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Case Report

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Management of Ketamine Abuse with Dextromethorphan-Bupropion & Naltrexone

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Abstract

Background: Ketamine abuse has been documented as early as the 1970s. Effects of Ketamine intoxication include, but are not limited to, sedation; dream-like states; auditory hallucinations; and visual hallucinations. Long-term abuse has been linked to a variety of pathologies including nephrotoxicity and urinary bladder dysfunction. Despite the degree of harm Ketamine abuse may cause patients, there remains a paucity of literature on how best to manage the condition. ***Case Presentation:*** Our case concerns a 20-year male with a history of depression and substance abuse. In the antecedent weeks, the patient had experienced worsening of his depressive symptoms and his Ketamine abuse. The patient was thereafter treated with psychotropic medication, including Dextromethorphan-Bupropion which led to a dramatic improvement in his condition and was thereafter also given Naltrexone therapy to better enhance his abstinence from substance abuse. ***Conclusion:*** This article highlights the challenges faced in the management of Ketamine abuse patients, especially in the context of comorbidities such as depression. Here we have highlighted the potential for Dextromethorphan & Bupropion based rapid acting antidepressant therapy along with Naltrexone for the management of patients suffering from this condition.

Keywords: ***Dextromethorphan, Ketamine, Substance Abuse, NMDA Receptor, Depression.***

Introduction

Ketamine is a dissociative anesthetic developed & derived in 1962 from Phencyclidine.

Reports of abuse date back as early as 1971 with Ketamine earning a reputation as a "club drug" by the 1980s. In view of the increasing misuse Ketamine was classified as a Schedule III controlled substance by 1999. Ketamine may be abused by intravenous injection or by using tablets, capsules or powders in oral, intranasal or smoked form. When used recreationally, Ketamine produces a plethora of effects including possible sedation, relaxation (K-land), a dream like state (K-hole), auditory/visual hallucinations but, less desirable effects such as chest pain, tachycardia, paralysis, blurred vision are also possible. Concerns related to Ketamine abuse include schizophrenia-like symptoms, driving under the influence, nephrotoxicity, urinary bladder dysfunction and fatty degeneration of liver and hepatic fibrosis [1,2]. In view of the above, it is imperative that Ketamine abuse in patients be managed and treated as best as possible.

Case Presentation

The patient is a 20-year-old, single male with a past history of treated clinical depression, ongoing marijuana abuse.

History

The patient presented to the clinic with complaints of depressive symptoms including decreased appetite, isolation and withdrawal. He expressed currently feeling empty, lonely and numb. He had ongoing sleep problems and anxiety symptoms in the form of panic attacks. He did not currently present with apparent manic symptoms or psychotic symptoms such as delusions & auditory or visual hallucinations. The patient revealed that he had been abusing 2cb (4-bromo-2,5-dimethoxyphenethylamine) and Ketamine for the past 2 years with an increase in substance abuse within the past few weeks, snorting as much as 1000 mg Ketamine most nights.

Treatment

In view of the above, substance/medication-induced depressive disorder was suspected and the patient was started on

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Dextromethorphan HBr - Bupropion HCl (Auvelity) 45-105mg PO OD for depression along with Mirtazapine, which was increased up to 15 mg PO HS for sleep.

Follow-up

On follow up 10 days later, the patient reported feeling better with decrease in substance use and complete abstinence in substance use for the past 48 hrs. However, sleep disturbance persisted, now with vivid nightmares and waking up drenched in sweat. In view of the above Quetiapine 100 mg PO HS was added to improve sleep. In an attempt to maintain abstinence and control depressive symptoms Auvelity 45-105 mg was increased to BID. Naltrexone 25 mg PO OD for 3 days followed by an increase to 50 mg PO OD was added to further strengthen abstinence.

Discussion

The above discussed patient suffered from Ketamine abuse along with depressive tendencies. Literature supports that underlying depression may contribute to substance abuse, given that both may share common predisposing factors and may have bidirectional effects [3]. In accordance with this, the patient was started on Dextromethorphan-Bupropion (Auvelity), a novel rapid acting antidepressant so as to break the reinforcing effects of depression on substance abuse. Bupropion is a norepinephrine dopamine reuptake inhibitor antidepressant itself and it enhances the antidepressant activity of Dextromethorphan (DXM) by CYP2D6 inhibition and thus increasing its half-life [4,5]. Moreover, DXM and ketamine act on similar neurobiological pathways in order to impart their psychiatric effects, such as rapid acting antidepressant activity, thus making DXM based therapy a potential option of interest in patients with a history of Ketamine abuse. Shared mechanisms include non-competitive antagonism at NMDA receptors, sigma receptor agonism and serotonin transporter inhibition. Both may cause an increase in mTOR activity, leading to increased AMPA signaling and synaptogenesis [6]. To be noted, it may be possible that not only does Dextromethorphan have antidepressant properties in these patients, it may to an extent also serve as “maintenance” therapy for their Ketamine abuse.

Previous treatment strategies discussed in the literature for the maintenance phase in patients who have abused Ketamine are limited and include few case reports on utilization of Naltrexone or Lamotrigine or the use of intramuscular Paliperidone palmitate with Bupropion [7]. Naltrexone is an opioid antagonist, first synthesized in 1963. It has shown to be beneficial across a plethora of addictive disorders including alcohol abuse, opioid abuse, nicotine abuse, stimulant use disorders and has been suggested to be a pan-addiction treatment. Possible mechanisms for the benefit of naltrexone may include mu-opioid receptor antagonism and consequent amelioration of impulsivity associated with addiction disorders [8]. Naltrexone in doses of 25 to 50 mg PO OD in these case reports has been shown to successfully maintain abstinence from Ketamine for prolonged periods, as long as 12 months [7,9,10]. In view of the above evidence, the patient was started on Naltrexone to further their maintenance.

As per our knowledge, this is the first instance in literature documenting the role of DXM & Bupropion based rapid acting antidepressant therapy along with Naltrexone being used for the treatment of patients suffering from Ketamine abuse.

Conclusion

Treatment for Ketamine abuse remains poorly documented in literature with treatment strategies including mu-opioid antagonists such as Naltrexone, mood stabilizers like Lamotrigine & antipsychotics like Paliperidone. This article highlights the challenges faced in the management of these patients, especially in the context of comorbidities such as depression. Here we have highlighted the potential for DXM & Bupropion based rapid acting antidepressant therapy along with Naltrexone for the management of patients suffering from this condition.

Declarations

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None

Conflict of Interest

Authors have no conflicts of interest to declare.

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