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Gratis

Case Report

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Use of Ketamine to Treat Depressive Symptoms in Schizoaffective Disorder

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Abstract

The use of subanesthetic ketamine infusions in treatment resistant depression and bipolar depression is becoming more common. Subanesthetic doses of ketamine cause the patient to dissociate, which was initially considered a side effect of this treatment; it is believed to play a role in a patient'sclinical improvement. Researchers attribute this result to an increase in brain-derived neurotrophic factor, a growth factor that stimulates the formation of new synaptic connections. Due to its psychogenic affect, ketamine treatment is less suitable for patients who experience mood disorders with psychotic features. Although symptomatic hallucinations seemingly conflict with the dissociative effects of ketamine, treatment of a patient with depressive type schizoaffective disorder revealed significant improvements in his depressive symptoms, demonstrating ketamine's potential to be safely administered to patients with a variety of complex disorders.

Keywords: Schizoaffective disorder, Depression, Ketamine

Abbreviations: ADHD: Attention-Deficit/Hyperactivity Disorder; BDNF: Brain Derived Neurotrophic Factor; HAM-D: Hamilton Rating Scale for Depression; NMDA: N-methyl-D-aspartate; QIDS-SR16: Quick Inventory of Depressive Symptomatology; TRD: Treatment Resistant Depression

Introduction

Schizoaffective disorder is a chronic mental disorder characterized by psychotic symptoms such as delusions, visual and/or auditory hallucinations, as well as symptoms of either treatment resistant depression (TRD) or bipolar depression . Patients are diagnosed with either depressive type or bipolar type schizoaffective disorder. The combination of psychotic symptoms and manic or depressive states can be debilitating. Ketamine is a dissociative anesthetic which primarily acts as an antagonist on the N-methyl-D-aspartate (NMDA) glutamate receptor. Research demonstrates that ketamine stimulates the expression of brain derived neurotrophic factor (BDNF), which is associated with its antidepressant effects [1]. Due to the complex and potentially dangerous interactions between the psychotic symptoms of schizoaffective disorder and ketamine, there are few reported cases in which doctors safely have administered ketamine to treat the depressive symptoms of the disorder on a short term basis. This case discusses a patient in whom ketamine treatment safely improved

the depressive symptoms of the disorder on a more long term basis. Although ketamine has yet to be used exclusively to treat the long term psychotic symptoms of this disorder, an alternate study showed that ketamine improved depressive symptoms from a 21 to a 4 on the Hamilton Rating Scale for Depression (HAM-D) over a four day hospitalization with a 300 mg ketamine treatment [2].

In the following case, a patient with depressive type schizoaffective disorder observed an improvement in mood and depressive symptoms and reported no exacerbation of psychotic symptoms after six ketamine treatments with one maintenance infusion. Additional research is needed to replicate these findings to gain a better understanding of the effects ketamine may have on patients with schizoaffective disorder. Yet, this is a promising start, demonstrating ketamine's ability to be safely administered to these patients.

Case Presentation

A 24-year-old man presented to our clinic with complaints of TRD and anxiety. His previous depression treatment included escitalopram, venlafaxine, and fluoxetine, all of which proved ineffective. Upon presentation, his depression was treated with a daily 90 mg dose of duloxetine. The patient never underwent electroconvulsive therapy, but received weekly neurofeedback psychotherapy, which continued throughout the duration of the ketamine treatment period. At age 16 he was diagnosed with depressive type schizoaffective disorder as well as panic disorder, and attention-deficit/hyperactivity disorder (ADHD). His schizoaffective symptoms included paranoia, delusions, and auditory hallucinations which were treated with 600 mg Lithium Carbonate and 40 mg lurasidone HCl. Prior to treatment, the patient reported hearing voices approximately twice a month for eight years. The patient was on a regimen of lisdexamfetamine dimesylate and trazodone for ADHD and sleep management, respectively. The initial treatment protocol at our clinic includes two weeks of every other day infusions with no change to regular medications. The patient was initially started on a ketamine dose of 0.5mg/kg, which was incrementally increased as tolerated to reach a desired target depression inventory rating (i.e., a 50% change from initial rating). The patient continued his treatments to reach this desired rating. Patient progress was tracked with self-reported scores on both the Beck's Depression Inventory and the Quick Inventory of Depressive Symptomatology (QIDS-SR16). The staff administered these inventories prior to each treatment with interpretation as follows:

QIDS: Scale 1-27. 1-5 = no depression, 6-10 = mild depression, 11-15= moderate depression, 16-20= severe depression, 21-27 = very severe depression

Beck: Scale 1-40+. 1-10 = normal, 11-16 = mild mood disturbance, 17-20 = borderline depression, 21-30 = moderate depression, 31-40 = severe depression, 40+ = extreme depression

Prior to the first treatment, the patient was categorized with severe depression according to both the Beck and QIDS scale with scores of 31 and 16, respectively. Following the first maintenance infusion, the patient's ratings improved significantly. The following data was observed for the first six treatments:

Table 1: Depression ratings for six treatments.

