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Review

British Association of Urological Surgeons Consensus statements on the management of ketamine uropathy

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Objectives

To provide guidance in the form of consensus statement in the management of ketamine uropathy.

Methods

A literature review of ketamine uropathy was performed. The consensus method was of a modified nominal group technique and has been use in the previous British Association of Urological Surgeons (BAUS) consensus documents and was led by the Female, Neurological and Urodynamic Urology Section of the BAUS.

Results

A number of consensus statements detailing the assessment and management of urological complications relate to the recreational use of ketamine (ketamine uropathy) in both elective and emergency urology settings.

Conclusion

Comprehensive management pathway for ketamine-related urinary tract dysfunction and uropathy has been detailed.

Keywords

ketamine bladder dysfunction, ketamine uropathy, lower urinary tract symptoms, Ketamine cystitis, ureteric stricture, urodynamics

Introduction

Although the use of ketamine historically has fluctuated, the prevalence of its use in adults aged 16 to 59 years has increased from 0.5% in the year ending March 2010 to 0.8% for the year ending March 2020. Use among those aged 16 to 24 years has almost doubled in the same period, from 1.7% to 3.2% [1].

Patients with ketamine abuse can present with urinary frequency, nocturia, urgency, incontinence, cystitis, bladder or loin pain and haematuria, which are debilitating symptoms causing a profoundly negative impact on quality of life [2]. Pain can promote the further use of ketamine or other recreational drugs to help suppress distressing symptoms, so compounding the condition. Onset of urinary symptoms is typically delayed from the time ketamine is first used, and the severity of symptoms appears to be related to the quantity and duration of drug intake [3].

Ketamine uropathy is a challenging condition to treat, and a core principle is patient abstinence from the drug. This usually requires collaboration with drug and alcohol support services and supportive urological management initially, followed by vigilance and management of complications when they arise.

A nationwide prevalence study in the UK has demonstrated that 26.6% of regular ketamine users experience at least a single urinary symptom, with 51% experiencing an improvement of symptoms on cessation [3]. Approximately 50% of ketamine users experiencing urinary symptoms do not seek medical attention immediately, with symptoms becoming more apparent after 2 years [4]. Nasal inhalation (or 'snorting') of ketamine causes more symptoms than oral ingestion [5]. It is essential when seeing patients with storage bladder symptoms that a direct question regarding recreational drug use, and in particular ketamine use, is asked to avoid delay in diagnosis and to consequently offer correct

management. Clinical effects of ketamine are shown in Table 1.

Background

Ketamine is a drug that was originally developed as an anaesthetic alternative to phencyclidine. It acts as a non-competitive antagonist of the N-Methyl-D-aspartate acid receptor complex and has various medical uses, including anaesthesia, epilepsy treatment, pain management, and depression treatment [12].

Recreationally, ketamine is known as a dissociative anaesthetic that provides feelings of detachment from oneself and the environment. It has analgesic, stimulant, and psychedelic effects. Most users prefer snorting the drug, with effects taking approximately 20 min to develop and lasting for 1 to 2 h [13].

Ketamine has gained popularity in rave culture and has been classified as a Class B drug since 2014. Its lower cost compared to other substances contributes to its widespread use [14]. Regular ketamine use can lead to tolerance and physiological dependence, with withdrawal symptoms such as abdominal pain, anxiety, fatigue, and changes in behaviour.

The effect of ketamine abuse on the urinary tract was first reported in Canada in 2007, with a case series of nine patients presenting with severe LUTS, haematuria and history of recreational ketamine abuse [15], which was followed by a large case series from Hong Kong of 59 patients who had abused ketamine for >3 months with severe storage LUTS and haematuria [16].

Staging System

Adapting and modifying a staging system from Wu et al. [17] (Table 2), patients can be classified into three stages of Ketamine uropathy. Stage 1 is the inflammatory phase where cessation of ketamine and oral medications can resolve the situation. Stage 2 is where structural changes to the bladder occur and the mainstay of treatment includes bladder instillations and intradetrusor botulinum toxin A injections. Stage 3 is the final stage with permanent changes to the bladder, upper tracts and renal function, and is best served by urinary tract reconstruction.

