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Is ketamine efficacious for rapid treatment of acute suicidal ideation in an emergency setting? Lessons learned from a pilot randomized controlled trial

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Abstract

Objective This study aimed to evaluate the efficacy of a single infusion of ketamine in inducing rapid remission of severe suicidal ideation, compared to Midazolam, in a population with acute suicidal thoughts. In a double-blind randomized controlled trial conducted in Tehran, Iran, from January to July 2022 (IRCT20220118053756N1), 36 inpatients with acute severe suicidal ideation were enrolled. Participants were randomly assigned to receive either a single dose of ketamine (0.5 mg/kg) or Midazolam (0.02 mg/kg). Suicidality was assessed using the Beck Scale for Suicide Ideation (BSSI) and the Suicide-Visual Analog Scale (S-VAS) before the intervention and at 12 and 24 h post-administration.

Results At baseline, the Midazolam group exhibited significantly higher BSSI scores and a higher rate of borderline personality disorder than the Ketamine group. Mean BSSI and S-VAS scores at 12 and 24 h after the treatment decreased significantly compared to baseline in both groups. Despite these observations, no statistically significant differences were found between the groups in terms of BSSI and S-VAS scores.

Trial registration The protocol for this RCT was registered at the Iranian Registry of Clinical Trials (IRCT). The trial registration details are as follows: IRCT registration number IRCT20220118053756N1, with the registration date being June 12, 2022 (1401/03/22). It is important to note that this trial was retrospectively registered.

Keywords Suicide, Ketamine, Midazolam, N-methyl-d-aspartate receptor antagonist, Depressive disorder

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Introduction

Background

Suicide causes a total of about 700,000 annual deaths globally [1]. The World Health Organization (WHO) has identified suicide as a priority condition in the Mental Health Gap Action Programme (mhGAP) launched in 2008 [2]. The mhGAP aims to scale up services for mental, neurological, and substance use disorders in low- and middle-income countries [2]. The WHO Mental Health Action Plan 2013–2030 has set a global target of reducing the suicide rate in countries by one-third by 2030 [2].

Suicidal ideation, especially when severe, is considered a medical emergency [3]. Although antidepressants reduce suicidal ideation by controlling other symptoms of depression, their optimal clinical effects usually take weeks to months [4]. Ketamine at subanesthetic doses is the only FDA-approved antidepressant with its onset of action within a few hours [5]. Ketamine has also been investigated for its rapid effects on reducing suicidal thoughts independent of its antidepressant effect [6–9].

A systematic review of studies demonstrated that the rapid antidepressant effect of ketamine can significantly reduce suicidal thoughts in patients with major depressive disorder who experience suicidal ideation. However, most of the research has focused primarily on this specific patient population, and the efficacy of ketamine may vary among individuals with different psychiatric diagnoses. Therefore, further trials are necessary to evaluate its safety and effectiveness across a broader range of psychiatric conditions and treatment settings [10].

Midazolam is a well-established benzodiazepine with anxiolytic, sedative, and amnesic properties, making it a suitable control for assessing the distinct effects of ketamine, particularly its rapid antidepressant and potential anti-suicidal effects. Unlike ketamine, which acts as a noncompetitive antagonist of the N-methyl-D-aspartate (NMDA) receptor and has unique mechanisms of action, midazolam primarily operates through GABAergic pathways. This contrasting pharmacological profile aids in isolating the specific effects of ketamine on mood and suicidality [11, 12]. Moreover, midazolam's sedative properties allow researchers to control for any sedation-related effects that may arise from ketamine administration, ensuring that any observed benefits in reducing suicidal ideation can be attributed to ketamine's antidepressant properties rather than sedation alone [11]. While midazolam does have pharmacological effects, its impact on mood and suicidal ideation is generally less pronounced than that of ketamine, establishing it as a suitable active comparator. This allows for a clearer measurement of ketamine's more potent effects on rapid changes in suicidal thoughts and depressive symptoms.

Objectives

We aimed to compare the anti-suicidal effects of Ketamine infusion to Midazolam for rapid remediation of acute suicidal thoughts in patients admitted to the hospital with severe suicidal ideation regardless of their primary diagnoses.

