STUDENTS' CORNER
SHORT COMMUNICATION

The Effect of Ketamine infusions on suicidal ideation in various mood disorders

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Abstract

Borderline Personality Disorder (BPD) is characterised by altered perception of self, mood changes, and suicidal ideation. The traditional treatments of BPD, including psychotherapy, fail to provide an immediate response in susceptible patients. However, recent literature has shed light on the use of Ketamine as intervention for suicidal ideation in BPD patients, as well as for patients with Major Depressive Disorder (MDD). Studies have shown that administering low doses of Ketamine intravenously has profound impact on reducing suicidality in susceptible patients. The mechanism of action of Ketamine is thought to be its regulation of neurotrophic factors, hence, eliciting a rapid response. Furthermore, Ketamine has also proved beneficial in alleviating other symptoms of BPD including mood dysregulation and impulsive behaviour. Provided the evidence, Ketamine could revolutionise the emergency management of suicidality; however, further research is required to establish its dose, safety, and contraindications.

Keywords: Ketamine, Mood disorders, Major depressive disorder, Borderline personality disorder, Suicidal ideation.

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Introduction

Borderline Personality Disorder (BPD) is a mental health disorder indicated by recurring instability in mood, self-perception, and interpersonal interactions.[1] BPD sufferers struggle to control their emotions, exhibit impulsive behaviour, and experience intense emotions, leading to impulsivity, self-harm, and suicidal ideation.[1] Approximately 10% of BPD patients are likely to commit suicide.[2] Suicidal ideation in people with BPD necessitates an effective intervention for susceptible individuals.[2] However, there is no current evidence to support the efficacy of any suicide prevention treatment. Similarly, MDD—also a mood disorder—is a devastating illness marked by low mood, a loss of interests, cognitive impairment, and vegetative symptoms, such as irregular eating or sleeping patterns.[3]

Nonetheless, recently, Ketamine—an N-methyl-D-aspartate (NMDA) receptor antagonist—has emerged as a potential intervention for the treatment of depression as well as reducing suicidal ideation in patients with psychiatric illnesses.[3] This short communication explores the potential benefits of Ketamine infusion in the management of suicidality in BPD patients.

This short communication explores the potential benefits of ketamine infusion in the management of suicidality in mood disorders patients like BPD. Given the high suicide risk in individuals with BPD and the lack of established, effective interventions, investigating novel treatment options like ketamine is crucial. Publishing this case may contribute to the growing evidence supporting ketamine's role in acute suicidality management, particularly in treatment-resistant populations.

Although suicidal ideation is common to all mood disorders and is not only specific to BPD, there is a greater clinical urgency in treating suicidality in the BPD population due to higher prevalence of self-harming behaviours in BPD individuals.5 While suicidal tendencies are also evident in people with MDD and other psychological disorders, the frequency and severity of suicidality in BPD necessitates a different therapeutic approach.[5] In addition, BPD patients frequently show resistance to treatment, which calls for rapid-acting medications like Ketamine, especially in crisis situations, whereas mood disorders may respond to standard antidepressant treatments.[5]

Methods and Results

A comprehensive literature search was carried out, and evidence was compiled from randomised controlled trials (RCTs) and meta-analyses. The studies which showed association between Ketamine intervention and its effect on suicide ideation in patients with psychiatric illnesses

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Table: Summary of RCTS and Meta-analysis conducted on the effect of Ketamine.

Study	Methodology	Conclusions
Grunebaum et al. 2018[7]	RCT with 80 adults, Ketamine vs. Midazolam, evaluated suicidal thoughts 24 hours post-infusion	Ketamine group showed significant reduction in SSI scores compared to Midazolam group.
Su et al. 2023[8]	RCT with 84 TRD patients, Ketamine vs. Midazolam, evaluated depressive and suicidal symptoms using MADRS and C-SSRS	Ketamine showed significant antidepressant effects up to 14 days; and anti-suicidal effect up to 5 days.
Witt et al. 2020[9]	Meta-analysis of 15 clinical trials with 572 participants	Single IV infusion of 0.5 mg/kg Ketamine effective in reducing suicidal ideation for up to 72 hours.
Shen et al. 2024[10]	Meta-analysis of Ketamine's effects on suicidal ideation in depression patients	Ketamine shown to alleviate suicidal ideation in patients with depression.
Fineberg et al. 2023[11]	Pilot RCT of Ketamine in BPD patients	Ketamine effective in reducing suicidal ideation in BPD patients.
Shivanekar et al. 2022[12]	Pilot study of Ketamine infusion post-suicide attempt	Ketamine showed promise in treating acute suicidality.

