Phenylephrine Bolus Versus Infusion During Cesarean Delivery Under Neuraxial Anesthesia: A Systematic Review, Meta-Analysis, and Trial Sequential Analysis

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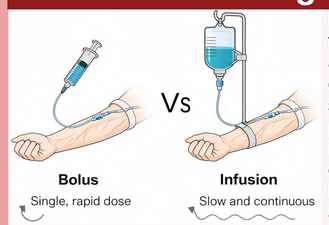
Background



Postspinal hypotension is a frequent complication of neuraxial anesthesia during cesarean delivery and may affect maternal safety and comfort, and utero-placental perfusion. Phenylephrine is widely used as the vasopressor of choice, yet clinical practice varies between intermittent bolus dosing and continuous infusion.

Prior studies and meta-analyses have yielded conflicting findings, and none have evaluated whether the evidence is sufficient to support firm conclusions.

Objectives

To compare phenylephrine (PE) bolus and infusion regimens for the prevention of postspinal hypotension (PSH) during cesarean delivery (CD) after spinal anesthesia (SA) and to evaluate maternal and neonatal outcomes. Trial sequential analysis was used to determine whether the accumulated evidence is conclusive or whether further trials are required.

Study Design

A PRISMA 2020 compliant systematic review and meta-analysis (MA) was prospectively registered PROSPERO-CRD420251081996. RCTs of IV bolus and infusion PE regimens during CD under SA or combined spinal epidural (CSE) anesthesia were included. Major databases were searched from inception to 2025. Primary outcome was pre-delivery maternal hypotension, defined as a systolic blood pressure (SBP) decrease to less than 80% of baseline. Secondary outcomes: reactive hypertension, bradycardia, nausea, vomiting, Apgar scores, and umbilical arterial blood gas parameters. Random-effects MA and trial sequential analysis (TSA) were performed.

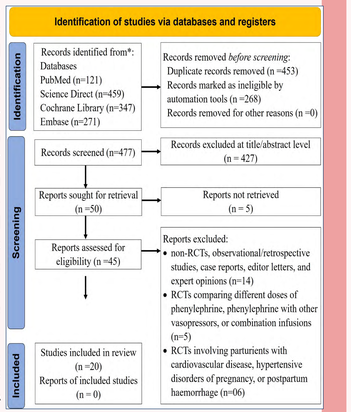


Figure 1: PRISMA Flow Diagram

Results

22 RCTs (N=2,742 parturients; PE Bolus: 1,314; PE Infusion: 1,428). There was no significant difference in the incidence of pre-delivery hypotension for infusion & bolus, although heterogeneity was very high. Subgroup analysis showed that fixed-rate prophylactic PE infusion significantly reduced pre-delivery hypotension.

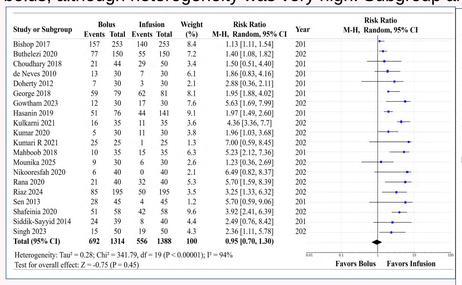


Figure 2. Forest Plots for the Incidence of Pre-Delivery Hypotension with PE Bolus and Infusion

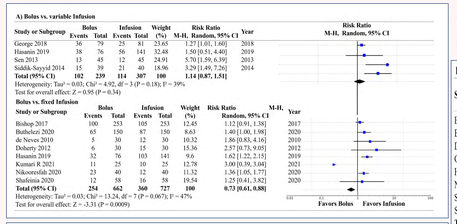


Figure 3. Forest Plots-Subgroups (A) PE Bolus vs Variable-Rate Infusion (above) and Fixed-Rate Infusion; (B) PE Therapeutic Bolus (above) or Prophylactic Bolus (below) vs Infusion

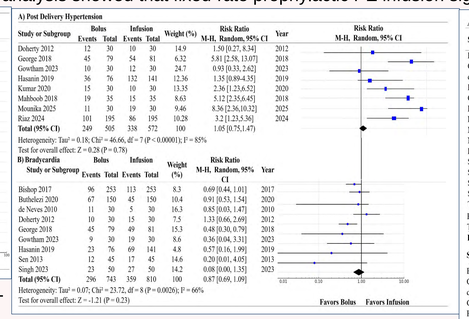


Figure 4. Forest Plots Maternal Hemodynamic Outcomes. (A) Hypotension following delivery (B) Bradycardia:

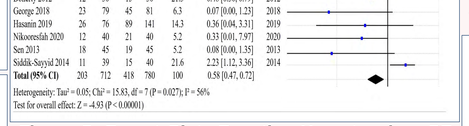


Figure 5. Forest Plots-Reactive Hypertension. PE Bolus vs Infusion.

