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Intravenously administered ketamine shown to reduce symptoms of chronic post-traumatic stress disorder

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Summary: For the first time, evidence that a single dose of IV-administered ketamine was associated with the rapid reduction of symptoms of post-traumatic stress disorder in patients with chronic PTSD was demonstrated in a proof-of-concept, randomized, double blind crossover study. These findings could be the first step toward developing new interventions for PTSD.

FULL STORY

For the first time, evidence that a single dose of IV-administered ketamine was associated with the rapid reduction of symptoms of post-traumatic stress disorder in patients with chronic PTSD was demonstrated in a proof-of-concept, randomized, double blind crossover study, undertaken by researchers at the Icahn School of Medicine at Mount Sinai in New York City. These findings, according to Mount Sinai researchers, could be the first step toward developing new interventions for PTSD.

The original investigation, titled "Efficacy of Intravenous Ketamine for Treatment of Chronic Post-Traumatic Stress Disorder -- A Randomized Clinical Trial," was first published online in *JAMA Psychiatry* on April 16.

"These findings may lead to novel approaches in the treatment of chronic PTSD -- a condition that affects a broad spectrum of adults in the United States and beyond, including victims of sexual assault, war veterans, those who have witnessed catastrophic events such as the September 11 terror attacks, and others," said Adriana Feder, MD, Associate Professor of Psychiatry at the Icahn School of Medicine at Mount Sinai and the lead author of the study. "However, this should be viewed as a proof of concept study. Additionally, longer term clinical trials with ketamine will be required to determine if ketamine will be a clinically useful treatment for PTSD."

Previously, few pharmacotherapies, such as selective serotonin reuptake inhibitors and serotonin norepinephrine reuptake inhibitors -- both of which are associated with significant levels of nonresponse and persistent residual symptoms of post-traumatic stress disorder -- have been shown to be effective in the treatment of chronic PTSD. However, these treatments were not shown to have the same rapid effects on symptoms of PTSD as IV-administered ketamine, which emerged as an effective, quick-acting intervention for patients with treatment-resistant depression when administered at sub-anesthetic doses (0.5 mg / kg).

Ketamine is used for anesthesia at doses of 2 mg/kg or higher, and as an analgesic (painkiller) at subanesthetic doses. It is considered particularly safe because, unlike other anesthetics, ketamine reliably preserves breathing reflexes. According to Mount Sinai's researchers, there have been no randomized clinical trials examining the effects of ketamine in patients with chronic PTSD; the few previous studies that have examined the effects of ketamine in trauma-exposed individuals were either retrospective or non-randomized.

"In recent years, we and others have shown that ketamine could often counter the symptoms of depression in treatment-resistant cases. In the present study, we hypothesized that ketamine would be associated with significantly greater reduction in core PTSD symptom levels 24 hours after a single IV infusion, and that it would also improve co-morbid depressive symptoms in patients diagnosed with PTSD," said Dennis Charney, MD, Anne and Joel Ehrenkranz Dean, Icahn School of Medicine at Mount Sinai, President for Academic Affairs, Mount Sinai Health System, and principal investigator. "This study has borne out that hypothesis, and we hope the results soon will be replicated and extended by other researchers."

Study Methodology Patients with chronic PTSD were enrolled in this study at the Icahn School of Medicine at Mount Sinai between May, 2012 and December 2012. Eligible participants were between 18 and 55 years of age; had a primary diagnosis of PTSD; and a score of at least 50 on the Clinician-Administered PTSD Scale (CAPS). Study participants were free of concomitant psychotropic medications for two weeks prior to randomization and for the duration of the study.

For each procedure day, patients were assigned to receive a single IV infusion of ketamine hydrochloride or midazolam administered over 40 minutes. The order of infusions was randomly assigned, and administrations were made two weeks apart. Midazolam was chosen as the active placebo because its pharmacokinetic parameters and nonspecific behavioral effects are similar to those of ketamine.

Administered ratings were administered at pre-infusion baseline and 24 hours (day 1) after infusion (before patients were discharged from the hospital), 48 hours (day 2) after infusion, 72 hours (day 3) after infusion, and seven days day 7) after infusion.

The primary outcome was PTSD symptom severity 24 hours after infusion, assessed with the Impact of Event Scale -- Revised (IES -- R). Total IES-R scores 24 hours after infusion were significantly improved with ketamine compared with midazolam (mean difference, 12.7 [95% CI, 2.5-22.8]; P = .02). There was no evidence of any period or residual effects for the crossover. Additionally, symptoms in seven patients randomly assigned to ketamine first remained significantly reduced two weeks after infusion, compared with only one patient randomly assigned to midazolam first.

Story Source:

The above post is reprinted from materials provided by **Mount Sinai Medical Center**. *Note: Materials may be edited for content and length.*

Journal Reference:

1. Adriana Feder, Michael K. Parides, James W. Murrough, Andrew M. Perez, Julia E. Morgan, Shireen Saxena, Katherine Kirkwood, Marije aan het Rot, Kyle A. B. Lapidus, Le-Ben Wan, Dan Iosifescu, Dennis S. Charney. **Efficacy of Intravenous Ketamine for Treatment of Chronic Posttraumatic Stress Disorder**. *JAMA Psychiatry*, 2014; DOI: 10.1001/jamapsychiatry.2014.62

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