INPLASY

Comparison of norepinephrine versus phenylephrine to prevent hypotension after spinal anesthesia for cesarean section: systematic review and meta-analysis

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ADMINISTRATIVE INFORMATION

Support - None.

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

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202380048

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 11 August 2023 and was last updated on 11 August 2023.

INTRODUCTION

Review question / Objective Is norepinephrine is safe for the fetus in terms of pH and base excess of umbilical artery and vein than phenylephrine in parturients undergoing cesarean section under spinal aneshesia?

Rationale n the past, ephedrine was the drug of choice because it maintains uterine blood flow due to its adrenergic beta-effect. However, after reports that ephedrine caused acid-base imbalance in the fetus, it has been replaced by phenylephrine nowadays.
However, phenylephrine reduces maternal cardiac output by causing bradycardia and increasing systemic vascular resistance. Thus, glycopyrrolate is recommended as a treatment for phenylephrine induced bradycardia, but the effect is temporary and ineffective. To overcome these problems, norepinephrine is being tried as a new alternative, but safety for the fetus has not been secured, so several clinical studies comparing norepinephrine with phenylephrine are being actively conducted.

Condition being studied Parturients undergoing cesarean section under spinal anesthesia.

METHODS

Search strategy Literature searches will be conducted in ovid-Medline, ovid-EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL) databasesCochrane Library, and Google Scholar at August 2023.

Participant or population Parturients undergoing cesarean section under spinal anesthesia.

Intervention Intravenous(IV) infusion of norepinephrine.

Comparator Intravenous(IV) infusion of phenylephrine.

Study designs to be included Inclusion criteria: Randomized controlled trial. Exclusion criteria: observational study, conference abstracts, posters, case reports, case series, comments or letters to the editor, reviews, and laboratory or animal studies.

Eligibility criteria Not any other inclusion or exclusion criteria not defined in the PICOS.

Information sources Ovid-Medline, ovid-EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL) databases and Google Scholar.

Main outcome(s) The umbilical artery (UA) or umbilical vein (UV) pH as neonatal condition at birthpH and base excess(BE) of umbilical artery and vein.

Additional outcome(s) Umbilical artery (UA) or umbilical vein (UV) base excess (BE) None.

Data management Two independent investigators will extract all interrelated data from the included studies and entered into a standardized form, and then will cross-check. Any discrepancy will be resolved through discussion. If an agreement can not be reached, the dispute will be resolved with the aid of a third investigator. Dataextracted will be as follows; (1) title, (2) name of first author, (3) name of journal, (4) year of publication, (5) study design, (6) registration of clinical trial, (7) competing interest, (8) country, (9) risk of bias, (10) inclusion criteria, (11) exclusion criteria, (12) age, (13) number of parturient (14) twins or not (15) primary outcome, and secondary outcomes. The primary outcome of this study was the umbilical artery (UA) or umbilical vein (UV) pH as neonatal condition at birth, and secondary outcome was umbilical artery (UA) or umbilical vein (UV) base excess (BE) as additional prognostic value over measurement of umbilical pH.
We will initially extract data from tables or text. In cases involving missing or incomplete data, we will try to contact the study authors to obtain the relevant information.

Quality assessment / Risk of bias analysis Two independent investigators will assessed the risk of bias of included studies using the Revised Cochrane risk of bias tool for randomized trials (RoB 2.0) version. RoB 2.0 consists of five domains: Bias arising from the randomization process; Bias due to deviations from the intended interventions; Bias due to missing outcome data; Bias in measurement of the outcome; Bias in selection of the reported result. Judgement of each domain lead to judgment of the overall risk of bias, which enables us to evaluate the overall risk of bias. Each domain and overall risk of bias were graded as low risk of bias, some concerns, and high risk of bias.

Strategy of data synthesis Meta-analysis will be conducted using meta package in the R software. Two investigators will independently input all data into the software. The weighted mean difference (MD) and their 95% confidence intervals (CIs) will be calculated for each outcome. A random-effects model will be used to account for clinical or methodological heterogeneity in the study. Statistical heterogeneity will be assessed using an I2 test, with I2 >50% indicating significant heterogeneity.
Meta-regression will be used to identify covariates (outcome (artery vs vein), administration method (bolus, infusion, both bolus and infusion), twin or not, and number of parturients) that could influence the estimates (umbilical artery (UA) or umbilical vein (UV) pH umbilical artery (UA) or umbilical vein (UV) base excess (BE)).
Publication bias will be assessed by Begg's funnel plot, Egger's linear regression test and Begg & Mazumdar Rank correlation test. If Begg's funnel plot were visually assessed for asymmetry, or a P value < 0.05 for Egger's linear regression test and Begg & Mazumdar Rank correlation test, publication bias was suspected.
Quality of the evidence**.**

Subgroup analysis Umbilical artery and vein.

Sensitivity analysis Not planned.

Language restriction We will not apply restriction on language.

Country(ies) involved Korea.

Other relevant information None

Keywords Anesthesia, Spinal; Cesarean Section; Meta-Analysis; Norepinephrine; Phenylephrine; Hypotension; Vasoconstrictor Agents.

Dissemination plans Peer reviewed journal.

Contributions of each author

Author 1 - Young Seok Jee - Jee YS will search literature, select literature, extract data, assess risk of bias and draft manuscript.
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Author 2 - Hyun Kang - Hyun Kang will search literature, select literature, extract data, assess risk of bias, analyze data and draft manuscript.
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