Methods

Setting, participants, and design

This double-blind randomized controlled trial was registered in the Iranian Registry of Clinical Trials (IRCT20220118053756N1). It was conducted from January to July 2022 at two university hospitals in Tehran, Iran.

Patients aged 18–65 with acute suicidal ideation associated with major depression were recruited. Acute suicidal thoughts were defined as thoughts starting within 72 h before admission, associated with serious risk, and requiring psychiatric hospitalization. Thirty-six patients meeting the inclusion criteria were enrolled via convenience sampling and randomized to receive either a single-dose ketamine or midazolam infusion.

Exclusion criteria included physical disorders (thyroid disorder, diabetes, hypertension, stroke, brain surgery, neurological disorders, seizures), allergy to ketamine or midazolam, pregnancy, and lactation. Patients taking antidepressants regularly in the previous month were also excluded.

The effect was evaluated using the suicide visual analog scale (S-VAS) and Beck Suicide Severity Inventory (BSSI) at baseline, 12 h (10–14 h), and 24 h after administering the medication (22–26 h).

Randomization, allocation concealment, and blinding

One researcher coded Ketamine and Midazolam as A and B. The second researcher who was unaware of the coding created a blocked random sequence of A and B using a computer-generated list of random numbers. The same researcher maintained the list. The recruiting researcher was unaware of the patient group at the time of assignment and would contact the second researcher to inquire the patient assignment.

Midazolam and Ketamine were prepared in packages with the same appearance and labeled as A and B. To prevent the sedative effects of Midazolam altering the masking, Midazolam was administered at a low non-sedative dose.

Interventions

The patients received either a single dose of Ketamine hydrochloride (Exir Pharmaceutical Company, Iran) infusion 0.5 mg/kg or Midazolam(Daroo Pakhsh Co. Iran) 0.02 mg/kg infusion in 100 cc sodium chloride 0.9% over 40 min. The patient's blood pressure, level

of consciousness, and blood oxygen saturation, heart and breathing rate during the injection were monitored throughout the infusion. Either a physician or a highly skilled anesthetist was on standby at the participant's bedside throughout the infusion to handle emergency tracheal intubation or cardiopulmonary resuscitation if required.

Outcome measurement

A psychiatrist, who was blinded to the intervention, interviewed all participants before, 12 h after, and 24 h after administration of the medication, and filled Hamilton's scale and BSSI. The same outcome assessor explained the protocol and administered the S-VAS to the participants. The main outcomes were suicidal ideation and the secondary outcome was the severity of depression.

Choosing the Beck Scale for Suicide Ideation (BSSI) and the Suicide-Visual Analog Scale (S-VAS) for assessing suicidal ideation is advantageous due to their complementary strengths. The BSSI is a well-established instrument with strong psychometric properties, providing a comprehensive evaluation of suicidal thoughts, including their presence, intensity, and associated risk factors [13]. This structured approach allows clinicians to gain nuanced insights into an individual's mental state. In contrast, the S-VAS offers a straightforward and immediate way for individuals to express their level of suicidal thoughts on a continuous scale, enhancing sensitivity in detecting changes over time. Together, these scales facilitate effective monitoring of suicidal ideation in response to interventions, such as ketamine treatment [5, 11, 14].

Hamilton's depression scale

Hamilton's scale measures the severity of depression through 17 questions encompassing symptoms of depression including mood, guilt, sleep pattern, and suicidal thoughts. Scores above 22 point to very severe depression [15, 16].

Beck scale for suicidal ideation

The Beck scale for suicidal ideation (BSSI) consists of 19 items that assess suicidality in detail. The score obtained from BSSI ranges from 0 to 38; the higher the score, the more severe the suicidal thoughts [15–17]. The Persian version of this instrument has also been deemed valid and reliable [17].

S-VAS (suicide visual analog scale)

The Visual Analogue Scale, a method for measuring the severity of an experience subjectively, has been standardized and widely used for assessing suicidal ideation [18].

