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Original Article

Comparison of Phenylephrine, Mephentermine and Ephedrine for Maintenance of Blood Pressure During Subarachnoid Block in Cesarean Section and their Effects on Fetal Outcome

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Abstract

Background

Globally, the incidence of hypotension has been very high during cesarean section under spinal anesthesia. Hence, to manage hypotension and maintain adequate blood pressure, vasopressors such as Phenylephrine, Mephentermine, and Ephedrine are commonly used.

Materials and Methods

A Prospective Comparative Interventional study was conducted among 102 singleton pregnant women undergoing cesarean section at Nobel Medical College Teaching Hospital Ltd. Following hypotension, group P received Phenylephrine 100 mcg IV, Group E received Ephedrine 6 mg IV and group M received Mephentermine 6 mg IV. Vital parameters like blood pressure (systolic, diastolic and mean), heart rate, and oxygen saturation were recorded preoperatively as well as intraoperatively.

Results

After administering vasopressors, Group P showed a significantly greater increase in blood pressure than Groups E and M at the 4, 6, 8, and 10 minute intervals. However, Group P also demonstrated a significant decrease in heart rate at 4, 6, 16, 18, 20, and 30 minutes compared with Groups E and M. Drug bolus requirements and maternal side effects were similar among groups. Neonatal outcomes were comparable, with Apgar scores >7 in all cases.

Conclusion

From our study, it can be concluded that all three vasopressors Phenylephrine, Ephedrine, and Mephentermine were able to restore hypotension during cesarean section, although Phenylephrine achieved faster blood pressure control, though it was associated with a reduction in heart rate. Therefore, phenylephrine is most suitable when rapid blood pressure control is required, provided that heart rate is closely monitored.

Keywords: *Ephedrine, Hypotension, Mephentermine, Phenylephrine*

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Introduction

Subarachnoid block is the most frequently used neuraxial anesthesia technique for cesarean sections due to its simplicity, rapid onset, and reliable effectiveness. It requires a small dose of local anesthetic, thereby minimizing the risk of toxicity and limiting fetal drug exposure [1]. This technique provides complete sensory and motor blockade, reduces the risk of pulmonary aspiration, and avoids fetal depression associated with general anesthesia [2]. However, like other anesthesia techniques, spinal anesthesia may cause complications, with maternal hypotension being the most common and clinically significant concern [3-6].

Hypotension after spinal anesthesia is primarily caused by sympathetic blockade, which leads to arterial and venous vasodilation, venous pooling, and a subsequent reduction in cardiac output. As described by Park and Choi (2024) [7], preventive strategies such as leg elevation, left uterine displacement, and intravenous fluid preloading are commonly practiced, although these measures alone may not adequately prevent hypotension. Sonika et al. (2024) [8] further emphasize that combining fluid administration with vasopressor therapy, such as Phenylephrine, Ephedrine, or Mephentermine, is the most effective approach to maintaining maternal blood pressure and ensuring adequate uteroplacental perfusion

Untreated maternal hypotension can decrease uteroplacental blood flow, causing fetal acidosis and maternal symptoms such as nausea, vomiting, and dizziness. Vasopressors like Phenylephrine, Ephedrine, and Mephentermine are commonly used to treat this condition [8-10]. The present study aims to compare these agents for the maintenance of maternal blood pressure during subarachnoid block in cesarean sections and assess their effects on fetal outcomes.

Materials and Methods

A Prospective Comparative Interventional study was conducted among 102 singletons pregnant women undergoing elective caesarean sections aged between 18-35 years old with ASA PS I and II at Nobel Medical College Teaching Hospital Ltd, Biratnagar, Nepal over a period of one year from June 2024 to June 2025, after getting ethical clearance from the Institutional Review Committee (IRC 14/2024) of Nobel Medical College Teaching Hospital. Written informed consent was obtained from all participants after they were informed of the study protocol. Inclusion criteria were singleton pregnancies beyond 36 weeks of gestation with no known fetal abnormalities, scheduled for elective cesarean section under spinal anesthesia. Exclusion criteria included patients who declined consent, those with diabetes mellitus, hypertension, rheumatic heart disease, severe anemia, cerebrovascular disease, and obstetric complications such as antepartum hemorrhage, pregnancy-induced hypertension, cord complications, fetal malformations, polyhydramnios, or contraindications to spinal anesthesia.

