Final Report for Beat Drugs Fund Project (Updated April 2012)

Research Title:

Clinical profile of lower urinary tract changes and urinary marker measurements in young adults using ketamine

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Executive Summary:

Ketamine abuse is becoming an increasing concern worldwide. Besides the neuro-cognitive complications, there are also reports on the associated voiding dysfunction in ketamine-abusers. The urinary tract problems range from irritative bladder symptoms to structural changes.

With the support from the Beat Drug Fund programme, we have improved our fast-track clinic service with ultrasound assessment to assess the effect of ketamine abuse on the urinary system. Also we have explored the possible structural and functional changes, as well as urinary marker changes, in these ketamine abusers. In this study, we have analysed the results from 47 subjects. We found that it is difficult to quantify the amount of ketamine abuse and there were also a wide variety of symptoms in these patients. We need to develop better assessment tools to assess the extent of problems in these patients. We also noted that there were changes in the urinary markers NGF and PGE2 in patients with ketamine abuse might be related to the duration of ketamine abuse. Also there were a weak correlation of the urine marker level and the symptom severity. This might give insight into the underlying pathophysiology of the problems. However, further studies are needed to confirm this initial observation.

We also take this opportunity to update the frontline staff, including nurses, urology specialists and family physicians on this clinical problem. Prompt and proper referral and management of ketamine abusers with urinary tract symptoms may also serve a good contact point to these patients, and maybe able to allow an early intervention and abstinence of the drug abuse.

青少年吸食氯胺酮已越來越被全球所關注。除了已知的神經認知損害外，也有醫療報告有關這些氯胺酮吸毒者的排尿功能障礙，包括由刺激性膀胱症狀以至泌尿系統結構性的變化。

承蒙禁毒基金的支持，我們引入了超聲檢查以改善我們的門診服務，這超音波評估可以幫助評估氯胺酮吸毒者的泌尿系統變化。此外，在這項研究中我們分別對47例作出分析，我們發現很難量化氯胺酮的用量，同時患者也有各種各樣的症狀。因此我們須要發展一套更完善的評估工具為這類別的案例作全面的評估。再者，我們注意到在這群濫藥病人中，他們的尿液中的生化指標 NGF 和 PGE2與氯胺酮使用的時間有關。此外尿液標記水平和症狀嚴重程度呈弱相關。這新發現也許可啟發病理生理的發展。然而，還需要進一步研究來證實這初步觀察。

在這個項目中我們也提供最新情況給前線人員包括護士、家庭醫生及泌尿科醫生。一個快捷及有效的轉介和治療系統，不僅能夠幫助這些吸食氯胺酮者的排尿症狀，也可以提供一個與氯胺酮吸毒者的接觸點，令我們能夠及早介入以致幫助他們盡早戒除及康復!

Background

The recreational usage of ketamine amongst young adults is a rising social and health problem worldwide. Since the early report of the possible association of ketamine usage and lower urinary tract symptom (LUTS) in 2007, [Chu 2007] [Chu 2008] ketamine-induced voiding dysfunction (KIVD) has become an established condition. KIVD is characterized by the association of predominant irritative LUTS in patients with ketamine usage. They may also suffer from on and off gross haematuria. In severe cases, there may also have upper tract dilatation and renal impairment. Despite the increase in awareness and understanding of the condition, there are still many uncertain areas, such as the underlying pathophysiology of the problem, the sequential changes of the lower urinary tract during the progress of the condition.

Most of the current studies were based on clinic parameters and investigations, such as cystoscopy and urodynamic study. However, the invasiveness of some of these tests may affect the compliance of patients for investigations and also limit the use in follow-up assessment of the disease progress. Therefore, developing non-invasive investigations, such as ultrasonography and possible urine markers may help in the management of these patients.

Moreover, the change in urine markers in patients may also provide us some hints on the underlying pathophysiology of the condition, such as inflammation-related, nerve damage- related, etc. Therefore, urinary marker changes become an important area for researches.

In this project we would like to assess the clinical profile of the lower urinary tract in ketamine users by non-invasive urological investigations and also the role of some potential urine markers in the diagnosis of the condition. The correlation of the results of investigations (including urine markers) with the amount of ketamine consumption and LUTS will also be assessed.

Planning and set up of the programme

Since April 2010, patients referred to the urological clinic for ketamine related voiding dysfunction would be assessed in a special fast track clinic at the Lithotripsy and Uro-investigation Centre (LUC) of our unit. During each consultation, patients would be assessed by urologists for their urological problem. Also information about their history of substance abuse would be collected. A standardized proforma would be used to collect necessary information for subsequent analysis. Self-administrative questionnaires (Pelvic pain-urgency-frequency score, PUF score) would also be done for the assessment of symptom severity and also for subsequent follow-up. Basic investigations, including urine for culture and microscopy, blood for renal and liver function, etc, would be performed. Besides performing uroflowmetry to assess the voiding status, patients would be referred to our radiologists for ultrasound assessment, including (1) the upper tract condition, such as presence of hydronephrosis etc, and (2) the bladder condition – including the bladder wall thickness, maximum capacity, etc.

With the support from the Beat Drug Fund programme, we have modified our clinic setting in order to improve the management of the patients. Ultrasound machine was set-up in our clinic to facilitate the screening of the patients' urinary tract, which would aid early identification of patients with severe damaged urinary system. This could overcome the problem of frequent default for the ultrasound examination. Additional 10 cc spot urine would also be collected from each patient for measurement of urine markers (details referred to the Material and Method section).

