INPLASY PROTOCOL

To cite: Huang et al. Implications of Perioperative Intravenous Esketamine Administration on Postpartum Depression in Cesarean Section Patients: A Comprehensive Systematic Review and Meta-Analysis. Inplasy protocol 202350024. doi: 10.37766/inplasy2023.5.0024

Received: 05 May 2023

Published: 05 May 2023

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Support: **None.**

Review Stage at time of this submission: **The review has not yet started.**

Conflicts of interest:
None declared.

Implications of Perioperative Intravenous Esketamine Administration on Postpartum Depression in Cesarean Section Patients: A Comprehensive Systematic Review and Meta-Analysis

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Review question / Objective: **The purpose of this systematic review and meta-analysis is to evaluate the efficacy and safety of perioperative intravenous esketamine administration in mitigating postpartum depression (PPD) among patients who underwent cesarean section.**
Information sources: **Searches will be conducted in electronic databases, including PubMed, Embase, Cochrane Library, Web of Science, Google Scholar, CNKI, Wanfang, and other relevant databases, without any restrictions on the country of publication. Reference lists of all selected articles will be independently screened to identify additional studies that may have been missed in the initial search.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 05 May 2023 and was last updated on 05 May 2023 (registration number INPLASY202350024).

INTRODUCTION

Review question / Objective: **The purpose of this systematic review and meta-analysis is to evaluate the efficacy and safety of perioperative intravenous esketamine administration in mitigating postpartum depression (PPD) among patients who underwent cesarean section.**

Condition being studied: **Postpartum depression (PPD) is a prevalent mental health condition that affects a significant proportion of women following childbirth, with potential long-term consequences for**

both the mother and the child. PPD not only impairs maternal-infant bonding but also increases the risk of cognitive, emotional, and behavioral difficulties in the child. Identifying effective interventions for the prevention and treatment of PPD is crucial to improving maternal and child health outcomes.

Cesarean section, as a major surgical procedure, has been associated with an increased risk of PPD, possibly due to factors such as pain, surgical complications, and a delayed recovery process. Therefore, it is essential to explore strategies that may reduce the risk of PPD in women undergoing cesarean section. Recent studies have suggested that perioperative intravenous esketamine administration may have a beneficial effect on PPD incidence among cesarean section patients.

Esketamine, an N-methyl-D-aspartate (NMDA) receptor antagonist, has been increasingly recognized for its rapid-acting antidepressant effects. It has been demonstrated to exert its therapeutic action through various mechanisms, including enhancing neuroplasticity, modulating the hypothalamic-pituitary-adrenal (HPA) axis, and reducing inflammation. However, the efficacy and safety of perioperative intravenous esketamine administration in cesarean section patients remain inconclusive, necessitating further research and a systematic review.

METHODS

Participant or population: Adult women (≥18 years) undergoing cesarean section, without any other psychiatric disorders or substance abuse history.

Intervention: Perioperative intravenous esketamine administration, either as a single agent or as part of a multimodal analgesic regimen.

Comparator: Placebo, no treatment, or standard analgesic regimen without esketamine.

Study designs to be included: Only randomized controlled trials (RCTs) examining the efficacy and safety of perioperative intravenous esketamine administration in reducing postpartum depression (PPD) among patients undergoing cesarean section will be included.

Eligibility criteria: Studies presenting insufficient data, unclear methodology, or involving participants with a history of psychiatric disorders, substance abuse, or contraindications to esketamine administration will be excluded. Moreover, case reports, case series, narrative reviews, commentaries, letters to the editor, editorials, animal studies, in vitro studies, and duplicate publications or studies with overlapping data will be excluded.

Information sources: Searches will be conducted in electronic databases, including PubMed, Embase, Cochrane Library, Web of Science, Google Scholar, CNKI, Wanfang, and other relevant databases, without any restrictions on the country of publication. Reference lists of all selected articles will be independently screened to identify additional studies that may have been missed in the initial search.

Main outcome(s): Main outcomes should include the incidence of postpartum depression, as assessed by a validated diagnostic tool (e.g., Edinburgh Postnatal Depression Scale or Postpartum Depression Screening Scale).

Additional outcome(s): Additional outcomes may include postoperative pain scores, analgesic consumption, and adverse events related to esketamine administration.

Quality assessment / Risk of bias analysis: Following the guidelines of version 5.1.0 of the Cochrane Handbook for Systematic Reviews of Interventions, the methodological quality of each study will be independently assessed by two authors. The main indicators evaluated include randomization, allocation concealment,

blinding, completeness of data, selective reporting, and other biases. In the case of any disagreement between the two authors, a third party will make the final judgment.

Strategy of data synthesis: We plan to conduct a meta-analysis using RevMan 5.4 software. A random-effects model will be employed to calculate the pooled risk ratios (RRs) and their corresponding 95% confidence intervals (CIs). The inverse variance method will be used to calculate the weighted mean differences (WMDs) and their corresponding 95% CIs. 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 dose, timing of esketamine administration, different postpartum depression (PPD) diagnostic methods and criteria, and patient characteristics. 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. If necessary, a meta-regression analysis will be conducted to explore the potential sources of heterogeneity. Finally, the quality of evidence will be evaluated using the GRADE approach.

Subgroup analysis: We plan to conduct subgroup analyses based on the dose of esketamine administered, timing of administration, various postpartum depression (PPD) diagnostic methods and criteria, and patient characteristics.

Sensitivity analysis: We intend to perform sensitivity analyses to investigate the robustness of the meta-analysis results. Specifically, we will exclude studies with a high risk of bias due to inadequate randomization or allocation concealment and incomplete data. Furthermore, we will conduct sensitivity analyses by iteratively excluding each study and re-analyzing the remaining studies to assess the impact of individual studies on the overall results.

Language restriction: None.

Country(ies) involved: China.

Keywords: Cesarean section; Esketamine; Intravenous administration; Postpartum depression.

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