Statistical methods

The obtained data were analyzed by SPSS-26 software. To describe qualitative variables, we used simple and relative frequencies, while quantitative data were summarized using mean, standard deviation, median, and range of variation. The comparison of baseline and clinical data between the two groups was conducted using chi-square tests and independent samples t-tests. Given that the data followed a normal distribution, as confirmed by the one-sample Kolmogorov-Smirnov test, we employed repeated measures ANOVA for data comparison. To compare the changes in VAS scores between the two groups, we calculated the differences from baseline at the 12-hour and 24-hour time points. After assessing the normality of the data using histograms, we compared the mean changes in VAS scores from baseline between groups using independent samples t-tests. Given that Levene's Test indicated unequal variances, we employed Welch's t-test to compare the mean changes in VAS scores between the two groups. This approach is appropriate for analyzing independent samples when the assumption of equal variances is violated. In all cases, $p < 0.05$ was considered significant.

We used a p-value threshold of 0.05 to determine statistical significance, as this is a widely accepted standard in the scientific community. This threshold effectively balances the risk of Type I errors—incorrectly rejecting the null hypothesis—while maintaining sufficient sensitivity to detect meaningful differences. By adhering to this conventional standard, we aimed to ensure consistency with previous research, facilitating comparisons of our findings with those in the field of acute suicidal ideation treatment.

Results

Baseline characteristics

A total of 36 patients were randomized 1:1 to the study groups (Fig. 1). Other baseline characteristics are shown in Table 1. Except for borderline personality disorder(BPD), there was no difference between the two groups. The severity of suicidal thoughts based on BSSI scores was higher in the midazolam group than in the ketamine group at the beginning of the study (Table 1).

Treatment effects

Repeated measure analysis of variance showed that the intensity of suicidal thoughts based on the Beck Scale for Suicidal Ideation(BSSI) decreased moderately in both of the intervention groups over time with a moderate to large effect size (Cohen's f was 0.61 for the BSSI). However, the change in the severity of suicidal thoughts according to the BSSI did not significantly differ between the ketamine and midazolam groups (Table 2). The independent samples t-test revealed that, after 12 h, the mean

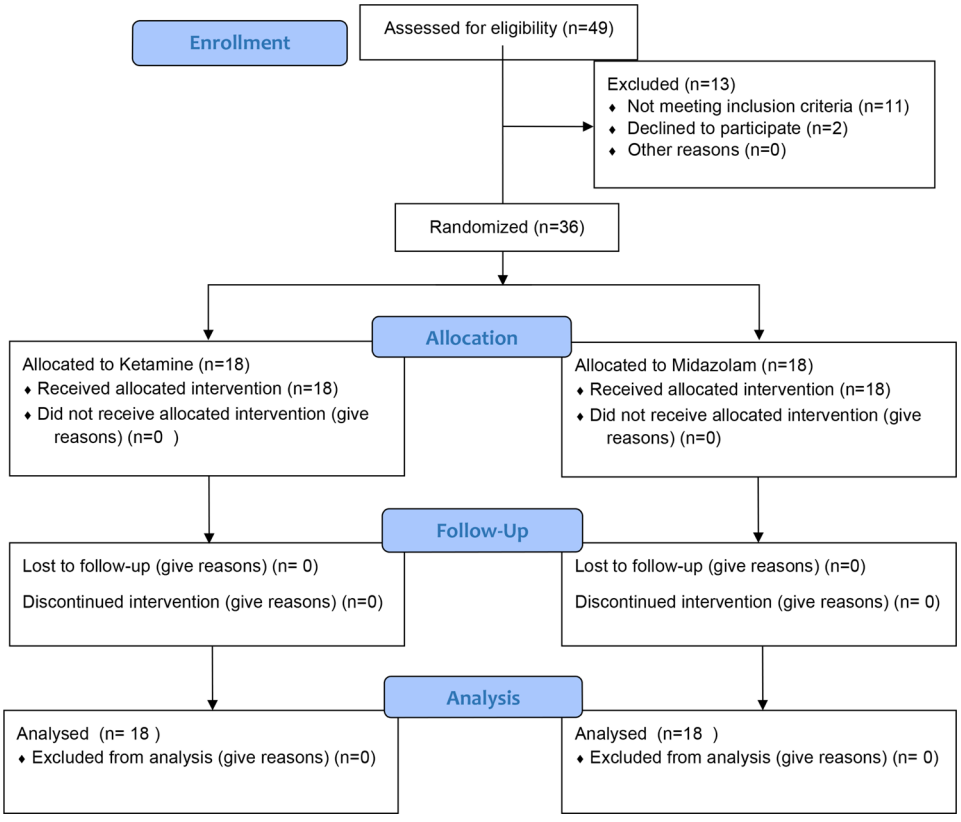

Fig. 1 The CONSORT diagram demonstartes the participants' flow during the trial. All patients received the intended treatment and none of them left the study

difference in VAS score changes from baseline between the ketamine and midazolam groups was 0.66 (95% CI: -0.33 to 1.66), with a p-value of 0.181. After 24 h, the mean difference was 1.16 (95% CI: -0.10 to 2.43), with a p-value of 0.069.