A series of lectures were organized in December 2010 for the education of urologists and also nursing staff about the latest management of ketamine cystitis, and this also serves as a platform for announcing the commencement of the new programme. The series of lectures for urologists were presented on 18th December 2010 in the ***Urology Symposium 2010*** organized by The Chinese University of Hong Kong. The topics included "Ketamine cystitis – a new disease entity?" "Multidisciplinary approach to ketamine abuse / ketamine cystitis" and "Management of ketamine cystitis". (Appendix 1) Other lectures were also presented in ***Nursing Workshop on Comprehensive management of bladder dysfunction*** on 19th December 2010. The topics included "Ketamine uropathy: a new epidemic?"

“Ketamine abuse – the role of a urology nurse” and “ketamine – psychiatric aspects”. (Appendix 2) The attendance for the Urology symposium 2010 and the Nursing workshop were 219 and 134 respectively.

In the subsequent section, we will report on the research project “Clinical profile of lower urinary tract changes and urinary marker measurements in young adults using ketamine”

Study Objective:

- To determine the relative risk of dosage, frequency of ingestion and duration of ketamine use for changes in lower urinary tract (LUT) function
- To evaluate the utility of urinary markers to correlate with the degree of bladder changes

Material and Method:

All patients suffered ketamine related voiding dysfunction under our care would be recruited for this study. As mentioned in the previous section, during the initial consultation, a standardized data form would be used for collecting patients' information. The information collected would include the history of ketamine consumption, voiding symptoms, and previous treatment, etc. Self-administrative questionnaires (PUF score, score ranged from 0 to 35), uroflowmetry and ultrasound assessment would also be performed for assessing symptom severity and degree of urinary tract dysfunction. Besides the usual urine and blood test assessment, 10 cc of spot urine would be collected for subsequent markers evaluation.

Spot urine were first centrifuged at 3000g for 10 minutes at 4°C. A portion of the spot urine (3cc) would be used for creatinine level measurement. The rest of the supernatant was then separated into aliquots in 1.5mL tubes and stored in -80°C before use.

In our project, we have selected three markers, nerve growth factor (NGF), prostaglandin E2 (PGE2) and interleukin-18 (IL-18), for measurement. Nerve growth factor (NGF) is produced by bladder smooth muscle and urothelium. Increased NGF level is found in patients with inflammatory lower urinary tract conditions, like interstitial cystitis / painful bladder syndrome (a condition similar to KIVD). [Ochodnický 2011] [Liu 2010] Other associated conditions are overactive bladder and detrusor overactivity. Prostaglandin E2 (PGE2) is a cyto-protective eicosanoid, which inhibit apoptosis of epithelium. An increased level of urinary PGE2 is associated with urinary tract infection and overactive bladder. [Liu 2010] IL-18 is an inflammatory marker and is used for evaluating the severity of inflammation of urinary bladder.

The level of all the three markers were determined by ELISA test according to manufacturer's instructions (NGF: Emax® ImmunoAssay System, Promega Corporation, Madison, WI; PGE2: R&D Systems, Minneapolis, Minnesota; IL-18: Medical & Biological Laboratories Co. Ltd., Naka-ku Nagoya, Japan) The urinary marker levels will be corrected with the concurrent the urinary creatinine level. Due to some technical errors, some of the urine ELISA tests was found to have problem and only 12 samples were available for analysis in this part of study.

Spot urine samples from 12 normal subjects, with no history of ketamine usage, were collected as controls for our study. The result of urine markers changes will be compared between patients and normal subjects. In addition, the results from investigations will be correlated to the patients' history of ketamine usage and also the severity of symptoms and complications. All the data would be collected and analyzed by SPSS 18.0.

Results:

From December 2010 to November 2011, there were 47 patients recruited for the study (24 male and 23 female). (Table 1) The mean age of the patient was 26.4 years old (range 16 to 41). The mean duration of ketamine usage was 65.6 months (about 5 years) (range 3-144 months). At the time of assessment, 64.9% already started detoxification and the mean time of abstinence was 2.9 months (range from less than 1 month to 12 months).

The mean and median duration of urinary symptoms were 28.2 months and 24 months, respectively (less than 1 month to 96 months). The mean time lag between ketamine usage and onset of urinary symptoms was 39.3 months (range 1.5 to 126months). Except for one patient, all patients had nocturia and the mean number of voids per night was 4.4 times (range from 1-20). Seventy percent (33 patients) of patients also had urgency. Sixteen patients (34.0%) experienced haematuria and 20 patients (42.6%) had history of loin pain.

The mean PUF symptom score and PUF bother score were 12.5 (range 9-16) and 7.2 (5-9) respectively. The mean total PUF score was 19.7 (range 15 – 24)

From the uroflowmetry and bladder scan study, the mean bladder capacity was 118.8 cc (range 10 to 431 cc). Ultrasound study shown the mean bladder emptying efficiency was 92.5% (range 61-100%). Fourteen patients (36.2%) had hydronephrosis shown during ultrasound examination.

The mean spot urine level for IL-18, NGF and PEG2 were 168.12 pg/ mg Cr (0-1362.88), 3.80 pg/ mg Cr (0.08 to 18.13) and 3639.27 pg/ mg Cr (1163.01 – 13316.40) respectively.

