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BRIEF REPORT

Micro-dose, macro-impact: Leveraging psychedelics in frontline healthcare workers during the COVID-19 pandemic

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ABSTRACT

Background and aims: The COVID-19 pandemic exacerbated pre-existing high-levels of physician stress and burnout[1]. In order to help treat frontline colleagues who were diagnosed with acute stress disorder, we chose a non-psychedelic, ketamine micro-dose treatment strategy for symptom management. *Methods:* We provided care virtually, and all patients were prescribed sublingual ketamine once daily. Each patient was evaluated using the NIH-PROMIS CAT assessments for stress, depression, anxiety, and PTSD via a remote, HIPAA compliant patient self-reporting platform. Progress was tracked and assessed against a baseline value obtained prior to the start of treatment. Patient progress was evaluated at a 4–6-week interval. Patients did not report any significant side effects to the treatment regimen. *Results:* 100% (25/25) of patients experienced improved anxiety, 92% (23/25) experienced improved stress, 96% (24/25) experienced improved PTSD, and 91% (20/22) experienced improved depression. *Conclusions:* While we cannot draw definitive conclusions from the association demonstrated by this data, we believe these results demonstrate that further research into the efficacy of daily, short-term ketamine micro-doses for treatment of acute stress disorder is warranted.

KEYWORDS

ketamine, micro-dose, COVID-19, mood disorders, acute stress disorder

INTRODUCTION

The COVID-19 pandemic exacerbated pre-existing high-levels of physician stress and burnout, threatening the safety and performance of front-line health care workers (West, Dyrbye, & Shanafelt, 2018). To help our frontline colleagues, we created a protocol based on our experience as a ketamine clinic to treat those healthcare workers diagnosed with acute stress disorder.

Ketamine is currently the only FDA approved drug with psychedelic properties. Since 2006, a large body of literature has been published on the efficacy of Ketamine for off-label treatment of mood disorders utilizing dissociative, psychedelic "macro-dose" protocols (Zarate et al., 2006).

For our study, we chose a non-psychedelic, micro-dose treatment strategy as an alternative to existing ketamine treatment strategies.

This study received the Institute of Cellular and Regenerative Medicine institutional review board approval for a retrospective chart review to assess the efficacy of our intervention. All patient data was de-identified and patient records kept confidential.

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This retrospective study is an open label, proof-of-concept trial, neither structured nor powered to reach a definitive conclusion, but rather intended to determine if this clinical strategy deserves further study.

METHODS

We provided all care virtually, and data was collected via the remote, HIPAA-compliant, patient self-reporting outcomes platform Outcome MD.

See Table 1 for Inclusion/Exclusion criteria.

Participants were recruited by email and word-of-mouth and admitted on a rolling basis from April of 2020 to July of 2021.

Retrospective chart review revealed 25 patients (of 26 total) with data for the 4–6-week treatment data interval.

The patient pool represented a heterogenous group of frontline healthcare worker roles and at various stages of training/experience across both academic and private hospitals. Ages ranged from 29 to 60 years old, with a mean age of 36.5 and a median age of 34.5. Patients self-reported gender with 15 male and 10 female patients.

Of the twenty-six study participants, sixteen were physicians. Of the sixteen, eight were resident physicians in post-graduate specialization programs and eight were attending-level physicians. Specialties represented were psychiatry, emergency medicine, anesthesiology, and internal medicine.

Of the remaining ten subjects, three were registered nurses, five were mental health professionals (Licensed Clinical Social Workers, Marriage and Family Therapists, and Clinical Psychologists), one was a medical student on clinical rotations, and one was a surgical technician.

After initial screening, all patients were confirmed to have a diagnosis of acute stress disorder by DSM V guidelines. All participants provided informed consent, were educated regarding potential side effects, and instructed in safe medication use practices.

All patients were prescribed 37.5 mg sublingual ketamine once daily. Patients were instructed to only take the medication as they were "winding down" from their day.

Each patient was evaluated using the NIH-PROMIS CAT assessments for stress, depression, anxiety, and PTSD via a remote, HIPAA compliant patient self-reporting platform OutcomeMD. OutcomeMD produces a normalized score of 0–100 for each metric with 0 representing the negative end of the scale. Progress was tracked and assessed against a baseline value obtained prior to the start of treatment. Follow-up visits were live, face-to-face telemedicine visits via a HIPAA-compliant platform.

Table 1. Inclusion/Exclusion criteria

Inclusion Criteria	Exclusion Criteria
Greater than 18 years of age	Currently on medication for psychiatric conditions
Demonstrate capacity to consent to study	Currently breastfeeding or attempting to procreate
A frontline health-care worker	History of seizure disorder, liver disease, or psychosis/mania
Experiencing acute stress disorder per DSM V criteria	Uncontrolled hypertension
	Study Physician discretion: any condition deemed inappropriate

We used OutcomeMD's method of calculating percentage improvement, defined as:

(Follow-up Score-Initial Score)/(Maximum Score-Initial Score) = % Improvement.

Data is stored and can be accessed within our HIPAA compliant electronic health record, DrChrono. OutcomeMD, our HIPAA compliant, virtual patient self-reported outcomes measures platform integrates directly with DrChrono and is accessed by the same portal.