Methods

The BAUS Female, Neurological and Urodynamic Urology Section (FNUU) Executive Committee comprises a group of urological surgeons elected by their peers due to their interest in the field of female urology, neurourology, urodynamics and reconstruction of the urinary tract. It was identified that ketamine-related uropathy is an important and challenging

Table 1 Clinical effects of ketamine.

Clinical effects of ketamine	
Lower urinary tract	Storage LUTS (frequency, urgency, urgency incontinence and nocturia), haematuria, dysuria and bladder pain
Upper urinary tract	Risk factors for developing hydronephrosis were increased duration of abuse, raised creatinine, abnormal LFTs and decreased functional bladder capacity [6]
Sexual dysfunction	Taiwanese survey of 1056 male ketamine users demonstrated 30.8% incidence of ED using validated questionnaires. Risk of ED was increased with duration of use and age > 30 years. The only protective factor was if use was <3 months [7]
Hepatobiliary effect	Epigastric pain with dilated bile ducts in 9.8% of ketamine abusers [8] Cholangiopathy due to CBD dilatation and liver fibrosis – related to disease severity and might suggest upper urinary tract abnormality [5]
Gastrointestinal effects	Gastritis, peptic ulcers and gastroduodenal erosions. Can precede urological symptoms [5]
Central nervous system effects	Long-term neurocognitive problems with impaired verbal fluency, decreased cognitive processing speed, decreased verbal learning and, if heavy use, issues with verbal and visual memory. Evidence of structural brain damage [9]
Long-term risk of malignancy	Rare – two case reports of development of leiomyoma [10] and primary yolk sac tumour [11] of the bladder after persistent ketamine misuse

ED, erectile dysfunction; LFT, liver function test.

Table 2 Typical finding of the stages of ketamine misuse [17]. Staging is indicated in the main text under 'Staging system'.

Staging	Stage 1	Stage 2	Stage 3
History of abuse, years	<1	1–2	>2
Dose of ketamine, g/week	<1 g	1-2 g	>2 g
Renal function	Normal	Normal	Abnormal
Liver function	Normal	Normal/Abnormal	Abnormal
Bladder change (capacity and thickening)	No	Yes	Yes
Upper tract involvement (hydronephrosis)	No	No	Yes

condition to diagnose and treat, and standardisation of urological practice in the UK would be helpful for both general and subspecialist urologists and would ultimately be beneficial for patients. Following FNUU Executive Committee discussion, a thorough literature search was performed on ketamine-related urinary tract dysfunction and this, along with UK best practice, provided the framework for this consensus on the assessment, investigation and management of these patients. The document underwent multiple rounds of review by all FNUU Executive Committee members and an additional two invited specialists with significant experience in ketamine uropathy, and then was submitted for external expert independent review by two further subspecialists. The revised document was further discussed at the Annual BAUS Meeting in June 2023 and amended. This document has been distributed to all the BAUS FNUU membership for widespread scrutiny and further comments from registered medical professionals working in the relevant field to help refine the guidance into a consensus statement. The consensus statement was approved by BAUS council in November 2023, and the recommendations, which are all consensus-based are summarised below.