Adverse events were sought and recorded in uniform notes at the outcome measurement time points. The most commonly reported side effect was mild nausea in the ketamine group. There were no events of serious adverse reactions to the study medications.

Discussion

In this double-blind randomized controlled trial, we compared the efficacy of ketamine compared to the active comparison of midazolam in the instant amelioration of suicidal thoughts in patients with severe suicidal ideation. Although the severity of suicidal thoughts decreased in both study arms, we did not find a significant difference between groups.

This outcome can be correlated with the pharmacological effects of both agents. Ketamine is known for its rapid antidepressant properties, primarily acting as an NMDA receptor antagonist, which leads to an increase in synaptic plasticity and a quick reduction in suicidal ideation [18]. Previous studies have shown that ketamine can significantly lower suicidal thoughts within hours of administration, often outperforming other treatments, including midazolam, in terms of efficacy and duration of effect [6, 7, 9].

Conversely, midazolam functions primarily as a GABAergic sedative, providing anxiolytic and calming effects without the same robust antidepressant action. While midazolam can effectively alleviate acute anxiety and distress, its impact on suicidal ideation is generally less pronounced compared to ketamine [19]. The finding that both groups experienced a reduction in suicidal thoughts suggests that midazolam's sedative and anxiolytic properties may have contributed to immediate relief from distress, which could explain the decrease in suicidal ideation observed in both arms of the study. However, the lack of significant difference indicates that while ketamine may offer superior long-term benefits for mood improvement and sustained reduction in suicidality, midazolam's immediate effects can also play a role in the short-term alleviation of suicidal thoughts. This highlights the complexity of treating severe suicidal ideation and suggests that further research is necessary to explore how different pharmacological profiles influence outcomes across various patient populations.

Table 1 Table of baseline characteristics of trial participants

Participant characteristics	Categories	Midazolam number(percent)	Ketamine number(percent)
Gender	Man	10(55.5)	13(72.2)
Marital Status	Single	11(61.1)	10(55.6)
	Married	5(27.8)	7(38.9)
	Divorced	2(11)	1(5.6)
Occupational Status	Employed	11(61)	9(50)
Education	Below high school diploma	4(23.2)	1(5.6)
	High school diploma	8(44.4)	8(44.4)
	University education	6(33.3)	9(50)
Personal History	Admission in psychiatric hospitals	14(77.8)	14(77.8)
	Suicidal attempt	13(72.2)	8(44.4)
	Borderline personality disorder	13(72.2)	6(33.3)
	Substance use disorder	10(55.6)	6(33.3)
Family history of	Mood disorders	15(83.3)	13(72.2)
	Suicidal attempt	8(44.4)	5(27.8)
Current Diagnosis	Major Depressive Disorder	5(27.8)	8(44.4)
	Bipolar Disorder-I Depressive Episode	0	1(5.6)
	Bipolar Disorder-I Manic Episode	2(11.1)	4(22.2)
	Personality Disorder	10(55.6)	3(16.7)
	Anxiety Disorders/ Obsessive Compulsive Disorder	1(5.6)	2(11.1)
Psychiatric comorbidities	Major Depressive Disorder	1(5.6	1(5.6)
	Obsessive Compulsive Disorder	0	2(11.1)
	Other Diagnoses	0	1(5.6)
The severity of baseline suicidal thoughts	Beck Suicide Inventory	26.2(9.3)	18.7(8.1)
	Visual Analog Scale	7.5(1.8)	7.1(1.7)

Table 2 Main treatment effects: BSSI: Beck scale for suicidal ideation, Jacob Cohen has suggested that the values of 0.10, 0.25, and 0.40 represent small, medium, and large effect sizes for Cohen's f, respectively

