# Suspected Ketamine-Associated Lower Urinary Tract Symptoms

Tzu-Rong Peng, <sup>1</sup> Ming-Chia Lee, <sup>1</sup> Ta-Wei Wu, <sup>1</sup> Chou-Chin Lan<sup>2,3</sup>

Buddhist Tzu Chi General Hospital, Taipei Branch, Taiwan. cine, Buddhist Tzu Chi General Hospital, Taipei Branch, Taiwan.

Division of Pulmonary Medicine, Bud-dhist Tzu-Chi General Hospital, Taipei

Tel: +886 2 6628 9779 Fax: +886 2 6628 9009 E-mail: bluescopy@yahoo.com.tw

Received November 2012 Accepted December 2012

**Keywords:** ketamine; urination disorders; lower urinary tract symptoms; etiology.

## INTRODUCTION

n increasing number of case reports of ketamine involving in urinary system complications, such as lower urinary tract symptoms (LUTS) or ulcerative cystitis, have been cited from the chronic abuse of ketamine. (1-7) Many health care professionals, however, are not aware of these under-diagnosed adverse effects. Thus, we report on a case of suspected ketamine associated contracted bladder and hydronephrosis and conduct a review of the related literature

## **CASE REPORT**

A 45-year-old male was admitted to our emergency department due to changed consciousness and renal function. He had a 3-year history of intranasal ketamine use and increased urinary frequency and urethral pain sine one year ago. The symptoms began only after the onset of ketamine use and resolved with treatment of oral propiverine 15 mg twice daily and oral tamsulosin 0.2 mg once daily and cessation of ketamine use. After two years then, however, the symptoms recurred after inhaled ketamine reused. In this admission, urine analysis showed hematuria and proteinuria. Urine cultures were sterile. The blood tests revealed white blood



**Figure**. The computed tomography imaging of the abdomen showed bilateral hydronephrosis (A), small bladder capacity (B) and gallbladder sludge (C).

cell 20,200/µL, neutrophil bands 3%, neutrophil segments 88%, C-reaction protein 21.25 mg/dL, serum creatinine 11.8 mg/dL, blood urea nitrogen 106 mg/dL, sodium 104 mmol/L, potassium 6.6 mmol/L, alkaline phosphatase 944 IU/L, gamma-glutamyltransferase 1998 IU/L, total bilirubin 2.46 mg/dL, direct bilirubin 2.25 mg/dL, lipase 1,165 IU/L, and amylase 212 IU/L. The computed tomography imaging of the abdomen showed bilateral hydronephrosis and small bladder capacity and no sign of pancreatitis. Besides, the echo imaging of abdomen revealed gallbladder sludge. A full screening confirmed the exclusion of other causes of liver disease. Ketamine associated lower urinary tract syndrome was diagnosed and ketamine associated gallbladder sludge was suspected (Figure). The hemodialysis and ureteral double-J placement were performed for poor renal function and bilateral hydronephrosis. Oral silymarin was given for poor liver function. Intravenous levofloxacin 750 mg single dose and 500 mg every other day was administrated for treating infection. After seven days, his renal and liver function improved, serum creatinine 1.7 mg/dL, blood urea nitrogen 38 mg/dL, total bilirubin 0.54 mg/dL, direct bilirubin 0.52 mg/ dL, gamma-glutamyltransferase 1,617 IU/L, lipase 1,405 IU/L, and amylase 328 IU/L, but no sign of pancreatitis, so he was discharged home due to stable condition. He also was referred to drug rehabilitation center for the problem of ketamine abuse.

