CASE REPORT

Intravenous Ketamine as an Adjunctive Treatment for Dysthymia: A Case Report

Pavan Kumar Thatisetti Venkata[1], Divya Bolla[2], Raj Kiran Donthu[3]

Received on: 28 November 2023; *Accepted on:* 11 January 2024; *Published on:* 26 July 2024

Abstract

Background: Dysthymia, characterized by persistent low mood without reaching the severity of depression, poses a challenge in terms of prolonged symptom duration and limited response to conventional antidepressant therapies.

Case description: This case report details the presentation of a patient with dysthymia inadequately responding to antidepressant treatments. Intravenous ketamine was given as an adjunctive treatment, resulting in significant clinical improvement.

Conclusion and clinical significance: Our findings suggest that ketamine could serve as a beneficial adjunct in the treatment of dysthymia. However, it is noteworthy that sustained efficacy may necessitate frequent infusions, ideally at intervals of at least 2 weeks. Further research is warranted to validate and expand upon these observations, offering new insights into the potential role of ketamine in the management of dysthymia.

Keywords: Case report, Dysthymic disorder, Investigational therapies, Ketamine, Mood disorder, Therapeutics.

Indian Journal of Private Psychiatry (2024): 10.5005/jp-journals-10067-0173

Introduction

Dysthymia means "being of bad mood"/"ill humor," and is an illness encompassing affective, cognitive, and neurovegetative symptoms. It made its entry into the classificatory system in the *International Classification of Disorder – Tenth Edition (ICD-10)*. Clinically, it exhibits a protracted course lasting over 2 years with milder severity compared to depressive disorder.[1] According to ICD-10, a long-standing low mood that is never or rarely severe enough to make a diagnosis of depressive disorder is required to reach a diagnosis of dysthymia along with other clinical features.[2] Antidepressants such as selective serotonin receptor inhibitors, tricyclic antidepressants, and monoamine oxidase inhibitors can be tried.[3]

Ketamine is a US Food and Drug Association (FDA) approved medication for anesthesia and is routinely used as an inducing agent as well as for maintenance. It acts as an antagonist at *N*-methyl-D-aspartate (NMDA) receptors. There is evidence for its use in the management of pain, and treating depression and suicidal ideation.[4] The use of ketamine in depression is not FDA-approved, but there is increasing evidence to support its efficacy.[5] According to the "disinhibition hypothesis" of possible ketamine action, there is preferential inhibition of NMDA receptors expressed on gamma-aminobutyric acid (GABA) interneurons, these, in turn, decreases the overall inhibition leading to pyramidal cell disinhibition and an enhancement of excitatory glutaminergic neurotransmission in the medial prefrontal cortex and other mood relevant corticolimbic brain regions.[6]

Dysthymia and depression share clinical similarities, with differing features in duration, severity, and functional impairment. The diagnosis of dysthymia is clinically made when the symptoms last for more than 2 years, and the severity is lesser than a depressive episode with no/mild impairment in functioning. The response to the available treatment options such as antidepressants is usually not adequate and patients can suffer from symptoms for a long duration.[7] From our understanding, there is limited literature on the use of ketamine in dysthymia and in this case report we share the experience of using intravenous ketamine in managing a case of dysthymia who was not responding to usual medications.

[1–3]Department of Psychiatry, NRI Academy of Sciences, Mangalagiri, Andhra Pradesh, India

Corresponding Author: Raj Kiran Donthu, Department of Psychiatry, NRI Academy of Sciences, Mangalagiri, Andhra Pradesh, India, Phone: +91 8309318045, e-mail: drdonthu@gmail.com

How to cite this article: Venkata PKT, Bolla D, Donthu RK. Intravenous Ketamine as an Adjunctive Treatment for Dysthymia: A Case Report. Ind J Priv Psychiatry 2024;18(2):94–95.

Source of support: Nil

Conflict of interest: None

Patient consent statement: The author(s) have obtained written informed consent from the patient for publication of the case report details and related images.