Date	QIDS	Rating	Beck	Rating
3/21/18	16	Severe	31	Severe
3/28/18	10	Mild	23	Moderate
2/4/2018	12	Moderate	28	Moderate
6/4/2018	12	Moderate	23	Moderate
4/23/18	15	Moderate	10	Normal
7/5/2018	14	Moderate	25	Moderate
5/15/18*	13	Moderate	21	Moderate

*maintenance infusion

Discussion

To date, the patient in this case has not yet reached the indicated target scores on his respective depression inventories, but remains in treatment. The patient responded positively to all aspects of ketamine infusions with minimal side effects. This case is one of the first examples of the safe treatment of schizoaffective disorder using ketamine with no exacerbation of psychotic symptoms. In fact, the patient even reported a decrease of certain psychotic symptoms. While this patient under our treatment appears to have marginal improvement in depressive symptoms associated with schizoaffective disorder, there are several more qualitative points to consider even with the fluctuation in quantitative scores.

First, the self-reported nature of the scores cannot be overlooked while interpreting results. Other symptoms of schizoaffective disorder, besides depression, may contribute to depression inventories and potentially confound results. Additionally, basic classification of schizoaffective disorder and other schizotypal disorders detail an episodic nature wherein patients experience episodes with intense symptoms followed by a recovery

period with little to no symptoms [3]. It is possible that the patient experienced a depressive episode during this highlighted six treatment period, thus inflating both inventory scores and the reported relief. The complexity of schizoaffective disorder makes it far more difficult to understand the effect of ketamine treatment when compared to the less variant symptoms of TRD and bipolar depression.

Additionally, the observations of clinical staff should be considered. The staff observed improvements in patient affect, morale, and appearance following just one treatment. Upon initial presentation the patient appeared removed and distant, but has since appeared friendlier and more energetic. Additionally, the staff reported that early in the patient's treatment course he demonstrated a lack of interest and compliance when filling in inventories and other paperwork.

Verbal patient reports indicated significant improvements in mood. When interacting with staff, the patient responded positively when questioned about progress. Interestingly, the patient reported a stabilization in auditory hallucinations. After initiation of treatment, the twice monthly hallucinations stopped entirely. This is a remarkable and unexpected improvement. It is possible that this improvement is indicative of the general mood stabilization brought about by the treatment. However, one also must consider the possibility that ketamine has a deeper neurologic effect on auditory hallucinations. The origins of such hallucinations are still in question, but research has shown patients who suffer from hallucinations display abnormalities in the brain's white matter upon F-MRI, as well as connectivity problems between the frontal and parietotemporal speech-related areas [4]. Ketamine stimulates the expression of BDNF, which effectively creates new neural connections and strengthening existing ones. Thus, ketamine may be able to positively effect the abnormal speech area connections. Additionally, chronic ketamine exposure damages white matter in the brains of cynomolgus monkeys [5]. If this observation translates to human physiology as well, it is possible that controlled ketamine exposure may balance out the increase in white matter brought about by auditory hallucinations. These hypotheses must be investigated thoroughly before any definitive conclusions can be drawn on ketamine's ability to treat auditory hallucinations.

Additional study of ketamine treatment for schizoaffective disorder is required to demonstrate replicability of these findings. With the popularization of the use of intravenous subanesthetic doses of ketamine to treat both mood and personality disorders, more research must be carried out to understand the complete long term effects of this type of treatment. One must consider the correlation between dissociation and depression recovery. This issue becomes more opaque when considering mood and personality disorders accompanied with psychotic symptoms, like those with schizoaffective disorder. The use of ketamine for various psychiatric disorders is in its infancy, however, our observations suggests a possible novel use for this agent.

Declarations

A signed consent from the patient was obtained prior to treatment to participate in this study and to have de-identifed data published. De-identified data is available for review upon written request of the Journal's Editor. Drs. Nandra and Wiesman have a financial interest in the Ketamine Centers of Chicago as owners/operators. The study has received no internal or external funding. Each author has contributed substantively to the study by data analysis, background research, delivery of care, and manuscript preparation.

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