	0.926	0.936	0.970
Q7a	12.2121	162.047	0.855	0.878	0.972
Q7b	12.3636	158.114	0.929	0.962	0.970
Q8	12.7273	172.267	0.764	0.811	0.974

of ketamine use and 15 patients with street-ketamine associated LUTS filled out the questionnaire. Of the former 20 individuals, 18 (9 males and 9 females) completed the questionnaire the second time 2 weeks after the initial assessment. Their mean age was 24 (range, 19-31) years. The mean PUF (± standard deviation [SD]) total score was 2.1 ± 2.4 (mean symptom score, 1.6 ± 1.5; mean bother score, 0.6 ± 2.0). Regarding the patients, eight were male and seven were female. Their mean age was 26 (range, 18-31) years. Their mean PUF (± SD) total score was 27.4 ± 7.3 (mean symptom score, 18.3 ± 4.7; mean bother score, 9.1 ± 2.8).

The test-retest reliability coefficients for symptom score, bother score, and total score were 0.753, 0.764, and 0.755, respectively (P<0.001 for all three). The equal-length Spearman-Brown coefficient for split-test reliability was 0.974, while the Guttman coefficient was 0.972. The overall Cronbach's alpha was 0.974. The Cronbach's alpha for any one of the questions being deleted are shown in Table 1. The Mann-Whitney U test revealed significant differences between scores of the 20 health care workers and 15 street-ketamine abusers (U=1.50, Z= –4.96 for symptom score: U=0, Z= –4.92 for bother score: U=0, Z= –4.94 for total score; P<0.001 for all three). The respective mean (± SD) score differences were 12.3 ± 0.8, 7.2 ± 0.5, and 19.5 ± 1.2.

Assessment results

Fifty-four street ketamine abusers attended the clinic during the study period. Altogether four patients were excluded: two had LUTS before abusing ketamine, one had psychiatric illness with active use of anti-psychotic medications, while the other had a history of childhood meningitis without definitive LUTS. As a result, 50 patients (20 males and 30 females) with a mean age of 24 (range, 14-48) years were eligible and included for analysis.

The mean (± SD) duration of ketamine abuse was 4.7 ± 2.8 years. The mean monthly amount spent on ketamine abuse was HK$5006 (range, $200-21 000). Common presenting LUTS included: urgency (46 patients, 92%), frequency (42 patients, 84%), nocturia (44 patients, 88%), dysuria (43 patients, 86%), and haematuria (34 patients, 68%). The mean (± SD) presenting PUF total score was 21.4 ± 7.5 and the corresponding symptom and bother scores were 13.6 ± 5.1 and 7.7 ± 3.0, respectively.

The PUF score correlated well with the presence/absence of each individual LUTS component: urgency (mean PUF, 22.5 ± 7.3 vs 15.1 ± 5.5; P=0.002), frequency (mean PUF, 23.8 ± 7.4 vs 17.3 ± 5.2; P=0.009), nocturia (mean PUF, 22.4 ± 7.5 vs 14.0 ± 1.4, P<0.001), dysuria (mean PUF, 22.7 ± 7.0 vs 13.3 ± 6.2; P=0.002), and haematuria (mean PUF, 24.8 ± 7.2 vs 16.2 ± 5.6; P<0.001) [Fig 2]. Quantitatively, the number

of day-time voids (frequency episodes) was shown to correlate with symptom score (R=0.475, P=0.001) and total score (R=0.408, P=0.004), while the number of nocturia episodes was correlated with all three: symptom, bother, and total scores (R=0.651, 0.557, and 0.669, respectively; all P<0.001). The correlations between PUF total score and the amount of ketamine consumption or duration of abuse were not statistically significant (R=0.17, P=0.909 and R=0.234, P=0.239, respectively).