Assessment

1. Take a full urological history including relevant medications, previous medical, surgical, and psychosocial histories (summarised in Fig. 1).
2. Establish if ketamine use is a potential cause of symptoms and, if so, take a ketamine-specific history detailing dosage (g) duration, frequency, route of administration and additional illicit drugs usage (Fig. 2).
3. Perform a chaperoned abdominal and pelvic examination where appropriate.
4. Check urine dipstick to assess for infection and/or haematuria.
5. Perform renal profile, liver function tests (LFTs) and full blood count as a baseline and document any future deterioration. Ketamine is known to affect liver function and can require referral to a hepatologist/gastroenterologist.
6. Bladder diary, uroflowmetry and postvoid residual urine volume measurement are helpful discriminators on a first clinic visit. They provide an objective assessment of functional bladder capacity when considered together.
7. Request renal tract ultrasonography. This is important as a baseline and to screen for any upper tract involvement in the form of hydronephrosis.
8. Complete validated questionnaires such as the Pelvic Pain and Urgency/Frequency (PUF) questionnaire which has been validated in ketamine uropathy populations internationally [18] or standardised questionnaires such as the International Consultation on Incontinence Questionnaire (ICIQ)-LUTS.
9. Perform a cystoscopy with or without a biopsy – most patients will have visible haematuria and require cystoscopic inspection. Local anaesthetic flexible cystoscopy can be used in milder forms of ketamine uropathy but is usually poorly tolerated in the majority of this patient group and is likely to result in

Fig. 1 Assessment of ketamine uropathy. ICIQ-LUTS, International Consultation on Incontinence Questionnaire-LUTS; PUF, Pelvic Pain and Urgency/Frequency.

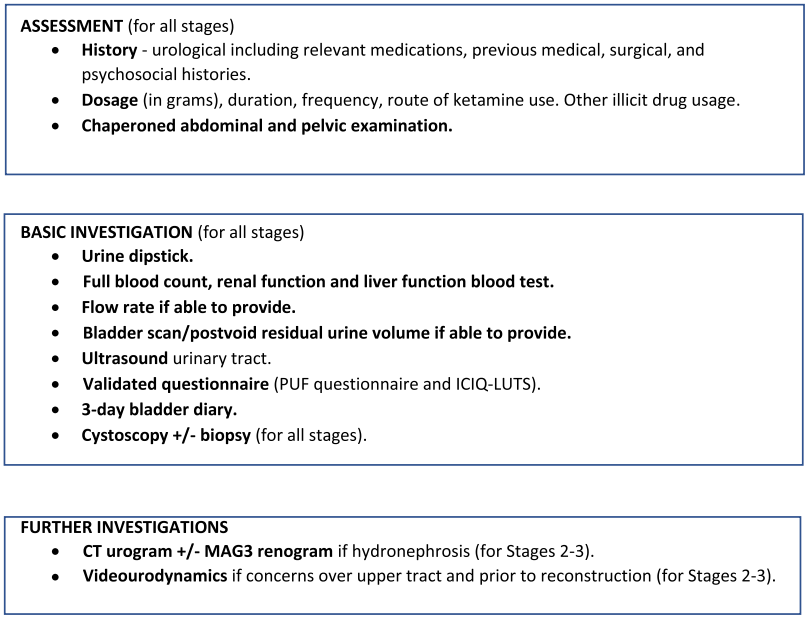
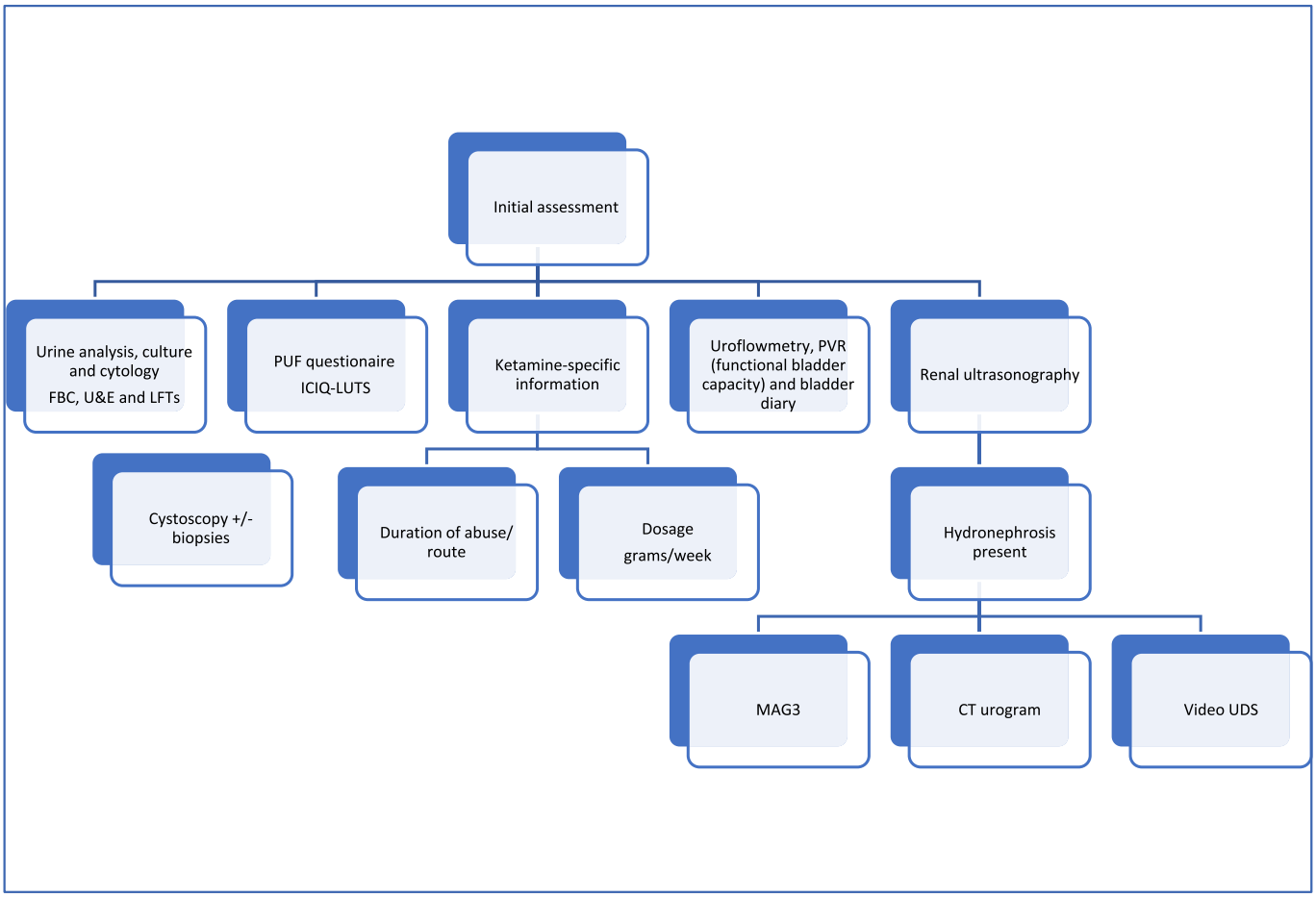


