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Case Report

Efficacy of Once-Weekly Esketamine in Major Depressive Disorder Accompanied by Suicidal Ideation

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Abstract

This case report presents a 26-year-old male diagnosed with major depressive disorder (MDD), who experienced a relapse despite treatment with high-dose Venlafaxine. The patient was administered Esketamine nasal spray once weekly at a starting dose of 56 mg. Following Esketamine treatment, the patient demonstrated significant clinical improvement, with a noticeable reduction in depressive symptoms. However, the patient self-discontinued the treatment after feeling better, leading to a relapse characterized by low mood, hopelessness, and suicidal ideation. This relapse prompted a reevaluation of the treatment plan, and Esketamine was reintroduced at the same weekly dosage, with a subsequent dose adjustment to 84 mg weekly due to clinical need. Although the patient experienced dissociative symptoms at higher doses, these occurred only after the first session. The patient ultimately achieved remission with the adjusted dosage, highlighting the rapid antidepressant effect of Esketamine. The report emphasizes the efficacy of Esketamine in the treatment of treatment-resistant depression (TRD), the importance of adherence, the need for careful monitoring for adverse effects, and the role of individualized management in optimizing outcomes.

Keywords: Treatment-resistant depression (trd); Smoking cessation; Dissociation; Venlafaxine; Esketamine; Major depressive disorder

Introduction

Major Depressive Disorder (MDD) is a chronic and recurrent mental health condition that affects mood, cognition, and physical health, often necessitating long-term pharmacological and psychological interventions [1]. Although a wide array of antidepressants is available, a substantial proportion of patients fail to achieve adequate symptom control. Treatment-Resistant Depression (TRD) is typically defined as the lack of satisfactory response to at least two different antidepressants of adequate dose and duration from different pharmacological classes [2]. It is estimated that 20-30% of individuals with MDD meet the criteria for TRD, leading to increased morbidity, functional impairment, suicidal risk, and healthcare utilization [3,4].

The neurobiology of TRD is complex and involves dysregulation of monoaminergic systems, as well as glutamatergic neurotransmission and neuroplasticity-pathways not fully addressed by conventional antidepressants [3,5]. Esketamine, the S-enantiomer of ketamine, is a rapid-acting NMDA receptor antagonist that modulates glutamatergic signaling and promotes synaptogenesis. In 2019, it received FDA approval for use in adults with TRD, offering a novel mechanism distinct from traditional monoaminergic antidepressants [4,6].

Clinical trials have shown that esketamine nasal spray, in conjunction with an oral antidepressant, significantly reduces depressive symptoms, with improvements evident within 24 hours in many cases [2,5]. Furthermore, its use has shown promise in patients with acute suicidal ideation or behavior, addressing an urgent unmet need in psychiatric care [7].

This case explores the clinical presentation and therapeutic journey of a patient with TRD, highlighting the impact of esketamine nasal spray on symptom relief, relapse risk after discontinuation, adverse effects, and the importance of adherence and multidisciplinary management.

Case Presentation

A 26-year-old male presented with complaints of persistent low mood, anhedonia, fatigue, and sleep disturbances. He is a known case of Major Depressive Disorder (MDD), currently in remission but with multiple recent relapses. There is no history

of psychotic features, manic/hypomanic symptoms, suicide attempts, or substance use. He is a heavy smoker and has shown interest in smoking cessation.

The patient had previously been treated at another facility, where he was prescribed Venlafaxine up to 450 mg daily; however, he reported inadequate response even at this maximum dose. Upon transfer to our care, Vortioxetine 20 mg daily was trialed but did not yield clinical improvement. Mirtazapine 15 mg at bedtime was then initiated for augmentation and later increased to 30 mg, with minimal additional benefit. Given the persistence of symptoms, Esketamine nasal spray (56 mg once weekly) was introduced in a controlled clinical setting.

The patient reported subjective improvement in mood and energy levels after four doses of Esketamine. However, he self-discontinued the medication without medical consultation. Shortly thereafter, he experienced a relapse characterized by low mood, hopelessness, and suicidal ideation, prompting him to self-increase Venlafaxine to 375 mg. This provided only partial relief, and at this time, his MADRS (Montgomery-Åsberg Depression Rating Scale) score was 34, consistent with severe depression.

Despite continued treatment with Venlafaxine 225 mg and addition of Vortioxetine 10 mg, the patient remained symptomatic, reporting ongoing sleep disturbances, emotional frustration, and impaired daily functioning. A decision was made to resume Esketamine under close psychiatric and nursing supervision at 56 mg once weekly, which led to modest improvement.