Of the 50 participants, 42 (84%) underwent flexible cystoscopy, 31 (62%) underwent urodynamic study, and 43 (86%) had renal ultrasonography. In all, 30/42 (71%) of the patients had cystitis revealed by cystoscopy, 10/31 (32%) had detrusor overactivity, 3/31 (10%) had vesico-ureteric reflux, 10/31 (32%) had poor bladder compliance, and 10/43 (23%) had hydronephrosis (8 unilateral and 2 bilateral).

Higher mean PUF total scores were noted in patients with positive cystoscopic, urodynamic and ultrasonographic investigation results, namely cystitis changes on flexible cystoscopy (mean PUF, 24.0 ± 6.4 vs 18.6 ± 7.4; P=0.024), detrusor overactivity (mean PUF, 25.3 ± 4.9 vs 19.4 ± 7.8; P=0.034), vesico-ureteric reflux (mean PUF, 30.0 ± 5.6 vs 20.3 ± 7.1, P=0.029), poor bladder compliance (mean PUF, 27.2 ± 5.0 vs 18.6 ± 6.9; P=0.001), and hydronephrosis (mean PUF, bilateral 30.0 ± 7.1 vs unilateral 22.5 ± 4.1 vs negative 20.6 ± 8.0; P=0.018) [Fig 3]. Biochemically, only four patients had mildly deranged serum creatinine levels (range, 105-118 µmol/L; upper limit normal, 100 µmol/L).

With a PUF total score of 14 or above, patients started to develop cystitis changes on flexible cystoscopy. Changes indicative of cystitis increased
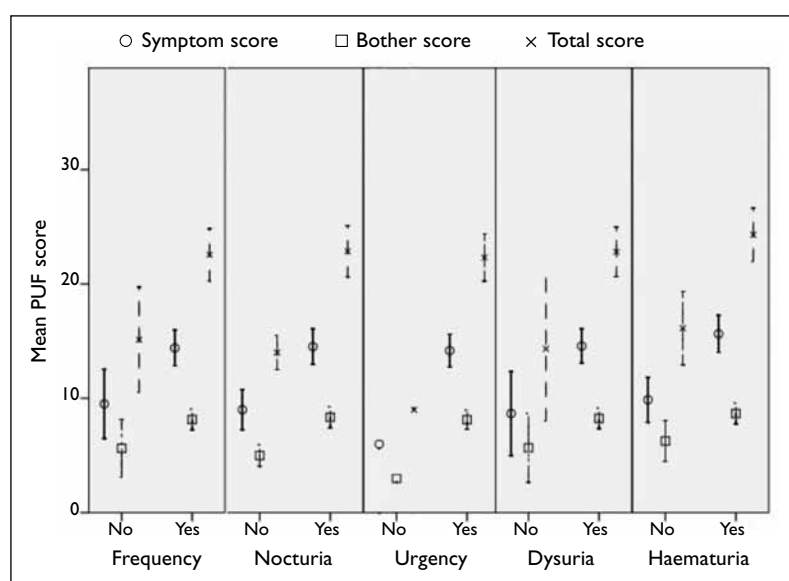

FIG 2. Mean pelvic pain and urgency/frequency (PUF) score in relation to specific lower urinary tract symptom component

TABLE 2. Sensitivity, specificity, positive likelihood ratios, negative likelihood ratios, positive predictive values, and negative predictive values when using different pelvic pain and urgency/frequency total score as cut-off in the detection of the presence of urodynamic or radiological upper urinary tract abnormalities[*]

