

From University of California, San Diego, School of Medicine

# Is Ketamine a Game Changer for Severe Depression?

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Hi. I'm Dr. David Feifel. I am Professor of Psychiatry at University of California, San Diego (UCSD) and Director of the Neuropsychiatry and Behavioral Medicine Program at the UCSD Medical Center.

Today I want to talk about some exciting positive developments in the treatment of depression, especially for depression in our most difficult-to-treat patients. What I really want to talk about is ketamine. You may have heard of ketamine -- it's not a new or novel medication. It has been around for many decades. Ketamine is approved as an anesthetic, and it works through the glutamate system.*[see reference 1]* A lot of research over the years suggests that glutamate plays an important role in regulating depression, but it has only been in the last few years that people have started to test this concept by actually doing clinical trials with ketamine to see how it may benefit people who have difficult-to-treat depression. This, of course, is our most challenging population, certainly in my caseload, and I'm sure most of you would agree.

The results are very exciting in several studies, and most seminally in a study by a group led by Carl Zarate out of the National Institutes of Health.*[see reference 2]* When they conducted a placebo-controlled study looking at intravenous ketamine (and these are small doses of ketamine, very safe), a large percentage of treatment-resistant patients improved -- up to 70% of the patients responded. What is really exciting is that the response was very rapid. Response was often within 24 hours, and many patients actually responded within a couple of hours. This is not something we are used to seeing in this difficult-to-treat population, and I think it's very exciting.

The big problem with intravenous ketamine is that the benefits of a single infusion are not sustained. So in the Zarate study, 35% of the patients did maintain some benefit a week after treatment, but most of the patients relapsed, and eventually all patients, we believe, will relapse after a single infusion. So we need to work out how to sustain that benefit in patients who do get a response. However, people are working on it, and there are some interesting protocols for multiple infusions over a series of weeks, similar to what we do with electroconvulsive therapy, for example, and that may solve this problem.

Is ketamine ready for prime time? It's very close to being ready for prime time. These are approved medications; they are very safe. Ketamine is used many times a day in this very institution, at UCSD Medical Center. We have a population of patients who have no other option; they are extremely ill, their lives are miserable; they have tried everything. For that reason, weighing the risks and benefits, we have actually begun a protocol here at UCSD Medical Center where we offer intravenous ketamine infusions for patients in this situation,

making it clear to them that this is not an approved medication, that this is not going to be covered by insurance, but that it could be very beneficial for them. If nothing else, sometimes it is helpful just to provide hope. Some people with treatment-resistant depression have not felt well for many years, and they start believing that nothing will make them feel better. If you can give them some hope, sometimes that itself is very beneficial. Keep an eye on intravenous ketamine; I think it could potentially be a real game changer in our field.

I want to briefly mention another medication that is showing similar, not as extensive, but still promising results, and that is intravenous scopolamine. Scopolamine is not a new drug; it has been around for a long time and was also used as part of a cocktail for anesthesia. Scopolamine is an anticholinergic medication, and a couple of placebo-controlled studies show rapid and very robust improvements in treatment-resistant patients. Therefore, intravenous ketamine and intravenous scopolamine might be what we need to treat these difficult patients. Keep an eye on these drugs. We are starting to use scopolamine here at UCSD Medical Center, so let's keep our fingers crossed. I want to thank you for watching. I am Dr. David Feifel.

## References

1. Zarate C Jr, Machado-Vieira R, Henter I, et al. Glutamatergic modulators: the future of treating mood disorders? *Harv Rev Psychiatry*. 2010;18:293-303. Abstract
2. Zarate CA Jr, Singh JB, Carlson PJ, et al. A randomized trial of an N-methyl-D-aspartate antagonist in treatment-resistant major depression. *Arch Gen Psychiatry*. 2006;63:856-864. Abstract

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## Disclosures

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