The sample size was calculated using G*Power version 3.1 for a one-way ANOVA comparing three vasopressor groups on mean arterial pressure (MAP) following subarachnoid block. Assuming a medium effect size (Cohen's f = 0.25), $\alpha = 0.05$, and 80% power, a minimum of 84 participants was required. Considering a 20% attrition rate, 102 patients were enrolled and randomly assigned into three groups (n = 34 each):

Group P: Phenylephrine 100 µg IV
Group E: Ephedrine 6 mg IV
Group M: Mephentermine 6 mg IV

Randomization was performed using a sealed-envelope technique. Both the patient and the anesthesiologist assessing outcomes were blinded to group allocation.

Routine pre-anesthetic check-up was done a day before surgery and all patients were explained about the anesthetic technique and prescribed tab. Ranitidine 150mg orally on the evening prior to surgery. Nil per oral for at least 8 hours before surgery was maintained. After briefing the patients about the procedure in the operative room, an 18G intravenous cannula was inserted in the non-dominant hand and ringer lactate (RL) was infused at a rate of 20ml/kg. Standard ASA monitors were attached where baseline heart rate, blood pressure, oxygen saturation and ECG were recorded. The vasopressor drug solutions were prepared in identical syringes by an anesthetist or nurse who was not involved in the study and the intraoperative monitoring and postoperative observation were done by the same anesthesiologist or nurse who administered the drugs, in

order to maintain blinding.

Subarachnoid block (SAB) was performed with all patients in the sitting position. A 25G Quincke's needle was inserted at L3-L4 vertebral inter-space and once free flow of clear cerebrospinal fluid was obtained hyperbaric bupivacaine 0.5%, 11 mg (2.2 ml) was injected over 10-15 seconds. Time of injection of the drug was noted and the patient was placed in supine position immediately with a left lateral tilt of 15-20 degrees. The sensory block height of T6 was considered appropriate. Alcohol swab method was used to assess the level of sensory block after 5 min of subarachnoid block. Oxygen 5 L/min was administered through a face mask until the delivery of the child. Immediately following SAB, patients received a 1 ml bolus of the study drug Phenylephrine 100 mcg IV, Ephedrine 6 mg IV, Mephentermine 6 mg IV according to the group allocated. Hemodynamic variables like blood pressure and heart rate were monitored every 2 minutes for the first 20 minutes and every five minutes for the next 40 minutes after?the spinal injection. For this study, hypotension was defined as a decrease in blood pressure greater than 20% from baseline. Whenever hypotension occurred, the study drug was given IV. On each occasion when maternal heart rate decreased to below 60 beats per minute (bpm), atropine 0.3 mg IV was administered. The induction delivery and incision delivery interval were recorded. Nausea and vomiting were scored on a scale of 0-2 (0 = none, 1 = nausea without vomiting, 2 = vomiting). After delivery, we gave oxytocin 5±10 IU by slow IV fluid. Adverse events like hypotension, bradycardia, nausea, vomiting, and shivering were recorded as secondary outcomes. The attending pediatrician, who was blinded to the patient's group, assessed Apgar scores 1 and 5 min after delivery.

Data were analyzed using SPSS version 26. Continuous variables were presented as mean ± standard deviation (SD), and intergroup comparisons were performed using one-way ANOVA. A p-value < 0.05 was considered statistically significant.

Results

The study was on the comparison of intravenous bolus Phenylephrine, Ephedrine and Mephentermine for maintenance of blood pressure during spinal anesthesia in caesarian section. In the study all three groups group P, group E and group M were comparable to each other with respect to age, weight, height, parity and surgery duration where none of the variables showed any significant differences as per Table-1.

