Ketamine Lifted Bipolar Depression in 40 Minutes

VITALS

Major Finding: In patients with treatment-resistant bipolar depression, an infusion of 0.5 mg/kg of ketamine significantly relieved depression within 40 minutes, an effect that lasted at least 3 days.

Data Source: Randomized, placebo-controlled, double-blind, crossover study involving 18 patients.

Disclosures: The National Institute of Mental Health and the National Alliance for Research on Schizophrenia and Depression funded the study. A patent application for the use of ketamine for depression has been submitted, listing two of the investigators among the inventors; they have assigned their rights on the patent to the U.S. government.

BY ROBERT FINN

FROM ARCHIVES OF GENERAL PSYCHIATRY

A single infusion of ketamine relieved bipolar depression within 40 minutes in patients with treatment-resistant bipolar disorder, according to a randomized, placebo-controlled, double-blind, crossover study involving 18 patients.

The effect lasted at least 3 days, wrote Dr. Nancy Diazgranados and her colleagues from the National Institute of Mental Health.

The participants in the study were an average of 48 years old, had suffered from bipolar I or bipolar II depression for an average of 28 years, and had failed an average of seven antidepressant treatments before the ketamine study. Fifty-five percent of the participants had failed to respond to electroconvulsive therapy. Two-thirds of participants were on psychiatric disability, and all but one were unemployed (Arch. Gen. Psychiatry 2010;67:793-802).

The investigators randomly assigned the patients to receive an infusion of 0.5 mg/kg of ketamine or placebo. Two weeks later, the patients who had been given ketamine were given placebo and vice versa.

Of the 17 patients who completed the ketamine phase of the study, 12 (71%) responded to ketamine. In contrast, of the 16 patients who completed the placebo phase of the study, only 1 (6%) responded to placebo.

The investigators assessed the patients at baseline using several rating scales, including the Montgomery-Åsberg Depression Rating Scale, the Hamilton Scale for Depression, and the Beck Depression Inventory.

Patients showed statistically significant improvements in depression with ketamine, compared with those who were on placebo on all three scales beginning at 40 minutes after ketamine infusion and continuing for at least 3 days. The mean scores on the rating scales did not differ from placebo on days 7, 10, and 14.

Within 40 minutes, 9 of 16 patients receiving ketamine (56%) responded and an additional 2 (13%) experienced complete remission of their depression. One day after the infusion of ketamine, 44% of the patients had responded and 31% had remitted.

None of the patients experienced serious adverse events during the study. Among the adverse events associated with ketamine and experienced by at least 10% of the patients were disassociation; feeling strange, weird, or bizarre; dry mouth; tachycardia; and increased blood pressure.

Ketamine has been used in human and veterinary medicine since 1962, most commonly for inducing and maintaining general anesthesia, sedation in intensive care, analgesia, and treatment of bronchospasm.

When used for general anesthesia, the initial dose of intravenous ketamine is typically 1.5-4.5 mg/kg, which is substantially higher than the level used in this study.

Ketamine is thought to act as a noncompetitive inhibitor of the *N*-methyl-D-aspartate (NMDA) receptor, which is part of the glutaminergic neurotransmitter system.

Several lines of evidence have implicated the glutaminergic system in bipolar disorder. ■