#### DISCUSSION

Ketamine, an N-methyl-D-aspartic acid (NMDA) receptor

antagonist, has been used in veterinary medicine and for anesthesia purposes more than 30 years. It has been abused as a recreational drug in nightclubs due to the effects of hallucination and "near-death experiences". (8) However, the detrimental effects of ketamine are not understood by many recreational users, in particular on the central nervous system, respiratory and cardiovascular systems. Since 2007, several case reports of ketamine associated LUTS have been described, (1-7) all patients had a history of ketamine use. The clinical presentations of LUTS include dysuria, frequent urination, small volume voids and painful hematuria. (1,8) In addition, some reports indicated that the computed tomography imaging of the abdomen showed a small bladder capacity and unilateral or bilateral hydronephrosis. (1,4,8) Our patient's LUTS, a small bladder capacity and bilateral hydronephrosis are consistent with previous reports. Cystoscopy and biopsy were both refused by the patient. However the LUTS of our patient resolved after cessation of ketamine and recurred when he re-inhaled ketamine. The Naranjo probability scale (7 points) indicated a probable relationship between ketamine and LUTS in this patient (10) Tsai and colleagues demonstrated that the time of onset of LUTS after ketamine abuse ranged from 1 month to a few years. (5) In our patient, the onset of symptoms was about 1-2 years and the doses of ketamine are unknown. The mechanism of ketamine associated LUTS is still not clear. High concentrations of ketamine and its metabolites can be detected in the urine of patients using ketamine. (11) The direct toxicity of ketamine and its metabolites may cause significant bladder irritation and kidney damage. (4,12) At the early stage of the disease, ketamine cessation may resolve the LUTS. Cheung and colleagues have indicated the subjects who had ceased ketamine use for less than 3 months had significantly more urinary symptoms than those who had stopped for 3 months or more. However, those persons who abused ketamine for 2 years or more and ceased for less than 3 months, endured significantly poorer quality of life. (13) In addition, pentosan polysulfate sodium, antihistamine, and corticosteroid may help alleviate the irritable voiding symptoms. As the disease becomes more severe, such as painful hematuria, or impaired renal function, enterocystoplasty may be required. It is important to note that delayed diagnosis and intervention will eventually lead to irreversible renal damage. (4,12) The biliary abnormality due to chronic ketamine use is fully reversible, so Lo and colleagues suggest that biliary stenting should be avoided unless absolutely necessary. (13) According to our patient, ketamine associated urinary tract and biliary abnormality could appear simultaneously. Therefore, ketamine abuse should be considered as a potential cause if patients have unexplained cholestatic liver function tests and urinary tract syndrome. Health care workers should be alert to this disease and at risk patients should be informed about these possible side effects.

### CONFLICT OF INTEREST

None declared.

#### **REFERENCES**

- Shahani R, Streutker C, Dickson B, Stewart RJ. Ketamine-associated ulcerative cystitis: a new clinical entity. Urology. 2007;69:810-2.
- 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-
- Chen LY, Chen KP, Huang MC. Cystitis associated with chronic ketamine abuse. Psychiatry Clin Neurosci. 2009;63:591.
- Chiew YW, Yang CS. Disabling frequent urination in a young adult. Ketamine-associated ulcerative cystitis. Kidney Int. 2009;76:123-4.
- 5. Tsai TH, Cha TL, Lin CM, et al. Ketamine-associated bladder dysfunction. Int J Urol. 2009;16:826-9.
- Middela S, Pearce I. Ketamine-induced vesicopathy: a literature review. Int J Clin Pract. 2011;65:27-30.
- Nomiya A, Nishimatsu H, Homma Y. Interstitial cystitis symptoms associated with ketamine abuse: the first Japanese case. Int J Urol. 2011;18:735.
- Mason K, Cottrell AM, Corrigan AG, Gillatt DA, Mitchelmore AE. Ketamine-associated lower urinary tract destruction: a new radiological challenge. Clin Radiol. 2010;65:795-800.
- Naranjo CA, Busto U, Sellers EM, et al. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther. 1981:30:239-45.
- Moore KA, Sklerov J, Levine B, Jacobs AJ. Urine concentrations of ketamine and norketamine following illegal consumption. J Anal Toxicol. 2001;25:583-8.
- 11. Shahani R, Stewart RJ. Reply to letter-to-the-editor, Re: Shahani R, Streutker C, Dickson B, et al: Ketamine-associated ulcerative cystitis: a new clinical entity. Urology 69: 810-812, 2007. Urology. 2008;71:987.

- Cheung RY, Chan SS, Lee JH, Pang AW, Choy KW, Chung TK. Urinary symptoms and impaired quality of life in female ketamine users: persistence after cessation of use. Hong Kong Med J. 2011;17:267-
- Lo RS, Krishnamoorthy R, Freeman JG, Austin AS. Cholestasis and biliary dilatation associated with chronic ketamine abuse: a case series. Singapore Med J. 2011; 52:e52-5.