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Dr. Faizal Rafik Kureshi
Senior Resident, Department of Anaesthesiology, GMERS Medical College, Gandhinagar, Gujrat, India

Dr. Shobhana Gupta
Professor & Head, Department of Anaesthesiology, GMERS Medical College, Gandhinagar, Gujrat, India

Dr. Bharti Rajani
Professor, Department of Anaesthesiology, GMERS Medical College, Gandhinagar, Gujrat, India

Dr. Urvashi Patel
Assistant Professor, Department of Anaesthesiology, Shri M P Shah Government Medical College, Jamnagar, Gujrat, India

Dr. Mukund Patel
Third Year Resident Doctor, Department of Anaesthesiology, GMERS Medical College, Gandhinagar, Gujrat, India

Corresponding Author:
Dr. Faizal Rafik Kureshi
Senior Resident, Department of Anaesthesiology, GMERS Medical College, Gandhinagar, Gujrat, India

Efficacy of phenylephrine in preventing hemodynamic responses of oxytocin during caesarean section under spinal anaesthesia: A randomized comparative study

Faizal Rafik Kureshi, Shobhana Gupta, Bharti Rajani, Urvashi Patel, Mukund Patel

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Abstract
Introduction: Postpartum hemorrhage (PPH) is a major cause of maternal morbidity and mortality, with uterine atony being the leading cause. Oxytocin is the first-line uterotonic for PPH prevention but can cause significant hypotension and tachycardia. This study evaluates the efficacy of two different doses of phenylephrine, 75 µg and 100 µg, in preventing oxytocin-induced hypotension during caesarean section under spinal anaesthesia, focusing on its effects on blood pressure, heart rate, and the need for rescue vasopressors.
Methods: This study involved 180 full-term pregnant women aged 18-35, it used a randomized, double-blind, controlled design with three groups: Group P75 (75 µg phenylephrine), Group P100 (100 µg phenylephrine), and Group NS (normal saline). Phenylephrine was administered just before IV oxytocin (3U) following cord clamping. Hemodynamic parameters, incidence of hypotension, need for rescue vasopressors, and side effects were recorded.
Results: While the mean age, weight, and height were similar across all groups, Phenylephrine administration significantly reduced oxytocin-induced hypotension. The incidence of hypotension was 8.3% in P75, 3.3% in P100, and 20% in NS (p=0.001). The mean dose of rescue vasopressors required was 45.1 µg in P75, 30.0 µg in P100, and 51.6 µg in NS (p<0.001). Group NS had the highest hypotension rate and required the most vasopressor, followed by Groups P75 and P100. Group P100 maintained the most stable hemodynamic profile with minimal side effects compared to Group P75 and Group NS.
Conclusion: Prophylactic administration of phenylephrine, particularly at 100 µg, significantly reduces oxytocin-induced hypotension during caesarean section under spinal anaesthesia. This strategy may enhance maternal hemodynamic stability, reducing the need for additional rescue vasopressor interventions.

Keywords: Phenylephrine, oxytocin, postpartum hemorrhage, hypotension, caesarean section, spinal anaesthesia

Introduction
Postpartum hemorrhage (PPH) is one of the leading causes of maternal morbidity and mortality, with uterine atony, amongst various etiologies, responsible for nearly 50% of cases. Oxytocin, the first-line uterotonic, is essential for prevention and treatment but often causes hemodynamic effects like hypotension and tachycardia due to its action on cardiovascular oxytocin receptors. Phenylephrine, a selective α1-adrenergic agonist, is gaining attention in obstetric anesthesia for counteracting oxytocin-induced hypotension. While widely used for post-spinal hypotension, its role in managing oxytocin-induced instability and optimal dosing remain under study. This study compares 75 µg and 100 µg of intravenous phenylephrine for preventing oxytocin-induced hypotension in cesarean sections under spinal anesthesia. The primary objective is to assess hypotension incidence, with secondary outcomes including HR, SBP, DBP, MAP, vasopressor requirements, and side effects.

Methods
This prospective, randomized, double-blind, controlled study was conducted at the Department of Anesthesiology, GMERS Medical College, Gandhinagar, between June 2021 and May 2022.

Institutional ethical committee approval was obtained, and written informed consent was secured from all participants.

Inclusion Criteria: ASA Grade I & II parturients undergoing elective or emergency caesarean section under spinal anaesthesia; Age range: 18-35 years; Body Mass Index (BMI) < 30 kg/m²; Singleton pregnancy with an otherwise uncomplicated gestation

Exclusion Criteria: Patient refusal; ASA Grade III & IV patients; Contraindications to spinal anaesthesia (e.g., coagulopathy, infection at the injection site, hypersensitivity to local anaesthetics); Pre-existing cardiovascular disease, hypertension, or autonomic dysfunction; Patients already administered oxytocin for augmentation of labor; or allergies to study drugs; Multiple gestation, placenta previa, abnormal placentation, severe preeclampsia/eclampsia

Randomization and Blinding: Participants were randomized into three groups: Group P75 (75 µg phenylephrine), Group P100 (100 µg phenylephrine), or Group NS (normal saline), using a computer-generated randomization sequence. To maintain double-blinding, an anaesthesiologist not involved in intraoperative management prepared the study drug solutions, ensuring that both the participants and the attending anaesthesiologists were unaware of group allocations.

