Ketamine A Cause of Urinary Tract Dysfunction



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KEYWORDS

• Ketamine • Urology • Urinary Tract Dysfunction • Inflammation • Bladder • Illicit

KEY POINTS

- Lower urinary tract symptoms such as urgency, frequency, dysuria, and hematuria are common urologic complaints in men and women and the differential remains broad.
- Illicit ketamine abuse is a growing problem and can lead to a cystitis symptom complex that mimics common genitourinary complaints.
- Ketamine abuse induces complex changes to the environment of the urinary tract, specifically the bladder, that can be observed clinically and at the molecular level.
- Currently, there is no standard for diagnosing and treating ketamine induced cystitis, however, treatment currently involves symptom management.
- More investigations should be done to develop standard and/or individually targeted diagnostic and treatment protocols for this emerging cause of cystitis.

INTRODUCTION

According to the 2014 national survey on drug use and health, approximately hundreds of thousands of people in the United States aged 12 and over have used illicit substances of varying types.¹ Drug addiction is a chronic relapsing disorder, and people who suffer with it tend to demonstrate binge use, intoxication, withdrawal associated with a negative emotional state, and anticipation of substance use that modifies the brain reward and stress systems.² The association between reward and stress has been demonstrated previously. For example, using a mouse model, Piazza and colleagues³ found that when mice were injected with corticosterone, self-administration frequency increased, particularly at higher doses. Interestingly, in

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this study, the investigators also found that different animals had different propensities to self-administer the steroids based on their individual sensitivities to drugs of abuse.

The neurobiological basis of addiction involves a complex array of circuitry and brain structures, and a detailed discussion of this topic is beyond the scope of this work. In brief, the mesocorticolimbic dopamine system involves forebrain structures like the nucleus accumbens, the midbrain's ventral tegmental area, and the amygdala, and is critical in modulating the reinforcing actions of many drugs of abuse (Fig. 1).

Aside from dopamine, other molecules like glutamate, dynorphin, corticotrophinreleasing factor, neuropeptide Y, and endocannabinoid also appear to be involved.^{2,4–6}

It is estimated that the lifetime prevalence for any prescription opiate use disorder in treated patients with chronic pain is approximately 42%.⁷ Other substances are also abused. For example, in a sample of 921 patients with prescriptions for opiates, a portion of these patients had promethazine- and benzodiazepine-positive urine. Of these individuals, only 50% had prescriptions for promethazine. In addition, the finding of benzodiazepine-positive urine without a prescription for it was associated with illicit promethazine use.⁸ Because of these kinds of findings, clinicians must be conscious of the abuse of other classes of medications.

In the urologic setting, a commonly abused drug that is becoming more of a problem worldwide is ketamine (Fig. 2).

Ketamine is important to the urologist because it can adversely impact the lower urinary tract. In addition, the clinical and objective findings can mimic a commonly

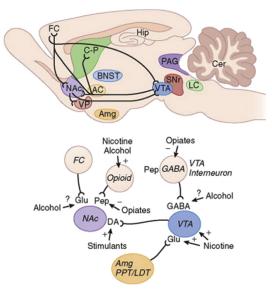


Fig. 1. Substances of abuse and complex interactions of brain neurocircuits. AC, anterior commissure; Amg, amygdala; BNST, bed nucleus stria terminalis; Cer, cerebellum; C-P, caudate-putamen; DA, dopamine; FC, cerebrofrontal cortex; Glu, glutamate; Hip, hippocampus; LC, locus ceruleus; NAc, nucleus accumbens; PAG, periaqueductal gray; Pep, opioid peptides; PPT/LDT, peduncular pontine tegmentum/lateral dorsal tegmentum; SNr, substantia nigra pars reticulata; VP, ventral pallidum; VTA, ventral tegmental area. (*From* Choi DS, Karpyak VM, Frye MA, et al. Drug addiction. In: Waldman SA, editor. Pharmacology and therapeutics: principles to practice. Philadelphia: Elsevier Saunders; 2009. p. 821; with permission.)

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