Fig. 2 Assessment of patients with urology complications of ketamine misuse. FBC, Full Blood count; ICIQ-LUTS, International Consultation on Incontinence Questionnaire-LUTS; LFT, liver function test; PUF, Pelvic Pain and Urgency/Frequency; U&E, Urea and Electrolytes; UDS, urodynamic study.



abandonment and proceeding to general anaesthetic. Therefore, a rigid cystoscopy under general anaesthetic is often preferred. In addition, a poor experience of flexible cystoscopy may mean the patient may be reluctant to consider bladder instillation treatment in the future. Bladder capacity under general anaesthetic may be a marker of disease severity and will help plan future reconstructive surgery. It may provide therapeutic relief of symptoms in a minor cohort of patients. A bladder biopsy is useful in the initial assessment. Cystoscopic findings are erythematous bladder mucosa with petechial haemorrhages, inflammation and neovascularisation. In severe forms, the bladder mucosa tends to be very friable and 'shed'. On distension ulcerations/lacerations can develop [19,20].

Further Investigations

1. CT urogram and MAG3 renogram may be useful for the assessment of any detected hydronephrosis on ultrasonography. The diuretic phase of a renogram may be poorly tolerated.
2. Video-urodynamics. This test can provide both the anatomical and functional information that is needed for accurate diagnosis of the underlying issues, particularly if there is a suspicion of upper urinary tract involvement or poorly compliant bladders. However, commonly, this tends to be poorly tolerated and can be reserved for whom urinary tract reconstruction might next be considered.

BAUS Recommendation

The recommendations are to ensure initial assessment of urinary tract with ultrasonography and renal function blood tests and for further investigation with additional imaging if abnormalities detected.

In addition, it is recommended to ensure a liver function blood test check and referral to hepatology if abnormal.

If possible, a joint clinic with drug cessation nurse is recommended or, failing that, significant input from the substance misuse team within the service.

Initial Management (Stages 1 and 2)

1. In the initial management, stopping ketamine should be the primary goal, with signposting to the local substance misuse services.
2. A trial of anticholinergic and/or beta 3 agonist medication for overactive bladder symptoms can be tried, especially at early stage of ketamine uropathy.
3. A referral to the pain team should be made and may aid the cessation of ketamine abuse. An analgesic ladder of NSAIDs, opioid analgesics and neuroleptic drugs (amitriptyline, gabapentin and pregabalin) has been used successfully for bladder pain [9].
4. Pentosan polysulphate (Elmiron), an oral glucosamine glycan (GAG) replacement may also be considered and commenced at the time of cessation of ketamine, but the evidence is limited [21].
5. After cessation of ketamine for 1 month, intravesical instillations such as Parson's cocktail or modified Whitmore cocktail (typically containing combinations of heparin, lignocaine, sodium bicarbonate +/− hydrocortison)Ketamien, chondroitin sulphate [Gepan] and sodium hyaluronate [Cystistat], alone or in combination [iAuril]) can be offered in these patients with ongoing symptoms. In general, regimens are weekly instillation for 4 to 6 weeks and then monthly instillations for 4 to 6 months initially, and may be continued after assessment if effective. In small case series these have been shown to be beneficial [22].
6. If the above measure fails to be of benefit, a trial of botulinium toxin A injection into the bladder under general anaesthesia can be considered to treat the urinary symptoms and has been shown to reduce urinary symptoms and increase bladder capacity [23].
7. A combination therapy of bladder instillations and or intradetrusor botulinium toxin A can be helpful in some patients [24].

BAUS Recommendation

The importance of ketamine cessation should be made clear to the users, emphasising the benefit of preventing deterioration of the urinary tract, with appropriate signposting to drug cessation and pain services.

Medication, bladder instillations and intradetrusor botulinium toxin A injections are the mainstay of managing Stages 1 and 2 of ketamine uropathy.

Stage 1 and Stage 2 ketamine uropathy can be managed in all urology centres but Stage 3 should be managed in specialist centres with the appropriate expertise.

Upper Tract Monitoring

Ongoing ketamine misuse can cause upper tract dysfunction, either due to vesico-ureteric reflux from a poorly compliant bladder or due to ureteric stricture formation. Obstruction due to stricture formation seems to occur more commonly in patients with deranged liver and kidney function. Patients who continue to abuse ketamine should have renal function and LFTs monitored regularly.

1. Renal function and LFTs are recommended to be monitored on a 3-monthly basis.
2. Renal tract ultrasonography should be performed on a 6-monthly basis.

BAUS Recommendation

Regular monitoring and surveillance are required in those with ketamine uropathy.

Upper Tract Management

Active ketamine users often have a poor tolerance to urethral catheters and ureteric stents. This should be considered when planning interventions or considering long-term management options. It is recommended to delay definitive reconstruction for end-stage bladder patients until they have stopped ketamine for at least 6 months.

1. In cases where ureteric strictures and hydronephrosis occur because of ketamine use, temporising with endourology interventions such as stents and nephrostomies may be necessary.
2. Nephrostomy is preferred in those who have poor tolerance to ureteric stents and concern with compliance for attending for regular stent changes.
3. Upper tracts should be re-evaluated if stents or nephrostomy are removed, with reimaging a few weeks later to ensure no ongoing obstruction.
4. Long-term nephrostomy is preferred over urinary reconstruction in those with continued ketamine use.
5. Definitive upper tract reconstruction may require reimplantation, ileal ureteric interposition or kidney auto-transplantation depending on the severity.

