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Case report

Case Report: Ketamine Cystitis

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Abstract

Ketamine was created in the early 1960s and is utilized as a dissociative anesthetic with sedative and analgesic effects in both human and veterinary medicine. Lately, the medication has been utilized in palliative medicine to treat a variety of conditions, including chronic pain and refractory depression [1-3]. Ketamine gained popularity as a recreational drug due to its ability to produce a variety of dissociative effects. Ketamine is a non-competitive antagonist of the N-methyl D-aspartic acid (NMDA) receptor for glutamate and a derivative of phenycyclidine. It may cause a variety of adverse effects because of its intricate metabolism and interacts with many receptors. The medication primarily undergoes liver transformation before being eliminated by urine, which has a toxic effect on the urinary system and can cause lower urinary tract syndrome (LUTS), which manifests as suprapubic discomfort, dysuria, frequency, urgency, incontinence, macroscopic haematuria, and dysuria with typically negative urine cultures.

Keywords: Ketamine cystitis; urinary tract infection; incontinence; haematuria, dysuria

Introduction

Ketamine was created in the early 1960s and is utilized as a dissociative anesthetic with sedative and analgesic effects in both human and veterinary medicine. Lately, the medication has been utilized in palliative medicine to treat a variety of conditions, including chronic pain and refractory depression. Ketamine gained popularity as a recreational drug due to its ability to produce a variety of dissociative effects. Ketamine is a non-competitive antagonist of the N-methyl D-aspartic acid (NMDA) receptor for glutamate and a derivative of phenycyclidine. It may cause a variety of adverse effects because of its intricate metabolism and interaction with many receptors. The medication primarily undergoes liver transformation before being eliminated by urine, which has a toxic effect on the urinary system and can cause lower urinary tract syndrome (LUTS), which manifests as suprapubic discomfort, dysuria, frequency, urgency, incontinence, macroscopic haematuria, and dysuria with typically negative urine cultures. In 2007, reports of the first cases of LUTS linked to ketamine and resistant to therapy were made. The term "ketamine induced vesicopathy" (KIV) [4], "ketamine-induced urologic insult" (KIUI), "ketamine associated (ulcerative) cystitis" (KA(U)C) [5], or "ketamine cystitis" (KC) [6] have all been used to describe this new entity in several published studies since its discovery.

Case presentation

We report the case of a 23-year-old woman who had been experiencing symptoms of recurrent lower urinary tract infection including frequency, urgency, nocturia, and discomfort during micturition for the previous two years and was not responding to antibiotics. The patient, who used ketamine recreationally, received treatment for chemical dependence in a specialist facility and was now drug-free. Nevertheless, the symptoms persisted. Only one of the several urinalyses performed during the 2-year follow-up verified the presence of white blood cells and red blood cells; all other urinalyses were sterile and showed no abnormalities. During the follow-up, many ultra sonographies were conducted to look for possible upper urinary tract injury, but no significant alterations were discovered. Nevertheless, the results of the computer tomography showed a 38 ml estimated decrease in bladder capacity, although no thickening of the bladder wall was seen. A

recent urodynamic exam verified decreased bladder capacity and showed a maximal urine flow rate (Qmax) of 9 ml/s for a voiding volume of 112 ml, along with a detrusor pressure of 40 cm H20.

The proposed and prescribed treatment of first intention, as recommended by the general practitioner, included the use of nitrofurantoin and norfloxacin. However, despite following this treatment, no improvement was observed. Subsequently, the patient consulted a urologist and treatment based on propiverine hydrochloride, solifenacin (5mg) and oxybutynin respectively was introduced. Nocturia, or the need to wake up during the night to urinate, was not found to be affected by the treatment. Nonetheless, there was a moderate improvement observed in urinary frequency during the day. In a subsequent course of treatment, tamsulosin was prescribed, however, it did not yield any noticeable effects on the patient's symptoms. In the present study, the patient is undergoing therapy with solifenacin, a medication known for its efficacy in managing urinary frequency. Although the treatment has resulted in mild improvement, the patient continues to experience urinary frequency during the day, with episodes occurring more than once per hour. To re-educate the bladder, it is recommended to incorporate voiding diary as an additional measure. Further follow-up is foreseen for early detection of upper urinary damage and observation of possible improvement of symptoms induced by ketamine abstinence.

Discussion

Thus far recognition of KC remains a non-standardized process since no strict diagnostic criteria were described to confirm the KC. Therefore, the presence of ketamine abuse in anamnesis and clinical presentation of LUTS including dysuria, frequency, urgency, and gross haematuria combined with no other possible explanations are usually sufficient to make a diagnosis of KC. Further investigation implies use of different exams involving ultrasonography, urine analysis, CT, cystoscopy and intravenous urography. In the case of our patient the diagnosis was made on the basis of history of ketamine abuse and clinical signs such as dysuria, frequency, urgency, nocturia. However, no haematuria was detected with one exception when urinalysis showed white blood cells and red blood cells without any bacterial growth. So far, no histopathological data is available in our case. Although CT-scan of mild KC may show no pathological changes, in severe form it usually shows bladder contraction and wall thickening [7]. Additionally, Ureter dilatation, ureter wall thickening, vesicoureteral reflux and hydronephrosis may be demonstrated in advanced cases of KC. In the presented case CT-scan done one year ago showed bladder capacity of 38ml whereas no significant changes in terms of wall thickness were observed.

