

Implications of Perioperative Intravenous Esketamine Administration on Perioperative Neurocognitive Disorders in Patients: A Meta-Analysis of Randomized Controlled Trials

INPLASY202510088

doi: 10.37766/inplasy2025.1.0088

Received: 21 January 2025

Published: 21 January 2025

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ADMINISTRATIVE INFORMATION**Support** - National Natural Science Foundation of China (NSFC:82160224).**Review Stage at time of this submission** - Formal screening of search results against eligibility criteria.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY202510088**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 21 January 2025 and was last updated on 21 January 2025.**INTRODUCTION**

Review question / Objective The purpose of this meta-analysis is to investigate the effects of esketamine on perioperative neurocognitive disorders in patients with general anesthesia in randomized controlled trials. P: Patients with general anesthesia. I: Perioperative intravenous esketamine. C: Esketamine was not used in the perioperative period. O: The incidence or occurrence of PND. S: Randomized controlled trials.

Condition being studied Cognitive impairment is frequently observed in patients after surgery and anesthesia, mainly characterized by impairments in memory, attention, orientation ability, thinking, information processing. The Consensus on Perioperative Cognitive Disorders (2018) recommends that cognitive changes associated with anesthesia and surgery be named

perioperative neurocognitive disorders (PND). Studies have shown that the incidence of PND ranges from 17% to 43%, which can be seriously detrimental to recovery, increase healthcare expenditures, reduce the quality of life, and even increase the postoperative mortality of patients. However, effective pharmacotherapies to prevent or reduce PND are not currently available.

Esketamine is the S-enantiomer of ketamine and has the advantage of reducing postoperative sleep disturbances and perioperative pain. Animal studies have shown that esketamine can effectively reduce perioperative neurocognitive disorders. However, The application of esketamine in general anesthesia is still in its initial stage and its effectiveness in reducing the incidence of PND remains controversial. Therefore, the availability of intraoperative esketamine usage for relieving PND need more study.

To date, the related perioperative clinical study of esketamine is limited, and the effect of esketamine

on PND unclear. Therefore, we conducted this study to investigate the effects of esketamine on perioperative neurocognitive disorders in patients with general anesthesia in randomized controlled trials.

METHODS

Search strategy We systematically searched the databases of PubMed, Embase, Cochrane and Web of Science for all relevant studies from inception to January 10, 2025. Search strategies will include free text and search strings related to the three groups of following core concepts: The first group will encompass keywords related to perioperative neurocognitive disorders. The second group will include esketamine, Boolean operators used to combine the search terms will include. The third group will include randomized controlled trial. (1) keywords within one group were combined using the OR operator; and (2) keywords across different groups were linked using the AND operator. The articles meeting inclusion criteria will be searched from inception to January 10, 2025.

Participant or population Patients with general anesthesia.

Intervention Perioperative intravenous esketamine.

Comparator Esketamine was not used in the perioperative period.

Study designs to be included Randomized controlled trials.

Eligibility criteria 1.The inclusion criteria were: (1) studies examining the association between esketamine vs. control and perioperative neurocognitive disorders under general anesthesia; (2) studies must be a randomized controlled trial. (3) articles are journal articles. (4)articles were available in English only.
2.The exclusion criteria were: (1) Participants < 18 years old; (2) The study is not general anesthesia; (3) the full text was not available; (4) involving participants with a history of psychiatric disorders, substance abuse, or contraindications to esketamine administration.

Information sources PubMed, Embase, Cochrane and Web of Science.

Main outcome(s) The incidence or occurrence of PND.

Data management EndNote.

Quality assessment / Risk of bias analysis

Cochrane risk bias assessment tool and Jadad scale.

Strategy of data synthesis We plan to conduct a meta-analysis using RevMan 5.4 and StataMP 15 software. A random-effects model will be employed to calculate the Odds Ratio. Heterogeneity among the included studies will be evaluated using the I^2 statistic. We will consider an I^2 value greater than 50% as substantial heterogeneity. In addition, we will perform subgroup analyses based on according to the assessed PND time and age. Sensitivity analysis will also be performed to assess the robustness of the meta-analysis results. A funnel plot and Egger's test will be used to evaluate the potential publication bias.

Subgroup analysis The assessed PND time and age.

Sensitivity analysis We will exclude studies with a high risk of bias due to in adequate randomization or allocation concealment and incomplete data. Furthermore, we will conduct sensitivity analyses, after deleting any of the studies, the combined results of the remaining literatures were not different from those without deletion, which means that the sensitivity analysis was passed.A funnel plot and Egger's test.

Language restriction English.

Country(ies) involved China.

Keywords Perioperative neurocognitive disorders, Esketamine, Cognitive impairment.

Contributions of each author

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