PAIN MEDICINE CASE REPORTS

ISSN 2768-5152

Volume 8, Number 2, pp. 45-47

KETAMINE INFUSION FOR REFRACTORY POST-COVID-19 FATIGUE: CASE REPORT

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Background: Post-COVID-19 syndrome (PCS) symptoms are common after COVID-19 infections and despite recent efforts to study and treat, limited progress has been made. The most common of the symptoms, fatigue, can be debilitating and lack effective treatment options, and as a result, the need for potential management options is paramount.

Case Report: We present a case report of a patient with refractory PCS fatigue. Following intravenous ketamine infusion, the patient noted significant improvement in his energy and fatigue symptoms.

Conclusions: We report the successful use of ketamine infusion for PCS fatigue symptoms.

Key words: Long COVID, post-COVID, ketamine, infusion, fatigue, case report

BACKGROUND

Since 2019, over 770 million cases of COVID-19 have been confirmed (1). Although most symptomatic individuals improve from the illness, > 30% may experience post-COVID-19 sequelae or lasting symptoms following the infection (2). Symptoms lasting for at least 4 weeks following the infection, referred to as long COVID, can comprise various symptoms, including fatigue and cognitive impairment (3,5,10). Various descriptions exist, including persistent post-COVID syndrome (PCS) symptoms referring to those symptoms lasting > 24 weeks (4). Despite fatigue being one of the most common features of PCS, there are no established nor effective treatments (5,6).

Ketamine is a dissociative anesthetic, which acts as a noncompetitive inhibitor at the N-methyl-D-aspartate receptor (NMDAR) commonly used for induction and maintenance of anesthesia (7). NMDAR mediates the excitatory glutamatergic synaptic transmission in the spinal cord and brain, which is strongly implicated in the amplification of pain signals and central sensitization. Consequently, NMDAR antagonists, such as ketamine, may be used to reduce the excessive nociceptive input and central pain sensitization and, more recently, have been used in refractory depression, as well as to treat pain in patients suffering from fibromyalgia (8).

In this case report, we describe a patient with refractory fatigue following COVID-19 that was successfully treated with ketamine infusion.

CASE STUDY

A 50-year-old man, who was diagnosed with COVID-19 infection 6 months prior, presented for evaluation for PCS fatigue symptoms for over 5 months. He was seen by Ear, Nose, and Throat, Neurology, and Rheumatology, as well as the institutional post-COVID-19 service. The patient noted generalized fatigue that was refractory to care and treatment. He was tired all day, with malaise limiting any physical activity. He noted the worsening of his fatigue with physical or mental effort. Additionally, the patient had constant headaches and had undergone a stellate ganglion block with successful improvement.

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Disclaimer: There was no external funding in the preparation of this manuscript.
Conflict of interest: Each author certifies that he or she, or a member of his or her immediate family, has no commercial association (i.e., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted manuscript.
Patient consent for publication: institutional policy does not require patient consent or institutional review board approval for case reports.
This case report adheres to CARE Guidelines and the CARE Checklist has been provided to the journal editor.
Accepted: 2024-01-04, Published: 2024-03-31

On evaluation, the patient noted > 90% improvement of his headaches with the stellate ganglion block, but no change of the fatigue symptoms. We discussed repeating the stellate ganglion block vs other options, including trial of a ketamine infusion.

The patient elected to try the ketamine infusion (subdissociative dosing of 0.25 mg/kg over 40 minutes). The patient experienced ~ 30% improvement in fatigue at the 2-week follow-up. He underwent a repeat infusion at 4 weeks and noted > 75% improvement in his fatigue symptoms, with improved activity level, including walks of over 1 mile at a time. At 6 months, the patient continued ~ 75% improvement of his fatigue.

Local institutional policy does not require patient consent or institutional review board approval for case reports.

