Therapeutic Vasopressor Use for Postspinal Hypotension in Low-Risk Planned Cesarean Deliveries: A Systematic Review, Network Meta-Analysis, and Trial Sequential Analysis

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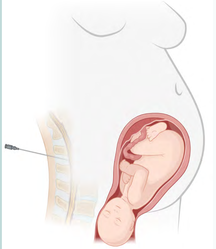
Background



Spinal anesthesia is the preferred technique for elective cesarean delivery yet postspinal hypotension remains a frequent and clinically relevant complication. Maternal hypotension can result in nausea, vomiting, dizziness, and compromised uteroplacental perfusion, potentially affecting neonatal acid–base status. Phenylephrine and ephedrine have traditionally been used to treat hypotension, but concerns regarding reflex bradycardia (phenylephrine) and fetal acidosis (ephedrine) have prompted increasing interest in norepinephrine.

Objectives

To compare the efficacy and safety of norepinephrine (NE), phenylephrine (PE), and ephedrine (EP) for the *treatment (not prophylaxis)* of PSH in low-risk women undergoing elective cesarean delivery (CD) under spinal anesthesia (SA).

Study Design

A systematic review & network meta-analysis (NMA) was conducted using PRISMA-2020 & PRISMA-NMA guidelines. RCTs enrolling low-risk parturients who developed hypotension *after* SA & received NE, PE or EP as *treatment* were included. Searches were performed across major databases up to 6/2025; the protocol was registered in PROSPERO CRD-420251074831. A frequentist NMA synthesized direct & indirect comparisons; treatment rankings were assessed using surface under the cumulative ranking curve (SUCRA) probabilities & trial sequential analysis (TSA) was applied to evaluate the conclusiveness of evidence. Bias & certainty of evidence were assessed using RoB-2, & GRADE.

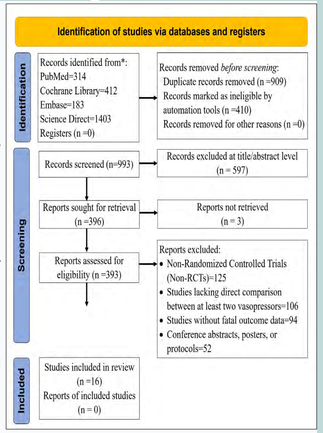


Figure 1: PRISMA Flow Diagram

Results

16 RCTs encompassing 2,102 low-risk parturients were included. NE demonstrated superior efficacy in reversing PSH (OR: 0.23; 95% CI: 0.09–0.58) and was associated with fewer adverse maternal events, including bradycardia (OR: 0.28) and nausea/vomiting (OR: 0.36), compared to PE and EP. Neonatal outcomes were generally comparable across groups, though NE showed a favorable trend in reducing the risk of neonatal acidosis (umbilical artery pH OR: 1.25; 95% CI: 1.06–1.54). SUCRA rankings and TSA supported the robustness of these findings.

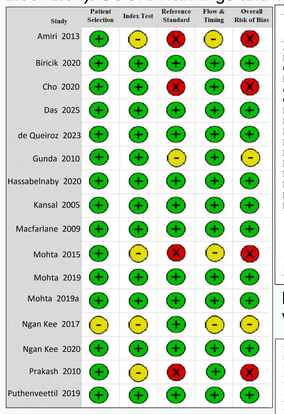


Figure 2. Risk of Bias. Green Circle with "+": Low Risk; Yellow Circle with "–": Unclear Risk; Red Circle with "×": High Risk

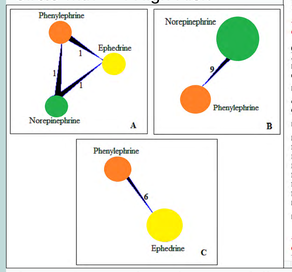


Figure 3. Panel A shows a fully connected network of PE, EP, and NE with one direct comparison per pair. Panels B and C indicate strongest evidence for NE vs PE.