However, the urodynamic exam showed voiding volume of 112ml, decreased bladder capacity, detrusor pressure of 40 cm H2O and bladder compliance of 112/40 [8]. The first symptoms included dysuria, urinary frequency and urgency suggested infection of lower urinary tract that's the reason why antibiotics were given at first. Urinalysis and bacterial cultures were done and permitted to exclude any infection, so the patient consulted the urology department. Further investigation involved broaden interview, ultrasonography toward diagnosis of overactive bladder conducted to treatment based on anticholinergic agents (solifenacin, oxybutynin) and others therapeutic options including propiverine hydrochloride and. A moderate attenuation of urinary frequency after solifenacin treatment was observed therefore it remains current medication. However, the physiopathology of ketamine associated cystitis remains unclear, recently presented hypothesis included: direct toxic effect, bladder barrier dysfunction, neurogenic inflammation, immunoglobulin-E-mediated inflammation, overexpression of carcinogenic genes, abnormal apoptosis and nitric oxide synthase-mediated inflammation [9].

However, the precise mechanism of KC pathogenesis remains unknown, no specific treatment is yet available. As a consequence, the therapy should be adapted at an individual level and depend mainly on gravity of the symptoms. The literature findings reported improvement of the symptoms after abstinence from ketamine, it seems to be a first-line therapy and should be applicated in all cases of KC. Anticholinergic agents can be used to improve the severity of symptoms whereas there is no evidence of its impact on pathogenesis of KC as LUTS are mostly caused by contracted bladder and chronic inflammation. As KC share some resembling in terms of histological presentation with IC the use of pain modulators such as tricyclic antidepressants and anti-inflammatories agents like H2 receptor antagonists, NSAID or COX2-inhibitors may have a positive impact on damaged epithelium. Non-steroidal anti-inflammatory drugs inhibitors seems to have poor impact on symptoms improvement therefore the steroid drugs can be used to decrease inflammation. However, the efficacy of this treatment remains limited even if combined with other therapies.

Other therapeutic strategies aimed at repairing the damaged urothelial involving sulphate GAG (pentosan polysulfide, chondroitin sulfate) and non-sulphate GAG (hyaluronic acid) resulted in symptom relief in some patients. What's more, one case of complete disappearance of the symptoms after intravesical hyaluronic acid instillation was reported [10]. Intravesical botulinum toxin injection showed successful results; however, its effectiveness might be limited by advanced damages and lack of ketamine abstinence. In severe, symptomatic cases, cystodistension was proposed to increase bladder capacity and reduce pain. The last line of treatment to relieve renal function includes subtotal cystectomy, cystoplasty, double J stent or nephrostomy. The bibliographic finding describes other potential complications of KC containing unilateral or bilateral hydronephrosis and vesicoureteral reflux (VUR) that can engender papillary necrosis. Cases of raised creatinine level were reported as well. Exempting deleterious effects of ketamine on urinary tract, potential affiliation between the drug and various pathologies including hepatobiliary complications, upper-GI symptoms, neuropsychiatric disorders, and sexual disorders in both genders have been reported [11].

Our patient's follow-up involved ultrasonography completed with two Ct-scans who allowed exclusion of hydronephrosis, vesicoureteral reflux and cholangiopathy. Neither epigastric pain nor recurrent vomiting were reported at this stage whereas those symptoms seem to anticipate LUTS. Blood analysis showed no increase of creatinine and no complaints indicating sexual disorders were reported. Nevertheless, it is essential to control these aspects in further follow-up and instore adequate treatment immediately in case of emergence of any supplementary complications to avoid exacerbation and potential irreversible damages. Because of absence of complications, the current treatment consists of solifenacin and ketamine abstinence. Although there is no proof of effectiveness of anticholinergic agents in KC, they may improve symptoms of some KC patients with mild symptoms. However, it is essential to find an effective therapy in the aim to prevent irreversible complications of KC therefore if the severity of symptoms persists, second-line strategies will be adapted. Additionally, further investigation by cystoscopy is foreseen.

Conclusion

Since the initial publications describing the association between ketamine abuse and lower urinary tract symptoms (LUTS), subsequent studies have been undertaken with the objective of comprehending the underlying mechanism responsible for the manifestation of these clinical symptoms. Despite the growing understanding of this condition, there appears to be a lack of corresponding awareness among medical professionals. The underdiagnosis of a condition known as (KC) is a prevalent issue, which suboptimal treatment can lead to an irreversible harm. The rising consumption of ketamine in both recreational and medical contexts requires medical professionals to possess a comprehensive understanding of its potential adverse impacts on the lower urinary tract and other bodily systems. The usage of ketamine should be carefully evaluated in cases where patients reveal lower urinary tract symptoms (LUTS) and no other underlying cause has been identified during the medical history assessment.

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