Study Groups: Group P75: Received 75 µg of intravenous phenylephrine; Group P100: Received 100 µg of intravenous phenylephrine; Group NS: Received normal saline placebo

Anaesthetic Protocol

Standard ASA monitoring was applied, including electrocardiography (ECG), non-invasive blood pressure (NIBP), and pulse oximetry (SpO_2). Intravenous (IV) access was established with an 18G cannula, and all patients were preloaded with 500 mL of Ringer's lactate solution prior to spinal anaesthesia. Spinal anaesthesia was administered in the L3-L4 or L4-L5 interspace using a 25G Quincke needle, delivering 2.0-2.2 mL of 0.5% hyperbaric bupivacaine. Immediately after the subarachnoid block (SAB), patients were positioned supine with 15° left uterine displacement using a wedge under the right buttock. At cord clamping, the study drug was administered as an IV bolus over 5-10 seconds, followed by oxytocin (3U IV over 15 seconds). An oxytocin maintenance infusion (20 IU in 500 mL normal saline at 125 mL/h) was initiated as per standard protocol. Hemodynamic parameters were monitored every minute for first 10 minutes and then every 5 minutes until the end of the surgery. Uterine tone was assessed, and interventions were made as necessary. Hypotension, defined as a MAP fall >20% from baseline, was treated with IV fluids and rescue phenylephrine. Bradycardia was managed with Atropine and patients were monitored in the postoperative care unit for 6 hours.

Outcome Measures: Primary Outcome: Incidence of hypotension, defined as a ≥20% decrease in MAP from baseline.

Secondary Outcomes: Hemodynamic parameters: HR, SBP, DBP, and MAP at predefined time intervals. Rescue vasopressor requirement (phenylephrine 50 µg IV administered in case of hypotension). Adverse effects: Bradycardia (HR <60 bpm), nausea, vomiting, arrhythmias

Statistical Analysis: Data was analyzed using SPSS version 25. Continuous variables were expressed as mean ± standard deviation (SD) and compared using ANOVA. Categorical variables were analyzed using the chi-square test. A p-value < 0.05 was considered statistically significant.

Results: Demographic and Baseline Characteristics: The three groups were comparable in terms of age, BMI, and baseline hemodynamic parameters ($p>0.05$), ensuring homogeneity.

Incidence of Hypotension: Group NS had the highest incidence of hypotension (20%), compared to 8.3% in P75 and 3.3% in P100, with the difference being highly significant. In Group P75, all 5 hypotensive cases had a single episode, and in P100, both hypotensive cases had one episode. In Group NS, 10 patients had a single episode, and 2 had two episodes, as mentioned in Table 3.

Hemodynamic Stability

At baseline, SBP, DBP, and MAP were comparable across all groups (P75, P100, and NS). After drug administration, no significant differences were observed at 1 and 5 minutes. However, at 10 minutes, Group P100 had significantly higher SBP (112 ± 9.2 mmHg), DBP (68 ± 6.4 mmHg), and MAP (83 ± 8.4 mmHg) than Group NS, with Group P75 also showing higher values ($p < 0.05$). SBP, DBP, and MAP were significantly better maintained in Group P100 compared to P75 and NS ($p<0.001$).

HR fluctuations were minimal in P100, with fewer cases of reflex bradycardia compared to P75. Baseline heart rates were comparable across groups ($p = 0.13$) and remained similar at 1 minute ($p = 0.41$). However, at 5 and 10 minutes, Group NS had significantly higher heart rates than P75 and P100 ($p = 0.01$, $p = 0.00$). Detailed data are shown in Table 2.

Rescue Vasopressor Requirement

Group NS required the highest vasopressor dose (51.6 ± 5.5 µg/min), followed by P75 (45.1 ± 6.1) and P100 (30.0 ± 5.1) ($p = 0.000$). Hypotension incidence was also highest in NS (20%) compared to P75 (8.3%) and P100 (3.3%) ($p = 0.001$). See Table 3.

Adverse Effects: Nausea and vomiting were more frequent in Group NS ($p=0.02$). No significant arrhythmias or serious cardiovascular events were observed.