The first objective of this study was to assess the relationship of the amount of ketamine abuse with the severity of urinary tract symptoms. Because of the diversity in dosage, frequency and duration of usage of ketamine and the recall bias, it was very difficult to accurately quantify the exposure of ketamine in each patient. Therefore, we try to correlate the duration of ketamine usage with the various parameters of the patients. In our sample, some patients had abstinence from ketamine for some time and we found that ketamine abstinence seemed to help to improve urinary symptoms. [Mak 2011] Therefore, in our analysis, two patients with abstinence greater than 6

months were excluded from the analysis. For the remaining 45 patients, the median duration of ketamine usage was about 54 months (about 5 years). These patients were further divided into two groups, ketamine usage more than 60 months (23 patients) and less than 60 months (22 patients). (Table 2) There was no statistical significant difference observed between the two groups regarding the severity of symptoms, ultrasound findings and urinary markers level.

Besides correlating the ketamine consumption with patients' clinical parameters, we also tried to correlate the patients' sex (male and female), age (using 25 year old as cut off to give two similar size groups) and co-ingestion habit (single drug user vs poly-drug user). (Table 3, 4 & 5) Except for significant lower PUF bother score and larger bladder capacity in male patients were observed, there was no significant different in the clinical parameters between different sex, age group and also single / multi-drug usage.

For the assessment of the role of urine markers in the management of ketamine cystitis, twelve normal subjects were recruited as control for the analysis. There was significantly less symptoms (as assessed by the PUF scores) when compared to the patients group ($p < 0.001$). The mean PUF Symptom score was 1.6 (0-5) vs 12.6 (5-22), PUF Bother Score was 0.6 (0-2) vs 7.2 (2-12) and the PUF total score was 2.2 (0-7) vs 19.8 (7-33). When combined with the urine levels of NGF and PEG2 of the test patients, there was a significant difference in NGF and PEG2 levels between the duration of exposure of ketamine (no vs less than 60 months vs more than 60 months). (Figure 1 and 2) By using independent-samples Kruskal-Wallis Test, the p value for urinary NGF level & duration of exposure and urinary PEG2 level & duration of exposure were 0.006 & 0.018 respectively. However, there was no difference observe for urinary IL-18 level.

Furthermore, we have also tried to correlate the symptom severity of the patients and the level of urinary markers. From our result, there was a statistically significant positive correlation between urine NGF level and PUF symptoms score ($r = 0.475$ with $p=0.019$, Spearman's correlation). Similarly, statistically significant positive correlation was found between urine PGE level and PUF symptoms score ($r = 0.644$ with $p=0.001$, Spearman's correlation). However, there was no correlation of the markers level with other symptoms and also ultrasound findings observed.

Discussion:

In this one-year study of patients suffering from KIVD, we observed certain features that may be important for the understanding and management of the condition.

From the information obtained from these patients, mean duration of ketamine consumption was about 5 years and the mean onset time for voiding symptoms was around 40 months (around 3.3 years). Therefore, the mean time lag between onset of symptom and assessment in our clinic was around 1.6 years. Certainly, some patients might have seeked medical advice prior to our consultation. However, if we could improve the public awareness and knowledge of the relationship of ketamine with voiding dysfunction, and also the possibility of reversing the disease progress by appropriate management, patients may seek medical advice earlier. This might also provide a chance for earlier intervention (including both urological management and detoxification) to the patients. This knowledge update could also be applied to other specialists (family physicians, urologists, etc), which might help to make an earlier diagnosis of the condition and provide appropriate management advice and necessary referral.

In this study, we have explored the possibility of using urine markers in the assessment of KIVD. From our results, two markers, NGF and PGE2, showed significant difference in their level among controls, patients that used ketamine < 5 years and patients that used ketamine ≥ 5 years. Also there was weak correlation of urinary levels of NGF and PGE2 with the total PUF score. Both of these markers had been used in the assessment of painful bladder syndrome / interstitial cystitis, a condition sharing some of the characteristics with KIVD. However, as the number of study subjects is relatively small, further studies maybe needed to verify our observations. These changes in urinary NGF and PGE2 levels might provide insights into the possible patho-physiology related to the development of KIVD. In future, further studies on the correlation of bladder biopsy result with the change in urine marker levels might give further information on the role of these markers in the condition and also their role in assessing the bladder conditions.

There were several limitations of our study. One of the main limitations is the small sample size (47 subjects, with 12 patients' urine sample analyzed), which may

affect the power of some of the statistical tests. Another problem in the quantification of the ketamine usage in our patients. From our data, the history and habit of ketamine consumption, including the frequency (from few times per days to few times per year) and dosage, the purity of ketamine, could be quite diversified and variable amongst the patients. Patients may consume different amount of ketamine over the years. Therefore, it was very difficult to quantify the amount of ketamine usage for analysis. Eventually, we only choose to use the duration of ketamine abuse for the correlation with some of the clinical parameters and also the urinary marker levels. In a similar study on the cross-sectional analysis of ketamine user, Mak *et al* used only the frequency of usage (times per week), duration of ketamine abuse and the duration of abstinence for correlation of symptoms. [Mak 2011] Therefore, better assessment tool or larger sample size would be needed to improve the quantification of ketamine consumption. Moreover, the performance of uroflowmetry might also be affected by various factors, such as whether the patient was in urge during the procedure, and the effect of voiding in a non-familiar environment, etc. Finally, there might also be recall bias due to the long history of ketamine abuse and other confounding factors, such as co-ingestion of other soft drugs and variable periods of abstinence of ketamine in the patients, which might all affect the analysis. Nevertheless, we believed our data still shown some important information, in particular the possible correlation of some urinary markers with the condition and would be helpful to guide future larger scale studies.