DISCUSSION

PCS is characterized by a wide range of symptoms and is defined as symptoms within 3 months after a probable COVID-19 infection, lasting at least 2 months with an impact on everyday function without an alternative diagnosis (9). Fatigue and exertion intolerance are common and have been well described. Unlike other PCS symptoms like anosmia, which may be self-limiting, a third of individuals experience persistent fatigue (2). The fatigue symptoms can be debilitating and may be like those suffering from chronic fatigue syndrome and fibromyalgia.

The pathophysiology of PCS is still unclear. Putative pathophysiology includes long-term tissue damage to organs, such as the lungs, heart, and brain (10). There is a suggestion that like autoimmune diseases and fibromyalgia, there may be pathological inflammation, including T-cell dysfunction (4). As a result, the condition may potentially respond to current treatments for autoimmune diseases or fibromyalgia.

The use of ketamine intravenously for treatment of fibromyalgia pain and related symptoms, including fatigue, has been explored due to its potential to reduce the induction of synaptic plasticity and maintenance of chronic pain states (8). By blocking NMDAR to mediate the glutamatergic synaptic transmission in the spinal cord and brain, ketamine has been proposed to impact the various receptors, such as the dopamine D2 receptors, resulting in the improvement of pain. Additionally, ketamine's effect on NMDAR may also improve sleep, cognition, and energy. The evidence for safety and efficacy has been growing. Most ketamine infusions for treatment of fibromyalgia have been explored using 0.3 mg/kg, ranging from 0.1-0.5 mg/kg (8). This dosing is considered subdissociative or subanesthetic and may be administered in various settings, including emergency rooms and in outpatient settings with appropriate monitoring and support.

With the evolving use of intravenous subdissociative ketamine infusions in refractory conditions like fibromyalgia and refractory chronic pain conditions, ketamine may be a potential treatment option in PCS. This case report describes improvement of PCS fatigue after COVID-19 with intravenous ketamine infusion.

CONCLUSIONS

The global pandemic COVID-19 has caused a huge public health burden. Patients with PCS, particularly fatigue, are suffering from lasting symptoms. Ketamine has been considered for use in various refractory conditions, such as depression and fibromyalgia. Its application in treating symptoms related to PCS may be promising and warrants further research.

REFERENCES

1. Coronavirus disease (COVID-19) – World Health Organization. Accessed September 30, 2023.
2. Tenforde MW, Kim SS, Lindsell CJ, et al. Symptom duration and risk factors for delayed return to usual health among outpatients with COVID-19 in a multistate health care systems network - United States, March-June 2020. *MMWR Morb Mortal Wkly Rep* 2020; 69:993-998.
3. Renaud-Charest O, Lui LMW, Eskander S, et al. Onset and frequency of depression in post-COVID-19 syndrome: A systematic review. *J Psychiatr Res* 2021; 144:129-137.
4. Nalbandian A, Sehgal K, Gupta A, et al. Post-Acute COVID-19 syndrome. *Nat Med* 2021; 27:601-615.
5. Davis HE, Assaf GS, McCorkell L, et al. Characterizing long COVID in an international cohort: 7 months of symptoms and their impact. *EClinicalMedicine* 2021; 38:101019.
6. Siegelman JN. Reflections of a COVID-19 long hauler. *JAMA* 2020; 324:2031-2032.
7. Littlejohn G, Guymer E. Modulation of NMDA receptor activity in fibromyalgia. *Biomedicines* 2017; 5:15.
8. Pastrak M, Abd-Elsayed A, Ma F, Vrooman B, Visnjevac O. Systematic review of the use of intravenous ketamine for fibromyalgia. *Ochsner J* 2021; 21:387-394.
9. Soriano JB, Murthy S, Marshall JC, Relan P, Diaz JV; WHO Clinical Case Definition Working Group on Post-COVID-19 Condition. A clinical case definition of post-COVID-19 condition by a Delphi consensus. *Lancet Infect Dis* 2022; 22:e102-e107.
10. Yong SJ. Long COVID or post-COVID-19 syndrome: Putative pathophysiology, risk factors, and treatments. *Infect Dis (Lond)* 2021; 53:737-754.