Naturalistic Clinical Evidence for the Use of Methylone in the Treatment of PTSD: A Case Series

Benjamin Kelmendi,[1,2,3] Christopher Pittenger,[1,4] Terence Ching,[1] Magí Farré,[5,6] Blake Mandell,[3] Martin Stogniew,[3] Mark Seelig,[7] Lynnette A. Averill,[1,2,8,9]

[1]Yale School of Medicine, Department of Psychiatry, New Haven, CT; [2] US Department of Veterans Affairs, National Center for PTSD – Clinical Neurosciences Division, West Haven, CT; [3]Transcend Therapeutics, New York, NY; [4] Yale Child Studies Center, New Haven, CT; [5]Department of Clinical Pharmacology, Hospital Universitari Germans Trias i Pujol and Institut de Recerca Germans Trias i Pujol, Barcelona, Spain; [6] Department of Pharmacology, Therapeutics and Toxicology, Universitat Autònoma de Barcelona, Spain; [7] Usona Institute, Madison, WI; [8] Baylor College of Medicine, Menninger Department of Psychiatry and Behavioral Sciences, Houston, TX; [9] Michael E. DeBakey VA Medical Center, US Department of Veterans Affairs, Houston, TX

Introduction

PTSD is a debilitating, and often chronic, condition with limited effective treatments and high risk for negative outcomes, including heightened suicidality.

SSRIs represent the first-line pharmacological treatment; paroxetine and sertraline are the only FDA-approved medications for PTSD. Despite their established efficacy, these treatments are sub-optimal. Even when optimally delivered, 40% of patients do not respond to SSRIs, only 20%-30% achieve remission, and the magnitude of the difference from placebo ranges from 10%-20%.[1,2]

Trauma-focused psychotherapy also shows efficacy in the treatment of PTSD and is often the first-line intervention selected, given the known limitations in pharmacotherapy; however, these too have significant limitations with high attrition and non-response rates.[3,4]

There is urgent need to identify novel rapid-acting interventions that support robust and durable clinical improvements, especially among patients who have been failed by traditional interventions.

The rapid acting empathogen methylone; also known as MDMC, βk-MDMA, and M1), is a phenethylamine compound with similarities to MDMA.

A recent observational study comparing the acute effects of methylone and MDMA in healthy participants reported that while the subjective pharmacological effects of the two drugs were categorically similar, methylone demonstrated physiological and pharmacological differences, including "softer" empathogenic and psychostimulant effects[5] that may have potential for accelerated adoption across a broader range of medical settings and clinical applications.

Here we report the first evidence of methylone's potential as a treatment for patients diagnosed with PTSD.

Methods

Archival data were obtained from 21 patients with a primary diagnosis of PTSD who received one or more oral methylone administrations.

Data was systematically compiled from information collected as part of routine clinical work.

Diagnoses were confirmed by an experienced clinician using semi-structured interviews. Baseline symptom severity and symptom improvement were evaluated using the Clinical Global Impressions Scale-Severity (CGI-S) and Clinical Global Impressions Scale-Improvement (CGI-I) respectively.

Patients were evaluated for observed or reported adverse effects during and after dosing sessions. Follow-up length varied.

Results

Twelve patients (57%) were female; 19 (90%) were White, and a mean age of 47.6 (range: 25 to 78).

Six patients (28.6%) were on concomitant SSRI or other psychotropic therapy. Methylone was administered orally, either as a single administration or with a boosted dose administered during the session (19 patients during at least one session). Starting doses were between 100 and 270 mg (selected on clinical judgement); the total dose administered ranged from 100 to 1,020 mg.

Baseline CGI-S scores ranged between 4 and 7 (i.e., moderately to severely ill; see Figure 1).

