Introduction

Ketamine, an N-Methyl-D-aspartate receptor antagonist, is an anaesthetic agent characterised by a rapid onset and short duration of action. It has been used for the induction and maintenance of anaesthesia for more than 30 years but has increasingly been abused as a ‘club-drug’ at dance and rave parties since the late 1980s. This is an increasing problem in Hong Kong and ketamine is now second only to heroin among psychotropic substances being abused.

Ten ketamine abusers (seven from Tuen Mun Hospital and three from Princess Margaret Hospital) were found to have severe bladder dysfunction—with markedly diminished functional bladder capacities of around 30 to 50 mL.

Case reports

From 2000 to 2007, seven male and three female patients, aged 20 to 30 years (mean, 25 years) who had all abused ketamine for 1 to 4 years (Table), came to the two hospitals with severe lower urinary tract symptoms. All presented with symptoms of dysuria, frequency (having to void once every 15 minutes), urgency, urge incontinence, and painful haematuria. None had positive urine cultures. Early morning urines were all negative for acid-fast bacilli. The urine and blood toxicology profiles of some of these patients were positive for ketamine and benzodiazepam.

The functional bladder capacities obtained from the voiding diaries of all of the 10 patients were between 30 to 100 mL only. Urodynamic studies were available for seven patients up to the time of this review. Three patients failed to attend the urodynamic test despite explanation of the need for it. All seven patients were found to have detrusor overactivity with urinary leakage when the bladder was filled to a capacity of 30 to 50 mL.

Key words
Ketamine; N-methylketamine; Urinary bladder, neurogenic

TABLE. Physical characteristics, clinical and radiological features of the 10 patients

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Sex/age (years)</th>
<th>Date of presentation</th>
<th>Duration of taking ketamine (years)</th>
<th>ALP/ALT* (U/L)</th>
<th>Serum creatinine (µmol/L)</th>
<th>USG† kidney</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F/25</td>
<td>Nov 2000</td>
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<td>400</td>
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<td>220</td>
<td>B hydro</td>
</tr>
<tr>
<td>3</td>
<td>M/30</td>
<td>Sep 2006</td>
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<td>413/83</td>
<td>177</td>
<td>B hydro</td>
</tr>
<tr>
<td>4†</td>
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<td>Jan 2007</td>
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</tr>
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<td>5†</td>
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<td>Unknown</td>
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<td>Apr 2007</td>
<td>1</td>
<td>229/48</td>
<td>100</td>
<td>B hydro</td>
</tr>
</tbody>
</table>

* ALP denotes alkaline phosphatase (reference range, 46-127 U/L); and ALT alanine aminotransferase (reference range, 10-57 U/L)
† USG denotes ultrasonography, and B hydro bilateral hydronephrosis
§ Patients 4 and 5 are a couple; patient 5 became a ketamine abuser after marrying patient 4
§§ Patient 8 was prescribed cimetidine while patient 9 was prescribed omeprazole for epigastric pain

‘Street ketamine’–associated bladder dysfunction: a report of ten cases

Ten young ketamine abusers presented with lower urinary tract symptoms to two regional hospitals in Hong Kong. Investigations demonstrated contracted bladders and other urinary tract abnormalities. These types of findings have never been reported before in ketamine abusers. The possible aetiology is also discussed.
Four of the patients had cystoscopies and random biopsies performed showed cystitis glandularis only. Three patients had magnetic resonance imaging of the lumbosacral spine, all of which were normal. All 10 patients had abnormal liver function tests with raised levels of alkaline phosphatase and alanine aminotransferase. Ultrasound examinations did not demonstrate any underlying obstructive cause in any of these patients, and none were found to have hepatitis B–associated chronic liver disease. Ketamine clearance is mainly hepatic and flow dependant, and it has been reported that the CYP3A4 is the principal microsomal enzyme involved in ketamine metabolism. Seven of these patients had complained of epigastric pain and had oesophagogastroduodenoscopies (OGD) performed. Although none had positive OGD findings some were given cimetidine or omeprazole, which are known to be CYP3A4 inhibitors, for a short period and this may have contributed to the abnormal liver function in these patients.

Patient 2 was given an augmentation enterocystoplasty with the aim of maintaining renal function and improving his quality of life. Despite our advice, he continued to abuse ketamine after the augmentation enterocystoplasty, and was admitted 3 months later in acute renal failure with a serum creatinine of 554 µmol/L and oliguria. An urgent ultrasound of the kidneys revealed gross bilateral hydronephrosis so bilateral percutaneous nephrostomy drainage was performed. The patient’s serum creatinine then improved slowly, falling to 170 µmol/L. A subsequent antegrade nephrostogram revealed complete right-sided ureteric obstruction just below the pelvic-ureteric junction (PUJ) and a markedly diminished flow of contrast in the left ureter suggestive of retroperitoneal fibrosis (Figs 4 and 5).

Discussion
An association between ‘street ketamine’ abuse, bladder dysfunction and subsequent renal impairment has not been previously reported. No animal studies into the effects of ketamine have revealed these types of disorders, nor has the pharmaceutical company marketing ketamine ever encountered such pathology after long-term exposure in both animals and humans. All 10 patients demonstrated an association between ketamine abuse and lower urinary tract pathology. This specific disease caused intractable urinary symptoms and severe impairment of their quality of life. Most importantly, the finding of hydronephrosis in most, and renal impairment in half, of our patients is suggestive of a progressive disease process that might end up as chronic renal failure. The aetiology of this disease is presently...
unknown. We initially postulated that damage to neurons in the brain or the spinal cord was the cause of the bladder dysfunction. Nonetheless, patient 2’s pathology—bilateral ureteric strictures suggestive of retroperitoneal fibrosis—implies that another aetiology like an intensive immunological response to ‘street ketamine’ may be a contributing factor. Possible causes include the direct toxic effect of ketamine and its metabolites on the lower urinary tract mucosa. Ketamine abusers are likely to be exposed to other drugs and chemicals either purposely added as a cutting agent or being co-abused in a soft drug cocktail. One sample of snorting ketamine powder was obtained from one of our patients and analysed but this failed to identify any additional ingredient likely to cause the bladder dysfunction. Further investigation is needed to determine the exact cause of the pathology. An epidemiological study would be helpful for assessing the actual size of the problem and may yield clues to the aetiology as well. The authors would like to alert frontline doctors, especially those working in primary care, emergency departments, and psychiatry, to this new form of uropathy and its association with ketamine abuse. Early urology referral for comprehensive investigation and management would help combat this new form of urinary tract disease.

References