During the course of treatment, a family medicine evaluation revealed microscopic hematuria and mild hypercholesterolemia. The patient was counseled on lifestyle and dietary modifications, and further evaluation was arranged. Esketamine was then titrated to 84 mg once weekly for greater efficacy. However, the patient developed transient dissociative symptoms observed by nursing staff. Consequently, the dose was reduced back to 56 mg, which was well- tolerated, with no further adverse effects reported.

Following the dose adjustment, the patient demonstrated progressive and sustained clinical improvement, with a repeat MADRS score of 7, indicating remission. The patient reported improved mood, restored sleep, enhanced concentration, and return to baseline functioning. As part of ongoing optimization, Venlafaxine was gradually tapered.

Currently, the patient is maintained on Venlafaxine 75 mg daily and Esketamine 84 mg once weekly, with continued clinical stability and no recurrence of adverse effects.

Discussion

This case underscores the potential of esketamine nasal spray as a rapid-acting intervention for treatment- resistant depression (TRD), particularly in patients with acute suicidal ideation. Clinical trials have demonstrated that esketamine, when combined with standard care, can lead to significant reductions in depressive symptoms within 24 hours of administration [1,2].

A 2019 randomized controlled trial by Popova et al. showed that flexibly dosed esketamine plus an oral antidepressant led to significant and sustained symptom reduction compared to placebo [2]. Similarly, Canuso et al. observed that esketamine rapidly reduced suicidal ideation in high- risk patients, even within 24 hours [3].

However, another major study by Ionescu et al. emphasized that while esketamine was effective in reducing depressive symptoms, its impact on suicidal ideation was not significantly better than placebo when combined with comprehensive standard care [5].

This highlights a crucial consideration: the magnitude of esketamine's effect may be amplified by robust supportive care, and it's important not to overestimate its independent impact on suicidality.

In this case, treatment discontinuation led to relapse, a known risk with esketamine therapy [1,7]. This emphasizes the need for continued maintenance treatment, careful tapering, and consistent follow-up to prevent symptom recurrence.

Regarding adverse effects, dissociation is the most frequently reported and often leads to dose adjustments or increased clinical monitoring [4,6]. A systematic review by Moeini et al. confirmed that dissociative symptoms can appear within hours of dosing and may be distressing for some patients [6]. These effects, although usually transient, reinforce the need for administering esketamine in medically supervised settings [6,7].

Of note, this case also involved integrating smoking cessation into the treatment plan, which is especially relevant as nicotine use is associated with worse depression outcomes and reduced response to antidepressants. A multidisciplinary approach that includes lifestyle interventions may optimize esketamine's therapeutic benefit.

While esketamine shows promise in TRD, the lack of robust long-term data and the need for ongoing dosing remain challenges [4,5]. Continued research and surveillance will be essential to refine protocols and ensure patient safety.

Conclusion

Esketamine nasal spray was effective in treating this patient's treatment-resistant depression (TRD), demonstrating rapid and significant symptom relief. However, relapse following discontinuation reflects the importance of maintenance treatment and long-term follow- up. This case also highlights the necessity of adherence and close medical supervision, especially given the potential for side effects like dissociation which may require dose adjustment or additional monitoring. Importantly, integrating smoking cessation efforts may enhance overall outcomes in TRD patients with comorbid nicotine dependence. Overall, esketamine provides a valuable option in the management of TRD when used with individualized care plans and multidisciplinary support.

References

1. Daly EJ, Trivedi MH, Janik A, et al. Efficacy of esketamine nasal spray plus oral antidepressant in reducing depressive symptoms in patients with treatment- resistant depression. J Clin Psychiatry, 2019; 76(9): 893-903.
2. Popova V, Daly EJ, Trivedi M, et al. Flexibly dosed esketamine nasal spray combined with a newly initiated oral antidepressant in treatment-resistant depression: A randomized double-blind active-controlled study. Am J Psychiatry, 2019; 176: 428-438. 10.1176/appi.ajp.2019.19020172.

3. Canuso CM, Singh JB, Fedgchin M, et al. Esketamine for treatment of major depression and suicidal ideation: A randomized double-blind study. Am J Psychiatry.
4. Wajs E, Aluisio L, Holder R, et al.: Esketamine nasal spray for rapid reduction of depressive symptoms in MDD with suicidal ideation. J Clin Psychopharmacol, 2019; 40: 610-617.
5. Ionescu DF, Mathews M, Zhan T, et al.: Esketamine nasal spray for treatment- resistant depression: Real- world evidence and safety profile. Ther Adv Psychopharmacol, 11: 1-11.
6. Moeini M, Jahangir N, Lee Y, et al.: Intranasal esketamine for depression and suicidality: A systematic review and meta-analysis. BMC Psychiatry, 2023; 23: Article number 587.
7. Zheng W, Cai DB, Yang XH, et al.: Esketamine's short-term efficacy for depression: A meta-analysis. Front Pharmacol.