



Spring 2023

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Ketamine for active-duty military and veterans with PTSD

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Abstract

The purpose of this research and systematic literature review is to compare the drug ketamine's efficacy at treating post-traumatic stress disorder for veterans and active-duty military compared to approved Food and Drug Administration (FDA) options and combination medication/psychotherapy. In this review, three databases were searched including Pubmed, ClinicalKey, and PsycInfo from October 3 to January 9, 2023. Additionally, the Veterans Affairs (VA)/Department of Defense (DOD) Clinical Practice Guidelines was utilized. A variety of key and mesh terms were utilized when database searching. Chosen works for review included randomized control trials, systematic reviews, meta-analysis, and retro-perspective studies. Sources that were excluded included those published prior to the year 2010, multiple comorbidities, non-veteran, and non-military. In total, 18 resources were selected. Most of the research presented shows evidence for the use of serotonin reuptake inhibitors (SSRIs) and cognitive behavioral therapy (CBT) as the gold standard of treatment for PTSD.

Introduction

According to the United States Department of Veterans Affairs (2017), "Post-Traumatic Stress Disorder (PTSD) is a debilitating psychiatric disorder estimated to affect 70% of the world's population and 25% of veterans." The Veteran Affairs defines PTSD as "the development of characteristic and persistent symptoms along with difficulty functioning after exposure to a life-threatening experience or an event that either involves a threat to life or serious injury." The American Psychiatric Association, as of 2013, re-classified PTSD in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) from anxiety disorders to trauma and stress-related disorders. The re-classification placed PTSD into four categories: intrusion, avoidance, negative cognition/mood, and arousal. PTSD may be acute or chronic, with acute episodes lasting no greater than three months and chronic PTSD lasting greater than three months. Reisman 2016 states that the two most widely used methods to measure PTSD is the PTSD Checklist for DSM-5 (PCL-5) and the Clinician-Administered PTSD scale for DSM-5 (CAPS-5), a clinician-administered questionnaire with 30 questions to complete during a face-to-face interview. Reisman (2016) states that cognitive behavioral therapy and selective serotonin reuptake inhibitors are first-line treatments that reduce PTSD-related symptoms; however, there is a need for improved pharmacological treatment and long-term studies to reduce symptoms and prevent chronic symptoms.

Statement of the Problem

According to the United States Department of Veteran Affairs, between 4 and 17 percent of veterans who served overseas in Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OEF) have been diagnosed with PTSD. To date, there currently is no firm estimate for the total number of all veterans that may be diagnosed with PTSD. There are limited psychotropic medications for the treatment of PTSD, but multiple cognitive behavioral therapy (CBT) treatments have been shown to reduce PTSD symptoms. Due to the chronicity and vicious cycle of PTSD with continuous symptoms, ketamine may help reduce symptoms and improve the overall quality of life. The Food and Drug Administration approved intravenous and intramuscular ketamine for the induction and maintenance of anesthesia. In 2019, intra-nasal (s)-ketamine was FDA-approved for treatment-resistant depression.

Research Question

In patients that are active-duty military or veterans diagnosed with post-traumatic stress disorder, is ketamine superior at reducing PTSD symptoms and more efficient at improving quality of life compared to FDA-approved psychotropic medications and cognitive behavioral therapy modalities?

Does ketamine have superiority at reducing PTSD symptoms compared to common therapeutic management techniques?

