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Inhaled nitric oxide and postoperative outcomes during cardiopulmonary bypass: a systematic review and meta-analysis

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ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - Preliminary searches.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 07 November 2023 and was last updated on 07 November 2023.

INTRODUCTION

Review question / Objective The effect of nitric oxide inhalation on postoperative outcomes during cardiopulmonary bypass assisted cardiac surgery.

Condition being studied As a major part of cardiac surgery, cardiopulmonary bypass (CPB) is associated with systemic inflammatory reactions, myocardial ischemia, and ischemia and reperfusion damage. Nitric oxide (NO) can exert anti-inflammatory effect by regulating endothelial function and microvascular inflammation. The benefit of NO on myocardial damage in during cardiopulmonary bypass has been demonstrated. However, the effect of NO inhalation on the postoperative recovery and outcomes was not well demonstrated. In addition, the concentration and duration for NO inhalation varies in different studies. Therefore, we conducted a systematic review and meta-analysis to explore the effect of NO inhalation on postoperative outcomes in cardiac surgical patients and will further explore the optimal NO inhalation that will lead to the most beneficial effect for these patient populations.

METHODS

Search strategy We searched the following electronic medical databases: Embase, PubMed, Web of Science, and Cochrane Library from inception to November 2023 in English language. The search query was as follow:("Cardiopulmonary Bypass" OR “Heart-Lung Bypass” OR “valve surgery” OR “cardiac surgery”) AND ("Nitric Oxide”) AND ("randomized controlled trial”).

Participant or population Patients undergoing cardiac surgery with cardiopulmonary bypass.

Intervention Inhaled NO.

Comparator Placebo or no therapy or standard care or other vasodilator.

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Study designs to be included Randomized controlled trial.

Eligibility criteria The inclusion criteria and exclusion criteria for this study were as follows: 1) randomized controlled trial (RCTs). 2) Inhaled NO was delivered during cardiac surgery with specific NO dosage or length of usage. 3) The control group is standard care or placebo or no therapy or other vasodilator. 5) Interest outcomes included hemodynamic index, the duration of postoperative mechanical ventilation, length of intensive care unit (ICU) stay, length of hospital stay or mortality and so on. 6) Case reports, retrospective studies, reviews, letters, comments, and editorials were excluded. 7) The publication language of the included studies was restricted to English.

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Main outcome(s) Postoperative outcomes: hemodynamic improvement (cardiac output, pulmonary arterial pressure, pulmonary resistence, etc), length of postoperative mechanical ventilation, length of intensive care unit (ICU) stay, length of hospital stay, mortality, the incidence of acute kidney injury, the incidence of major adverse cardiac events, and so on.

Data management Data extraction from each study was performed by two authors independently. Patients' basic characteristics, sample size, age, sex, CPB transit time, dosage and length of usage of NO, and outcome data were exacted from each study using a predesigned data extraction form. For the missing information, we tried to contact the authors of original articles. During the process of data extraction, any disagreement was resolved by discussion.

Quality assessment / Risk of bias analysis The study quality assessment /risk of bias analysis was conducted by two reviewers independently. Study quality was assessed by Cochrane risk-of-bias instrument, which encompasses the aspect of random sequence generation and allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting and other bias.

Strategy of data synthesis We used random-effects models to calculate risk ratios with 95 % confidence intervals in the pooled analyses. The continuous outcomes and the binary outcomes were separately reported as mean difference and risk ratios (RRs). Heterogeneity was assessed with the I-squared index. Publication bias was assessed via funnel plot. Statistical significance was at the two-tailed 0.05 level. Meta-regression for the relationship between the dosage of Inhaled nitric oxide and postoperative outcomes during cardiopulmonary bypass was performed.

Subgroup analysis Pediatric patients and adult cardiac surgical patients, dosage of NO, duration of NO inhalation, different comparators.

Sensitivity analysis We will omit each study that is included in the meta-analysis one by one if there are sufficient studies. Trial sequential analysis, Meta-regression, or Net-work meta-analyses will be used as appropriate.

Language restriction English.

Country(ies) involved China, Russia, and USA.

Keywords Inhaled nitric oxide, Postoperative outcomes, Cardiopulmonary bypass, cardaic surgery.

Contributions of each author

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