Ketamine infusions for the treatment of mental health conditions

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Abstract

Globally, mental health conditions impose a large burden of disease. Although mental disorders react positively to current pharmacotherapy, ketamine, an anaesthetic, has displayed favourable results in the treatment of depression, anxiety, pain and other mood disorders. Treatment with ketamine could provide an effective, non-invasive treatment option. The background, mechanism of action, uses and benefits of ketamine in the treatment of mood ailments are discussed.

Keywords: ketamine, mental health, infusions

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Introduction

Mental health conditions are ubiquitous and expensive. Effectual treatments have been available for many years; however, the remission is low and relapse is high. A stable remission of symptoms is not achieved in one-third of subjects receiving conventional antidepressant treatment, and it takes a long time before a therapeutic effect is achieved (about two weeks).[1] A single dose of ketamine has been shown to have fast-acting mood-enhancing and anxiolytic effects.[2,3] In the 1960s ketamine was presented as a safe anaesthetic in humans.[4] Ketamine has been seen as a hopeful therapeutic option for treatment-resistant mood ailments.[4] Intravenous (IV) doses of ketamine showed easing of symptoms of major depression in the space of three days.[5] A single dose of ketamine results in a quick reduction in depressive and suicidal ideation 40 minutes post-infusion.[6] In comparison, traditional antidepressants used to treat depression usually take up to four weeks to work. Recent research has indicated that intravenous ketamine may be able to lessen depressive symptoms within a 24-hour period.[2] Ketamine has been shown to quickly reduce suicidal thoughts, with effects that typically last for a week or longer.[7] This review highlights the background, mechanism of action and benefits of ketamine in mood disorders.

Background

Ketamine was discovered by Calvin Stevens in 1962. It was found to have anaesthetic effects, and analgesic effects.[7] It was approved as an anaesthetic by the Food and Drug Administration (FDA) in 1970. Even though the routine use of ketamine is limited, it is often the anaesthetic of choice in developing countries, in situations in which respiratory systems cannot be easily monitored, or where dosing is difficult (e.g. out of hospital emergencies, disaster situations, paediatrics and veterinary medicine).[7]

Mechanism of action

Ketamine is water and lipid soluble and is a racemic mixture of its two enantiomers, (S)-ketamine and (R)-ketamine. It is an antagonist of the ionotropic glutamate N-methyl-D-aspartate (NMDA) receptor.[4] The G protein-coupled NMDA receptors require binding of glutamate and glycine a membrane depolarisation sufficient to expel magnesium (Mg^{2+}) blocking the channel pore, before allowing the influx of calcium (Ca^{2+}) and the propagation of excitatory neurotransmission.[4,7] It is proposed that through disinhibition, low doses of ketamine affect postsynaptic α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptors which result in brain derived neurotrophic factor (BDNF) activation that leads to increased synthesis of proteins required for the growth of new synapses.[7] This development of new synapses is thought to be related to antidepressant effects.[7]

Benefits

Ketamine causes analgesia and sedation at doses below a threshold. However, the characteristic dissociative state appears abruptly once the critical dosage threshold is reached, which is approximately 1 to 1.5 mg/kg when given intravenously (IV) or 3 to 4 mg/kg when given intramuscularly (IM).[2,7] Recently, IV ketamine has shown the possibility in reducing symptoms of depression in the space of 2–24 hours.[2] Ketamine has been found to decrease suicidal ideation rapidly with effects usually lasting up to a week.[7] Ketamine has been shown to be effective in reducing drinking in patients with alcohol use disorder (AUD).[7] Several studies have explored the effect of ketamine on anxiety disorders. Reductions in social anxiety disorder and generalised anxiety disorder have been noted in animal models.[8] A decrease in obsessive compulsive disorder (OCD) has been seen but further studies are necessitated.[9] Benefits reported for post-traumatic stress disorder (PTSD) is limited.[9]

Drug interactions

The effectiveness of ketamine may be impacted by the following drugs:[10]

- Benzodiazepines: Ketamine's antidepressant effects may be less effective when taken with high doses of benzodiazapines. Doctors may lower the dosage of any benzodiazepines, like Ativan® and Xanor®, before starting treatment.
- Lamotrigine: This anticonvulsant drug is useful in the treatment of bipolar disorder and epilepsy. The medication treats bipolar disorder by reducing or postponing manic, depressive, or rapid cycling episodes.
- Memantin: Memantin is a type of NMDA blocker. It has an effect on NMDA receptors, which affects how effective ketamine is.
- Any medication that modifies NMDA receptors.

Conclusion

The worldwide burden of mental health conditions is significantly high. There is a need for novel pharmacotherapies that are efficient and rapid. Future studies should focus on optimising administration to better translate the use of ketamine into clinical settings.

Conflict of interest

The author has no conflict of interest.

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References

1. Mandal S, Sinha VK, Goyal N. Efficacy of ketamine therapy in the treatment of depression. Indian Journal of Psychiatry. 2019;61(5):480-485. https://doi.org/10.4103/psychiatry.IndianJPsychiatry_484_18.
2. Phillips JL, Norris S, Talbot J. Single, repeated, and maintenance ketamine infusions for treatment-resistant depression: a randomized controlled trial. American Journal of Psychiatry. 2018;176(5):401-409. https://doi.org/10.1176/appi.ajp.2018.18070834.
3. Price RB, Spotts C, Panny B, et al. A novel, brief, fully automated intervention to extend the antidepressant effect of a single ketamine infusion: a randomized clinical trial. American Journal of Psychiatry. 2022;179:12. https://doi.org/10.1176/appi.ajp.20220216.
4. Tully JL, Dahlén AD, Haggarty CJ. Ketamine treatment for refractory anxiety: A systematic review. British Journal of Clinical Pharmacology. 2022;88:4412-4426. https://doi.org/10.1111/bcp.15374.
5. Berman RM, Cappiello A, Anand A, et al. Antidepressant effects of ketamine in depressed patients. Biological Psychiatry. 2000;47(4):351-354. https://doi.org/10.1016/S0006-3223(99)00230-9.
6. Singh I, Morgan C, Curran V, et al. Ketamine treatment for depression: opportunities for clinical innovation and ethical foresight. Lancet Psychiatry. 2017;4(5):419-426. https://doi.org/10.1016/S2215-0366(17)30102-5.
7. Grabski M, Morgan C. Ketamine. Encyclopedia of Mental Health. 2023;3:328-335. https://doi.org/10.1016/B978-0-323-91497-0.00236-8.
8. Silote GP, de Oliveira SF, Ribeiro DE. Ketamine effects on anxiety and fear-related behaviors: current literature evidence and new findings. Progress in Neuro-Psychopharmacology & Biological Psychiatry. 2020:100:109878. https://doi.org/10.1016/j.pnpbp.2020.109878.
9. Rodriguez CI, Kegeles LS, Levinson A, et al. Randomized controlled crossover trial of ketamine in obsessive-compulsive disorder: proof-of-concept. Neuropsychopharmacology. 2013;38:2475-2483. https://doi.org/10.1038/npp.2013.150.
10. Veraart JKE, Smith-Apeldoorn SY, Bakker IM, et al. Pharmacodynamic interactions between ketamine and psychiatric medications used in the treatment of depression: a systematic review. International Journal of Neuropsychopharmacology. 2021;24(10):808-831. https://doi.org/10.1093/ijnp/pyab039.