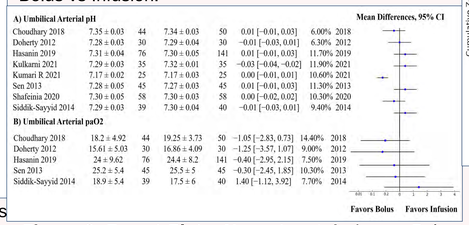


Figure 6. Forest Plots. Neonates. Infusion vs Bolus (A) UA pH: Marginally Higher with Infusion (B) UA paO_2

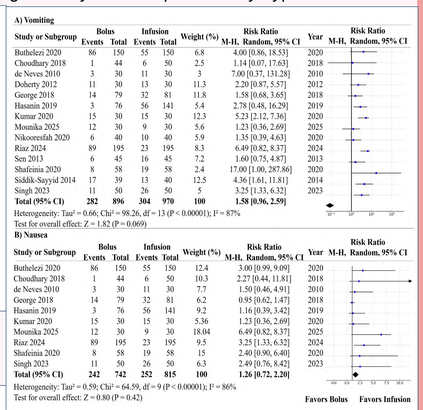


Figure 7. Forest Plots-Intraoperative Nausea & Vomiting (IONV). PE Infusion & Bolus. (A) Vomiting: Trend Toward Increased Incidence With Bolus, (B) Nausea

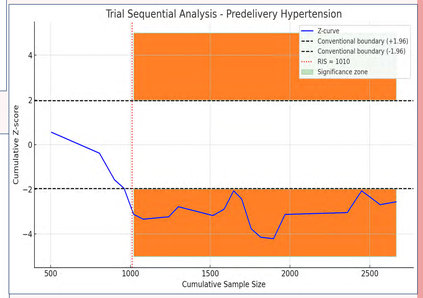


Figure 8. Trial Sequential Analysis (TSA)-Predelivery Hypotension. The cumulative Z-curve crossed neither the monitoring boundary nor the required information size (RIS), yielding inconclusive evidence.

Results

Outcomes	RR Infusion (%)	RR Bolus (%)	RR (95% CI)	N (clinical trials)	Evidence Certainty (GRADE)	Comments
Predelivery HoTN	25-42	30-55	1.40 [1.08, 1.82]	2742 (20)	[a]Moderate ⊕⊕⊕◯	Higher hypotension incidence in bolus group
Reactive HTN	5-15	3-11	0.48 [0.30, 0.79]	1532 (8)	[b]Moderate ⊕⊕⊕◯	Lower reactive hypertension with bolus
Bradycardia	8-15	6-13	0.91 [0.53, 1.54]	1553 (9)	[c]Very Low ⊕◯◯◯	No clear difference
Vomiting	3-8	5-11	2.20 [0.87, 5.57]	1906 (14)	[d]Very Low ⊕◯◯◯	Uncertain increase in vomiting with bolus
Nausea	5-10	6-12	0.95 [0.62, 1.47]	1157 (10)	[e]Low ⊕⊕◯◯	No significant difference in nausea
Apgar	8.5 ± 1.5	8.9 ± 1.2	0.50 [0.19, 0.81]	1232 (11)	[f]Moderate ⊕⊕⊕◯	Slight improvement with bolus
UA pH	7.30 ± 0.05	7.31 ± 0.04	−0.03 [−0.04, −0.02]	643 (8)	[g]Moderate ⊕⊕⊕◯	Minimal clinical difference
UA paO2	19.2 ± 4.0	18.5 ± 5.0	−1.05 [−2.83, 0.73]	540 (5)	[h]Low ⊕⊕◯◯	Uncertain impact on neonatal oxygenation

Table 1. Summary of Findings & GRADE Evaluation-Maternal & Fetal Outcomes Bolus & Infusion. High Risk: (**a**) 5/20 studies (Bishop 2017, Buthelezi 2020, Choudhary 2018, Hasanin 2019, Kumari 2021); (**b**) 3/8 studies (Bishop 2017, Buthelezi 2020, Hasanin 2019); (**c**) 3/9 studies (Bishop 2017, Buthelezi 2020, Hasanin 2019); (**d**)3/14 studies (Bishop 2017, Buthelezi 2020, Hasanin 2019); (**e**) 3/10 studies (Bishop 2017, Buthelezi 2020, Hasanin 2019); (**f**) 3/11 studies (Buthelezi 2020, Hasanin 2019, Kumari 2021); (**g**)2/8 studies (Choudhary 2018, Hasanin 2019); (**h**) 2/5 studies Choudhary 2018, Hasanin 2019).

Conclusion

Fixed-rate prophylactic PE infusion reduces the incidence of predelivery hypotension; however, overall evidence does not demonstrate clear superiority vs. bolus due to substantial heterogeneity. Trial sequential analysis confirms that only the fixed-rate infusion subgroup provides conclusive benefit. Neonatal outcomes are equivalent between dosing regimens. The choice of PE administration method should be individualized based on maternal cardiovascular profile.

References

1. **Doherty et al.** Phenylephrine infusion versus bolus regimens during cesarean delivery under spinal anesthesia: A double-blind randomized clinical trial to assess hemodynamic changes. Anesth Analg 2012;115:1343-50.
2. **Page et al.** PRISMA 2020 explanation and elaboration: Updated guidance and exemplars for reporting systematic reviews. BMJ 2021;372: 1-36.
3. **Kang H.** Trial sequential analysis: Novel approach for meta-analysis. Anesth Pain Med 2021;16:138-50.