BAUS Recommendation

Temporising measures, such as endourology interventions, should be considered during the waiting period for ketamine cessation prior to reconstructive surgery in those with upper tract changes.

Surveillance of Complications and Reconstructive Management

After cessation of ketamine for 6 months, reconstruction can be considered in those with end-stage ketamine bladder. Referral to a tertiary centre is highly recommended.

All reconstruction has been associated with a high complication rate and all patients need to be carefully counselled [14,23] (Fig. 3). Cessation should be confirmed with random urine toxicology testing.

1. Videourodynamic testing is useful to determine the compliance, bladder capacity and any reflux prior to surgery.
2. Augmentation enterocystoplasty has been the main reconstructive option to increase bladder capacity and improve compliance and reduce pressure [25,26].
3. Supratrigonal cystectomy to preserve the micturition reflex can be combined with augmentation [27].
4. Benign cystectomy (ideally nerve sparing) can be combined with an ileal conduit or orthotopic neobladder formation.
5. Ureteric involvement may require reimplantation, ileal substitution / interposition or kidney auto-transplantation depending on the severity.
6. All reconstructive cases should be discussed in a reconstructive urology multidisciplinary team meeting and a bespoke solution provided, depending on patient factors and clinical findings. This should include a psychological assessment to determine the risk of ketamine relapse.
7. Life-term follow-up is recommended after performing reconstructive surgery.

BAUS Recommendations

It is recommended to delay definitive reconstruction for end-stage ketamine uropathy until ketamine cessation has occurred for at least 6 months.

Ketamine cessation should be confirmed with urine testing prior to any major surgical intervention.

All reconstructive surgery should be discussed in a reconstruction or functional multidisciplinary team meeting and referred to a tertiary unit with the appropriate experience.

Fig. 3 Further management of patients with upper tract complications relating to ketamine misuse. MDT, multidisciplinary team.