Conclusion:

From our study, we noticed that there was a wide spectrum of symptoms, uroflowmetry and ultrasound findings in patients suffered from ketamine induced voiding dysfunction (KIVD). Due to the limitation of small sample size, there was no correlation found between various patients' parameter and the clinical & ultrasound findings. On the other hand, there seems to have a trend of urine markers, NGF and PGE2, level with the exposure of ketamine in patients and normal subjects. Moreover, there were a weak correlation of the level of urine markers and the severity of urinary symptoms. Further studies maybe needed to characterize the role of these markers in the assessment of patients suffered KIVD and also their possible role in the pathogenesis of KIVD.

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Table 1 Patient's and clinical parameters for study subjects and control

	Ketamine users	Control	
	N=47	N=12	
Sex			
Male	24 (51.1%)	8 (66.7%)	
Female	23 (48.9%)	4 (33.3%)	
Age	Mean = 26.4 (SD = 5.4)	Mean = 21.2 (SD = 0.84)	
	Range: 16-41	Range: 21-23	
Duration of abuse (months)	Mean = 65.6 (SD = 35.7)	--	
	Range: 3-144		
No. of abstinence	30 (63.8%)	--	
Period of abstinence (months)	Mean = 2.9 (SD = 2.7)	--	
	Range: 0-12		
	Median = 2 [1.5-3.5]		
Onset of Urinary symptoms (months)	Mean = 28.2 (SD = 20.3)	--	
	Range 0-96		
	Median 24 [12-39]		
Loin pain	20 (42.6%)	--	
Hematuria	16 (34.0%)	--	
Nocturia	Mean = 4.4 (3.7)	--	
	Range: 0-20		
	Median = 3.5 [2 – 5.5]		
Difficulty in passing urine	29 (61.7%)	--	
Urgency	33 (70.2%)	--	
Dysuria	33 (70.2%)	--	
Incontinence	10 (21.3%)	--	
PUF symptoms score	Mean = 12.5 (SD = 4.4)	Mean = 1.6	<0.001

	Range: 5-22	Range: 0-5	
	Median = 12.5 [9 – 16]	Median = 1.5 [0 – 3]	
PUF bother score	Mean = 7.2 (SD = 2.8)	Mean = 0.6	<0.001
	Range: 2-12	Range: 0-2	
	Median = 8 [5 – 9]	Median = 0 [0 – 1]	
PUF total score	Mean = 19.7 (SD = 6.8)	Mean = 2.2	<0.001
	Range: 7-33	Range: 0-7	
	Median = 20 [15 – 24]	Median = 1.5 [0 – 4]	
Bladder capacity	Mean = 118.8 (SD = 99.6)	--	
	Range: 10-43		
	Median = 88 [54 – 152]		
Bladder thickening	32 (68.1%)	--	
Emptying efficiency	Mean = 92.5 (SD = 8.6)	--	
	Range: 61-10		
	Median = 95 [90.5–98.75]		
Bladder vol. and thickness indes	Mean = 25.8 (SD = 26.9)	--	
	Range: 0-106		
	Median = 17 [8 – 31]		
Hydronephrosis		--	
Unilateral	7 (14.9%)		
Bilateral	7 (14.9%)		
IL18	Mean = 168.12 (SD = 393.14)	Mean = 11.53 (9.88) (0-27.39)	0.713
	Range: 0-1362.88	8.95 [2.71 – 20.30]	
NGF	Mean = 3.80 (SD = 5.49)	Mean = 0.54 (SD = 1.13)	0.001
	Range: 0.08 – 18.13	Range: 0.0022 – 3.28	
PEG2	Mean = 3639.27 (SD = 3319.42)	Mean = 1575.46 (SD = 781.30)	0.004
	Range (1163.01–13316.4)	Range (760.37 – 3395.77)	

Table 2 The comparison of patient and clinical parameters for patients with ketamine abuse more than or less than 5 years

History of Ketamine abuse	Less than 5 years N=22	More than 5 years N=23	P-value
Hematuria	8 (36.4%)	7 (30.4%)	0.835
Nocturia	Mean =4.3 (SD = 4.5) Range (0-20) Median = 3 [2 – 4.38]	Mean = 4.6 (SD = 2.8) Range (1-10) Median = 4 [1.88 – 6.5]	0.259
PUF symptoms score	Mean = 12.6 (SD = 3.6) Range: 6-19 Median = 13.5 [10.5 – 15.25]	Mean = 12.6 (SD = 4.9) Range: 5-22 Median = 11.5 [9 – 16.25]	0.663
PUF bother score	Mean = 7.1 (SD = 2.5) Range: 2-11 Median = 8 [5 – 9]	Mean = 7.4 (SD = 3.0) Range: 2-12 Median = 7.5 [5 – 10]	0.776
PUF total score	Mean = 19.7 (SD = 5.8) Range: 8-29 Median = 21 [16 – 24.25]	Mean = 19.9 (SD = 7.4) Range: 7-33 Median = 19 [14.5 – 25]	0.814
Bladder capacity	Mean = 127.23 (SD = 102.95) Range: 10-375 Median =84.5[55–170.75]	Mean = 98.24 (SD = 72.63) Range: 18-279 Median = 88 [41 – 148.5]	0.411
Bladder thickening	17 (77.3%)	15 (65.2%)	0.492
Emptying efficiency	Mean = 91.45 (SD = 10.13) Range: 61-100 N = 5	Mean = 93.44 (SD = 6.67) Range: 75-100 N = 7	0.816
IL18	Mean = 294.10 (SD = 598.13) Range: 0.15 - 1362.88	Mean = 78.13 (SD = 148.91) Range: 0.00 – 404.65	0.368

