Researchers studying ketamine as suicide prevention drug

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(Medical Xpress)—University of Alabama at Birmingham (UAB) researchers think ketamine, an anesthesia medication in use since the 1970s, might be a valuable tool in treating severe depression and reducing suicidal urges; they have launched two studies to explore the possibility. One of the studies, ketamine is administered to suicidal patients in the UAB Hospital emergency department (ED), is the only such trial actually being conducted in an ED in the nation.

"There is a growing body of evidence that indicates that lower doses of

ketamine can reduce suicidal feelings and relieve symptoms of severe depression in a very short period of time, as little as a few hours, which makes it an extremely attractive candidate for treating acute depression," said Richard Shelton, M.D., professor in the Department of Psychiatry and Behavioral Neurobiology and lead investigator on the studies.

Shelton said ketamine appears to work on depression by blocking a neurotransmitter called glutamate from binding to the NMDA receptor on neurons. Too much glutamate on an NMDA receptor leads to the opening of a calcium ion channel, releasing too much calcium downstream. This then affects a brain chemical, brain derived neurotrophic factor (BDNF), which increases connections between neurons in the brain. These connections help the brain regulate emotions better.

In the trial, patients presenting to the ED with suicidal thoughts can be enrolled in the ketamine trial. The drug is administered via infusion, which takes about five minutes.

"We have seen a decrease in depression scores and suicide scores, sometimes within 15 minutes after giving ketamine," said Cheryl McCullumsmith, M.D., Ph.D., assistant professor and director of hospital psychiatry. "The antidepressants commonly used to treat depression and suicidal thoughts take weeks or months to begin to show positive effects. When a patient is actively suicidal, we don't have that much time."

McCullumsmith said patients entered in the ketamine trial at the ED are admitted to the psychiatric inpatient unit for observation.

"We are attempting to determine just how quickly the drug produces a beneficial result, as well as how long that result lasts," McCullumsmith said.

Shelton said a second trial, sponsored by Janssen Research & Development, LLC., is a multi-site trial of patients with severe depression and possible suicidal thoughts who are seen in an outpatient setting. Patients receive two or three infusions of ketamine or placebo each week for four-to-six weeks. Patients who do not benefit from study treatment after the first two weeks are offered two weeks of treatment with ketamine without the chance of placebo.

"We're interested in knowing how long each infusion will sustain the beneficial effect," said Shelton. "Ketamine does not appear to be curative, and we have a lot of work to do to see if it might be a useful drug for depression and suicide prevention on a long-term, regular-use basis."

A third trial underway at UAB is testing a compound called Glyx-13, produced by Naurex, Inc. Glyx-13 may produce similar results as ketamine by blocking an amino acid called glycine, which works in tandem with glutamate. Glycine regulates glutamate signaling, so it is like an added layer of fine-tuning. When glycine and glutamate bind to NMDA together, the calcium ion channel opens widely. Blocking glutamate with ketamine can reduce the release of calcium. Blocking glycine with Glyx-13 may achieve the same result, but more subtly and with fewer side effects.

"Glyx-13 may prove to be a more promising candidate than ketamine in terms of potential side effects," said Shelton. "Glyx-13 is being evaluated with just one infusion per week."

Ketamine, when used in anesthesia, has some side effects, including hallucinations and psychotic symptoms. It has also been a drug of abuse, known on the street as Special K. Shelton said the dose used in the depression trials is much lower, and given over a longer period. Side effects observed thus far in the ketamine trials have been minimal, he

said.

More information: UAB is enrolling patients in the outpatient trials of ketamine and Glyx-13. Male and female patients ages 19-64 with a diagnosis of depression, who have failed two drug regimens for depression, are candidates for the trials. Total time involved in the studies, with treatment and follow-up, is about 13 weeks. Individuals interested in more information can contact the study coordinator at 205-975-2911 or hammond@uab.edu.

Provided by University of Alabama at Birmingham