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Case Report

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Potential Role of Ketamine in the treatment of Schizoaffective Disorder, Depressive Type

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Abstract

Ketamine use for patients with severe treatment-resistant depression continues to be an area of interest due to the relatively limited number of treatment options for those patients. Although its use as a treatment option for patients with schizophrenia and schizoaffective disorder may seem counterintuitive, in this case report, we explore the efficacy of ketamine for depressive episodes in schizoaffective disorder. This patient who carried a diagnosis of schizoaffective disorder was given 300 mg of intramuscular ketamine for agitation. However, over the course of four days of inpatient stay, her depression drastically improved. She met criteria for remission with the Hamilton Rating Scale for Depression (HAM-D) score of 4, down from an initial score of 21. We advocate for a better understanding of the pros and cons of using ketamine for depression in schizoaffective disorders considering the controversy over the diagnosis of schizoaffective disorder, especially in African American population. At the urging of reducing the risk of suicide among this group and improving their quality of life as well as reducing financial burden by shortening total duration of hospitalization, it may be worthwhile to explore the feasibility of ketamine as a treatment option for severe depression in these patients, possibly as a last resort.

Keywords: Ketamine, Schizoaffective, Depression, African Americans, Hamilton Rating Scale for Depression (HAM-D)

Introduction

Recently, there has been remarkable interest in the use of ketamine as a rapid-acting antidepressant to treat depressive episodes, both unipolar and bipolar disorders [1-3]. However, due to its dissociative and psychogenic effects, Ketamine has not been suitable for mood symptoms when associated with psychotic disorders [4]. It may need to be further investigated especially in a case of depression in the course of the schizoaffective disorder. Since misdiagnosis of affective disorders with psychotic features as schizoaffective disorder is not uncommon especially in minorities in the United States, it may be worthwhile to explore the efficacy of ketamine for depressive episodes in schizoaffective disorder [5, 6]. Here we report a case where a female African American patient with a diagnosis of schizoaffective disorder who received a dose of ketamine as a chemical restraint. Although ketamine was not effective in treating agitation, the patient's depressive symptoms remitted four days after she received a single dose of ketamine. With this case, we argue for a better understanding of the pros and cons of using ketamine for depression in schizoaffective disorders.

Case Presentation

The patient was a 38-year-old African-American female who presented to the emergency room (ER) after her family members had called the police since the patient had been threatening them. At the time of admission, she was highly combative, restless, uncooperative, providing minimal information, and needing to be in four-point restraints in the ER. Initial measures were unsuccessful in reducing combative behavior, and before completing a psychiatry consult, the patient had received 300 mg of intramuscular ketamine. The patient was unwilling to participate in an interview, and the collateral history indicated a diagnosis of schizoaffective disorder and the patient was not adherence to her medications. The psychiatry consultation liaison team recommended 5 mg intramuscular olanzapine for combative behavior and mood lability since ketamine did not show any acute benefits. After receiving olanzapine, the patient was far more cooperative and endorsed using synthetic cannabinoids as well as cannabis use. Her laboratory workup was significant for creatine phosphokinase (CPK) of 661 IU/L, thyroid-stimulating hormone of 0.36 mU/mL and free T4 of 1.2 NG/DL (which was within normal range), asymptomatic hematuria (negative urine nitrite and esterase), and positive urine toxicology for cannabis. The psychiatry consultation-liaison team recommended inpatient psychiatric stabilization. The patient's mental status examination by the time of admission to the psychiatric unit had improved, but she remained depressed with restricted affect. The next morning, she was calm, cooperative, and pleasant, denied thoughts of aggression towards family members, and reported no suicidal ideations, no auditory or visual hallucinations or delusional thoughts. On day 4 of admission, the patient completed HAM-D twice. First, she was instructed to consider her mood in the 2-week period before admission, which produced an HAM-D score of 21. For the second evaluation, she

was told to focus on her mood at the time of completing the HAM-D assessment, which produced an HAM-D score of 4. On hospital day six, follow up with her outpatient providers was established and she was discharged to home with her family members who welcomed her back.

Discussion

Ketamine is a NMDA receptor antagonist that has been used for decades as an anesthetic but has recently been found to have potential use in cases of severe treatment-resistant depression both in unipolar and bipolar disorders [1]. Ketamine is not FDA approved for depression, and its off-label use has become controversial because of its history as a substance of abuse. However, the use of ketamine in the treatment of severe depression continues to be an area of interest by many in the field of psychiatry due to the relatively limited number of treatment options for patients with severe treatment-resistant depression [1-3, 12].