Literature Review

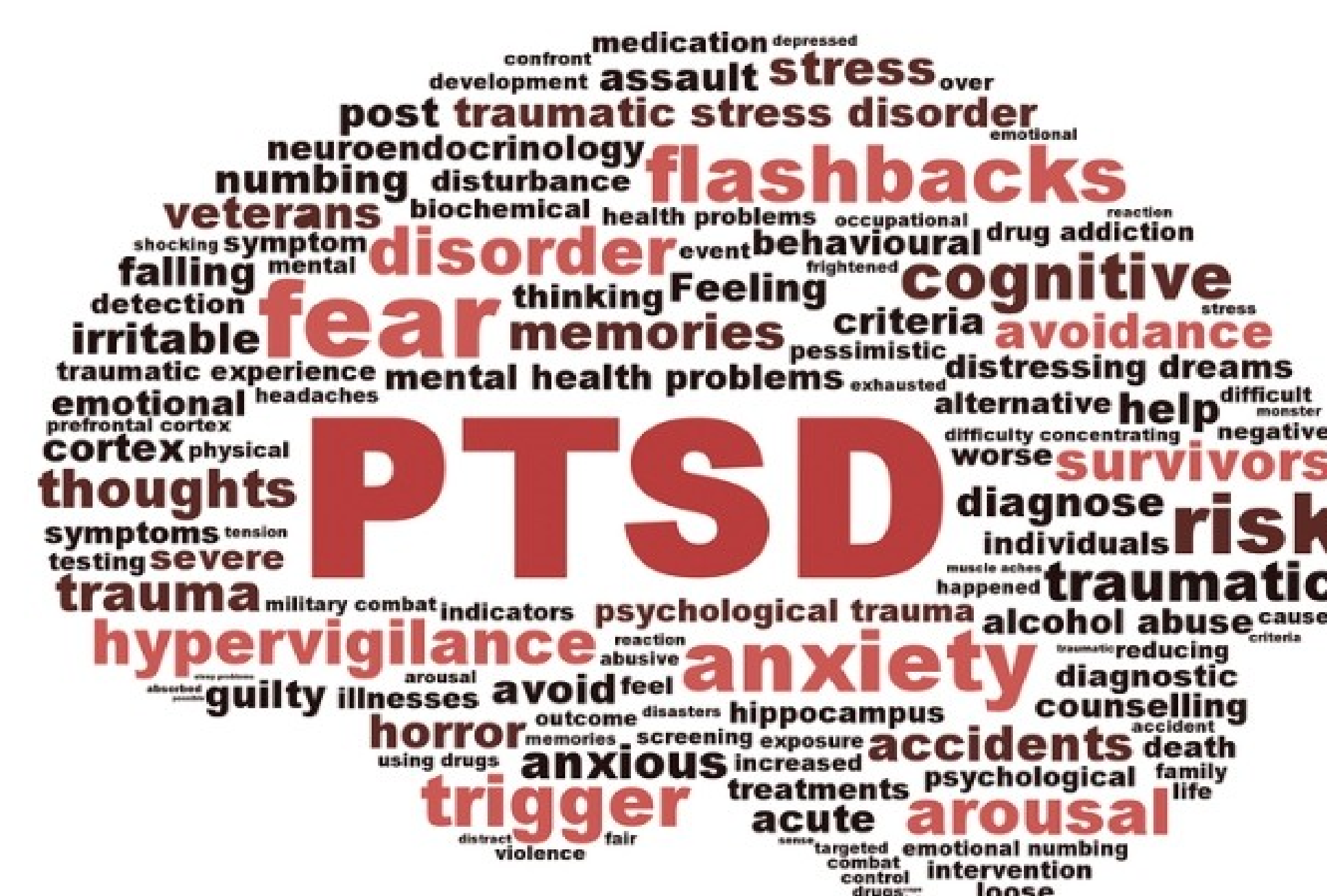
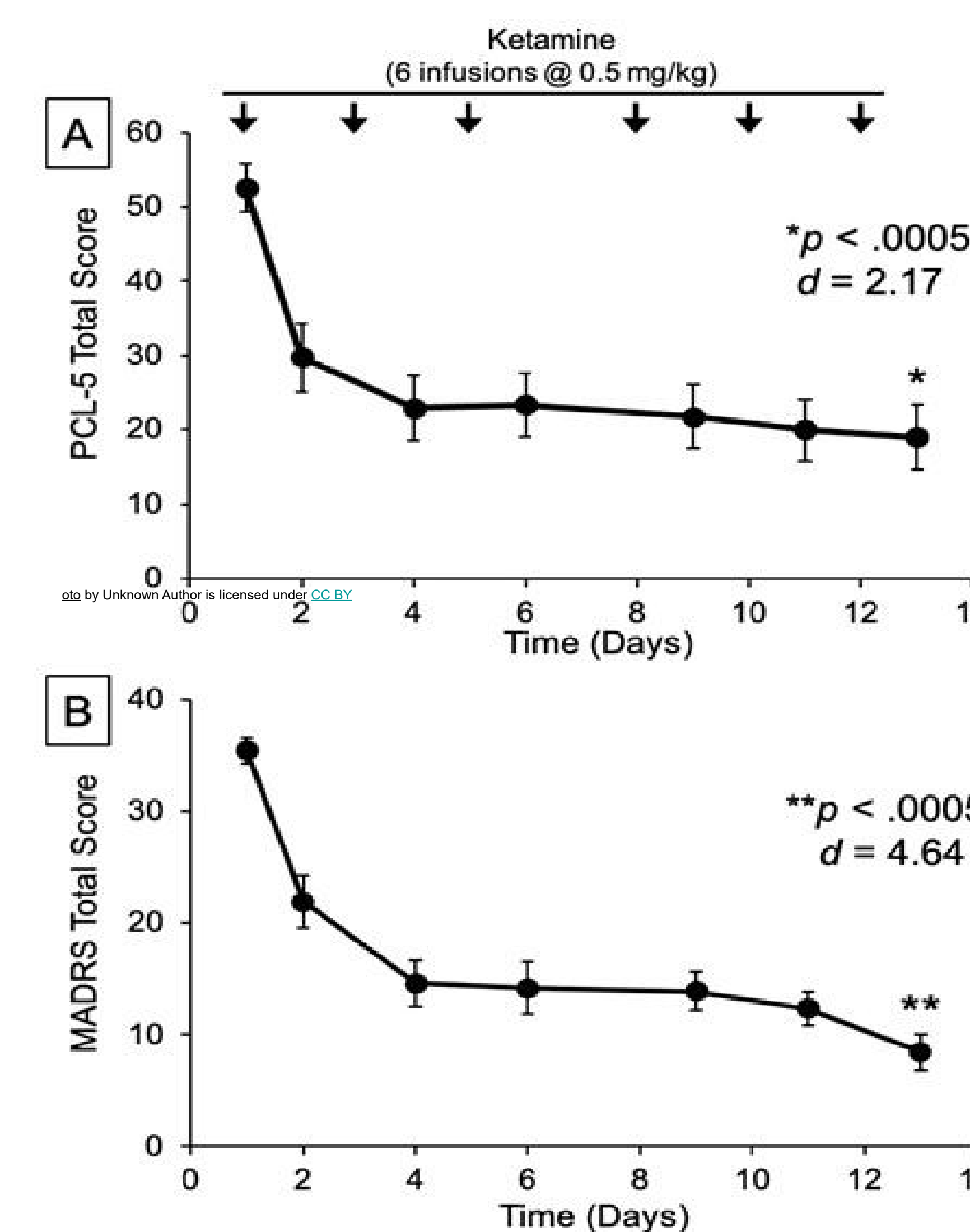
Active duty, reservist, national guard, and retired military personnel are frequently exposed to traumatic experiences in theater, overseas deployments, or within the United States. Military personnel are exposed to austere environments, warfare, and stressful situations and experience many life changes throughout their career. Therefore, mental health illness is a common complaint for this group. This scholarly project will investigate if novel ketamine therapy is superior compared to standard treatment options for PTSD.

