Medical Xpress

Ketamine shows significant therapeutic benefit in people with treatment-resistant depression

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Patients with treatment-resistant major depression saw dramatic improvement in their illness after treatment with ketamine, an anesthetic, according to the largest ketamine clinical trial to-date led by researchers from the Icahn School of Medicine at Mount Sinai. The antidepressant benefits of ketamine were seen within 24 hours, whereas traditional antidepressants can take days or weeks to demonstrate a reduction in depression.

Led by Dan Iosifescu, MD, Associate Professor of Psychiatry at Mount Sinai; Sanjay Mathew, MD, Associate Professor of Psychiatry at Baylor College of Medicine; and James Murrough, MD Assistant Professor of Psychiatry at Mount Sinai, the research team evaluated 72 people with treatment-resistant depression—meaning their depression has failed to respond to two or more medications—who were administered a single intravenous infusion of ketamine for 40 minutes or an active placebo of midazolam, another type of anesthetic without antidepressant properties. Patients were interviewed after 24 hours and again after seven days. After 24 hours, the response rate was 63.8 percent in the ketamine group compared to 28 percent in the placebo group. The response to ketamine was durable after seven days, with a 45.7 percent response in the ketamine group versus 18.2 percent in the placebo group. Both drugs were well tolerated.

"Using midazolam as an active placebo allowed us to independently

assess the antidepressant benefit of ketamine, excluding any anesthetic effects," said Dr. Murrough, who is first author on the new report. "Ketamine continues to show significant promise as a new treatment option for patients with severe and refractory forms of depression."

Major depression is caused by a breakdown in communication between nerve cells in the brain, a process that is controlled by chemicals called neurotransmitters. Traditional antidepressants such as selective serotonin reuptake inhibitors (SSRIs) influence the activity of the neurotransmitters serotonin and noreprenephrine to reduce depression. In these medicines, response is often significantly delayed and up to 60 percent of people do not respond to treatment, according to the U.S Department of Health and Human Services. Ketamine works differently than traditional antidepressants in that it influences the activity of the glutamine neurotransmitter to help restore the dysfunctional communication between nerve cells in the depressed brain, and much more quickly than traditional antidepressants.

Future studies are needed to investigate the longer term safety and efficacy of a course of ketamine in refractory depression. Dr. Murrough recently published a preliminary report in the journal *Biological Psychiatry* on the safety and efficacy of ketamine given three times weekly for two weeks in patients with treatment-resistant depression.

"We found that ketamine was safe and well tolerated and that patients who demonstrated a rapid antidepressant effect after starting ketamine were able to maintain the response throughout the course of the study," Dr. Murrough said. "Larger placebo-controlled studies will be required to more fully determine the safety and efficacy profile of ketamine in depression."

The potential of ketamine was discovered by Dennis S. Charney, MD, Anne and Joel Ehrenkranz Dean of the Icahn School of Medicine at

Mount Sinai, and Executive Vice President for Academic Affairs of The Mount Sinai Medical Center, in collaboration with John H. Krystal, MD, Chair of the Department of Psychiatry at Yale University.

"Major depression is one of the most prevalent and costly illnesses in the world, and yet currently available treatments fall far short of alleviating this burden," said Dr. Charney. "There is an urgent need for new, fast-acting therapies, and ketamine shows important potential in filling that void."

Dr. Murrough will present his research on Sunday, May 19, 2013 from 1:00 pm to 3:00 pm in the Moscone exhibit hall at the APA meeting.

Provided by The Mount Sinai Hospital

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