Patients were not questioned regarding other potentially relevant psychosocial history and variables such as financial, psychological, or familial stressors. We did not inquire about any self-care regimens or other behaviors that may have also affected outcomes.

RESULTS

Patient progress was evaluated at a 4–6-week interval. The assessment closest to 35 days after treatment start was used for patients with multiple assessments within this interval. One patient was excluded from the data for failure to complete the treatment parameters; three others were excluded from depression data due to non-completion of baseline depression assessments. Patients did not report any significant side effects to the treatment regimen.

100% (25/25) of patients experienced improved anxiety, 92% (23/25) experienced improved stress, 96% (24/25) experienced improved PTSD, and 91% (20/22) experienced improved depression (Fig. 1).

DISCUSSION

The rising popularity of ketamine macro-doses as treatment options for a wide array of mood disorders often does not discuss the burden that is imposed by these treatments, which are time and financial-resource intensive (Witt, 2021). Furthermore, many patients are averse to undergoing a dissociative, psychedelic experience.

In comparison, the relatively low-cost and potential to scale ketamine micro-dosing, along with the minimal disruption that it poses to patients' routines, supports its promise as an effective tool to help combat our worsening mental health epidemic (Reinert, Fritze, & Nguyen, 2021). In contrast to benzodiazepines, ketamine's apparent lack of physical dependency and safety profile further adds to its potential promise (Van Amsterdam & Van Den Brink, 2022).

While we cannot draw conclusions from the association demonstrated by this data, we believe these results

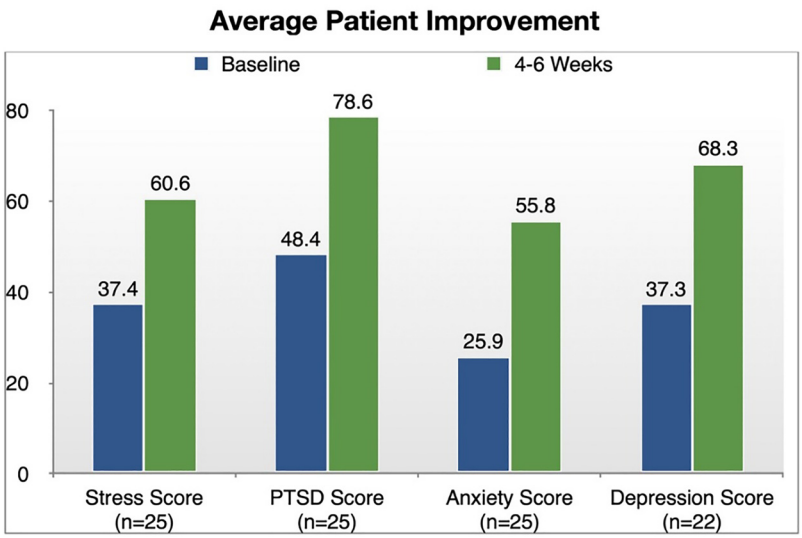

Fig. 1. Average patient improvement

demonstrate the significant potential of this treatment strategy, and that further research into the efficacy of ketamine micro-doses for acute stress disorders, and for mood disorders more broadly, is warranted.

Ethics: Institutional Review Board: Institute of Cellular and Regenerative Medicine; approval number: IRCM-2021-279.

Authors' contribution: AA and NB. had full access to all of the data in the study and take responsibility for the integrity of the data and accuracy of the data analysis. Concept and design: AA, HB, SA, DT. Acquisition, analysis, or interpretation of data: AA, SG, NB. Drafting of the Manuscript: AA, HB, NB, SA. Critical revision of the manuscript for important intellectual content: AA, DT. Statistical Analysis: AA, NB. Administrative, technical, or material support: SA, SG. Supervision: AA.

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Conflict of interest: AA reports he is an investor in OutcomeMD. No other author has any declaration of conflicting interests to disclose.

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REFERENCES

Reinert, M., Fritze, D., & Nguyen, T. (October 2021). *The state of mental health in America. 2022.* Alexandria VA: Mental Health America. Available at: https://mhanational.org/sites/default/files/2022%20State%20of%20Mental%20Health%20in%20America.pdf

Van Amsterdam, J., & Van Den Brink, W. (2022). Harm related to recreational ketamine use and its relevance for the clinical use of ketamine. A systematic review and comparison study. *Expert Opinion on Drug Safety*, *21*(1), 83–94. https://doi.org/10.1080/14740338.2021.1949454.

West, C. P., Dyrbye, L. N., & Shanafelt, T. D. (2018). Physician burnout: Contributors, consequences and solutions. *Journal of Internal Medicine*, *283*(6), 516–529. https://doi.org/10.1111/joim.12752.

Witt, E. (2021, December 29). *Ketamine therapy is going mainstream. Are we ready?* The New Yorker. https://www.newyorker.com/culture/annals-of-inquiry/ketamine-therapy-is-going-mainstream-are-we-ready.

Zarate, C. A. M. D., Singh, J. B., Carlson, P. J., Nancy, E., Brutsche, N. E., Ameli, R., Luckenbaugh, D. A., Charney, D. S., & Manji, H. K. (2006). Randomized trial of an N-Methyl-D-Aspartate antagonist in treatment-resistant major depression. *Archives of General Psychiatry*, *63*(8), 856–864. https://doi.org/10.1001/archpsyc.63.8.856.