Table 1:Comparison of demographic profiles

Variables	Group P(n=34)	Group E(n=34)	Group M(n=34)	p-value
Age(mean±SD) in yrs.	24.68±3.55	23.26±3.52	24.12±3.39	0.245
Weight(mean±SD)in kg	57.22±6.36	56.71±5.66	56.59±5.43	0.894
Height(mean±SD) in cm	149.28±3.51	149.71±4.21	148.87±4.34	0.690
Parity(mean±SD)	1.32±0.61	1.41±0.58	1.28±0.51	0.626
Duration of surgery (mean±SD) in min	39.34±10.82	36.43±10.41	38.11±9.62	0.507

There was a significant decrease in systolic and diastolic blood pressure in all three groups after the spinal anesthesia, but after administration of study drugs Phenylephrine, Ephedrine, Mephentermine, there was a rise in mean Systolic blood pressure and mean diastolic blood pressure at all the time intervals and were within normal range and were comparable among all three groups. In intergroup comparison, there was a significant rise in systolic blood pressure in group P than group E and M and were statistically significant ($p<0.05$) at 4,6,8 minute time interval [Table -2,3].

Table 2: Changes in mean systolic blood pressure among the groups(mmhg)(mean±SD)

Time interval (in min)	Group P	Group E	Group M	P vs E (p value)	P vs M(p value	E vs M(p value)
0	120.25 ± 10.78	119.70±8.86	120.11± 10.25	0.819	0.958	0.868
2	104.75 ± 17.76	103.40 ± 12.51	102.40 ± 17.23	0.705	0.527	0.780
4	116.42± 10.12	108.55 ± 13.81	107.15 ± 13.88	0.005	0.001	0.646
6	120.65± 10.81	113.85 ± 10.41	112.50 ± 14.11	0.003	0.001	0.633
8	119.80± 17.33	112.55 ± 9.18	115.45 ± 10.07	0.021	0.193	0.182
10	120.85± 10.38	115.60 ± 13.47	115.85 ± 13.99	0.088	0.072	0.939
12	121.85 ±12.62	118.90 ± 9.54	115.75 ± 13.09	0.248	0.023	0.194
14	118.85± 10.20	116.65 ± 11.28	115.70 ± 11.14	0.346	0.217	0.305
16	119.11±9.83	114.25±8.90	116.85±7.86	0.024	0.239	0.193
18	120.45±10.38	116.70±8.90	116.38±10.46	0.082	0.080	0.902
20	118.50±10.12	115.90±7.36	114.25±9.56	0.207	0.045	0.403
25	120.00± 11.18	118.80 ± 7.36	116.25± 11.67	0.586	0.108	0.274
30	117.88±10.61	115.90±8.78	115.82±9.12	0.374	0.382	0.974

Table 3: Changes in mean diastolic blood pressure among the groups(mmhg)(mean±SD)

Time interval (in min)	Group P	Group E	Group M	P vs E (p value)	P vs M(p value	E vs M(p value)
0	75.57±4.68	76.35±5.02	76.78±4.89	0.510	0.320	0.720
2	64.50±6.42	64.24±6.27	64.84±6.01	0.860	0.810	0.660
4	78.82±7.28	64.54±5.88	63.85±5.38	<0.001	<0.001	0.610
6	80.28±7.92	69.34±6.28	69.56±6.45	<0.001	<0.001	0.880
8	77.81±8.11	72.81±7.21	71.91±6.77	0.003	<0.001	0.550
10	76.38±8.42	74.81±7.05	74.63±7.82	0.370	0.310	0.920
12	76.25±9.11	75.81±8.10	76.55±8.34	0.820	0.870	0.680
14	72.90 ± 9.34	69.20 ± 10.28	69.37 ± 10.06	0.097	0.099	0.940
16	71.00 ± 9.68	69.50 ± 10.64	68.81 ± 10.88	0.530	0.340	0.760
18	71.25 ± 9.52	69.15 ± 9.49	69.15 ± 8.83	0.330	0.330	1.000
20	70.44 ± 8.26	71.90 ± 9.41	71.03 ± 9.68	0.460	0.760	0.670
25	73.50 ± 9.33	72.85 ± 9.86	72.15 ±9.16	0.760	0.500	0.740
30	76.50 ± 8.45	74.82 ± 7.56	75.09 ± 7.82	0.350	0.430	0.880

Heart rate was comparable among all three groups. There was a significant rise in heart rate in all groups during hypotension. However, following drug administration, a significant drop-in heart rate was observed in the Phenylephrine group (Group P) at (4, 6, 16, 18, 20, and 30 minutes) compared to the Ephedrine (Group E) and Mephentermine (Group M) groups. In contrast, Groups E and M showed a steady rise in heart rate post drug administration, with no significant difference between them throughout the given time interval [Table-4].

