Clinical Use of Ketamine in Psychiatry

C. Sophia Albott, MD, MA
Assistant Professor
Department of Psychiatry and Behavioral Sciences
University of Minnesota Medical School

November 17, 2018

Disclosure Information

● I have no financial relationships to disclose.

● I will discuss the off label use of ketamine in this presentation.

Mental health disorders impact the population worldwide.

1.5 billion people 1.1 Million Minnesotans

64 Million Americans
Depression is the leading cause of disability worldwide.

400 million people

$210 billion

$12 billion in lost workdays

Psychiatrists face 3 epidemics:

Depression

Suicide

Psychiatrists face 3 epidemics:

Ketamine

Depression

Suicide

Opioid Epidemic
Outline

• Historical overview of antidepressant development and treatment-resistant depression
• Review of research on ketamine for depression
• Ketamine mechanism(s) of action → new developments on safety
• Future directions

All antidepressant pharmacotherapies target the monoaminergic system.

STAR*D Study Design
(Sequenced Treatment Alternatives to Relieve Depression)
All antidepressant pharmacotherapies target the monoaminergic system.
Ketamine Timeline

- **1980s**: Glutamate and N-methyl-D-aspartate (NMDA) receptors play a key role in cortical functions.
- **1990s**: Probe to examine mechanisms in schizophrenia, alcoholism, and mood disorders.
- **2000**: Berman et al. Pilot study demonstrates rapid (hours) antidepressant response.
- **2006**: Zarate et al. RCT replicates Berman’s study.
- **2010**: Zarate et al. Single doze of ketamine leads to an increased number and function of new synapses in the rodent prefrontal cortex.

Single-infusion studies of ketamine

A single ketamine infusion rapidly improves symptoms of depression.

Zarate et al., Arch Gen Psychiatry, 2006
Single Ketamine Infusion

Comparison of outcomes in meta-analyses of single ketamine infusion:

Repeated-infusion studies of ketamine
Repeated infusions increase response & durability.

Shiroma et al., J Affect Disord 2014.

Median time to relapse (9/1/12): 14 days

Repeated infusions increase response & durability.

Murrough et al., Biol Psychiatry 2013.

Repeated infusions increase response & durability.

Rasmussen et al., J Pharmacol 2013.
Ketamine for Suicidal Ideation

A greater proportion of patients who received ketamine were without suicidal ideation compared to placebo.

Effect of a single infusion of ketamine on suicidal ideation per clinician administered scales.
Effect of a single infusion of ketamine on suicidal ideation per self-reported scales.

Continuation & Maintenance

Longer-term outcomes in patients receiving maintenance ketamine infusions.
Acute + continuation ketamine infusions prolong depression remission.


Acute + continuation ketamine infusions prolong depression remission.


Summary of reports describing maintenance ketamine infusions.

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<thead>
<tr>
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<tbody>
<tr>
<td>Subjects</td>
<td>14</td>
<td>11</td>
<td>45</td>
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<tr>
<td>Mean No. Maintenance Treatments (SD)</td>
<td>25 (10.5)</td>
<td>12</td>
<td>8.6 (9.0)</td>
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<tr>
<td>Length between treatments (weeks)</td>
<td>3.2</td>
<td>1.95</td>
<td>2.8</td>
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<tr>
<td>Baseline score</td>
<td>17 (QIDS)</td>
<td>38.2 (BDI-II)</td>
<td>Not available</td>
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<tr>
<td>Final score</td>
<td>10.5 (QIDS)</td>
<td>26.8 (BDI-II)</td>
<td>Not available</td>
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Ketamine Mechanism of Action

Chronic stress causes neuronal atrophy in the rodent prefrontal cortex.

Synaptogenic model of depression as a form of chronic stress.
Ketamine rapidly reverses the effects of chronic stress.

Synaptogenic Model of Chronic Stress and Treatment Response

Depression, as a syndrome of chronic stress, is treated by ketamine.
Naltrexone reduces antidepressant effects of ketamine compared to placebo. ($N = 12$)

Where are we now?

Naltrexone blocks antidepressant effects in ketamine-responders. ($n = 7$)
Increased numbers of physicians are providing ketamine off-label to treat psychiatric disorders.


Potential Risks of Poorly Monitored Ketamine Use in Depression Treatment

Ketamine treatment for depression: opportunities for clinical innovation and ethical foresight

APA recommends 7 components for evaluating appropriateness of ketamine treatment.

- Comprehensive diagnostic evaluation
- Objective measurement of baseline symptoms
- Thorough history of antidepressant treatment
- Review of medical systems
- Physical exam and laboratory screening
- Careful review of past medical and psychiatric records
- Informed consent process

MN Ketamine Task Force

- Registry
- Development of a state-wide community standard of practice
- Creation of an evidence-based treatment algorithm
- Informed recommendations on dose titration, monitoring, transitioning to alternative treatment modalities

Psychiatrists face 3 epidemics:

- Depression
- Ketamine
- Suicide
- Opioid Epidemic
Thank you.

Please email me if you are interested in joining MN Ketamine Task Force:

albot002@umn.edu