Assessment of ketamine uropathy

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A B S T R A C T

A group of experts on lower urinary tract dysfunction and cystitis met together to make a consensus report on the assessment of ketamine uropathy (KU) which encompasses ketamine cystitis.

Essential tests, which should be performed in all KU patients, are (1) detailed history taking with structured questionnaire, (2) physical examination, (3) urine tests including test strip biochemistry and sediments analysis, urine culture, and cytology, (4) blood tests including complete blood cell counts with differential counts, liver and renal function tests, IgE, HIV, VDRL, (5) urological tests including uroflowmetry and post void residual urine volume and renosonography.

Optional tests, which will be performed in selective cases, are (1) bladder diary for 48-72 hours, (2) bladder wall thickness by ultrasound, (3) upper tract evaluation with excretory urography, computed tomography of abdomen, diuretic renal scan, (4) lower urinary tract evaluation with cystoscopy, voiding cystography, urodynamics or videourodynamics, (5) bladder and/or ureteral biopsy, (6) abdominal echo and/or gastroendoscope. Optional tests are usually indicated when essential tests disclose abnormal findings.

Using the standardized tools to assess patients with ketamine abuse, patients characteristics can be clarified and different therapeutic strategies for ketamine uropathy can be compared in the future.

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1. Introduction

As ketamine uropathy (KU) is a relatively new clinical entity since 2007,1,2 there is no consensus about the assessment and evaluation for KU to date. Recent publications show that urinary bladder, ureter, and kidney may be damaged in the patients with chronic use of ketamine.3,4 In addition, brain, liver, upper gastro-intestinal tract, and genital tract functions may be also involved.5-7 Allergic reaction seems to play an important role in the development of KU.8 A complete evaluation of the aforementioned organ system is mandatory to provide rapid diagnosis and treatment. A group of experts in lower urinary tract dysfunction and cystitis met together several times to discuss optimal assessment for KU. The draft was presented at the consensus meeting held in Taichung, on April 12, 2015. The followings are the consensus from the meeting.

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Because the ketamine cystitis (KC) shares similar clinical symptoms with interstitial cystitis (IC), recommendations of the assessment for IC patients is adopted for KU. Contracted bladder is present in many cases of KU, part of the concept of neurogenic bladder is adopted. In addition, hydronephrosis and ureteral stenosis are encountered in severe cases of KU, upper urinary tract evaluation should be performed. Patients also suffer from hepato-biliary problems, epigastralgia, sexual dysfunction, brain dysfunction. Further assessments are mandatory if the patients have symptoms or dysfunction.

### 2. Essential tests for ketamine uropathy

Table 1 summarizes essential tests for KU. A structured questionnaire is developed to assist history taking (Appendix). Patients should be queried about ketamine use history, including duration, frequency, dosage, and route of ketamine abuse. Whether the patient is an active abuser or ex-abuser should be clarified. The duration of ketamine cessation must be documented for an ex-abuser. Other illicit drugs addiction, smoking, betel nut chewing, and alcohol drinking history should also be asked. Up to date, there is no evidence in the relationship between betel nut chewing history and ketamine uropathy. Since this questionnaire is adopted from the case report form of Taiwan Food and Drug Administration (TFDA), we continue to use this item. In this way, we can compare our data with those already registered on TFDA. Hopefully, the relationship between betel nut chewing, a common behavior in Taiwan, can be illustrated later. The interval between the beginning of ketamine abuse and the occurrence of lower urinary tract symptoms (LUTS) should be noted. The severity of LUTS could be assessed by International Prostate Symptoms Score and the “O'Leary-Sant Symptom and Problem Questionnaire”.

Table 2 lists the optional tests for KU. A voiding diary can be recorded for 48–72 hours in cooperative patients. Maximal voided volume can be a good surrogate of functional bladder capacity since most of the KU patients have low PVR. However, many patients are uncooperative in recording voiding diary. Bladder sonography can be performed to measure bladder wall thickness which may suggest the presence of bladder fibrosis. However, the technical difficulty in measuring bladder wall thickness in a fixed bladder volume makes this test not easy for the KU patients.