Outcome	Interaction of time and intervention group					The effect of time				
	Power	Cohen's f	$^2\eta$	p	F	Power	Cohen's f	$^2\eta$	p	F
BSSI	0.16	0.022	0.02	0.46	0.75	1	0.61	0.38	< 0.001	21.10

Contrary to our findings, a similar randomized clinical trial in 2017 with 80 adult participants with major depressive disorder and severe suicidal ideation reported that patients receiving ketamine experienced a larger reduction in Suicidal Ideation Scores (4.96 points) after 24 h (95% CI = 2.33, 7.59; Cohen's d = 0.75) [20]. Our smaller sample size and the differences in study arms at baseline may explain the lack of a significant difference in our study. Moreover, a relatively large proportion of the patients receiving midazolam in our study had comorbid BPD in contrast to the 2017 trial wherein the opposite was true. Also, 54% of their patients were receiving antidepressants which may have interacted with the pharmacological effects of ketamine and midazolam [11].

Another randomized double-blind trial compared ketamine with a placebo in 156 individuals across a spectrum of psychiatric diagnoses. They reported that two 40-minute IV doses of ketamine significantly reduced suicidal ideation on day three (to a score of lower than 3) (odds ratio 3.7 (95% CI 1.9 to 7.3), $P < 0.001$) [21]. The largest effects in their study were observed in patients with bipolar disorder and the results were not significant for the depression subgroup [22]. They proposed that the underlying diagnoses may affect the efficacy of ketamine in the reduction of suicidal thoughts [22]. Their study's large effect sizes may be due to their pharmacologically inactive comparison(placebo) or the nature of their participants' diagnosis.

The high rate(19/36 [52%] of BPD in our study participants and especially in the midazolam group(13/18(72%) was notable. Although there is no direct evidence that these individuals respond differently to ketamine or midazolam, the common notion is that patients with BPD may experience spontaneous resolution of suicidal thoughts. On the other hand, some individuals with BPD may have a higher tendency to act upon these temporary thoughts. Thus, while the effects of ketamine may have been underestimated in our study due to the higher

rate of spontaneous resolution of suicidal thoughts in the comparison group which contained a high rate of patients with borderline personality disorder the higher impulsivity among some of the patients with BPD signifies the importance of managing suicidal thoughts among this group of patients.

The high rate of Borderline Personality Disorder (BPD) among our study participants—19 out of 36 (52%)—is particularly notable, especially within the midazolam group, where 13 out of 18 participants (72%) were affected. Although there is no direct evidence suggesting that individuals with BPD respond differently to ketamine or midazolam [23], it is commonly believed that patients with BPD may experience spontaneous resolution of suicidal thoughts.

Conversely, some individuals with BPD may exhibit a higher propensity to act on these transient thoughts [24, 25]. This raises a significant consideration: while the effects of ketamine may have been underestimated in our study due to the elevated rate of spontaneous resolution of suicidal thoughts in the comparison group—which included a substantial number of patients with BPD—the heightened impulsivity observed in some of these patients underscores the critical need for effective management of suicidal thoughts within this population.

Our results are significant in that suicidal thoughts were considerably reduced in both study groups compared to baseline. However, the effects of ketamine did not demonstrate superiority over midazolam. One possible explanation for our small effect size is the use of a pharmacologically active comparison. This may have influenced the observed reductions in suicidal thoughts. Specifically, the heightened placebo effect associated with any drug that produces side effects—unlike an inactive placebo—could have played a role [12, 26]. Additionally, there may be potential antisuicidal activity associated with midazolam itself [12].

These factors highlight the complexity of assessing treatment efficacy in this context and suggest that further investigation is warranted to fully understand the dynamics at play. The effects of ketamine may vary based on the underlying diagnoses [5, 7, 9, 10]. Specifically, it is unclear how suicidal thoughts may respond to ketamine or other pharmacological agents among patients with borderline personality disorder. Since there is no evidence that individuals with borderline personality may respond differently to ketamine, the issue warrants further evaluation in larger and adequately powered trials. We suggest trials with larger sample sizes and stratification for borderline personality and other important diagnoses to facilitate subgroup analyses based on psychiatric comorbidities.