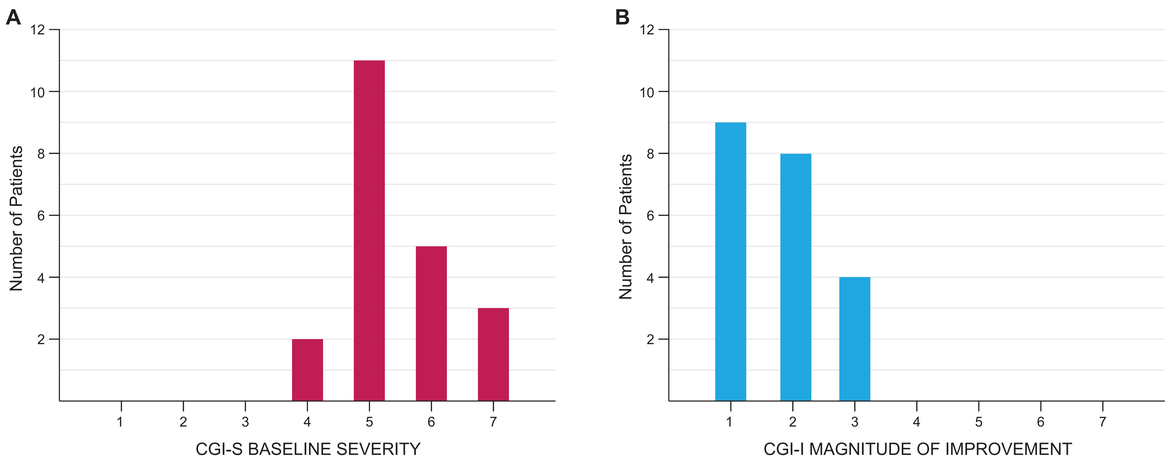
All patients achieved at least minimal improvement (CGI-I 1, 2 or 3) following treatment,
- 17 achieved "much" or "very much improved" ratings (see Figure 1).
- Remarkably, this benefit was observed for patients who received only a single dose (n=9), 8 (89%) achieved CGI-I scores of 1 or 2.
- For patients treated with multiple methylone sessions (n=12), initial improvement was noted after the first session in 83% (n=10).

Benefits were durable.
- 16 reported a durable effect (> six months in 11 patients).
- One patient each reported a sustained effect of 3 months, 2 months, and 1 week respectively.
- One patient's information was reported as, "no longer qualified for the disease (i.e., PTSD)" after the 4th methylone dosing session.

Methylone was well tolerated, and no patients discontinued treatment due to adverse events. A total of four adverse events were noted in three patients; none were considered severe, and none required medical intervention. AEs included light headedness, change in appetite and impaired sleep the day following dosing, and a flashback like experience.

Methylone produced acute and durable improvements in PTSD symptoms, without any notable adverse effects.

Fig. 1: Baseline symptom severity and magnitude of improvement following methylone dosing



Abbreviations: CGI-S = Clinical Global Impressions – Severity, where the higher the score the greater the severity of symptoms; CGI-I = Clinical Global Impressions – Improvement, where the lower the score the greater the magnitude of improvement.

Conclusion

This case series provides encouraging initial evidence that methylone may have utility in the pharmacological treatment of PTSD.

Methylone produced rapid symptom improvement, as measured by CGI-I ,in highly complex patients with significant disease (baseline CGI-S scores: 4 to 7).

The **majority (81%) of patients** achieved scores per CGI-I corresponding to **"much improved" or "very much improved."**

Methylone was well-tolerated over a broad dose range (100 to 1,020 mg) with both single and multiple administrations.

Adverse events were reported only in three older patients, age ≥70; these were mild and required no intervention. Notably, none of these adverse events occurred in patients receiving concomitant SSRI therapy, which is noteworthy as MDMA trials have required patients to taper off these medications.

Strengths/Limitations

Participants were treated clinically; data for this report were collected retrospectively from review of clinical records. Dosing and follow-up were variable and there was no randomization, control, or blinding to treatment condition. Further, the sample lacks diversity.

However, this data from a complex patient population constitutes the clinical evidence for the efficacy of methylone in the treatment of PTSD. The complexity of the sample aids in generalizability.

It is premature to draw conclusions regarding efficacy, optimal dosage and duration of treatment from this preliminary report; controlled trials are required

Disclosures

Dr. Kelmendi is a Co-founder, advisor, and has equity in Transcend Therapeutics and consults for Ceruvia Lifesciences. Dr. Pittenger serves as a consultant for Biohaven, Teva, Lundbeck, Brainsway, Ceruvia Lifesciences, Transcend Therapeutics, and Freedom Biotech, receives royalties and/or honoraria from Oxford University Press and Elsevier, and is PI for a sponsored study funded by Transcend Therapeutics. Dr. Stogniew is an employee and has equity in Transcend Therapeutics. Mr. Mandell is an employee and has equity in Transcend Therapeutics. Dr. Seelig has served as a consultant for Transcend Therapeutics. Dr. Averill has served as a consultant, speaker and/or advisory board member for Guidepoint, Transcend Therapeutics, Source Research Foundation, Reason for Hope, Beōnd, and Ampelis. All other authors declare no conflicts. The work on this poster was funded by Transcend Therapeutics.