Criterion	Sensitivity	95% CI	Specificity	95% CI	+LR	95% CI	-LR	95% CI	+PV	95% CI	-PV	95% CI
>15	100.00	80.5-100.0	33.33	18.0-51.8	1.50	0.9-2.4	0.00	0.0-0.0	43.6	27.8 - 60.4	100.0	69.2-100.0
>16	100.00	80.5-100.0	42.42	25.5-60.8	1.74	1.2-2.6	0.00	0.0-0.0	47.2	30.4 - 64.5	100.0	75.3-100.0
>17	94.12	71.3-99.9	51.52	33.5-69.2	1.94	1.4-2.8	0.11	0.02-0.8	50.0	31.9 - 68.1	94.4	72.7-99.9
>18	94.12	71.3-99.9	54.55	36.4-71.9	2.07	1.5-2.9	0.11	0.02-0.7	51.6	33.1 - 69.8	94.7	74.0-99.9
>19	82.35	56.6-96.2	60.61	42.1-77.1	2.09	1.5-3.0	0.29	0.10-0.9	51.9	31.9 - 71.3	87.0	66.4-97.2
>20	70.59	44.0-89.7	63.64	45.1-79.6	1.94	1.3-2.9	0.46	0.2-1.1	50.0	29.1 - 70.9	80.8	60.6-93.4
>21	64.71	38.3-85.8	69.70	51.3-84.4	2.14	1.4-3.2	0.51	0.2-1.2	52.4	29.8 - 74.3	79.3	60.3-92.0
>23	58.82	32.9-81.6	69.70	51.3-84.4	1.94	1.2-3.1	0.59	0.3-1.3	50.0	26.6 - 73.4	76.7	57.7-90.1

* CI denotes confidence interval, +LR positive likelihood ratio, -LR negative likelihood ratio, +PV positive predictive value, and -PV negative predictive value
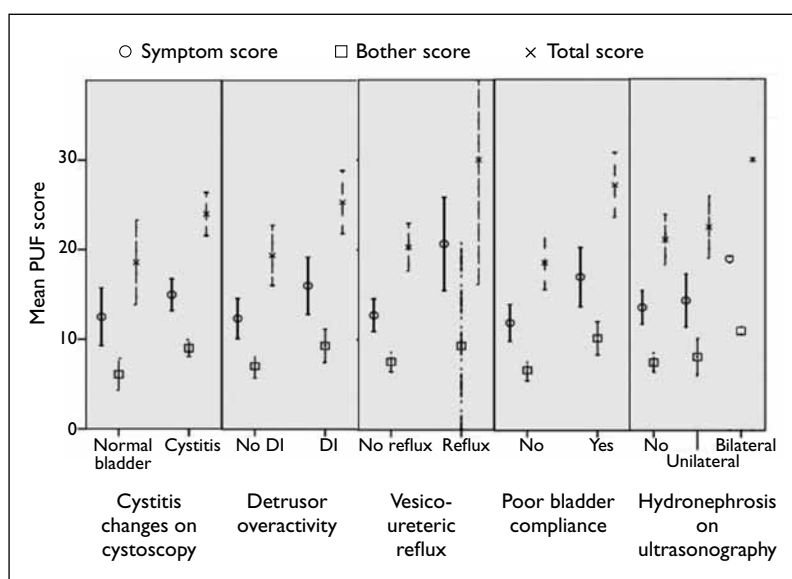

FIG 3. Mean pelvic pain and urgency/frequency (PUF) score and investigation results
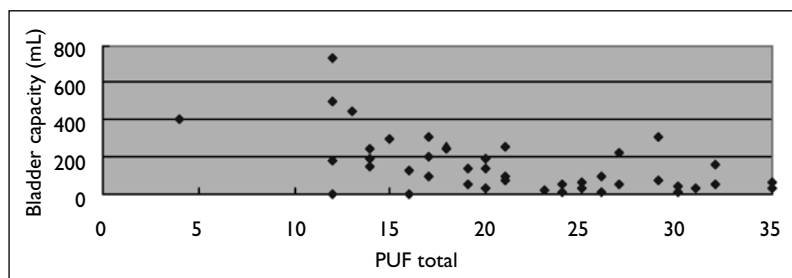DI denotes detrusor instability

