The future of ketamine in psychiatry

Bushra S. Qureshi, MD, and Steven Lippmann, MD

Ketamine, a high-affinity, noncompetitive *N*-methyl-D-aspartate (NMDA)-glutamate receptor antagonist, is used in human and veterinary medicine for its anesthetic and analgesic properties.[1] NMDA receptors could trigger cellular and behavioral responses, and ketamine blocks neuronal communication pathways.

How ketamine works

Water- and lipid-soluble, ketamine is available in oral, topical, IM, and IV forms. Plasma concentrations reach maximum levels minutes after IV infusion; 5 to 15 minutes after IM administration; and 30 minutes after oral ingestion.[1] The duration of action is as long as 2 hours after IM injection, and 4 to 6 hours orally. Metabolites are eliminated in urine.

Ketamine, co-prescribed with stimulants and some antidepressant drugs, can induce unwanted effects, such as increased blood pressure. Auditory and visual hallucinations are reported occasionally, especially in patients receiving a high dosage or in those with alcohol dependence.[1] Hypertension, tachycardia, cardiac arrhythmia, and pain at injection site are the most common adverse effects.

Some advantages over ECT in treating depression

The efficacy of electroconvulsive therapy (ECT) in alleviating depression depends on seizure duration. Compared with methohexital, an anesthetic used for ECT, ketamine offers some advantages:

- increased ictal time
- augmented mid-ictal slow-wave amplitude
- shortened post-treatment re-orientation time
- less cognitive dysfunction.[2]

Uses for ketamine

Treatment-resistant depression. The glutamatergic system is implicated in depression.[2,3] Ketamine works in patients with treatment-resistant depression by blocking glutamate NMDA receptors and increasing the activity of α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptors, resulting in a rapid, sustained antidepressant effect. Response to ketamine occurs within 2 hours and lasts approximately 1 week.

Bipolar and unipolar depression. Ketamine has rapid antidepressant properties in unipolar and bipolar depression. It is most beneficial in people with a family history of alcohol dependence, because similar glutamatergic system alterations might be involved in the pathophysiology of both disorders.[3,4] An antidepressant effect has been reported as soon as 40 minutes after ketamine infusions.[3]

continued

Dr. Qureshi was an observer physician in the Department of Psychiatry, University of Louisville School of Medicine, Louisville, Kentucky, where Dr. Lippmann is a faculty professor, when this article was written.

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Ketamine's rapid antidepressant effect could be beneficial when used in severely depressed or suicidal patients

Suicide prevention. A single sub-anesthetic IV dose of ketamine rapidly diminishes acute suicidal ideation.[1] This effect can be maintained through repeated ketamine infusions, episodically on a clinically derived basis. The exact duration and period between ketamine readministrations are not fully established. A variety of clinical-, patient-, and circumstance-related factors, history, response, and physician preferences alter such patterns, in an individualized way. This is also a promising means to reduce hospitalizations and at least mitigate the severity of depressive patient presentations.

Anesthesia and analgesia. Because ketamine induces anesthesia with minimal effect on respiratory function, it could be used in patients with pulmonary conditions.[5] Ketamine can provide analgesia during brief operative and diagnostic procedures; because of its hypertensive actions, it is useful in trauma patients with hypotension. A low dose of ketamine effectively diminishes the discomfort of complex regional pain and other pain syndromes.

Abuse potential

There is documented risk of ketamine abuse. It may create psychedelic effects that some people find pleasurable, such as sedation, disinhibition, and altered perceptions.[6] There also may be a component of physiological dependence.[6]

Conclusion

Ketamine's rapid antidepressant effect results could be beneficial when used in severely depressed and suicidal patients. Given the potential risks of ketamine, safety considerations will determine whether this drug is successful as a therapy for people with a mood disorder.

Further research about ketamine usage including pain management and affective disorders is anticipated.[7] Investigations substantiating relative safety and clinical trials are still on-going.[8]

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Related Resources

- Nichols SD, Bishop J. Is the evidence compelling for using ketamine to treat resistant depression? Current Psychiatry. 2015;15(5):48-51.
- National Institute of Mental Health. Highlight: ketamine: a new (and faster) path to treating depression. www.nimh.nih.gov/about/strategic-planning-reports/highlights/highlight-ketamine-a-new-and-faster-path-to-treating-depression.shtml.

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