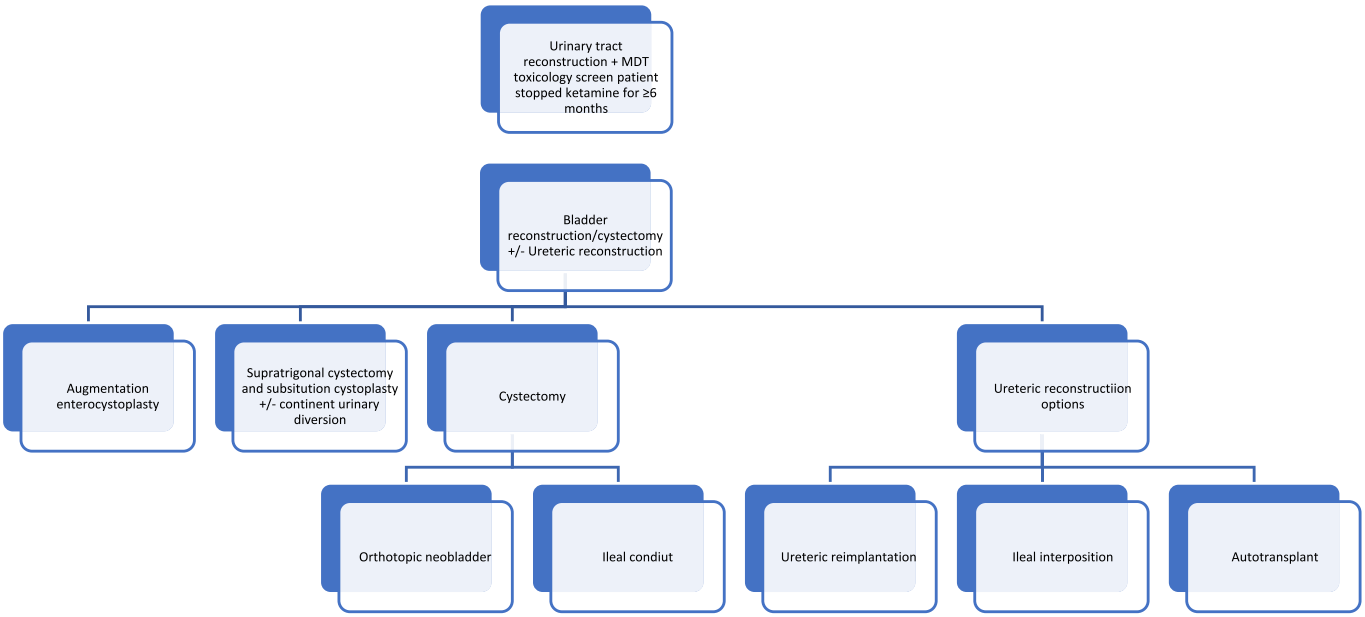


Table 3 Methods of ketamine testing.

Ketamine testing	Detection time	Advantage	Disadvantage
Urine laboratory testing	3–5 days	Accurate	Costly and time consuming
Urine dipstick	3–5 days	Cheap and accessible, immediate result	May not be as accurate as laboratory testing
Saliva	24 h	Easily performed	Short window
Blood	24 h	Accurate	Short window
Hair	3 months	Long window of detection	Time consuming

Ketamine Testing

Table 3 shows the different methods of detecting ketamine. Urine tests are commonly used in detecting ketamine use. The standard detection time for ketamine in urine is up to 5 days. However, in some cases, traces of ketamine may be found in the urine for up to 14 days in those with an excessive use of ketamine [28]. The advent of commercially available CE-marked and US Food and Drug Administration-approved ketamine urine dipstick tests means such testing may prove to be the best practical method of monitoring abstinence.

Conclusion

Ketamine misuse has a significant effect on the urinary tract. Every effort should be made to help with the cessation of the drug and prevent irreversible damage to the urinary tract. Detailed assessment of patients is key in areas of high ketamine misuse. A multidisciplinary approach is required in dealing with the consequences of misuse and for consideration of urinary tract reconstruction.

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Disclosure of Interests

The authors declare no conflicts of interest.