Table 1: Mean Blood Pressure Measurements (SBP, DBP, and MAP) Across Groups at Different Time Points

Timeline (mins)	Measurement	Group P75 (mean)	Group P100 (mean)	Group NS (mean)	P value
Baseline	SBP (mmHg)	123 ± 10.1	122 ± 10.2	122 ± 10.1	0.63
	DBP (mmHg)	79 ± 6.7	78 ± 7.1	78 ± 8.0	0.33
	MAP (mmHg)	94 ± 8.8	93 ± 8.5	93 ± 8.5	0.54
After Injection					
1 min	SBP (mmHg)	118 ±, 10.5	120 ±, 10.0	117 ± 9.9	0.12
	DBP (mmHg)	74 ± 6.5	76 ± 6.8	73 ± 6.9	0.22
	MAP (mmHg)	89 ± 8.7	91 ± 8.8	88 ± 8.4	0.33
5 min	SBP (mmHg)	112 ± 9.8	116 ± 9.9	110 ± 9.8	0.09
	DBP (mmHg)	68 ± 6.0	72 ± 6.6	66 ± 6.0	0.08
	MAP (mmHg)	83 ± 8.4	87 ± 8.7	81 ± 8.0	0.1
10 min	SBP (mmHg)	105 ± 9.4	112 ± 9.2	103 ± 9.5	0.01
	DBP (mmHg)	61 ± 5.0	68 ± 6.4	59 ± 5.8	0.01
	MAP (mmHg)	76 ± 7.5	83 ± 8.4	74 ± 7.3	0.00

Table 2: Mean Heart Rate (per minute) Before and After Administration of Phenylephrine Across Groups

Timeline (mins)	Group P75 (mean)	Group P100 (mean)	Group NS (mean)	P value
Before giving inj. Phenylephrine (Baseline)	91 ± 7.6	91 ± 7.6	92 ± 7.5	0.13
After giving inj. Phenylephrine				
At 1 min	92 ± 7.6	91 ± 7.7	93 ± 7.8	0.41
At 5 min	96 ± 7.8	94 ± 7.7	99 ± 7.9	0.01
At 10 min	100 ± 7.9	97 ± 7.9	103 ± 8.0	0.00

Table 3: Incidence of Hypotension and Vasopressor Dose Required in Study Groups

Parameter	Group P75 (n=60)	Group P100 (n=60)	Group NS (n=60)	P value
Incidence of Hypotension (%)	5 (8.3)	2 (3.3)	12 (20.0)	0.001
Mean Dose of Vasopressor (µg/min)	45.1 ± 6.1	30.0 ± 5.1	51.6 ± 5.5	0.000

Discussion

Oxytocin is widely used during caesarean sections to prevent postpartum haemorrhage, but its vasodilatory effects can lead to hypotension, tachycardia, and decreased systemic vascular resistance (SVR). These changes can be particularly concerning in parturients receiving spinal anaesthesia, where sympathetic blockade further contributes to hypotension. Phenylephrine, a selective α1-adrenergic receptor agonist, has been well-established in obstetric anaesthesia for preventing spinal-induced hypotension. Its role in counteracting oxytocin-induced hemodynamic instability, however, is less studied. Our findings suggest that prophylactic phenylephrine administration significantly improves maternal hemodynamic stability, with 100 µg proving more effective than 75 µg.

Comparison with Existing Literature: Previous studies have demonstrated that phenylephrine coadministration with oxytocin reduces hypotension (Dyer *et al*., 2009; Stewart *et al*., 2010). However, the optimal dose remains debated. Hasan *et al*. (2012) found that 200 µg provided superior BP control, but it also led to more bradycardia. Our study confirms that 100 µg offers a better balance between efficacy and safety, reducing the need for rescue vasopressors while maintaining stable blood pressure.

Hemodynamic Stability and Reflex Bradycardia: Phenylephrine's α1-mediated vasoconstriction raises blood pressure but can trigger baroreceptor-mediated bradycardia. While some studies highlight bradycardia concerns with phenylephrine, our results show that 100 µg was well-tolerated, with minimal heart rate fluctuations compared to 75 µg. This suggests that doses up to 100 µg are both safe and effective in parturients undergoing caesarean sections. Compared to ephedrine, which has β-adrenergic activity and can cause maternal tachycardia and neonatal acidosis, phenylephrine is the preferred vasopressor in obstetric anaesthesia due to its predictable action and better foetal safety profile.

Clinical Implications: 1. 100 µg phenylephrine should be the preferred prophylactic dose for mitigating oxytocin-induced hypotension. 2. Prophylactic administration is more effective than reactive management in preventing severe BP drops. 3. Phenylephrine bolus administration is practical in resource-limited settings, though infusions may offer smoother BP control. 4. Maternal safety and neonatal outcomes remain favourable with phenylephrine use, making it a safe first-line choice.

Limitations and Future Research: Single-center study; multi-center trials are needed for broader validation. Neonatal outcomes were not assessed; future studies should evaluate foetal acid-base balance.

Conclusion

Our findings show that both phenylephrine doses effectively manage oxytocin-induced hypotension, with 100 µg providing better hemodynamic stability. These results support using 100 µg phenylephrine to prevent significant blood pressure drops during cesarean sections, improving maternal blood pressure management.

Conflict of Interest
Not available

Financial Support
Not available

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