VASOPRESSORS FOR PREVENTION OF POSTSPINAL HYPOTENSION DURING HIGH-RISK CESAREAN DELIVERY: A NETWORK META-ANALYSIS

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Abstract

Background: Post-spinal hypotension is frequent in high-risk cesarean delivery, and the optimal vasopressor remains unclear.

Methods: Eighteen RCTs (n=2,843) comparing norepinephrine, phenylephrine, and ephedrine were evaluated via network meta-analysis.

Results: Vasopressors lowered hypotension (OR 1.50; 95% CI 1.12–1.67). Norepinephrine and phenylephrine were more effective than ephedrine. Norepinephrine caused less bradycardia, while ephedrine caused more nausea/tachycardia. Neonatal outcomes were comparable.

Conclusion: Norepinephrine and phenylephrine are the most effective prophylactic choices, with norepinephrine offering superior hemodynamic stability.

Objectives

To compare **norepinephrine (NE), phenylephrine (PE), ephedrine (EP)** for **prophylaxis (prevention) of PSH in high-risk cesarean delivery** (CD), and to evaluate maternal hemodynamics, adverse effects, and neonatal outcomes.

Study Design

This systematic review and network meta-analysis (NMA) compared 18 RCTs of NE, PE and EP administered via IV bolus or infusion for the prevention of PSH in high-risk CD. PROSPERO registration number CRD420251050322. Endpoints included maternal hemodynamics, fetal outcomes, and AEs. Pairwise meta-analyses for direct comparison conducted using a random-effects model, and for NMA, using a frequentist approach.

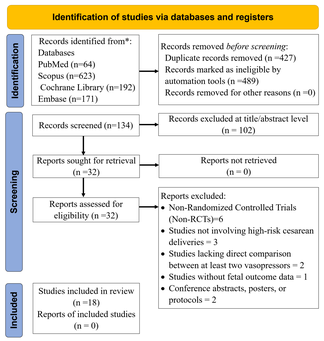

Figure 1: PRISMA flow diagram

Heterogeneity was assessed using the I² statistic and Cochran's Q test. Subgroup analysis, data quality, sensitivity analysis and publication bias were examined.

Results

Intrathecal Anesthetic Regimens: Most trials used hyperbaric bupivacaine (8–12 mg) with fentanyl or morphine adjuvants. Regimens were balanced between groups and did not influence vasopressor efficacy. Sample sizes ranged from 30 to 664. Interventions included prophylactic infusions of EP, PE, NE, or comparators (placebo, saline, mephentermine). Reported AEs included nausea, vomiting, bradycardia, and hypertension.

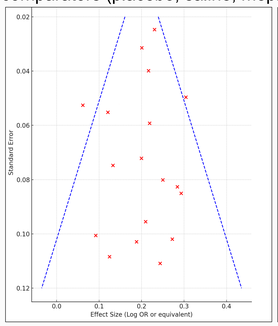

Figure 2. Risk of Bias Assessment: The funnel plot demonstrated a symmetric distribution with most studies within 95% limits (low publication bias).

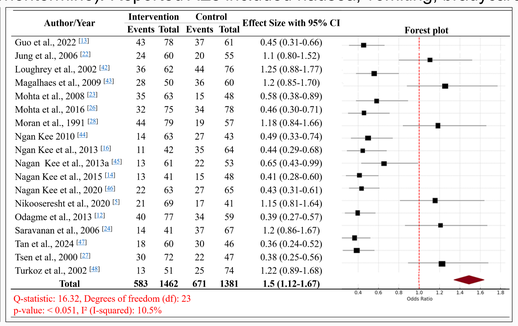

Figure 3. Meta-analysis: Primary Outcome—Prevention of PSH. In 18 RCTs (1107 intervention; 1028 control), vasopressors significantly reduced PSH: OR 1.50 (95% CI 1.12–1.67) with low heterogeneity (I² = 10.5%). Most trials favored vasopressors, with consistent maternal benefit and no differences in neonatal outcomes (Apgar, UA pH).