FIG 4. Scatter chart of bladder capacity against pelvic pain and urgency/frequency (PUF) total score

with increasing PUF total score. None of the patients with PUF total scores of 16 or below had detrusor instability, vesico-ureteric reflux, poor bladder compliance, or hydronephrosis. With a higher PUF total score, the prevalence of detrusor instability, vesico-ureteric reflux, poor bladder compliance, and hydronephrosis increased. Receiver operating characteristics (ROC) curve analysis was performed. The area under the ROC curve was 0.723 (95% confidence interval, 0.578-0.840; P=0.0017) for using a PUF score to detect the presence of any urodynamic or radiological upper urinary tract abnormalities. Table 2 summarises the sensitivity, specificity, positive likelihood ratios, negative likelihood ratios, positive predictive values, and negative predictive values for assessing urodynamic abnormalities and upper urinary tract damage when using different PUF total scores as the cut-off.

A higher PUF score was associated with smaller bladder capacity (correlation= –0.497, P=0.001; Fig 4).

Of the 50 patients, 24 attended one or more follow-up and 18 out of these patients had PUF scores documented during follow-up. Only those who stopped the medications prescribed (by self or by doctor) for symptomatic control were included in the analysis. Only nine patients were available for analysis (three were active ketamine abusers and six had quit the habit). The mean (± SD) abstinence period was 24 ± 12 months for the six patients who had quit ketamine. After stopping medications for symptomatic control, the post-treatment mean change in PUF total score in the abstinence group was -4.33 (range, -16 to +3), and mean change among those who were still abusing ketamine was +3.33 (range, +1 to +5).

Discussion

Ketamine abuse has been well reported by the Narcotics Division of the Hong Kong SAR Government. From 2007 to 2010, it was the most common type of drug abused by persons aged 21 years or under and the second most common among all ages (next to heroin). Local urologists and family physicians were involved in managing and treating ketamine abusers presenting with

urological symptoms. While there had been no standardised assessment tool for this clinical entity, in 2007 we started using the PUF symptom scale in our patients and since then attained our objective, namely to obtain clinical information on the severity of urological sequelae in abusers. As investigations like flexible cystoscopy and urodynamic study are invasive and not readily accepted by ketamine abusers, a non-invasive diagnostic tool that can truly reflect the symptomatology of these patients is needed. An ideal scoring system should also predict the outcome of invasive investigations and help in counselling patients before they consent to those investigations. As in the entity of interstitial cystitis, Kushner and Moldwin[20] revealed that questionnaires do not demonstrate sufficient specificity to serve as sole diagnostic indicators, but they can be used to screen patients with urinary tract symptoms to identify those who should be further examined or followed up if they had already been diagnosed.

Different assessment tools for interstitial cystitis have been considered. The NIDDK criteria for interstitial cystitis were established in 1987. They were intended to be used as a guideline for research.[14] The criteria also involved invasive procedures, were purposely designed to be restrictive, and therefore were not widely applicable.[23] While there were several other diagnostic tools for interstitial cystitis, including the UWI and the OSI,[15] Parsons et al[18] proposed the PUF scale as a non-invasive and accurate diagnostic tool in the assessment of patients with interstitial cystitis. A PUF score of 15 or higher was associated with an 84% chance of a positive with the intravesical potassium sensitivity test.[24]

Among the Chinese-speaking communities including those in mainland China and Taiwan, the Chinese version of PUF questionnaire was translated for individual use only, and no formal validation has been reported in the western literature. We therefore translated and validated the questionnaire locally, and tested its linguistic and cultural suitability in Hong Kong users. The test-retest reliability was demonstrated based on 18 pairs of PUF scores completed 2 weeks apart by healthy individuals, which resulted in a reliability coefficient of 0.755. Bias by memory of questionnaire answers was reduced by the 2-week interval between filling of the two questionnaires. As only healthy subjects were used for analysing test-retest reliability, its usefulness cannot be taken to reflect the full range of the scores. A more appropriate way of testing the test-retest reliability would be to do so in patients with street-ketamine–associated LUTS, which was not achieved because of the high default rate of the patients. For the construct validity of the questionnaire, the split-half reliability and the internal consistency were good. The Mann-Whitney U test for the scores between healthy individuals and ketamine abusers confirmed the good discriminatory ability of the questionnaire in patients with different severity of LUTS.

