

IV Ketamine Therapy for Long COVID

A Rapid Systematic Review

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About this report

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About the Evidence-Based Practice Group

The Evidence-Based Practice Group was established to address the many medical and policy issues that WorkSafeBC officers deal with on a regular basis. Members apply established techniques of critical appraisal and evidence-based review of topics solicited from both WorkSafeBC staff and other interested parties such as surgeons, medical specialists, and rehabilitation providers.

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Objectives

- To determine whether there is any evidence on the efficacy and/or effectiveness of IV Ketamine in treating patients diagnosed with Post-COVID Conditions (Long COVID).

Methods

- A comprehensive and systematic literature search was conducted on February 4, 2025.
- The search was done on commercial medical literature databases, including Cochrane Database of Systematic Reviews (2005 to January 29, 2025), ACP Journal Club (1991 to January 2025), Cochrane Clinical Answers (January 2025), Cochrane Central Register of Controlled Trials (December 2024), Embase (1974 to 2025 Week 05), Medline and Epub Ahead of Print, Medline In-Process, In-Data-Review & Other Non-Indexed Citations, Medline Daily and Medline (1946 to February 03, 2025), Joanna Briggs Institute Evidence-Based Practice Database (Current to January 29, 2024), that are available through the Ovid platform.
- A combination of keywords, as proposed by the Canada's Drug Agency (formerly Canadian Agency for Drugs and Technology in Health) in 2021 to search for COVID-19 studies (<https://www.cda-amc.ca/literature-searching-tools/covid-19-search-strings#covid-19-medline>), were employed in this systematic review. These keywords included:
 - (COVID-19 **OR** (COVID-19 Testing) **OR** (COVID-19 Vaccines) **OR** SARS-CoV-2)
 - ((coronavirus **OR** betacoronavirus **OR** (coronavirus infections)) **AND** ((disease outbreaks) **OR** epidemics **OR** pandemics))
 - (nCoV* **OR** 2019nCoV **OR** 19nCoV **OR** COVID19* **OR** COVID **OR** SARS-COV-2 **OR** SARSCOV-2 **OR** SARS-COV2 **OR** SARSCOV2 **OR** (SARS coronavirus 2) **OR** (Severe Acute Respiratory Syndrome Coronavirus 2) **OR** (Severe Acute Respiratory Syndrome Corona Virus 2))
 - ((new **OR** novel **OR** 19 **OR** 2019 **OR** Wuhan **OR** Hubei **OR** China **OR** Chinese) **ADJ3** (coronavirus* **OR** (corona virus*) **OR** betacoronavirus* **OR** CoV **OR** HCoV))
 - ((coronavirus* **OR** corona virus* **OR** betacoronavirus*) **ADJ3** (pandemic* **OR** epidemic* **OR** outbreak* **OR** crisis))
 - ((Wuhan **OR** Hubei) **ADJ** pneumonia)
 - ((long COVID*) **OR** (post COVID*) **OR** (post coronavirus*) **OR** (post SARS*) **OR** (long-COVID*) **OR** (post-COVID*) **OR** post-coronavirus* **OR** post-SARS*)
 - 1 **OR** 2 **OR** 3 **OR** 4 **OR** 5 **OR** 6 **OR** 7
 - limit 8 to yr="2019 -Current"
 - (ketamine **ADJ** infusion*) **OR** (ketamine **ADJ** injection*) **OR** (intravenous **ADJ** ketamine) **OR** (intra **ADJ** venous **ADJ** ketamine)
 - #9 **AND** #10
- No limitations, such as on the language of publication, were implemented in this literature search.
- A manual search on the references of the articles that were retrieved in full was also conducted.

Results

- Search results:
 - Twenty-nine¹⁻²⁹ published studies were identified from search #11. Upon examination on the titles and abstracts of these twenty-nine¹⁻²⁹ studies, ten^{3,6,7,12,13,14,22,23,28,29} studies were retrieved in full for further appraisal.

- No further study was identified from the manual searches conducted on the references of these ten^{3,6,7,12,13,14,22,23,28,29} studies that were retrieved in full.
- Of the ten^{3,6,7,12,13,14,22,23,28,29} studies that were retrieved in full, nine^{3,6,7,12,13,14,22, 28,29} studies were not relevant or did not provide relevant data to the objective of this systematic review and will not be discussed further.
- A case report (level of evidence 4. Appendix 1) on a post-Covid 19 patient with refractory fatigue that was treated with ketamine infusion was reported by Remick et al²³. A 50-year-old man, who was diagnosed with COVID-19 infection 6 months prior, presented for evaluation for post-Covid 19 fatigue symptoms for over 5 months. The patient reported generalized fatigue that was refractory to care and treatment. He was tired all day, with malaise limiting any physical activity and reported the worsening of his fatigue with physical or mental effort. The patient also had constant headaches and had undergone a stellate ganglion block with successful improvement but no change to the fatigue symptoms. The patient received ketamine infusion (sub-dissociative dosing of 0.25 mg/kg over 40 minutes) and reported approximately 30% improvement in fatigue at the 2-week follow-up (it is not clear how fatigue was assessed). He then 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 reported approximately 75% improvement of his fatigue. It should be noted that it was not clear how this patient was selected for the report and it was not clear the effect of cointervention, if any, in this patient.
- It should be noted that Mallet¹², Mallet et al¹³ and Wendel-Garcia et al²⁸ reported cases of cholestatic liver injury due to ketamine infusion in ventilated patients with Covid-19.

Summary

- At present, there is a case report (level of evidence 4. Appendix 1) on the effectiveness of IV ketamine in treating post-Covid-19 fatigue. There are also reports on cholestatic liver injury due to ketamine infusion in ventilated patients with Covid-19.

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Appendix 1

WorkSafeBC — Evidence-Based Practice Group levels of evidence (adapted from 1-6)

1	Experimental, randomized controlled trial (RCT), systematic review RCTs with or without meta-analysis.
2	Evidence from controlled trials without randomization (quasi-experimental studies) or systematic reviews of observational studies.
3	Evidence from cohort or case-control analytic studies, preferably from more than 1 centre or research group.
4	Evidence from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled experiments.
5	Opinions of respected authorities, based on clinical experience, descriptive studies or reports of expert committees based on scientific evidence.

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