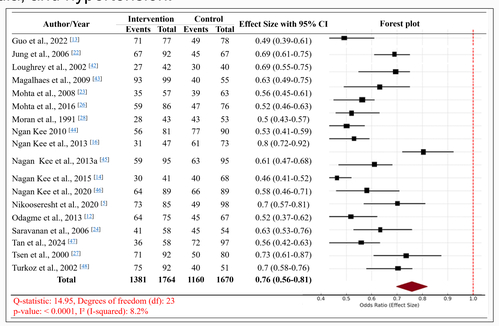

Figure 4. Secondary Outcomes — Hemodynamic Stability. Across 2554 parturients, vasopressors improved maternal hemodynamics: OR 0.76 (95% CI 0.56–0.81), a 24% reduction in AE with low heterogeneity (I² = 8.2%).

Table 1: Quality assessment of included randomized controlled trials using the RoB 2 tool

Author	Randomization Described	Allocation Concealment	Blinding (Participants/Personnel)	Blinding (Outcome Assessors)	Baseline Characteristics Similar	Incomplete Outcome Data Addressed	Free of Selective Reporting	Other Bias Addressed	Overall Quality Judgment	GRADING
Guo et al., 2022[13]	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Unclear	Some concerns	⭐⭐⭐
Jung et al., 2006[22]	Yes	Unclear	Yes	Yes	Yes	Yes	Unclear	Unclear	Some concerns	⭐⭐
Loughrey et al., 2002[41]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low risk	⭐⭐⭐
Magalhães et al., 2009[42]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low risk	⭐⭐
Mohta et al., 2008 [23]	Yes	Unclear	Unclear	Unclear	Yes	Unclear	Yes	Yes	Some concerns	⭐⭐⭐ ⭐⭐
Mohta et al., 2016[25]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low risk	⭐⭐⭐
Moran et al., 1991[27]	Yes	Unclear	Unclear	Unclear	Yes	Unclear	Yes	Yes	Some concerns	⭐⭐⭐ ⭐⭐
Ngan Kee 2010[43]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low risk	⭐⭐
Ngan Kee et al., 2013[16]	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	Low risk	⭐⭐⭐
Nagan Kee et al., 2013a[44]	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Unclear	Some concerns	⭐⭐
Nagan Kee et al., 2015[24]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low risk	⭐⭐⭐
Nagan Kee et al., 2020[45]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low risk	⭐⭐⭐
Nikooseresht et al., 2020[5]	Yes	Unclear	Yes	Unclear	Yes	Yes	Yes	Unclear	Some concerns	⭐⭐
Fyneface-Ogan et al., 2013[12]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low risk	⭐⭐⭐
Saravanan et al., 2006[24]	Yes	Unclear	Yes	Unclear	Yes	Yes	Yes	Unclear	Some concerns	⭐⭐
Tan et al., 2024[46]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low risk	⭐⭐⭐
Tsen et al., 2000[26]	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Low risk	⭐⭐⭐
Turkoz et al., 2002[47]	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Unclear	Some concerns	⭐⭐

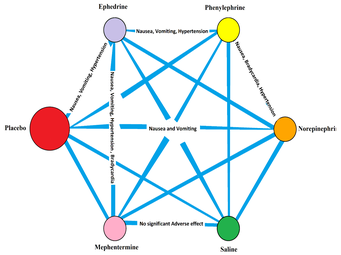

Figure 5. NMA: Network showed strong comparative evidence for EP, PE, and NE, with EP–PE & EP–placebo most common.

Table 1. Quality Assessment of RCTs using Cochrane RoB Tool

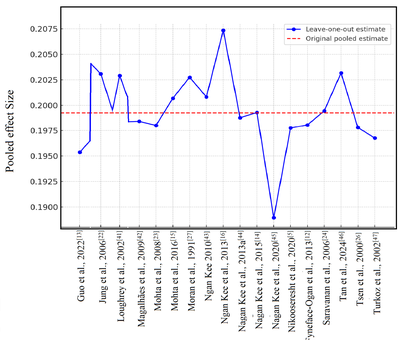

Figure 6. Sensitivity Analysis: Leave-one-out testing showed minimal fluctuation in pooled estimates, indicating no study disproportionately influenced results.

