Comparison of Psychotherapy to MDMA-Assisted Psychotherapy in the Treatment of Patients with PTSD

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Abstract

Post traumatic stress disorder (PTSD) is a devastating disease that has high morbidity and mortality. Despite therapy, almost half of patients with PTSD will have chronic and devastating symptoms. The novel agent methylnedioxymethamphetamine (MDMA) has shown promise in phase 3 clinical trials; and, investigation into other therapies is warranted given our current treatment resistance. The objective of the research is to compare the use of MDMA assisted psychotherapy to psychotherapy alone.

Introduction

- PTSD is characterized by the affected individual re-experiencing a traumatic event through flashbacks, intrusive thoughts, or nightmares
- Significant impact on daily function, increased risk of comorbid psychiatric diagnoses, increased risk of suicide
- Symptoms include hyperarousal, impulsivity, detachment, illusions, difficulty concentrating, sleep disturbances, avoidance, withdrawal, depersonaalization, derealization, etc
- Symptoms must be present > 1 month
- Mechanism is unknown
- US and Canada adult prevalence is 6-9 % of general population, with higher prevalence in special populations such as Veterans, refugees, indigenous people, non-binary people, front-line workers during the COVID pandemic
- Risk factors: female gender, race, low socioeconomic class, less education, childhood adversity, poor social support, personal or familial psychiatric history
- Current mainstay treatment is CBT, pharmacotherapy such as SSRIs show some efficacy when treating comorbid anxiety/depression
- Despite therapy, half of patients will have chronic and devastating symptoms
- Clinician Administered PTSD Scale (CAPS) gold standard survey that measures symptom severity

Methods

- Search Strategy
  - Pub Med Database
  - October 2021
  - Key Terms= “PTSD and MDMA and CAPS”
  - 15 resulting articles
- Inclusion and Exclusion Criteria
  - Free articles
  - Full text articles
  - 11 articles total
  - 8 articles selected based on relevance to research question, design, and outcome measures

Results

Table 1 compares the mean reduction in CAPS scores between the control/placebo group compared to the treatment groups. CAPS scores were measured before treatment sessions and then 1-2 months following treatment, which consisted of 2-3 therapy sessions with placebo or MDMA. Two of the studies, Jerome at al and Jardim et al, only evaluated the reduction in CAPS in a treatment group without a control. All studies found statistically significant ($p < 0.005$) reduction in CAPS scores for treatment groups except for Oehen et al compared to the control groups, with no statistically significant reduction in CAPS.

- 7/8 studies found a statistically significant reduction in CAPS score in the treatment group

Table 1. Comparison of Results

Study	Mean reduction in CAPS post therapy, control	Mean reduction in CAPS post therapy, treatment
Mithoefer et al	-10.5	-30.4
Jerome et al	N/A	-44.8
Mitchell et al	-13.9	-24.4
Jardim et al	N/A	-48
Ponte et al	-12.4	-34.0
Gorman et al	-12.8	-35.1
Oehen et al	-3.2	-15.6
Wagner et al	-15.0	-40.2

Discussion

- Mithoefer et al: 6 randomized, double blind, controlled clinical trials. 56% of participants no longer met diagnostic criteria at treatment exit and 67% at 12 month follow up
- No adverse events occurred including increased suicidality, QTC prolongation, or abuse potential
- Most side effects included temporary somatic pains, sweating, or feeling flushed
- Jardim et al: specifically in patients with PTSD from sexual assault. All CAPS scores reduced greater than 30%
- Ponte et al: sleep quality improved significantly in the treatment group vs control
- Gorman et al: double blinded study, improved post traumatic growth inventory
- Fedduccia et al: non-tapered group had lower CAPS then taper group

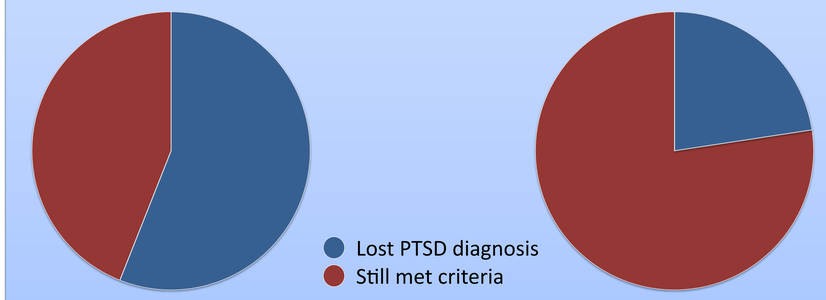

Figure 1. Percentage of patients after 2 treatment sessions who no longer met diagnosis criteria for PTSD using CAPS in the treatment group (left) vs control group (right)

Conclusion

MDMA assisted-psychotherapy shows promising results in the treatment of patients suffering from PTSD with minimal side effects. There is a good safety profile without any adverse events seen yet in current research. There is sufficient evidence that CAPS score improvement following MDMA-assisted psychotherapy is greater than psychotherapy alone. Research comparing the use of MDMA assisted psychotherapy with SSRIs and psychotherapy would be an interesting avenue for future research. However, the benefits of patients needing only two to three therapy sessions with MDMA compared to a much longer course of SSRIs, to be taken daily, offers a more cost effective treatment approach for the patient. There is also the potential for future drug development using the pharmacological profile of MDMA.

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