Limitations

This pilot trial had several limitations that should be considered when interpreting the results and in designing future trials. First, the small sample size, which is typical for pilot trials, likely hindered the detection of significant effects and restricted the ability to perform subgroup analyses or adjust for confounding factors.

Secondly, the groups were not comparable at baseline in terms of depression severity and the rate of borderline personality disorder, despite randomization. Baseline imbalances can occur in some variables in randomized controlled trials due to random chance, especially in small sample sizes, where differences may arise purely by luck. This suggests the observed effects may not be attributed solely due to the drugs.

Thirdly, our study included patients with various psychiatric diagnoses, enhancing its practical relevance in emergency settings. However, this diversity may have decreased statistical power because ketamine's efficacy can vary significantly across different disorders.

Conclusions

The findings show that although suicidal thoughts were reduced in both groups, ketamine was not superior to midazolam for the reduction of suicidal thoughts. This raises questions about the efficacy of ketamine among a diverse patient population.

Abbreviations

BPD	Borderline Personality Disorder
BSSI	Beck Suicide Severity Inventory
FDA	Food and Drug Administration
GABA	Gamma-Amino-Butyric Acid
mhGAP	Mental Health Gap Action Programme
NMDA	N-methyl-D-aspartate
S-VAS	Suicide Visual Analog Scale
WHO	World Health Organization

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None.

Author contributions

M.B. K.A. AH. JN. contributed to the study design. M.B. conducted the main assessments and the data gathering. K.A. conducted the statistical analysis and supervised methodological aspects. K.M. and M.N.L. contributed to patient recruitment, medication administration, and data gathering. F.B. and MA. KA interpreted the data and prepared the tables and the manuscript. All authors reviewed the manuscript.

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Data availability

The data are available upon request to the corresponding author.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics committee at Iran University of Medical Sciences (Ethics reference: IR.IUMS.FMD.REC.1399.069). Written informed consent was obtained from patients and their legal guardians(as an additional ethical safeguard) prior to enrollment. This decision was made to ensure

transparency and to inform guardians about their loved ones' involvement in the research, particularly given the sensitive nature of the study topic.

Consent for publication
All participants provided written informed consent that their anonymous data be shared.

Competing interests
The authors declare no competing interests.

