Esketamine Produces Rapid Effects in Treatment-Resistant Depression

Reports new study in Biological Psychiatry

Philadelphia, PA, September 8, 2016 – A new study in Biological Psychiatry reports that esketamine, a component of the general anesthetic ketamine, shows rapid and significant improvement in depressive symptoms in patients who do not respond to currently available therapies. The study aimed to demonstrate the efficacy and safety of esketamine in hopes to fulfill a long-awaited clinical need for therapies that can crack treatment-resistant depression.

Ketamine piqued researchers’ interest when a study demonstrated that low doses of the drug have rapid antidepressant effects, alleviating symptoms within just 2 hours. This stood in stark contrast to conventional antidepressant drugs, which can take 1 to 3 months to produce an effect. In addition, ketamine appeared to work in patients who did not see improvement in symptoms with conventional antidepressant drugs, about one third of patients with major depressive disorder.

Although ketamine entered the field as a promising new antidepressant a decade ago, no strategy has been established to maintain its efficacy. Studies have primarily focused on the effects of a single IV dose, but patients who initially respond tend to relapse within a week after the infusion.

In this study, first author Jaskaran Singh from Janssen Research & Development, LLC in San Diego, California and colleagues examined for the first time the safety and efficacy of esketamine in patients with treatment-resistant depression. In a double-blind study, the researchers randomly assigned 30 patients to receive a placebo, or a lower (0.2 mg/kg) or higher (0.4 mg/kg) dose of esketamine. The patients received two IV doses during the double-blind phase, which was followed by a 2-week follow up phase in which patients could receive up to 4 additional optional open-label doses.

The earliest onset of an antidepressant effect was measured 2 hours after the first infusion. Within 3 days, over 60% of patients receiving either dose of esketamine saw improvement in depressive symptoms. None of the patients in the placebo group responded. The authors compare this response rate to only 37–56% of patients after 6–12 weeks with conventional antidepressants.

“The study shows clear benefits of the drug over placebo and suggests that the lowest of the two doses may be equally efficacious but also safer,” said Murray Stein, of the University of California San Diego and a deputy editor of Biological Psychiatry. Seventeen percent of patients taking the higher dose experienced transient perceptual changes immediately after infusion, which subsided within 4 hours.

“Though the mechanism of ketamine (and esketamine) antidepressant effects remains unclear, this study clearly demonstrates a benefit, at least in the short term, of this drug for treatment-resistant depression,” said Stein.
Clinical trials are underway by Janssen to test a wider range of doses to determine the optimal dosing, assess other possible side effects, and establish the safety of esketamine in the longer term.

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Notes for editors

Copies of this paper are available to credentialed journalists upon request; please contact Rhiannon Bugno at +1 214 648 0880 or biol.psych@utsouthwestern.edu. Journalists wishing to interview the authors may contact Jaskaran Singh at jsingh25@its.jnj.com.

The authors’ affiliations, and disclosures of financial and conflicts of interests are available in the article.

Murray B. Stein MD, MPH, FRCPC is Distinguished Professor of Psychiatry and Family Medicine & Public Health, and Vice Chair for Clinical Research in Psychiatry at the University of California San Diego. His disclosures of financial and conflicts of interests are available here.

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Media contact
Rhiannon Bugno
Editorial Office, Biological Psychiatry
+1 214 648 0880
biol.psych@utsouthwestern.edu