Table 4: Changes in mean heart rate among the groups(bpm) (Mean ± SD)

Time interval (in min)	Group P	Group E	Group M	P vs E (p value)	P vs M (p value	E vs M(p value)
0	85.63± 8.24	87.37± 8.33	87.89± 6.36	0.33	0.251	0.814
2	82.55± 7.24	87.35± 6.61	84.70± 6.11	0.007	0.296	0.067
4	72.05 ± 8.36	88.90± 7.09	87.45± 08.99	<0.001	<0.001	0.49
6	78.70 ± 5.04	84.40± 09.20	87.15± 09.85	0.022	0.001	0.211
8	82.65 ± 7.32	85.10± 07.35	85.55± 05.72	0.167	0.042	0.75
10	83.00 ± 6.74	85.45± 08.00	85.95± 08.95	0.124	0.053	0.818
12	83.15 ± 8.24	85.10± 6.48	87.00± 07.21	0.372	0.022	0.285
14	82.10 ± 8.52	86.10± 08.05	85.75± 08.63	0.024	0.032	0.859
16	80.70 ± 7.23	85.85± 7.10	86.10± 08.93	0.002	0.004	0.892
18	79.65 ± 7.36	87.80± 6.44	87.70± 6.41	<0.001	<0.001	0.939
20	82.25 ± 8.14	87.25± 7.37	88.05± 6.38	0.008	0.001	0.617
25	85.85 ± 8.74	88.60± 7.06	89.60± 05.83	0.113	0.018	0.494
30	80.25 ± 03.92	86.60± 8.38	87.35± 06.95	<0.001	<0.001	0.629

The number of patients who received bolus drugs were comparable in all three groups**.** In Group P, 47.06% (16) of patients required one bolus, 32.36% (11) required two boluses, and 20.58% (7) required three boluses; in Group E, 47.06% (16) of patients required one bolus, 29.41% (10) two boluses, and 23.53% (8) three boluses; whereas Group M required one bolus in 44.12% (15), two boluses in 35.29% (12), and three in 20.59% (7). No statistically significant differences were observed among groups (χ^2 test, p-value >0.05) [Table-5].

In Group P, five patients developed bradycardia following the drug bolus at 4 and 6 minutes, a finding not observed in the other groups. Additionally, six patients in Group E and four patients in Group M experienced intraoperative nausea during episodes of hypotension. There were no shivering cases in any groups. There was no significant difference in APGAR score, all three groups had a mean APGAR score of more than 7.

Table 5:Number of patients receive bolus drug among the three groups

No. of bolus received	Group P(n=34)	Group E(n=34)	Group M(n=34)
Bolus 1	16(47.06%)	16(47.06%)	15(44.12%)
Bolus 2	11(32.36%)	10(29.41%)	12(35.29%)
Bolus 3	7(20.58%)	8(23.53%)	7(20.59%)

Discussion

Spinal anesthesia is the preferred option for cesarean delivery as it offers effective muscular relaxation and sensory blockade with less physiological impact than general anesthesia [11-12]. Cesarean section is arguably the most executed surgery in modern medicine [13]. One of the challenges with spinal anesthesia is the risk of inducing hypotension which is commonly seen due to sympathetic blockade coupled with vasodilation. This is particularly challenging for both the mother and fetus if not appropriately treated [14,15,16]. While the practice of pre-loading with intravenous fluids remains commonplace, the strategy often falls short and therefore, vasopressors alongside fluids provide stronger results [17].

Vasopressors are nowadays becoming one of the mainstays of management of spinal hypotension. Prophylactic use of vasopressors, intramuscular and subcutaneous routes rule out

the possibility of dose titration and may result in either inadequate treatment or more seriously hypertension. Intravenous infusion and bolus of vasopressors have the advantage of side-to-side monitoring of patient response, better flexibility and greater margin of safety. However, infusions have been associated with a large amount of drug used, increasing the possibility of side effects and toxicity. Various vasopressors are available for counteracting spinal hypotension, each with a different pharmacological profile [4,17]. The current study was undertaken to compare the efficacy of IV bolus Phenylephrine, Ephedrine and Mephentermine for maintenance of blood pressure following spinal anesthesia in caesarean section. We chose an equipotent dose of Phenylephrine 100mcg, Ephedrine 6mg and Mephentermine 6mg in our study.