NGF	Mean = 2.16 (SD = 3.14) Range: 0.08 – 7.57	Mean = 4.98 (SD = 6.70) Range: 0.46 – 18.13	0.167
PGE2	Mean = 2996.25 (SD = 1811.55) Range: 1786.79 – 6181.87	Mean = 4098.57 (4173.99) Range: 1163.01 – 13316.40	0.808

Table 3 Relationship of patient's sex and clinical parameters

	Female N=22	Male N=23	P-value
Age at attendance	25.7 （SD＝ 4.6) Range: 16-34	27.3 (SD = 6.1) Range: 19-41	0.353
Duration of abuse	74.5 (SD = 40.8) Range: 12-144 Median=60 [46.5 – 120]	60.0 (SD = 26.8) Range: 24-120 Median=54 [36 – 84]	0.269
No. of abstinence	12 (54.5%)	16 (69.6%)	0.299
Poly drug user	10 (45.5%)	12 (52.2%)	0.546
Hematuria	6 (27.3%)	9 (39.1%)	0.396
Nocturia	Mean = 5.3 (SD = 4.2) Range: 2-20 Median = 4 [2.75 – 6.38]	Mean = 3.53 (SD = 2.9) Range: 0-10 Median = 3 [1.38 – 5.13]	0.072
PUF symptoms score	13.5 (SD = 4.2) (7-21) Median = 13 [9.75 – 17]	11.64 (SD = 4.2) (5-22) Median = 11 [7.75 – 15]	0.179
PUF bother score	Mean = 8.3 (SD = 2.3) Range: 5-12 Median = 8 [6 – 10]	Mean = 6.2 (SD = 2.8) Range: 2-10 Median = 6 [4 - 9]	0.028
PUF total score	21.8 (5.9) (12-33) Median = 21 [18.75 – 26.5]	17.8 (6.7) (7-31) Median = 17 [12.5 – 24]	0.086
Bladder capacity	69.00 (SD = 37.35) Range: 18-158 Median = 56.4 [43.5 – 94.5]	157.98 (SD = 104.24) Range: 10-375 Median = 145.5 [74 – 237.5]	0.003
Bladder thickening	14 (63.6%)	18 (78.3%)	1.000

Emptying efficiency	90.97 (SD = 11.13) Range: 61-100 N = 9	93.53 (SD = 5.93) Range: 79-100 N = 3	1.000
IL18	219.79 (SD = 447.65) Range: 0.00 - 1362.88	13.12 (SD = 21.45) Range: 0.00 – 37.87	0.482
NGF	4.81 (SD = 6.07) Range: 0.08 – 18.13	0.78 (SD = 0.41) Range: 0.47 – 1.25	0.864
PGE2	2717.56 (SD = 1534.78) Range: 1714.63 – 6181.87	6404.29 (SD = 5990.76) Range: 2710.95 – 13316.40	0.145

Table 4 Relationship of patient's age and clinical parameters

	Age <=25 N=24	Age >25 N=21	P-value
Gender			0.873
Female	12(50%)	10(47.6%)	
Male	12(50%)	11(52.4%)	
Duration of abuse	Mean = 64.3 (SD = 33.4) Range = 18-144 Median=57 [42 – 84]	Mean = 70.3 (SD = 36.7) Range = 12-132 Median = 60 [39 – 111]	0.615
No. of abstinence	12 (50%)	16 (76.2%)	0.071
Poly drug user	14 (58.3%)	8 (38.1%)	0.131
Hematuria	10 (41.7%)	5 (23.8%)	0.205
Nocturia	Mean = 3.88 (SD = 2.713) Range: 1-10 Median = 3.5 [1.5 – 5]	Mean = 4.9 (SD = 4.398) Range: 0-20 Median = 3.5 [2 – 6.5]	0.622
PUF symptoms score	Mean = 11.9 (4.2) (5-19) Median = 12 Range = 8 – 15	Mean = 13.3 (SD = 4.3) (7-22) Median = 13 Range = 10.5 – 16	0.383
PUF bother score	Mean = 7.0 (SD = 2.5) Range = 2-11 Median = 7 [5 – 9]	Mean = 7.5 (3.0) Range = 2-12 Median = 8 [5 – 9.5]	0.492
PUF total score	Mean = 18.9 (SD = 6.3) Range = 7-29 Median = 20 [13 – 24]	Mean = 20.8 (SD = 6.9) Range = 9-33 Median = 20 [16.5 – 25]	0.444

Bladder capacity	Mean = 96.83 (SD = 75.17) Range = 10-279 Median = 72 [50.5 – 148.5]	Mean = 128.71 (SD = 100.54) Range = 18-375 Median = 104.5 [49.5 – 170.75]	0.334
Bladder thickening	17 (70.8%)	15 (71.4%)	0.932
Emptying efficiency	Mean = 90.78 (SD = 10.73) Range = 61-100 N = 8	Mean = 94.03 (5.59) Range = 80-100 N = 4	0.636
IL18	Mean = 243.59 (SD = 472.09) Range = 0.00 - 1362.88	Mean = 17.18 (SD = 33.38) Range = 0.00 – 67.25	0.283
NGF	Mean = 5.42 (SD = 6.19) Range = 0.42 – 18.13	Mean = 0.57 (SD = 0.49) Range = 0.08 – 1.25	0.154
PGE2	Mean = 2727.87 (SD = 1640.39) Range: 1163.01 – 6181.87	Mean = 5462.08 (SD = 5241.89) Range: 2631.46 – 13316.40	0.154

Table 5 Relationship of patient's drug usage history (single or poly drug usage) and clinical parameters (1 case's information was missed)