Abbreviations: RCT, randomised control trial; SSI, Scale for Suicidal Ideation; TRD, treatment-resistant depression; MADRS, Montgomery-Åsberg Depression Rating Scale; C-SSRS, Columbia-Suicide Severity Rating Scale; IV, intravenous; BPD, Borderline Personality Disorder.

were included. The exclusion criteria were the studies that were more than 10 years old. The critical outcome under investigation was the reduction in suicidal ideation among BPD patients. The results were assessed under standardised scales such as the Columbia-Suicide Severity Rating Scale (C-SSRS) and the Beck Scale for Suicide Ideation (BSSI), which are frequently used to analyse suicide risk in susceptible individuals.[6,7]

A randomised control trial (RCT) was conducted at Columbia University Medical Center and the New York State Psychiatric Institute in New York.[8] The research was published in the American Journal of Psychiatry on April 1, 2018.[8] Specific dates of the study's conduct are not provided in the available sources.[8] In the study, 80 adults suffering from major depressive disorder and suicidal thought were randomly assigned to receive either a Ketamine or Midazolam infusion.[8] The primary goal was to measure suicidal thoughts 24 hours after the infusion by utilising the Scale for Suicidal Ideation (SSI).[7] The study noted that the Ketamine group showed a more significant reduction in SSI scores as compared to the Midazolam group.[5] However, in the aforementioned RCT, it was not disclosed if the participants suffered from BPD or not.

Similarly, another RCT was conducted at Taipei Veterans General Hospital in Taiwan.[9] The research was published in the International Journal of Neuropsychopharmacology on May 31, 2023.[9] Specific dates of the study's conduct are not provided in the available sources.[9] The study sought to explore the potential benefits of administering low-dose Ketamine to patients with treatment-resistant depression (TRD) and suicidal ideation. The trial involved 84 treatment resistant patients (TRD) patients, identified by a score ≥4 on the Montgomery-Åsberg Depression Rating Scale (MADRS).[9] Participants were randomly assigned to receive either 0.5mg/kg of Ketamine or 0.045mg/kg of Midazolam.[9] Evaluation of depressive and suicidal symptoms took place before and after the infusion, with follow-up assessments continuing until day 14.[9] Based on the MADRS score, Ketamine demonstrated a significant antidepressant effect (p=0.035) for up to 14 days compared to the Midazolam group.[9]

Moreover, a meta-analysis conducted in 2022 gathered reports from 15 independent clinical trials with a total of 572 participants.[10] It demonstrated how a single intravenous infusion of Ketamine, i.e. 0.5mg/kg, proved to be beneficial in mitigating suicidal ideation in patients with major depressive disorder for up to 72 hours.[10]

Furthermore, a meta-analysis in 2024 proved the role of Ketamine in alleviating suicidal ideation in patients suffering from depression, hence, reinforcing the concept of Ketamine as an acute treatment for suicidal ideation.[11] Most importantly, the RCT done in 2023 extended the aforementioned results to BPD patients and gave evidence on the efficacy of Ketamine in mitigating suicidality in BPD patients.[12] The study also pointed out the success of Ketamine in regulating other symptoms of BPD including mood dysregulation.[12]

Ketamine causes rapid onset of anti-depressant and anti-suicidal effects that persist from days to up to a week, thus proving beneficial in managing suicidal ideation in psychiatric patients.

Discussion

The data from current literature, including several meta-analyses, supports the use of Ketamine in managing suicidal ideation. One noteworthy fact is that Ketamine induces a rapid response in reducing suicide ideation as compared to the traditional treatment given to such patients.

The underlying mechanism of action of Ketamine lies in reversing neuroplasticity changes in patients with depression or mood disorders.[13] Due to chronic stress in such patients, the signalling of a neuroprotective factor, brain-derived neurotrophic factor (BDNF) is greatly reduced, leading to neuroplasticity changes in the

hippocampus.[13] Consequently, there is impairment in cognition and decision-making, along with prefrontal inhibition, making such patients susceptible to suicidal ideation.[13] Ketamine has been seen to rapidly reverse these neuroplasticity changes, hence improving the patients' condition within two to 24 hours.[13]

The data indicate that Ketamine infusions can be a potential emergency intervention for individuals at high risk of suicide. However, its long-term effects, contraindications, and optimal dosing requires further investigation. Additionally, due to Ketamine's potential for abuse and its dissociative side effects, its administration should be carefully monitored.

Limitations and Future Directions: Current studies are limited by small sample sizes and short follow-up periods. Larger RCTs with extended follow-up are necessary to confirm these findings and establish long-term safety and efficacy, particularly considering BPD population.

Conclusion

Preliminary data suggest that Ketamine could serve as a valuable tool in the acute management of suicidality in BPD, providing rapid relief when traditional treatments fail. Continued research is essential to fully understand its potential and to develop comprehensive treatment protocols.

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Author Contribution:

MBM, ZAS & SS: Concept, design, data acquisition, analysis, interpretation, drafting, revision, final approval and agreement to be accountable for all aspects of the work.