Our results demonstrated that the PUF score related well to symptom severity, both qualitatively (presence of frequency, nocturia urgency, dysuria, and haematuria) and quantitatively (number of day-time voids and number of nocturia events). It was closely related to investigation outcomes in all aspects: endoscopically, urodynamically and radiologically, and as a tool for assessing urological sequelae in patients with ketamine-induced cystitis. The sequence of progressive urodynamic changes with increasing PUF scores may provide hints to the cause of upper urinary tract damage, as it is suggested that the lower urinary tract is primarily affected before the upper tracts, which results from a small, shrunken bladder with time.[7] Further studies to determine the actual pathophysiology of ketamine-induced cystitis are required. The persons performing the cystoscopic, radiological, and urodynamic investigations were not blinded to the history of ketamine use, LUTS and PUF score, which may have caused possible bias.

The cut-off value of 17 is suggestive of more severe disease status. A total PUF score of higher than 16 was associated with a significantly higher rate of urological sequelae: endoscopically confirmed cystitis (83% vs 47%), detrusor instability (48% vs 0%), vesico-ureteric reflux (14% vs 0%), poor bladder compliance (48% vs 0%), and hydronephrosis (37% vs 0%). This cut-off had a sensitivity of 100%, specificity of 42%, positive predictive value of 47%, and negative predictive value of 100% in assessing the presence of any urodynamic abnormalities and upper tract damage in patients with ketamine-induced cystitis. This cut-off value may spare patients with lower PUF scores from invasive investigations and those with higher scores may warrant more thorough investigation.

Our study failed to demonstrate any correlation of PUF score and the serum creatinine level as a result of prolonged abuse or progression of the disease. This was probably due to the small number of patients with renal impairment in our group of patients. The highest serum creatinine level among the recruited patients was 118 µmol/L only. The predictability of the PUF score for biochemical renal impairment is uncertain.

The frequency, amount, and monthly spending on ketamine did not show any significant correlation with PUF scores. This could be due to the difficulty in quantifying the actual amount of ketamine being consumed. For most of the patients, the frequency of ketamine consumption was irregular and the amount consumed each time varied. Furthermore, many abusers shared ketamine between friends, so

the analysis based on monthly spending on ketamine may be inaccurate. Besides, the street-ketamine powder obtained by abusers varied as to the degree of its purity. There is also the possibility of different susceptibility to street-ketamine metabolism in different abusers.

Abstinence from ketamine is thought to be associated with improved PUF scores but serial follow-up of a larger number of patients is needed for confirmation. Due to the high default rate in the current study, we failed to obtain a large cohort of ketamine abusers who abstained. The social and psychological complexity of ketamine abusers rendered them difficult to follow-up. Only nine patients without medical intervention were available to evaluate this aspect of the study. Our limited results nevertheless showed a different trend for mean changes in PUF score in the abstinence group (-4.33) and the continuously abusing group (+3.33). This suggests reversibility of LUTS with abstinence and may motivate abusers to stop further use of ketamine. More concrete proof of recovery is required to document PUF score improvements together with follow-up urodynamic studies on patients with ketamine abstinence.

Conclusion

The Chinese version of PUF questionnaire is reliable and has good discriminatory ability for assessment in patients with street-ketamine–associated LUTS. The PUF score correlates well with symptom severity as well as endoscopic, urodynamic, and radiological abnormalities in patients with ketamine-induced cystitis. A cut-off PUF total score of 17 or more may suggest more serious urological sequelae from ketamine abuse. Abstinence from ketamine appears to help reduce urinary tract symptoms, but the reversibility of the urinary tract damage is yet to be evaluated.