	Single drug user	Multidrug user	p-value
	N=22	N=22	
Sex			
Male	10 (45.5%)	12 (54.5%)	0.546
Female	12 (54.5%)	10(45.5%)	
Age	Mean 26.4 (SD = 5.4)	Mean 21.2 (SD = 0.84)	
	Range: 16-41	Range: 21-23	0.032
Duration of abuse (months)	61.1 (SD = 37.1)	72.3 (SD = 32.7)	0.117
	Range: 12-132	Range: 18-144	
	Median 48 [30-93]	Median 60 [54-93]	
Onset of Urinary symptoms (months)	22.8 (SD = 15.1)	34.1 (SD = 23.7)	0.103
	Range: 4-54	Range: 0-96	
	Median 24 [10.5-36]	Median 30 [16.5-48]	
Loin pain	10 (45.5%)	9 (40.9%)	0.761
Hematuria	8 (36.4%)	7 (31.8%)	0.835
PUF symptoms score	13.4 (SD = 4.6)	11.8 (SD = 3.8)	0.220
	Range: 7-22	Range: 5-19	
	Median = 13 [9.75 – 16.25]	Median = 12 [8.75 – 14.5]	
PUF bother score	7.6 (SD = 2.9)	6.8 (SD = 2.6)	0.328
	Range: 2-12	Range: 2-10	
	Median = 8 [5 – 10]	Median = 7.5 [5 – 9]	
PUF total score	21 (SD = 7.0)	18.6 (SD = 6.0)	0.228
	Range = 9-33	Range: 7-28	
	Median = 20.5 [15.75 – 26.5]	Median = 19 [14.5 – 24]	

Bladder capacity	91.7 (SD = 62.7)	132.1 (SD = 105.9)	0.268
	Range: 10-243	Range: 18-375	
	Median = 64.2 [49.5 – 136]	Median = 100 [49 – 189.5]	
Bladder thickening	15 (68.2%)	17 (77.3%)	0.932
Emptying efficiency	92.5 (SD = 9.8)	92.3 (SD = 7.8)	0.883
	Range: 61-100	Range: 75-100	
Hydronephrosis			0.546
Unilateral	2 (9.1%)	5 (22.7%)	
Bilateral	4 (18.2%)	2 (9.1%)	
IL18	238.74 (SD = 551.36)	97.50 (SD = 155.11)	1.000
	Range: 0-1362.88	Range: 0-404.65	
NGF	1.70 (SD = 2.90)	5.90 (SD = 6.88)	0.065
	Range: 0.85 – 7.57	Range: 0.474 – 18.126	
PEG2	4799.35 (SD = 4461.24)	2479.19 (SD = 1052.77)	0.394
	Range: 1786.79 – 13316.40	Range: 1163.01 – 4040.19	

Figure 1

The correlation of the exposure of ketamine and the urine level of NGF (pg/ mg Cr). (p value = 0.006, independent-samples Kruskal-Wallis Test)