Results

Table 2: Subgroup analysis of vasopressor effectiveness and safety across clinical and methodological domains

Variables	Subgroups	No. of studies	Sample Size	Effect Size and 95% CI	P Value	Heterogeneity I² (%)
Population	Elective CD under SA	19	2180	0.85 (0.70, 1.05)	0.1	30.94
	Elective CD; Neuraxial anaesthesia vs. single-shot SA	1	70	0.78 (0.60, 0.95)	0.03	10.64
Intervention	Preeclampsia; CD under SA	2	772	0.8 (0.70, 0.90)	<0.01	15.84
	Preeclampsia: prevention of SAIH	2	248	0.82 (0.65, 1.05)	0.07	26.04
	EP bolus vs. Saline (Placebo)	2	86	0.72 (0.54, 1.06)	<0.01	6.24
	EP infusion vs. EP bolus	1	30	0.66 (0.46, 0.95)	0.3	20.84
	EP vs. MP	1	46	0.82 (0.60,0.95)	<0.01	46.04
	EP vs. PE	13	1718	0.65 (0.50,0.85)	0.07	10.84
	Glycopyrrolate pre-treatment before PE infusion	1	104	0.78 (0.62,0.88)	<0.01	15.54
	NE infusion combined with crystalloid or colloid	1	200	0.7 (0.55,0.88)	0.15	20.84
	NE vs. PE	5	1086	0.84 (0.72,0.96)	0.7	50.74
Maternal Hemodynamic Outcomes	SBP	23	3230	0.75 (0.65,0.85)	0.05	20.84
	DPB	22	3120	0.68 (0.54,0.78)	0.5	25.64
	MAP	23	3160	0.67 (0.52,0.82)	0.2	41.04
	CI	2	144	0.71 (0.60,0.83)	0.05	35.74
	HR	18	1940	0.76 (0.61,0.95)	<0.01	45.75
Fetal Outcomes	Apgar scores, UA pH	20	2190	1.1 (0.8–1.5)	0.15	30.74
	Apgar scores, UA pH, Lactate	1	30	1.2 (0.9–1.6)	0.7	25.84
	Apgar scores; Neonatal outcomes	1	138	0.9 (0.6–1.4)	0.5	30.64
	Fetal acidosis	1	712	0.82 (0.42–1.61)	0.2	10.74
Adverse Events	No complications	1	200	1.4 (1.0–1.9)	0.25	35.74
	Bradycardia, Hypertension, Nausea	6	1136	1.1 (0.9–1.3)	0.04	40.74
	Hypertension, Dry mouth, Nausea	1	104	1.0 (0.7–1.5)	0.02	35.54
	Nausea, Bradycardia	2	210	1.15 (0.89–1.48)	0.05	20.84
	Nausea, Hypertension	1	200	0.92 (0.73–1.17)	0.3	21.04
	Nausea, Vomiting	2	70	1.25 (1.10, 1.40)	0.03	10
	Nausea, Vomiting, Bradycardia	2	130	1.10 (0.95, 1.25)	0.12	15
	Nausea, Vomiting, Bradycardia, Tachycardia	3	212	1.35 (1.20, 1.50)	0.01	20
	Nausea, Vomiting, Hypertension, Bradycardia	4	948	1.50 (1.20, 1.80)	0.02	25
	No significant adverse events	2	160	1.20 (1.15, 1.25)	0.001	5

Table 2. Vasopressors improved SBP, DBP, and MAP (OR **0.67–0.75**) without affecting neonatal outcomes but increased nausea/vomiting and bradycardia (**OR 1.50; P=0.02**).

Conclusion

This SR and NMA shows strong evidence supporting intravenous vasopressors for preventing PSH in high-risk cesarean delivery. NE and PE were most effective, with NE demonstrating a potentially better safety profile, though not statistically significant. EP caused more adverse effects. Overall, findings support using PE or NE based on patient risk.

References

1. **Sun L et al.** Norepinephrine or phenylephrine for the prevention of post-spinal hypotension after caesarean section: A double-blinded, randomized, controlled study of fetal heart rate and fetal cardiac output. *J Clin Anesth*. 2024;97:111533.
2. **Veroniki AA et al.** Update to the PRISMA guidelines for network meta-analyses and scoping reviews and development of guidelines for rapid reviews: A scoping review protocol. *JBI Evid Synth* 2025;23:517-26.