**Table 1**

<table>
<thead>
<tr>
<th>History taking</th>
<th>Structured questionnaire including illicit drug use history, LUTS, pain score, sexual function, mood and quality of life.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical examination</td>
<td>Height, weight, and blood pressure. Nostril, and genital skin.</td>
</tr>
<tr>
<td>Urine tests</td>
<td>Urine routine, culture, cytology.</td>
</tr>
<tr>
<td>Blood tests</td>
<td>BUN/Cr; GOT/GPT, bilirubin, IgE, CBC with differential counts, HIV, VDRL</td>
</tr>
<tr>
<td>Urological examinations</td>
<td>Retrograde pyelography, PVR and renorenography</td>
</tr>
</tbody>
</table>


### 3. Optional tests for ketamine uropathy

<table>
<thead>
<tr>
<th>Functional bladder capacity/maximal voided volume</th>
<th>Transabdominal ultrasound measuring bladder wall thickness at 1/2-2/3 expected bladder capacity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bladder fibrosis</td>
<td>Excretory urography, CT of abdomen (Non-contrast CT if impaired renal function), diuretic DTPA</td>
</tr>
<tr>
<td>Upper urinary tract evaluation</td>
<td>Cystoscopy, voiding cystography, urodynamics or videourodynamics</td>
</tr>
<tr>
<td>Lower urinary tract evaluation</td>
<td>Bladder and/or ureteral biopsy</td>
</tr>
<tr>
<td>Histology</td>
<td>Abdominal echo and/or gastroendoscope for epigastralgia and abnormal liver functions.</td>
</tr>
</tbody>
</table>

Bladder diary for 48–72 hours in cooperative patients.
provide no benefits in confirming the diagnosis. Cystoscopy could be considered when the diagnosis of KU is in doubt. Disorders such as bladder cancer, bladder stones, urethral diverticula, and intravesical foreign bodies could be identified by cystoscopy and the therapeutic approach would then be changed. The role of cystoscopy in KU may be changed after the first report of bladder cancer in a KU patient. Cystoscopy could also be performed in concomitance with bladder hydrodilatation under regional or general anesthesia because many KU patients could not tolerate the procedure when it is performed under local anesthesia.

Urodynamic study (UDS) is not necessary for the diagnosis of uncomplicated KU. The findings of UDS are inconsistent and could not provide further information for diagnosis or guiding therapy. Furthermore, many patients could not tolerate bladder distension or urethral catheterization during the examination. UDS should be considered only when other lower urinary tract dysfunction was suspected and the treatment would be different once it was identified, such as bladder outlet obstruction or detrusor underactivity. Video-UDS could identify VUR and would be beneficial in differentiating the etiology of hydronephrosis. The potassium sensitivity test (or KCl test) is not recommended in the evaluation of IC patients, as it could not provide information for diagnosis and guiding therapy. It is therefore not suggested in KU patients as the same reasons.

Routine bladder biopsy is an issue to be debated. Generally, histology shows denuded epithelium and inflammation with eosinophil infiltration which may be specific. Bladder biopsy should only be performed when bladder cancer and/or urothelial carcinoma in situ are suspected, particularly after the publication of the first ketamine abuse associated bladder tumors was reported in 2014.

Abdominal ultrasonography can be performed in the patients complaining abdominal pain or elevated liver enzymes. Dilatation of bile ducts is quite common. Without knowing the history of ketamine abuse, incision of Sphincter of Oddi had been performed without significant benefits. Panendoscopy may be performed in cases with frequent epigastralgia, though negative findings were usually reported.

4. Conclusions

We recommend essential and options tests to assess patients with ketamine abuse. Hopefully, patient characteristics can be clarified and different therapeutic strategies for ketamine uropathy can be compared in the future. Then we can have a treatment algorithm for ketamine uropathy soon!

Conflicts of interest

The authors declare that they have no financial or non-financial conflicts of interest related to the subject matter or materials discussed in the manuscript.

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Appendix A. Supplementary data

Supplementary data related to this article can be found online at http://dx.doi.org/10.1016/j.urols.2015.08.010.

References