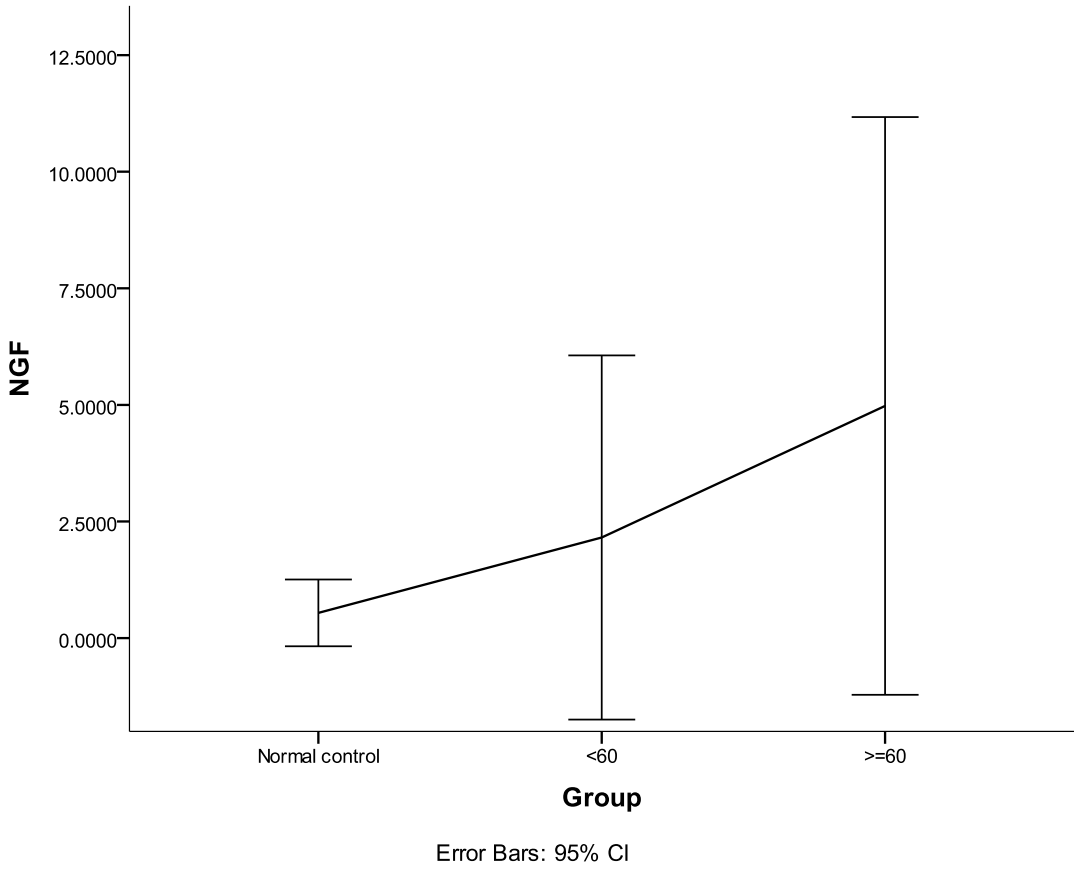
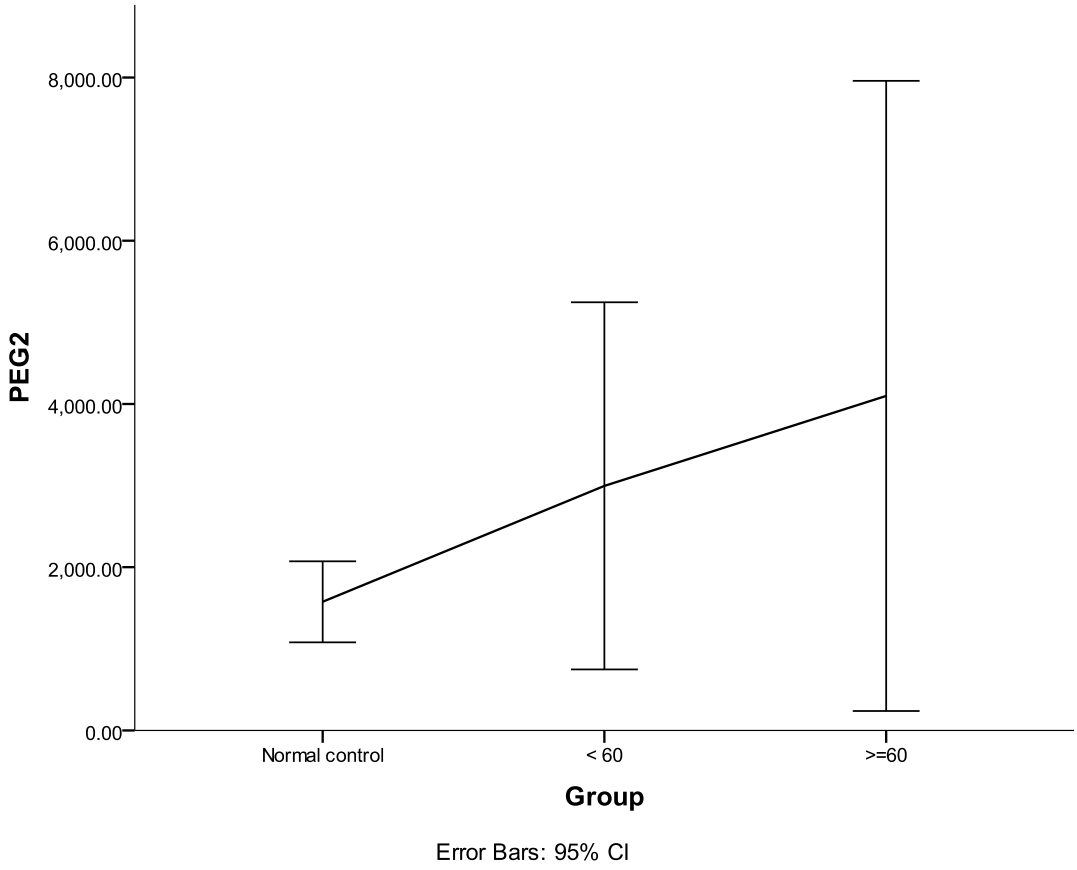


Figure 2

The correlation of the exposure of ketamine and the urine level of PGE2 (pg/ mg). (p value = 0.018, independent-samples Kruskal-Wallis Test)



Appendix 1

The programme of the Urology Symposium 2010

Appendix 2

The programme of the Nursing Workshop on Comprehensive management of bladder dysfunction

SCIENTIFIC PROGRAMME

Saturday, 18 December 2010 (Shaw Auditorium, Postgraduate Education Centre)

0830 – 0900	Registration G/F, PEC
0900 – 0920	Welcome Speech Eddie SY CHAN, Hong Kong Hong FUNG, Hong Kong Anthony CH YING, Hong Kong

0920 – 1020 Bladder Cancer (Part 1)

Moderators: Peggy SK CHU, Hong Kong
Chi Kwok CHAN, Hong Kong

0920 – 0935	Impact of Bladder Cancer - Worldwide and Local Perspective Eddie SY CHAN, Hong Kong
0935 - 0950	Bladder Cancer Pathology Ka Fai TO, Hong Kong
0950 – 1005	Urine Markers of Bladder Cancer Anthony Chi Fai NG, Hong Kong
1005 – 1020	Neoadjuvant and Adjuvant Chemotherapy in Invasive Bladder Cancer Wing Ming HO, Hong Kong
1020 - 1040	Tea Break

1040 - 1200 Bladder Cancer (Part 2)

Moderators: Anthony Chi Fai NG, Hong Kong
Berry TC FUNG, Hong Kong

1040 - 1100	BCG is Standard of Care for High-Risk, NMI Bladder Cancer Steven CAMPBELL, USA
1100 - 1120	Nerve-sparing Radical Cystectomy – Indications and Technique Urs E STUDER, Switzerland
1120 - 1200	Panel Discussion – Different Approaches of Radical Cystectomy

