INPLASY PROTOCOL

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Comparison of dexmedetomidine versus propofol in mechanically ventilated patients with sepsis: A meta-analysis of randomized controlled trials

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Review question / Objective: The aim of the present study was to evaluate the effects of dexmedetomidine compared with propofol in mechanically ventilated patients with sepsis. Condition being studied: Sepsis, which is defined as lifethreatening organ dysfunction caused by a dysregulated host response to infection, contributes the highest mortality to intensive care units (ICU) worldwide. Because of the high incidence of respiratory failure in sepsis care, mechanical ventilation is always adopted to give life support and minimize lung injury . And sedation is a necessary component of sepsis care who suffers from mechanical ventilation. The Society of Critical Care Medicine suggested using either propofol or dexmedetomidine for sedation in mechanically ventilated adults. However, it remained unknown whether patients with sepsis requiring mechanical ventilation will benefit from sedation with dexmedetomidine.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 17 April 2022 and was last updated on 17 April 2022 (registration number INPLASY202240103).

INTRODUCTION

Review question / Objective: The aim of the present study was to evaluate the effects of dexmedetomidine compared with propofol in mechanically ventilated patients with sepsis.

Condition being studied: Sepsis, which is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection, contributes the highest mortality to intensive care units (ICU) worldwide. Because of the high incidence of respiratory failure in sepsis care, mechanical ventilation is always adopted to give life support and minimize

lung injury. And sedation is a necessary component of sepsis care who suffers from mechanical ventilation. The Society of Critical Care Medicine suggested using either propofol or dexmedetomidine for sedation in mechanically ventilated adults. However, it remained unknown whether patients with sepsis requiring mechanical ventilation will benefit from sedation with dexmedetomidine.

METHODS

Search strategy: We systematically searched EMBASE, PubMed (MEDLINE), Cochrane Library from inception to December 2021.No language restrictions were imposed. We used the following combined text and Mesh terms: "sepsis" and "dexmedetomidine" in PubMed. The complete search strategies were shown in Supplemental file.1. In addition, Clinical.gov was searched for ongoing studies and unpublished data. A hand search through relevant conference papers and reference lists of relevant articles or reviews was also performed for completeness.

Participant or population: All patients were diagnosed as sepsis and required mechanical ventilation.

Intervention: Dexmedetomidine with or without other sedatives, irrespective of dose and duration.

Comparator: Proposol without dexmedetomidine, irrespective of dose and duration.

Study designs to be included: Randomized controlled trials (RCTs).

Eligibility criteria: Inclusion criteria: (1) Study design: Randomized controlled trials (RCTs). (2) Participants: All patients were diagnosed as sepsis and required mechanical ventilation. (3) Intervention: dexmedetomidine with or without other sedatives, irrespective of dose and duration. (4) Comparison: propofol without dexmedetomidine, irrespective of dose and duration. (5) Outcomes: the primary outcome: 28/30-day mortality.the

secondary outcomes: ventilator-free days and the length of ICU stay. Exclusion criteria: pediatrics, duplicated data, reviews, commentaries, meeting abstract, meta-analyses, animal and cell experiments, no clear diagnosis of sepsis.

Information sources: We systematically searched EMBASE, PubMed (MEDLINE), Cochrane Library from inception to December 2021.No language restrictions were imposed. We used the following combined text and Mesh terms: "sepsis" and "dexmedetomidine" in PubMed. The complete search strategies were shown in Supplemental file.1. In addition, Clinical.gov was searched for ongoing studies and unpublished data. A hand search through relevant conference papers and reference lists of relevant articles or reviews was also performed for completeness.

Main outcome(s): 28/30-Day Mortality.

Additional outcome(s): Ventilator-free days; Length of ICU Stay.

Quality assessment / Risk of bias analysis:

The Cochrane Collaboration's tool[12] was used to assess the qualities of included studies by two authors assessed the qualities of all eligible studies in Review Manager 5.3 (Cochrane Collaboration, Oxford, UK), which contains seven aspects: allocation concealment, random sequence generation, blinding of outcome assessment, blinding of participants and personnel, selective reporting, incomplete outcome data, and other bias. Each item was assessed as high risk, uncertain risk, or low risk.

Strategy of data synthesis: We assessed the effect of dexmedetomidine on three outcomes:28/30-day mortality, ventilator-free days, and the length of ICU stay. The statistical data analyses were performed by the software Review Manager 5.3. Since that some studies[10,13–16] described the data by median and interquartile range, we asked first and corresponding authors for raw data by email but failed, so we adopted the suggestions of Luo et al. and Wan et al. to estimate the mean values and standard

deviation. Pooled risk ratio (RR) along with 95% confidence intervals (CI) were used to express the primary outcome, 28/30-day mortality, while for secondary outcomes including ventilator-free days and the length of ICU stay, mean difference (MD) with 95% CI were calculated. The heterogeneity was evaluated using the Chisquare test and Higgins I2 test[19]; the fixed-effect model was used when I2 \leq 50% and P \geq 0.10; otherwise, we applied the random effect model to describe the heterogeneity.

Subgroup analysis: No.

Sensitivity analysis: The sensitivity analysis was involved to omit one study and assess whether the other results were substantially affected. We designed the sensitivity analysis of 28/30-day mortality to test the robustness of the primary outcome by STATA 15.0(Stata Corp, College Station, TX).

Language: English.

Country(ies) involved: China.

Keywords: dexmedetomidine, propofol, sepsis, sedation, mechanical ventilation.

Contributions of each author:

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