

## Serial Ketamine Infusions More Effective for Depression?

Deborah Brauser | June 06, 2013

Serial infusions of the *N*-methly-D-aspartate (NMDA) antagonist ketamine at a lower dosage than commonly used may be more effective than a single infusion in reducing symptoms of depression, new research suggests.

A small study of 10 patients with major depressive disorder (MDD) showed that half achieved remission after receiving up to 4 intravenous (IV) infusions of ketamine 0.5 mg/kg twice weekly. Of those who experienced remission, 2 had sustained improvement 4 weeks later.

In addition, overall scores on 2 different suicidal ideation measures were significantly decreased post infusion. And there were no significant increases in adverse events reported between baseline and post treatment.

"It's surprising both that [this treatment] works and how rapidly it has effects," said coinvestigator Timothy Lineberry, MD, from the Department of Psychiatry and Psychology at Mayo Clinic in Rochester, Minnesota, in a release.

"It sometimes can work in hours to reduce depressive symptoms and suicidal ideation. Our goal is to begin to determine how the drug can be administered safely in routine treatment," said Dr. Lineberry.

The investigators add that future ketamine-for-depression research should also focus on determining the optimal frequency of infusions, test relapse prevention strategies, and optimal dosing parameters.

The study [was published](#) in the May issue of the *Journal of Psychopharmacology*.

### Single vs Multiple Infusions

The researchers note that although previous research has shown improvement in depressive symptoms with a single infusion of ketamine, side effects during treatment are common.

In addition, "it is not known whether serial infusions or lower infusion rates result in greater efficacy."

Last year, [as reported](#) by *Medscape Medical News*, results from a small study were presented at the New Clinical Drug Evaluation Unit Annual Meeting showing that patients with treatment-resistant depression had significant symptom improvement after receiving 6 low-dose infusions of ketamine.

For the current study, 10 adult patients (mean age, 47.2 years) who had experienced a severe depressive episode as part of their MDD or bipolar II disorder were enrolled. All had failed to respond to at least 2 previous antidepressants.

They received twice-a-week infusions of ketamine 0.5 mg/kg over 100 minutes until remission was achieved or until 4 infusions had been administered.

Depressive symptoms were measured the morning of each scheduled treatment session, 2 hours post infusion, and the following morning using the Montgomery-Åsberg Depression Rating Scale (MADRS). Remission was defined as a score of 9 or less on the MADRS.

The Young Mania Rating Scale (YMRS), the Brief Psychiatric Rating Scale (BPRS), the Scale for Suicide Ideations (SSI), and the Suicide Status Form (SSF) were also administered to monitor for possible treatment-related adverse events.

All participants were asked about altered sensory experiences during the infusions and were kept in a recovery room 30 minutes post infusion. Although they were hospitalized for the first infusion, all were treated as outpatients for

subsequent infusions.

Weekly follow-up was conducted in person or by phone up to 4 weeks after infusion completion.

### **More Is More?**

Results showed significant improvement in total mean MADRS scores from baseline to endpoint (33.3 vs 16.7, respectively;  $P = .0009$ ), and 8 patients were classified as responders with at least 50% improvement in symptom scores.

Interestingly, 3 of these participants "responded after only one infusion, while the other five responders needed two infusions," report the investigators.

Five of the participants achieved remission, as measured on the MADRS, with only 1 of these receiving a single infusion.

"Thus, a preliminary conclusion is that limiting ketamine trials to only one infusion may result in remission rates less than what might be achieved with serial infusions," write the researchers.

Two of the patients who achieved remission remained depression-free 4 weeks after treatment.

The total mean score on the SSI for all 10 patients also improved significantly from baseline to endpoint ( $P = .007$ ), as did the mean SSF score ( $P = .026$ ).

Scores on the YMRS and BPRS did not change significantly. When asked about specific side effects, one patient reported having brief and limited hallucinations during treatment, and some reported experiencing drowsiness or dizziness. None experienced a significant increase in blood pressure or a heart arrhythmia during infusion.

The investigators note that future studies will need to determine which patients will respond best to this type of treatment and "to test relapse prevention strategies."

"While patients and clinicians are excited about ketamine's potential, we know that more and more research lies ahead before we know which depressive conditions can be addressed with ketamine safely...in routine clinical practice," said Dr. Lineberry.

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