- Intranasal and intravenous ketamine therapy has supporting evidence as a treatment option for veterans suffering from PTSD. Intranasal ketamine revealed a decrease in PCL-5 scores between treatments 1 and 2 ($p = 0.005$). Between treatment 4 and treatment 8, veterans showed a mean 5-point (SEM 2) reduction in PCL-5 scores ($p = 0.03$). Intravenous ketamine decreases acute PTSD symptoms up to 2 hours post infusion.
- Sertraline continues to provide benefit for PTSD patients (33.8 points for sertraline plus enhanced medication management [$P < .001$], 32.7 points for prolonged exposure therapy plus sertraline [$P < .001$])
- Internet based intervention, a form of cognitive behavioral therapy reduces PTSD symptoms. Zhou et al. (2020) revealed that the overall effects of IBI on veterans with PTSD show a in scores with an average of 0.29 (95% CI -0.48 to -0.11, $p < .001$)
- CBT and IR help reduce debilitating nightmares. According to Hart et al. (2019), "For the number of nights with nightmares both treatments showed a reduction in the frequency of approximately one night per week at six months, decreasing 3.6 to 2.6.
- Antipsychotic therapy helps to reduce insomnia significantly patients with PTSD. There were no significant effects of risperidone treatment on the primary outcome measure, the change in CAPS total score from baseline to 24 weeks ($P = 0.11$).

Discussion

According to the most currently accepted and approved standards for veteran PTSD treatment guidelines per the Veterans Affairs and Department of Defense, monotherapy utilizing cognitive behavioral therapy and/or selective serotonin reuptake inhibitors are still the gold standard to treat PTSD according the latest 2017 published guidelines. In fact, it is advised against the use of ketamine for veterans suffering from PTSD due to the lack of research. The VA/DoD guidelines for PTSD was published in 2017; therefore, this recommendation was made before the available ketamine studies found on PubMed.

PCL-5 and MADRS scores decrease within 2 weeks.



Applicability to Clinical Practice

Currently, ketamine is a topic of discussion rather than being applied in practice within family medicine. Ketamine does have clear benefits in emergency medicine and may benefit patients receiving care under psychiatry. In many areas of the country, there are low-dose ketamine infusion clinics that have been helping individuals with treatment-resistant depression. A long term controlled intravenous dose of ketamine has potential to provide symptom relief to patients in the outpatient setting. However, due to the lack of available long-term data, this option offers no long-term safety data and patients would have to consent to the risks and benefits of such treatment options.

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Acknowledgements

I want to thank all of my family, friends, and mentors that have served our country and shared their personal stories from World War 2, The Vietnam Conflict, The Gulf War, Operation Enduring Freedom and Operation Iraqi Freedom. All of you made a tremendous impact on my life. I know many conversations we had were topics that had been tucked away and out of sight for many years but you chose to talk with me because I had a great interest in your personal story and wanted to learn about these experiences. Thank you!