References

1. Peck TE, Hill SA, Williams M. Pharmacology for anaesthesia and intensive care. 3rd ed. Cambridge: Cambridge University Press; 2008: 111.
2. Ivani G, Vercellino C, Tonetti F. Ketamine: a new look to an old drug. Minerva Anestesiol 2003;69:468-71.
3. Narcotics Division. Report on a study on the cognitive impairment and other harmful effects caused by ketamine. Hong Kong: Narcotics Division, Security Bureau, HKSAR Government; 2005.
4. United Nations Office on Drugs and Crime (UNODC). Global amphetamine-type stimulants assessment report. 2008.
5. Shahani R, Streutker C, Dickson B, Stewart RJ. Ketamine-associated ulcerative cystitis: a new clinical entity. Urology 2007;69:810-2.
6. Chu PS, Kwok SC, Lam KM, et al. 'Street ketamine'–associated bladder dysfunction: a report of 10 cases. Hong Kong Med J 2007;13:311-3.
7. 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.
8. Cottrell A, Warren K, Ayres R, Weinstock R, Kumar V, Gillatt D. The destruction of the lower urinary tract by ketamine abuse: a new syndrome? BJU Int 2008;102:1178-9.
9. Huang YC, Jeng CM, Cheng TC, et al. Ketamine-associated ulcerative cystitis. Tzu Chi Med J 2008;20:144-6.
10. 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.
11. 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.
12. Ng SH, Tse ML, Ng HW, Lau FL. Emergency department presentation of ketamine abusers in Hong Kong: a review of 233 cases. Hong Kong Med J 2010;16:6-11.
13. Ho CC, Pezhman H, Praveen S, et al. Ketamine-associated ulcerative cystitis: a case report and literature review. Malays J Med Sci 2010;17:61-5.
14. Chu PS, Ma WK, Yu C, et al. Destruction of the urinary tract by ketamine abuse: Hong Kong local experience. Surg Pract 2010;14:44-8.
15. Ma WK, Chu PS, Wong S, et al. Street-ketamine associated bladder dysfunction and cystitis: pathological review. Indian J Urol 2008;24 Suppl 2:210.
16. Gillenwater JY, Wein AJ. Summary of the National Institute of Arthritis, Diabetes, Digestive and Kidney Diseases Workshop on Interstitial Cystitis, National Institutes of Health, Bethesda, Maryland, August 28-29, 1987. J Urol 1988;140:203-6.
17. O'Leary MP, Sant GR, Fowler FJ Jr, Whitmore KE, Spolarich-Kroll J. The interstitial cystitis symptom index and problem index. Urology 1997;49(5A Suppl):58-63.
18. Parsons CL, Stanford EJ, Kahn BS, et al. Tools for diagnosis and treatment. Female Patient 2002;(Suppl):12-7.
19. Rosenberg MT, Hazzard M. Prevalence of interstitial cystitis symptoms in women: a population based study in the primary care office. J Urol 2005;174:2231-4.
20. Kushner L, Moldwin RM. Efficiency of questionnaires used to screen for interstitial cystitis. J Urol 2006;176:587-92.
21. Parsons CL. Interstitial cystitis: epidemiology and clinical presentation. Clin Obstet Gynecol 2002;45:242-9.
22. Son HC, Jung YJ, Chang JS, et al. Translation and linguistic validation of the Korean version of the pelvic pain and urgency/frequency patient symptom scale. Int Neurourol J 2010;14:112-21.
23. Hanno PM, Landis JR, Matthews-Cook Y, Kusek J, Nyberg L Jr. The diagnosis of interstitial cystitis revisited: lessons learned from the National Institutes of Health Interstitial Cystitis Database study. J Urol 1999;161:553-7.
24. Parsons CL, Dell J, Stanford EJ, et al. Increased prevalence of interstitial cystitis: previously unrecognized urologic and gynecologic cases identified using a new symptom questionnaire and intravesical potassium sensitivity. Urology 2002;60:573-8.