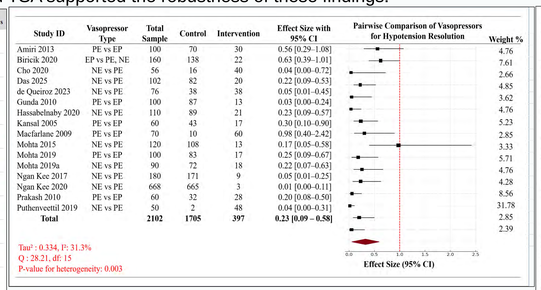


Figure 4. Forest Plot – Pairwise Comparison of Vasopressors for PSH Resolution

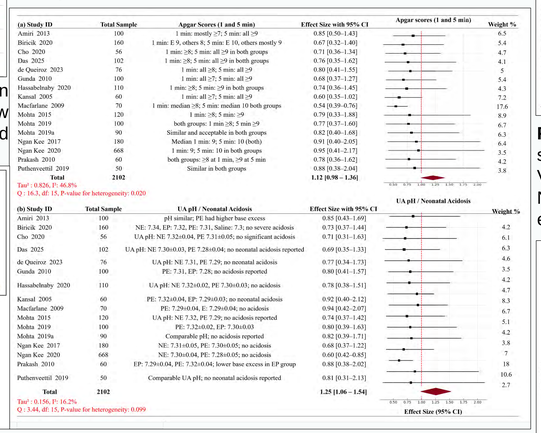


Figure 5. Forest Plot – Bradycardia and N/V outcomes. (a) Bradycardia incidence: NE significantly reduced risk compared to PE/EP (pooled OR 0.28 [0.10–0.43]). (b) N/V incidence: Intervention VPs, especially NE, associated with lower odds (pooled OR 0.36 [0.21–0.69]).

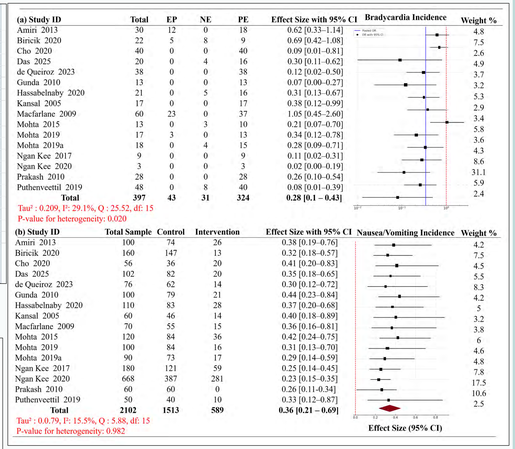


Figure 6. Forest Plot – Neonatal Outcomes. (a) Apgar scores at 1 and 5 minutes: No significant difference between VPs; pooled effect size 1.12 (95% CI: 0.98–1.36). (b) UA pH / Neonatal acidosis: Slightly favors intervention VPs; pooled effect size 1.25 (95% CI: 1.06–1.54).

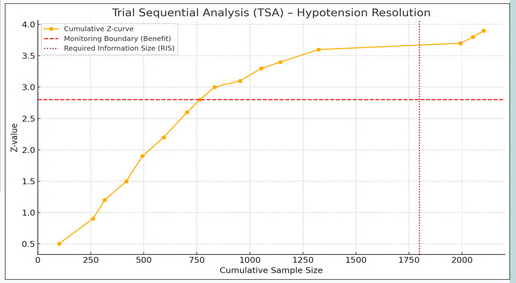


Figure 8. Trial Sequential Analysis Plot – PSH Resolution

Results

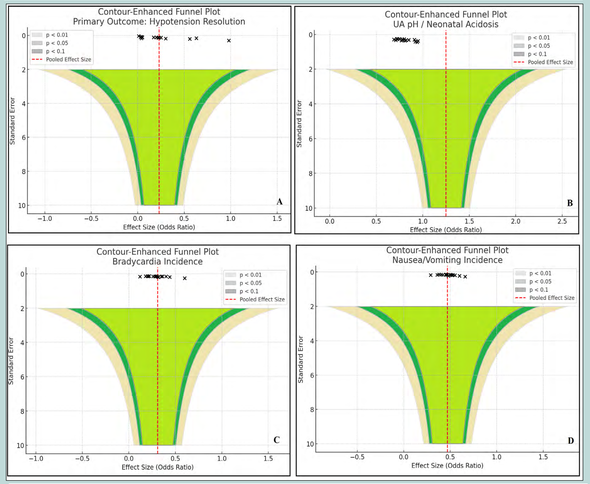


Figure 7. Contour-Enhanced Funnel Plots (Publication Bias). (A) Primary-PSH Resolution; (B) UA pH/Neonatal Acidosis; (C) Bradycardia; (D) N/V. No major asymmetry observed; contour shading indicates statistical significance thresholds ($p < 0.1$, $p < 0.05$, $p < 0.01$). Red dashed line represents pooled effect size.

Conclusion

In low-risk elective CD under SA, NE is the most effective and best-tolerated vasopressor for the *treatment* of PSH, with superior maternal hemodynamic stability, fewer AEs and without compromising neonatal safety., supporting NS as the preferred first-line therapeutic vasopressor in this clinical setting.

References

1. **Ng et al.** Spinal versus epidural anaesthesia for caesarean section. Cochrane Database Syst Rev. 2004;2004(2):CD003765. doi: 10.1002/14651858.CD003765.pub2. PMID: 15106218
2. **Wei et al.** Wei C et al. Norepinephrine for the prevention of spinal-induced hypotension during caesarean delivery under combined spinal-epidural anaesthesia: Randomised, double-blind, dose-finding study. Eur J Anaesthesiol. 2020 Apr;37(4):309-315. doi: 10.1097/EJA.0000000000001152. PMID: 31977628..
3. **Page et al.** The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. bmj. 2021;372.