Combining Intravenous Ketamine and Evidence-Based Psychotherapy for the Treatment of Chronic Pain and Chronic Posttraumatic Stress Disorder

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Introduction

- Intravenous infusion of ketamine hydrochloride has been demonstrated as effective for treating various chronic pain syndromes, especially CRPS [1].
- Recently Ketamine infusion has shown to be a potential treatment for Posttraumatic Stress Disorder (PTSD) [2].
- The current gold standard for treating PTSD is cognitive-behavioral psychotherapy [3].
- We report physical and psychological measures for a treatment that combines psychotherapy with a ketamine infusion for a patient with co-occurring chronic pain and PTSD.

Ketamine Dosing

- Patient was admitted to the ICU and started on a weight based ketamine infusion at 2mcg/kg/min. Over the next 24 hours the dose of ketamine was slowly titrated in 1-2mcg/kg/min increments every 3-4 hours until a final dose of 11mcg/kg/min was achieved. At this dose, the patient tolerated all side effects and her pain had completely resolved. The ketamine was continued at this maximum dose for a period of 48 hours at which time the infusion was discontinued. The patient was monitored for 4 hours and discharged home in stable condition.

Medical History

- Chronic Spondylolisthesis & Fusion
- Tuberculosis treatment → Lobectomy (oxygen-dependent since 2008), and PTSD secondary to late
- 33-year-old female with past medical history significant for left lower extremity
- Pain and PTSD.
- Recently Ketamine infusion has shown to be a potential treatment for Posttraumatic Stress Disorder (PTSD) [2].
- The current gold standard for treating PTSD is cognitive-behavioral psychotherapy [3].
- We report physical and psychological measures for a treatment that combines psychotherapy with a ketamine infusion for a patient with co-occurring chronic pain and PTSD.

Case Report

- 33-year-old female with past medical history significant for left lower extremity CRPS, lower back pain, Reynaud's syndrome, bronchiectasis with right upper lobectomy (oxygen-dependent since 2008), and PTSD secondary to late adolescent sexual assault.
- Patient completed fourteen day taper off 75mcg/hr/72hrs fentanyl patch and oral hydromorphone (32mg daily dose) prior to ketamine infusion
- Medical management consisted of continuous subanesthetic ketamine infusion over a four day period. Psychiatric treatment consisted of one hour evidence based psychotherapy session prior to infusion, daily one hour sessions during the four day ketamine infusion, and five one hour follow-up sessions.

Timeline

<table>
<thead>
<tr>
<th>Timeline</th>
<th>Psychology Intervention (focus of treatment in parentheses)</th>
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</thead>
<tbody>
<tr>
<td>Ketamine (K)</td>
<td>Cognitive Behavioral Therapy (CBT) Session 1 (Education about Pain &amp; PTSD Connection; treatment rationale)</td>
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<tr>
<td>K Day 1</td>
<td>CBT Session 2 (Application of connecting thoughts &amp; PTSD)</td>
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<tr>
<td>K Day 2</td>
<td>CBT Session 3 (Exposure: Patient voice records traumatic event &amp; listens to recording five times between sessions)</td>
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<tr>
<td>K Day 3</td>
<td>CBT Session 4 (Exposure: Voice recording of traumatic event with more details &amp; listen five times between sessions)</td>
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<tr>
<td>K Day 4</td>
<td>CBT Session 4 (Challenging/modifying maladaptive beliefs)</td>
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<tr>
<td>K + 7 days</td>
<td>CBT Session 5 (Insomnia, managing invasive thoughts)</td>
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<tr>
<td>K + 14 days</td>
<td>CBT Session 6 (Challenging/modifying maladaptive beliefs)</td>
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<tr>
<td>K + 20 days</td>
<td>CBT Session 7 (Challenging/modifying maladaptive beliefs)</td>
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<tr>
<td>K + 34 days</td>
<td>CBT Session 8: Inpatient session due to fainting/loss of consciousness incident (coping with illness)</td>
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<tr>
<td>K + 42 days</td>
<td>CBT Session 9: Oxygen discontinued (Improving insomnia)</td>
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<tr>
<td>K + 55 days</td>
<td>CBT Session 10 (Improving nutrition, exercise, social activities) – patient starts pulmonary rehab K + 62</td>
</tr>
</tbody>
</table>

Results

- Combined Ketamine / Psychotherapy: PCL
- Psychotherapy (Post-Ketamine): PCL
- Combined Ketamine / Psychotherapy: Pain
- Psychotherapy (Post-Ketamine): Pain

Discussion

- Ketamine (2-[2-chlorophenyl]-2-(methylamino)-cyclohexadone) is a potent analgesic at subanesthetic doses. It is also a noncompetitive agonist of the N-Methyl-D-Aspartate (NMDA) receptor, a glutamate system receptor responsible for brain synaptic plasticity/connectivity, fear learning/ extinction, and memory function [4].
- Ketamine also down-regulates the prefrontal cortex (PFC) resulting in decreased central sensitization and the re-gain of normal function in the Amygdala. When over-activated by the PFC, the amygdala manifests increased anxiety, irritability, and hypothalamic-pituitary-adrenal activity [2,4].
- Exposure/Cognitive-behavioral therapy (CBT) efficacy depends in part on the patient’s ability to recall and subsequently extinguish over time the most feared event(s). The theorized effectiveness of Ketamine is based on: a) increased access to the traumatic memory via enhanced synaptic connectivity; b) decreased central sensitization via down-regulation of the PFC; and c) enhanced extinction of previously paired pain related memories (e.g., walking = pain; talking about trauma = pain). Theoretically these conditions set the conditions for enhanced modification of core maladaptive fears underlying PTSD and fear/avoidance thoughts and behaviors that sustain both PTSD and chronic pain following the ketamine infusion.
- Other agonists of the NMDA receptor (D-cycloserine) have been used successfully in conjunction with CBT to treat acute stress disorder, generalized anxiety disorder, and panic disorder [5].

Conclusion

This case provides preliminary support for use of ketamine and psychotherapy yielding rapid reduction in PTSD and chronic pain symptom severity. These findings may lead to additional novel approaches to combining pharmacologic and psychotherapeutic treatments for patients with this co-occurring condition.

References


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