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References

1. Kastrup MC. Health Coverage and Mental Illness: the ongoing issue of Mental Health gap (mhGAP). Indian J Social Psychiatry. 2016;32(3):251–3.
2. World Health O. mhGAP intervention guide for mental, neurological and substance use disorders in non-specialized health settings: mental health Gap Action Programme (mhGAP). version 2.0 ed. Geneva: World Health Organization; 2016 2016.
3. Weber AN, Michail M, Thompson A, Fiedorowicz JG. Psychiatric emergencies: assessing and managing suicidal ideation. Med Clin North Am. 2017;101(3):553–71.
4. Caddy C, Giaroli G, White TP, Shergill SS, Tracy DK. Ketamine as the prototype glutamatergic antidepressant: pharmacodynamic actions, and a systematic review and meta-analysis of efficacy. Therapeutic Adv Psychopharmacol. 2014;4(2):75–99.
5. Matveychuk D, Thomas RK, Swainson J, Khullar A, MacKay MA, Baker GB, et al. Ketamine as an antidepressant: overview of its mechanisms of action and potential predictive biomarkers. Therapeutic Adv Psychopharmacol. 2020;10:2045125320916657.
6. Ballard ED, Fields J, Farmer CA, Zarate CA Jr. Clinical trials for rapid changes in suicidal ideation: lessons from ketamine. Suicide Life-Threatening Behav. 2021;51(1):27–35.
7. Siegel AN, Di Vincenzo JD, Brietzke E, Gill H, Rodrigues NB, Lui LM, et al. Antisuicidal and antidepressant effects of ketamine and esketamine in patients with baseline suicidality: a systematic review. J Psychiatr Res. 2021;137:426–36.
8. Siegel AN, Di Vincenzo JD, Brietzke E, Gill H, Rodrigues NB, Lui LMW, et al. Antisuicidal and antidepressant effects of ketamine and esketamine in patients with baseline suicidality: a systematic review. J Psychiatr Res. 2021;137:426–36.
9. Wilkinson ST, Ballard ED, Bloch MH, Mathew SJ, Murrough JW, Feder A, et al. The Effect of a single dose of intravenous ketamine on suicidal ideation: a systematic review and individual Participant Data Meta-Analysis. Am J Psychiatry. 2018;175(2):150–8.
10. Witt K, Potts J, Hubers A, Grunebaum MF, Murrough JW, Loo C, et al. Ketamine for suicidal ideation in adults with psychiatric disorders: a systematic review and meta-analysis of treatment trials. Australian New Z J Psychiatry. 2019;54(1):29–45.
11. Grunebaum MF, Galfalvy HC, Choo TH, Keilp JG, Moitra VK, Parris MS, et al. Ketamine for Rapid reduction of suicidal thoughts in Major Depression: a midazolam-controlled Randomized Clinical Trial. Am J Psychiatry. 2018;175(4):327–35.
12. Wilkinson ST, Farmer C, Ballard ED, Mathew SJ, Grunebaum MF, Murrough JW, et al. Impact of midazolam vs. saline on effect size estimates in controlled trials of ketamine as a rapid-acting antidepressant. Neuropsychopharmacology. 2019;44(7):1233–8.
13. Ballard ED, Luckenbaugh DA, Richards EM, Walls TL, Brutsche NE, Ameli R, et al. Assessing measures of suicidal ideation in clinical trials with a rapid-acting antidepressant. J Psychiatr Res. 2015;68:68–73.
14. Esfahani M, Hashemi Y, Alavi K. Psychometric assessment of Beck scale for suicidal ideation (BSSI) in general population in Tehran. MJIRI. 2015;29(1):862–71.
15. Ahmadpanah M, Sheikhbabaei M, Haghighi M, Roham F, Jahangard L, Akhondi A, et al. Validity and test-retest reliability of the Persian version of the Montgomery-Asberg Depression Rating Scale. Neuropsychiatr Dis Treat. 2016;12:603–7.
16. Bagby RM, Ryder AG, Schuller DR, Marshall MB. The Hamilton Depression Rating Scale: has the gold standard become a lead weight? Am J Psychiatry. 2004;161(12):2163–77.
17. Esfahani M, Hashemi Y, Alavi K. Psychometric assessment of Beck scale for suicidal ideation (BSSI) in general population in Tehran. Med J Islam Repub Iran. 2015;29(1):268.
18. Mion G, Villevieille T. Ketamine pharmacology: an update (pharmacodynamics and molecular aspects, recent findings). CNS Neurosci Ther. 2013;19(6):370–80.
19. Hauge MS, Willumsen T, Stora B. Changes in symptoms of anxiety, depression, and PTSD in an RCT-study of dentist-administered treatment of dental anxiety. BMC Oral Health. 2023;23(1):415.
20. Abbar M, Demattei C, El-Hage W, Llorca P-M, Samalin L, Demaricourt P et al. Ketamine for the acute treatment of severe suicidal ideation: double blind, randomised placebo controlled trial. BMJ. 2022;376.
21. Domany Y, Shelton RC, McCullumsmith CB. Ketamine for acute suicidal ideation. An emergency department intervention: a randomized, double-blind, placebo-controlled, proof-of-concept trial. Depress Anxiety. 2020;37(3):224–33.
22. Domany Y, Shelton RC, McCullumsmith CB. Ketamine for acute suicidal ideation. An emergency department intervention: a randomized, double-blind, placebo-controlled, proof-of-concept trial. Depress Anxiety. 2020;37(3):224–33.
23. Chen KS, Dwivedi Y, Shelton RC. The effect of IV ketamine in patients with major depressive disorder and elevated features of borderline personality disorder. J Affect Disord. 2022;315:13–6.
24. LINKS PS, Boggild A, Sarin N. Modeling the relationship between affective lability, impulsivity, and suicidal behavior in patients with borderline personality disorder. J Psychiatric Practice®. 2000;6(5):247–55.
25. Rizk MM, Choo T-H, Galfalvy H, Biggs E, Brodsky BS, Oquendo MA, et al. Variability in suicidal ideation is associated with affective instability in suicide attempters with borderline personality disorder. Psychiatry. 2019;82(2):173–8.
26. Barlati S, Nibbio G, Vita A. Evidence-based psychosocial interventions in schizophrenia: a critical review. Curr Opin Psychiatry. 2024;37(3):131–9.

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