

Efficacy of IV Ketamine in Refractory/Super-Refractory Status Epilepticus

A Systematic Review and Meta-Analysis

Abhijit Vijay Lele,¹ Alex Raquer,² Jorge Mejia-Mantilla,³ Samuel Ern Hung Tsan,⁴ Gentle Sunder Shrestha,^{5,6} Victor Lin,⁷ Samuel Neal Blacker,⁸ Sean Marinelli,⁷ Peter Chee Seong Tan,⁹ Sarah Wahlster,¹⁰ and Andres Gempeler³

Correspondence
Dr. Lele
abhijit2@uw.edu

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Abstract

Background and Objectives

Intravenous ketamine is increasingly used for refractory and super-refractory status epilepticus (RSE/SRSE), yet its efficacy and optimal use remain uncertain. We therefore aimed to synthesize the available evidence to quantify the effectiveness of ketamine in achieving seizure cessation and to explore differences in treatment characteristics between patients who respond and those who do not.

Methods

We conducted a systematic review and meta-analysis to estimate the pooled seizure cessation rate associated with intravenous ketamine. Secondary analyses compared ketamine initiation timing, dosing, and infusion duration between patients who achieved seizure cessation (responders) and those who did not (nonresponders).

Results

Fourteen studies comprising 388 adult patients (249 responders, 139 nonresponders) were included. The pooled seizure cessation rate with ketamine was 64% (95% CI 49%–76%) with moderate heterogeneity ($I^2 = 54.1\%$). Sensitivity analysis showed no single study substantially influenced results, supporting robustness. Responders received ketamine earlier (3.2 ± 2.6 days) than nonresponders (4.3 ± 2.6 days), mean difference of -0.90 days (95% CI: -1.31 to -0.49 ; $p < 0.0001$). The mean maintenance dose was 2.5 ± 1.4 mg/kg/hr (responders: 2.5 ± 1.3 ; nonresponders: 2.6 ± 1.4), with no significant difference between groups (mean difference -0.14 mg/kg/hr; 95% CI -0.45 to 0.18 ; $p = 0.39$). Infusion duration averaged 5.0 ± 4.2 days in both groups, with no significant difference (mean difference -0.07 days; 95% CI -1.02 to 0.88 ; $p = 0.88$). Ketamine discontinuation due to adverse events was rare (0.7%, 3/55 patients).

Discussion

Intravenous ketamine demonstrates consistent effectiveness and safety as an adjunctive therapy in RSE/SRSE. However, the timing of initiation cannot be reliably linked to improved clinical outcomes given current methodological limitations and heterogeneity across studies. Future prospective research using standardized definitions and rigorous temporal data collection is needed to clarify whether the timing of ketamine initiation independently influences therapeutic success and to define its optimal integration within established status epilepticus (SE) treatment algorithms.

Registration

The systematic review was registered (June 7, 2024) with the International Prospective Register of Systematic Reviews (PROSPERO, CRD42024549523).

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Supplementary Material

¹Departments of Anesthesiology, Neurology, and Neurological Surgery, University of Washington, Harborview Medical Center, Seattle; ²Washington State University, Elson S. Floyd College of Medicine, Spokane; ³Department of Critical Care Medicine, Fundación Valle del Lili, Cali, Colombia; ⁴Department of Anaesthesiology and Critical Care, Faculty of Medicine and Health Sciences, University of Malaysia Sarawak, Malaysia; ⁵Department of Critical Care Medicine, Tribhuvan University Teaching Hospital, Kathmandu, Nepal; ⁶Australian and New Zealand Intensive Care Research Centre (ANZIC-RC), School of Public Health and Preventive Medicine, Monash University, Melbourne, VC; ⁷Department of Neurology, University of Washington, Harborview Medical Center, Seattle; ⁸Department of Anesthesiology, University of North Carolina, Chapel Hill, NC; ⁹Sarawak General Hospital, Malaysia; and ¹⁰Departments of Neurology, Anesthesiology, and Neurological Surgery, University of Washington, Harborview Medical Center, Seattle.