In our study, a fair comparison was ensured by the groups having similar demographic characteristics, including age, height, weight, parity, and duration of surgery. As expected, the initial blood pressure in all groups declined significantly following spinal anesthesia. However, after administration of the respective study medications, blood pressure returned to normal in all three groups.

Phenylephrine resulted in a marked increase in systolic blood pressure at 4, 6, and 8 minutes, more than Ephedrine and Mephentermine, also keeping the diastolic pressures significantly elevated at 4 and 6 minutes. These findings correlate with the works of Mohammad A et al. [1], Sonika S et al. [8], and Dua D et al. [18], who had shown that Phenylephrine, a pure α-adrenergic agonist, is characterized by a very rapid peak effect within one minute, with sharp peripheral vasoconstriction and effective restoration of vascular tone. On the other hand, Ephedrine and Mephentermine, both mixed α and β agonists with some indirect sympathomimetic activity, have slower onsets of action (2–5 minutes for Ephedrine and about 5 minutes for Mephentermine), relying on the release of endogenous catecholamines, which likely accounts for the slower pressor action.

In the present study, heart rate increased in all three groups at the onset of hypotension, with mean values of 85.6, 87.3, and 87.8 beats per minute, respectively. Following administration of the study drugs, a highly significant reduction in heart rate ($p < 0.001$) was observed in Group P at 4, 6, 18, and 30 minutes when compared with Groups M and E. At the remaining time intervals, the differences were not statistically significant. These findings are consistent with those reported by Lonkar et al. [19] and Bhattarai et al. [11], as well as with other research demonstrating the heart rate–lowering effect of phenylephrine in obstetric patients [6,14,20,21].

This is probably due to beta beta-adrenergic effect of Ephedrine and Mephentermine which the Phenylephrine lacks. In spinal anesthesia, since there is decreased venous return, decreased venous pressure and a decreased right heart pressure thus slowing of the heart rate is expected based on the Brain-bridge reflex [19]. Bradycardia is also expected in high spinal, probably due to some paralysis of the cardiac accelerator nerve [11,19]. Bradycardia in the Phenylephrine group was effectively managed with atropine and did not result in adverse outcomes.

The requirement for additional repeat bolus doses was similar across the three groups in our study, as observed by Mohammad A et al. [1] and DuaD et al. [18], indicating that the duration of action for each vasopressor within this dosing regimen is roughly equivalent. Larger doses of Ephedrine are associated with maternal symptoms like tachycardia and nausea and vomiting as reported by many authors [22,23]. Intraoperative nausea was observed more frequently in the Ephedrine and Mephentermine groups in this study, an observation correlating with Lonkar S et al. [19] possibly due to increase β adrenergic activity and the subsequent tachycardia.

Outcomes for newborns evaluated with Apgar scores at 1 and 5 minutes showed comparable scores across all groups and a mean score greater than 7 which suggests no clinically significant compromise. These findings are consistent with prior literature done by Mohammad A et al. [1], Sonika S et al. [8] and Dua D et al. [19] which showed that small incremental bolus doses of Phenylephrine, Ephedrine, or Mephentermine are safe for the fetus when used to manage spinal anesthesia-induced hypotension during caesarean sections. While studies done by Cooper DW et a. [23] and Lonkar Set al. [19] proposed a link between the use of Ephedrine and lower pH of the umbilical artery, this effect is dose-dependent and not seen at the doses used in our study.

Conclusion

This study evaluated intravenous bolus doses of Phenylephrine, Ephedrine, and ephentermine for managing spinal anesthesia–induced hypotension during cesarean section. All three effectively restored blood pressure. Phenylephrine produced the most rapid hemodynamic correction but tended to lower heart rate, whereas Ephedrine and Mephentermine maintained heart rate more effectively but were associated with greater intraoperative nausea. Repeat bolus requirements and Apgar scores were comparable among the groups. Overall, Phenylephrine is preferred for rapid stabilization, with careful heart rate monitoring.

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Conflict of interest: None

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