Ketamine is a dissociative anesthetic that can cause psychosis [4]. Thus, it is thought that ketamine would not be appropriate as a treatment option for patients with schizophrenia and schizoaffective disorder [4]. However, considering the controversy over the diagnosis of schizoaffective disorder and the over diagnosing of mood disorders with psychotic features, especially in African American population [7, 9-11], it may be worthwhile to explore the feasibility of ketamine as a treatment option for severe depression in these patients, possibly as a last resort.

The dichotomous view of schizophrenia and mood disorders with psychotic features was less than desirable; thus the diagnosis of schizoaffective disorder was introduced [7]. This category created a challenge of its own. Compared to schizophrenia, the diagnosis of schizoaffective disorder is less stable over time, with patients later being diagnosed with either schizophrenia or mood disorders with psychotic features [9]. The question of how to differentiate mood disorder with psychotic features and schizophrenia spectrum disorders has remained debatable for the past century [7]. Even today, with shared genetic variations and endophenotypic characteristics, the differentiation between schizophrenia and affective disorders remains a challenge [8]. The challenge is even greater for African Americans and women [7]. It is known that psychotic disorders are over diagnosed in African American populations [10, 11]. Moreover, in a study of a Danish population of over 2 million, Laursen et al. reported that the chance of a bipolar woman being admitted with the diagnosis of schizoaffective disorder was 103 times higher than the general population of the same age [7]. Due to the unfavorable side effect profile of ketamine and safety and efficacy of antipsychotics, ketamine is used less often but successfully in the emergency setting for agitation [13-15]. The patient, who carried a diagnosis of schizoaffective disorder, in this report, was given 300 mg of intramuscular ketamine for combative behavior. In our patient, behavioral and mood changes responded better to olanzapine, but over the course of four days of inpatient stay, her depression scores drastically improved and she met criteria for remission with the HAM-D score of 4, down from an initial HAM-D score of 21.

This case advocates for considering ketamine as a possible intervention for depression in schizoaffective disorder and possibly schizophrenia. Depressive symptoms are common in schizophrenia [17] and are associated with increased morbidity and mortality [16]. As in the general public, patients living with schizophrenia and schizoaffective disorders are more likely to die by suicide if they have depressive symptoms. It is reported that as many as 40% of patients with schizophrenia and schizoaffective disorder will attempt suicide and 10% will complete suicide in their lifetime [18]. In a meta-analysis of over 25,000 patients, Palmer et al. reported that about 5% of patients with schizophrenia would die by suicide [19]. Kuo et al. reported a strong association between depressive symptoms in residual periods and completed suicide (OR= 23.07, $p < .005$) [20]. Similarly, in a systemic review of 29 studies, Hawton et al. reported a robust association between depressive symptoms and completed suicide in patients with schizophrenia (OR=3.03) [21]. Compared to schizophrenia, schizoaffective patients are more likely to attempt to take their lives if they have depressive symptoms [22]. Thus, identifying measures to improve depressive symptoms will improve the quality of life and reduce the premature death in patients with a diagnosis of schizoaffective disorder. There are very few treatments for acute suicidal behaviors in patients with schizoaffective disorders. Early studies showed that electroconvulsive therapy reduced suicide in patients with the schizoaffective disorder [23]. Ketamine has been found helpful in both unipolar and bipolar depression [1-3]. In bipolar depression, Zarate at al. reported an 80% response rate in a small clinical population [2]. Thus, ketamine may be valuable in treating depressive symptoms in schizoaffective disorder depressed type or bipolar type. Although further studies are needed, the preliminary data suggests ketamine as a promising rapid-acting anti-suicidal intervention [12]. Currently, there are some US clinical trials underway examining ketamine's variety of applications beyond anesthesia and sedation, including suicidality and treatment-resistant depression. The case report presented here (albeit N=1) advocates for considering ketamine in schizoaffective disorder.

Conclusions

Although it is counterintuitive to think of ketamine as a treatment option for patients with schizophrenia and schizoaffective disorder, this agent may contribute to an acute improvement of depressive symptoms in a select group of this population who experience severe depressive symptoms. We also have a hope that it may improve the quality of life for a selected group of such patients. It also can help in reduce financial burden by shortening total duration of hospitalization and may mitigate the risk of suicide among this group. Thus, we advocate for inclusion of patients with schizophrenia and schizoaffective disorders who also have significant depressive symptoms in well-designed studies using ketamine as acute antidepressant measure.

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