Case Description

A 29-year-old patient presented with persistent low mood, decreased interest in activities, disturbed sleep, diminished appetite, body pains, social withdrawal, and fleeting suicidal ideation over 6 years. Despite continuing to work, the patient expressed discontent with the job. Throughout the past 6 years, there was no significant improvement in the above symptoms. There was no history suggestive of hypomania or mania attempts of suicide or head injury. Past psychiatric history was unremarkable but was a known case of epilepsy and was maintained well with the tablet carbamazepine 300 mg twice daily and tablet clobazam 5 mg once daily for the past 5 years. There was no family history of psychiatric illness or substance use. Premorbidly was described to be well adjusted. The physical examination was within normal limits. Mental status examination (MSE) revealed unkempt, poor eye contact, downcast gaze, difficulty in establishing rapport; decreased psychomotor activity, speech was coherent and relevant, decreased tone and volume with increased reaction time; thought showed feelings of worthlessness, helplessness, and hopelessness; subjectively mood was reported to be low and objectively it was

dull. Most of the higher mental functions were within normal limits with insight being five out of six. Considering the presentation and examination a diagnosis of dysthymia was made based on the *International Classification of Disorders, Tenth Edition* (ICD-10). Investigations like complete blood picture, liver function tests, renal function tests, and thyroid function tests were within normal.

For the above history, patient was started on tablet sertraline 100 mg twice daily, tablet mirtazapine 15 mg once daily, and tablet tianeptine 12.5 mg thrice daily for more than 6 months from the previous psychiatrist but with no noteworthy improvement. The patient reports being compliant with the treatment and maintaining regular follow-ups. The baseline rating scales in our outpatient assessment were 30 on the Montgomery–Asberg Depression Rating Scale (MADRS); and 50 on the Cornell Dysthymia Rating Scale (CDRS). As the patient was already on a trial of three antidepressants with adequate dose and duration an option of adjunctive ketamine trial was considered and the same was discussed. the patient accepted to take the trial of ketamine and gave written informed consent to proceed.

The patient was started on ketamine intravenous infusion at the dose of 0.5 mg per kg in 100 mL of normal saline solution over 60 minutes under continuous supervision. Before the start of the session, the patient was assessed on rating scales, and during the infusion his blood pressure, pulse rate, and orientation were monitored. The plan was to give sessions with gradual spacing out, the patient was given a total of 14 sessions, starting at the frequency of 3 sessions per week for 2 weeks (5 sessions) and gradually reduced from 2 to 1 per week (4 + 2 sessions), later once every 2 weeks (2 sessions) and finally once in a month (1 session). Through the sessions, rating scales showed a gradual decline in scores: MADRS – 30, 24, 20, 16, 8, 6, 0, 0, 0, 0, 0, 0, 0, and 6; and CDRS –50, 48, 43, 40, 38, 35, 30, 24, 20, 16, 14, 12, 6, and 12. The final scores except the last one, showed improvement in the symptoms, and the same was corroborated by the clinical examination. Throughout the ketamine sessions, the patient continued to take oral medications. There were no abnormalities in vitals, or any adverse events noted during or after the sessions and serial MSEs showed improvement in mood with no other abnormalities noted. From the MADRS and CDRS scores, we found that the symptoms did improve with ketamine when they were given at regular intervals but when spacing was increased from 2 weeks to a month the response was not sustained. The patient lost for follow-up after the last session to further see the improvement in the long term.

Discussion

Treatment of dysthymia involves the use of antidepressants but the evidence suggests that although they have better efficacy than placebo, their effect is not marked as in the case of depressive disorder. Also, the efficacy of antidepressants is optimal in patients with sub-affective presentation rather than full-spectrum disorder. Relapse rates can be as high as 89% within 4 years of discontinuation of antidepressants.[1] There is good evidence to support the use of intravenous ketamine in depression and treatment-resistant depression.[8,9] The dose, rate of infusion, mode of administration, and duration were based on previous studies.[10–13] In the current case as the patient was not having adequate improvement a trial of intravenous ketamine was started. Within a few sessions patient started reporting improvement in the symptoms and by the end of 13 sessions, there was significant clinical improvement. But when the duration between sessions was increased to 1 month, the effect was not sustained, and the patient started having re-emergence of symptoms as evidenced both clinically and objectively through rating scales. So, we believe that intravenous ketamine is a good adjunct in dysthymia but needs to be given at regular intervals. As the patient did not follow up after the last session there was no follow-up data.

