# INPLASY PROTOCOL

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# The efficacy and safety of ketamine in treating refractory and super-refractory status epilepticus in pediatric and adult populations, A systemic review

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**Review question / Objective:** This study is to assess the efficacy and safety of ketamine in treating refractory and super-refractory status epilepticus in pediatric and adult populations.

Rationale: Refractory status epilepticus (RSE) is either generalized or complex partial status epilepticus (SE) that fails to respond to first and second-line therapies. Super refractory status epilepticus (SRSE) is SE that remains unresponsive despite 24 hours of therapy with general anesthesia [1, 2]. Both RSE and SRSE pose significant challenges for the managing intensivist. There exists a race against time for control of epileptic activity in the RSE/SRSE patient to preserve cortical function and reduce morbidity/ mortality. However, despite the best intentions, and not uncommonly, standard frontline antiepileptic drugs (AEDs) fail to control or reduce seizure activity once seizures approach the 30-minute mark. The following review provides an analysis of ketamine in treating RSE/SRSE, focusing on the potential target population, dosing, concerns, and the role of early administration.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 03 November 2022 and was last updated on 03 November 2022 (registration number INPLASY2022110011).

## INTRODUCTION

Review question / Objective: This study is to assess the efficacy and safety of ketamine in treating refractory and superrefractory status epilepticus in pediatric and adult populations. **Rationale:** Refractory status epilepticus (RSE) is either generalized or complex partial status epilepticus (SE) that fails to respond to first and second-line therapies. Super refractory status epilepticus (SRSE) is SE that remains unresponsive despite 24 hours of therapy with general anesthesia [1, 2]. Both RSE and SRSE pose significant

challenges for the managing intensivist. There exists a race against time for control of epileptic activity in the RSE/SRSE patient to preserve cortical function and reduce morbidity/mortality. However, despite the best intentions, and not uncommonly, standard frontline antiepileptic drugs (AEDs) fail to control or reduce seizure activity once seizures approach the 30-minute mark. The following review provides an analysis of ketamine in treating RSE/SRSE, focusing on the potential target population, dosing, concerns, and the role of early administration.

**Condition being studied:** Refractory and Superrefractory Status Epilepticus.

### **METHODS**

Search strategy: We conducted a systematic review and reported it according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist. We performed a MEDLINE literature search using PubMed to identify all articles published as of April 2022 with the following research details: "ketamine" [MeSH Terms] OR "ketamine" [All Fields]) AND ("status epilepticus" [MeSH Terms] OR ("Refractory status epilepticus" [All Fields] AND "epilepticus" [All Fields]) OR "Refractory Status Epilepticus" [All Fields]. We also searched the Cochrane Database for related systematic reviews and the ClinicalTrials.gov website for ongoing clinical studies on RSE.

Participant or population: Adult and Pediatric patients.

Intervention: Ketamine.

**Comparator:** With or without other agents.

Study designs to be included: All type of studies.

Eligibility criteria: KE efficacy and safety as primary outcome in SE, both in the paediatric and adult populations; only studies published in English. Information sources: Pubmed , Embase , Cochrane , ClinicalTrials.gov and google scholar.

Main outcome(s): Efficacy and safety of KE in Refractory and Superrefractory Status Epilepticus ,RSE and SRE.

Quality assessment / Risk of bias analysis: 1- case reports and case series will be assessed according to the CARE; 2- (STROBE) for cohort studies.

Strategy of data synthesis: i. Provide a general summary of the characteristics and findings of the included studies.

ii. Analyze the relationships between studies, exploring patterns and investigating heterogeneity.

iii. Discuss the applicability of the body of evidence to the review's question within the PICO structure.

iv. Explain the meta-analysis (if one is conducted) and interpret and analyze the robustness of its results.

v. Critique the strengths and weaknesses of the body of evidence as a whole, including a cumulative assessment of the risk of bias across studies.

vi. Discuss any gaps in the evidence, such as patient populations that have been inadequately studied or for whom results differ.

vii. Compare the review's findings with current conventional wisdom when appropriate.

Subgroup analysis: No.

Sensitivity analysis: Reporting of sensitivity analyses in a systematic review was done by producing a summary table.

Country(ies) involved: Saudi Arabia.

Keywords: ketamine, status epilepticus, seizures, efficacy, safety.

Contributions of each author:

Author 1 - Asaad Suliman Shujaa. Author 2 - Qasem Almulihi.