References

1 https://www.ons.gov.uk/peoplepopulationandcommunity/crimeandjustice/articles/drugmisuseinenglandandwales/yearendingmarch2020
2 **Wood D, Cottrell A, Simon C et al.** Recreational ketamine: from pleasure to pain. *BJU Int* 2011; 107: 1881–4
3 **Winstock AR, Mitcheson L, Gillatt DA, Cottrell AM.** The prevalence and natural history of urinary symptoms among recreational ketamine users. *BJU Int* 2012; 110: 1762–6
4 **Li CC, Wu ST, Cha TL, Sun GH, Yu DS, Meng E.** A survey for ketamine abuse and its relation to the lower urinary tract symptoms in Taiwan. *Sci Rep* 2019; 9: 1–6
5 **Castellani D, Pirola GM, Gubbiotti M et al.** What urologists need to know about ketamine-induced uropathy: a systematic review. *Neurourol Urodyn* 2020; 39: 1049–62
6 **Yee CH, Teoh JYC, Lai PT et al.** The risk of upper urinary tract involvement in patients with ketamine-associated uropathy. *Int Neurourol J* 2017; 21: 128–32
7 **Stephen Y, Mei-Yu J et al.** Sexual and bladder dysfunction in male ketamine abusers: a large scale questionnaire study. *PLoS One* 2018; 11: e0207927
8 **Wong SW, Lee KF, Wong J, Ng WW, Cheung YS, Lai PB.** Dilated common bile ducts mimicking choledochal cysts in ketamine abusers. *Hong Kong Med J* 2009; 15: 53–6
9 **Hong YL, Lee CH, Tam YH.** Management of complications of ketamine abuse: 10 years experience in Hong Kong. *Hong Kong Med J* 2018; 24: 175–81
10 **Zhong D, Feng Y, Chen J, Lin C, Luo H.** Bladder leiomyosarcoma in a patient with chronic ketamine abuse: a case report. *Can Urol Assoc J* 2015; 9: E514–6
11 **Mui WH, Lee KC, Chiu SC et al.** Primary yolk sac tumour of the urinary bladder: a case report and review of the literature. *Oncol Lett* 2014; 7: 199–202
12 **Peltoniemi MA, Hagelberg NM, Olkkola KT, Saari TI.** Ketamine: a review of clinical pharmacokinetics and pharmacodynamics in anesthesia and pain therapy. *Clin Pharmacokinet* 2016; 55: 1059–77
13 https://www.drugwise.org.uk/ketamine
14 **Sihra N, Ockrim J, Wood D.** The effects of ketamine cystitis on urinary tract reconstruction – a surgical challenge. *BJU Int* 2018; 121: 458–65
15 **Shahani R, Streutker C, Dickson B, Stewart RJ.** Ketamine- associated ulcerative cystitis: a new clinical entity. *Urology* 2007; 69: 810–2
16 **Chu PSK, Ma WK, Wong SCW et al.** The destruction of the lower urinary tract by ketamine abuse: a new syndrome? *BJU Int* 2008; 102: 1616–22
17 **Wu P, Wang Q, Huang Z, Wang J, Wu Q, Lin T.** Clinical staging of ketamine-associated urinary dysfunction: a strategy for assessment and treatment. *World J Urol* 2016; 34: 1329–36
18 **Ng C, Ma W, To K, Yiu M.** 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. *Hong Kong Med J* 2012; 18: 123–30
19 **Chan E, Chan V, Tang T et al.** Systematic review and meta-analysis of ketamine-associated uropathy. *Hong Kong Med J* 2022; 28: 466–74
20 **Lai Y, Wu S, Ni L et al.** Ketamine-associated urinary tract dysfunction: an underrecognized clinical entity. *Urol Int* 2012; 89: 93–6
21 **Chung-Hsien C, Ming-Huei L, Yi-Chang C, Ming-Fong L.** Ketamine-snorting associated cystitis. *J Formos Med Assoc* 2011; 110: 787–91
22 **Smart C, Kabir M, Pati J.** Treatment of ketamine-associated cystitis with chondroitin sulphate. *Br J Nurs* 2013; 22(18): S4
23 **Jianbo JS, Keji X, Yuebin C et al.** Treatment ketamine-related bladder dysfunction by intravesical injection of botulinum toxin A. *J Third Mil Med Univ* 2012; 11: 32
24 **Zeng J, Lai H, Zheng D et al.** Effective treatment of ketamine- associated cystitis with botulinum toxin type a injection combined with bladder hydrodistention. *J Int Med Res* 2017; 45: 792–7
25 **Vizgan G, Huamán M, Rychik K, Edeson M, Blaivas J.** Ketamine-induced uropathy: a narrative systemic review of surgical outcomes of reconstructive surgery. *BJUI Compass* 2023; 4: 377–84
26 **Ng CF, Chiu PKF, Li ML et al.** Clinical outcomes of augmentation cystoplasty in patients suffering from ketamine-related bladder contractures. *Int Urol Nephrol* 2013; 45: 1245–51
27 **Chung SD, Wang CC, Kuo HC.** Augmentation enterocystoplasty is effective in relieving refractory ketamine-related bladder pain. *Neurourol Urodyn* 2014; 33: 1207–11
28 **de Jong LAA, Qurishi R, Stams MPJ et al.** Prolonged ketamine and norketamine excretion profiles in urine after chronic use: a case series. *J Clin Psychopharmacol* 2020; 40: 300–4

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Abbreviations: FNUU, Female, Neurourology and Urodynamic Section; LFT, liver function test.