Moderator: Sidney KH YIP, Hong Kong
Murali SUNDRAM, Malaysia

1. Open Radical Cystectomy, Urs E STUDER
2. Laparoscopic Radical Cystectomy, Simon SM HOU
3. Single-port Radical Cystectomy, Jian HUANG
4. Robotic Radical Cystectomy, Steven CAMPBELL

1200 - 1240	**Case Discussion – Controversies in Bladder Cancer Management**
	Moderator: Simon SM HOU, Hong Kong Panel: Urs E STUDER, Steven CAMPBELL, Bill WONG
1240 - 1400	**Olympus Lunch Symposium** **Narrowband Imaging in Bladder Cancer** **Paolo PUPPO, Italy**
	Moderator: Eddie SY CHAN, Hong Kong
1400 - 1440	**Keys to Success with Orthotopic Bladder Substitution** **Urs E STUDER, Switzerland**
	Moderator: Ka Lun CHUI, Hong Kong
1440 - 1600	**Benign Bladder Conditions**
	Moderator: Wing Hang AU, Hong Kong Ka Lun CHUI, Hong Kong
1440 - 1500	Overactive Bladder – The perspective in Hong Kong Chi Kwok CHAN, Hong Kong
1500 - 1520	Medical and Surgical Treatment of Overactive Bladder Richard KY LO, Hong Kong
1520 - 1540	Ketamine Cystitis – A New Disease Entity? Peggy SK CHU, Hong Kong
1540 - 1600	Multi-disciplinary approach to Ketamine Cystitis Siu King MAK, Hong Kong
1615 - 1725	**Storz Urology Forum** **Opportunities and Challenges Encountered in Next Generation Urologist** **Young urologists from China, Singapore, Taiwan, India, Hong Kong**
16:15 – 16:20	Welcome Speech – Anthony Chi Fai NG, Hong Kong
16:20 – 16:30	Urology Training: Past and Present – Jian HUANG, China
16:30 – 16:40	Challenges in Hong Kong Urologists – J. TSU, Hong Kong
16:40 – 16:50	Challenges in Singapore Urologists – Qing Hui WU, China
16:50 – 17:00	Challenges in Taiwan Urologists – Y.J. HSUEH, Taiwan
17:00 – 17:10	Challenges in China Urologists – P. WU, China
17:10 – 17:20	Introduction of UAA young urologist session – Rajeev KUMAR, India
17:20 – 17:25	Closing Remarks – Peggy SK CHU, Hong Kong

SCIENTIFIC PROGRAMME

Sunday, 19 November 2010 (Kai Chong Tong, Postgraduate Education Centre)

0800 – 0815 Registration
G/F, PEC

0815 – 0830 Welcome Speech
Hoi Chu TO, Hong Kong
Sidney KH YIP, Hong Kong

0830 – 1000 Bladder Cancer (Module 1)

Moderators: Farrah T CHU, Hong Kong
Hoi Chu TO, Hong Kong

1. Post cystectomy: Ileal condut or neobladder?
2. Interstitial cystitis: Facts and myths

Rachel Busuttil LEAVER, United Kingdom

1000 - 1130 Post-Surgery Continence Care (Module 2)

Moderators: Crystal SY LI, Hong Kong
Helen KL YAU, Hong Kong

Understanding of urodynamics (UDS)
Lay Guat NG, Singapore

1. Nursing interventions for patients discharged after prostatectomy
2. Continence care post - Prostatectomy

Hamimah AHMAT, Singapore

1130 - 1230 Lunch

1230 – 1530 Urodynamics and Uro-diagnostic Evaluation (Module 4)
Hands-On Training

Station	Hands-on Training	Instructor
1	- Calibration, standardization and quality control of Urodynamics - Handling of diagnostic equipment	Chi Kwok CHAN, Hong Kong Helen WY LEUNG, Hong Kong Lay Guat NG, Hong Kong
2	- Intermittent catheterization	Hamimah AHMAT, Singapore Pui Hing WU, Hong Kong Mei Sum YIM, Hong Kong
3	- Handling of flexible cystoscopy	Ho Man TAM, Hong Kong Wing Yee YUNG, Hong Kong
4	- Handling of transrectal ultrasound with biopsy	Yi CHIU, Hong Kong Yuen Ching KAM, Hong Kong
5*	- Continence control - Pelvic anatomy training	For Shing CHIU, Hong Kong Rachel Busuttil LEAVER, United Kingdom Mei Nok LEUNG, Hong Kong
6*	- Tissue handling laboratory - Stoma siting	Hon Ming WONG, Hong Kong Ka Wai YUEN, Hong Kong

**** Venue: CUHK Jockey Club Minimally Invasive Surgical Skills Centre***
3/F Li Ka Shing Specialist Clinic (North Wing),Prince of Wales Hospital, Shatin, Hong Kong

1530 - 1800	**Ketamine Cystitis and Pelvic Pain (Module 3)**

Moderators: Miu Ling LI, Hong Kong
Siu Wan WONG, Hong Kong

15:30-16:00 Ketamine uropathy: A new epidemic?
Peggy SK CHU, Hong Kong

16:00-16:30 Ketamine abuse – The role of a urology nurse
Grace LP CHIU, Hong Kong

16:30-17:00 Ketamine – Psychiatric aspects
Alan KL TANG, Hong Kong

17:00-18:00 Group discussion and sharing
Moderator: Siu King MAK, Hong Kong
Sidney KH YIP, Hong Kong
Invited guest: Charles CHAN (Service Director, HK SKH Welfare Council)

Siu Cheuk CHAN, Grace CHIU, Sau Kwan CHU, Yuk Kiu LEUNG,
Alan KL TANG, Bonnie WU

18:00 Closing Remark