Conclusion

This single case experience suggests that ketamine may be a valuable adjunct option for treating dysthymia. However, rigorous future studies are warranted to validate this finding and also to explore the long-term effects and sustainability of ketamine treatment for dysthymia.

Limitation

This is a single case of administering ketamine, hence the results cannot be generalized. The patient was not followed up after the last ketamine dose to understand the long-standing effect of ketamine on the symptoms.

Orcid

Raj Kiran Donthu https://orcid.org/0000-0001-7738-2084

References

1. Griffiths J, Ravindran AV, Merali Z, et al. Dysthymia: A review of pharmacological and behavioral factors. Mol Psychiatry 2000;5(3):242–261. DOI: 10.1038/sj.mp.4000697.
2. World Health Organization. The ICD-10 Classification of Mental and Behavioural Disorders. Geneve, Switzerland: World Health Organization, 1993.
3. Ishizaki J, Mimura M. Dysthymia and apathy: Diagnosis and treatment. Depress Res Treat 2011;2011:893905. DOI: 10.1155/2011/893905.
4. Rosenbaum SB, Gupta V, Patel P, et al. Ketamine. In: StatPearls. Treasure Island (FL): StatPearls Publishing. Available at: http://www.ncbi.nlm.nih.gov/books/NBK470357/. Accessed on: 10 November 2023.
5. Andrade C. Ketamine for depression, 4: In what dose, at what rate, by what route, for how long, and at what frequency? J Clin Psychiatry 2017;78:e852–e857. DOI: 10.4088/JCP.17f11738.
6. Zanos P, Gould TD. Mechanisms of ketamine action as an antidepressant. Mol Psychiatry 2018;23(4):801–811. DOI: 10.1038/mp.2017.255.
7. Sansone RA, Sansone LA. Dysthymic disorder: Forlorn and overlooked? Psychiatry (Edgmont) 2009;6(5):46–51. PMID: 19724735.
8. Nikolin S, Rodgers A, Schwaab A, et al. Ketamine for the treatment of major depression: A systematic review and meta-analysis. EClinicalMedicine 2023;62:102127. DOI: 10.1016/j.eclinm.2023.102127.
9. Marcantoni WS, Akoumba BS, Wassef M, et al. A systematic review and meta-analysis of the efficacy of intravenous ketamine infusion for treatment resistant depression. January 2009–January 2019. J Affect Disord 2020;277:831–841. DOI: 10.1016/j.jad.2020.09.007.
10. Krystal JH, Karper LP, Seibyl JP, et al. Subanesthetic effects of the noncompetitive NMDA antagonist, ketamine, in humans. Psychotomimetic, perceptual, cognitive, and neuroendocrine responses. Arch Gen Psychiatry 1994;51(3):199–214. DOI: 10.1001/archpsyc.1994.03950030035004.
11. Zarate CA Jr, Singh JB, Carlson PJ, et al. A randomized trial of an *N*-methyl-D-aspartate antagonist in treatment-resistant major depression. Arch Gen Psychiatry 2006;63(8):856–864. DOI: 10.1001/archpsyc.63.8.856.
12. Loo CK, Gálvez V, O'Keefe E, et al. Placebo-controlled pilot trial testing dose titration and intravenous, intramuscular and subcutaneous routes for ketamine in depression. Acta Psychiatr Scand 2016;134(1):48–56. DOI: 10.1111/acps.12572.
13. Berman RM, Cappiello A, Anand A, et al. Antidepressant effects of ketamine in depressed patients. Biol Psychiatry 2000;47(4):351–354. DOI: 10.1016/s0006-3223(99)00230-9.