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Original Article

Anaesthesia Section

Mephentermine vs. Phenylephrine for Prevention and Management of Maternal Hypotension during Caesarean Section under Spinal Anaesthesia and their Effects on Foetal Outcome- A Randomised Control Trial

SRINIVASAN DIVYABHARATHI[1], SINAM NEETU DEVI[2], JONAN PUNI KAY[3], RAKESH NONGTHOMBAM[4], BALUSAMY DEVANATHAN[5], LAKSHMINARAYANAN SOWRIRAJAN[6], ADEENPA CHARA[7], NAVANEETHA PRIYA NANDINIE[8]

ABSTRACT

Introduction: For the best maternal and foetal outcome during caesarean section under spinal anaesthesia, maintaining Systolic Blood Pressure (SBP) at 100% of the baseline is necessary. Mephentermine and Phenylephrine are both sympathomimetic drugs used for timely correction of maternal hypotension.

Aim: To compare the effect of intravenous bolus administration of mephentermine and phenylephrine for prevention and management of maternal hypotension and to evaluate the foetal outcome.

Materials and Methods: In this randomised double-blinded controlled trial, a total of 150 American Society of Anaesthesiologist (ASA) II scheduled for elective Lower Segment Caeserean Section (LSCS) were randomly allocated into three groups to receive the study drugs: group A received mephentermine 6 mg in 2 mL Normal Saline (NS), group B received phenylephrine 100 mcg in 2 mL NS, and group C received 2 mL NS immediately following sub-arachnoid block. Whenever hypotension occurred (Systolic Blood Pressure (SBP) <90 mm Hg) rescue boluses were given. Maternal haemodynamic parameters, umbilical cord blood gases, and complications were recorded from the time of sub-arachnoid block till the end of surgery.

Results: There was no significant difference in the maternal haemodynamics and neonatal outcome among the three groups. It was observed that phenylephrine had quick peak effect, higher foetal umbilical pH and better neonatal outcome though statistically insignificant. Incidence of significant bradycardia (16%) and absence of intraoperative nausea and vomiting were also reported among group B. None of the neonate had APGAR (Appearance, Pulse, Grimace, Activity, and Respiration) score <7 and the umbilical pH was comparable in all the three groups (p >0.05). The time of first rescue vasopressor and the total volume of requirement was earlier and higher in group C with the mean timing of 5.87±4.37 min and mean volume of 2.68±1.58 mL, respectively.

Conclusion: There was a significant improvement of arterial blood pressures and better neonatal outcome observed when phenylephrine (100 mcg) and mephentermine (6 mg) are given as a prophylactic intravenous (i.v.) bolus dose immediately after subarachnoid block; especially in the initial time period between skin incision and delivery of the baby. When given as a prophylactic i.v. bolus, it had the advantage of lesser total dose requirement of the vasopressor used and better haemodynamic maintenance till the delivery of the baby.

Keywords: Blood pressure, Elective procedure, Prophylactic bolus, Sub-arachnoid block, Vasopressors

INTRODUCTION

Single shot spinal anaesthesia is by far the most common method of anaesthesia for elective and emergency caesarean section. Despite the many advantages offered by subarachnoid block for caesarean deliveries, one most common complication is development of hypotension. Hypotensive effects of sympathectomy after neuraxial anaesthesia are compounded by the physiological changes of pregnancy especially compression of the vena cava by gravid uterus. This being a detrimental condition to the mother and foetus, maintenance of maternal blood pressure to baseline is necessary to give the best outcome for both the mother and the baby [1].

For timely correction of maternal hypotension, uses of vasopressors are warranted. Numerous vasopressors have been studied viz; Ephedrine, Mephentermine, Methoxamine, Metarminol, Phenylephrine etc. for correction of maternal hypotension. Mephentermine is a direct and indirectly acting sympathomimetic drug with both alpha and beta adrenergic agonistic action. This increases both systolic and diastolic pressures by augmenting the cardiac output and increase in peripheral vascular resistance [2]. Literature mentions only few studies [3,4] in pregnant women that compared mephentermine and other vasopressors for management of spinal anaesthesia induced hypotension in obstetric patients.

Phenylephrine is a directly-acting sympathomimetic drug and a selective alpha-1 adrenergic agonist [5,6]. This increases systolic blood pressure by peripheral vasoconstriction and causes baroreceptor-mediated reflex bradycardia in a dose dependent manner [7]. Over the last two decades, evidences have been generated based on well-designed, randomised trials in Europe, United States and Asia [8-10], supporting the proposition that phenylephrine is as safe and effective as and probably preferable to traditionally used ephedrine for the treatment or prevention of hypotension during caesarean section. Few studies compared prophylactic infusions of phenylephrine with other vasopressors (metarminol, ephedrine) for prevention of maternal hypotension [11,12]. Another study [13], that compared phenylephrine infusion versus bolus regimens concluded that the infusion regimen required a higher total dose of phenylephrine to maintain maternal arterial blood pressure.

Therefore, the present study was designed in which the administration of study drugs or vasopressor was given intravenously soon after the establishment of spinal subarachnoid block even before

the development of hypotension as prophylactic bolus dose and then a rescue bolus was given, whenever hypotension occurred. The primary outcome was to compare the effect of prophylactic i.v. bolus administration of mephentermine and phenylephrine in the prevention and management of maternal hypotension during caeserean delivery under spinal anaesthesia. The seconday outcome was to study the effect on the foetal outcome and the incidence of any (maternal) adverse outcome.

MATERIALS AND METHODS

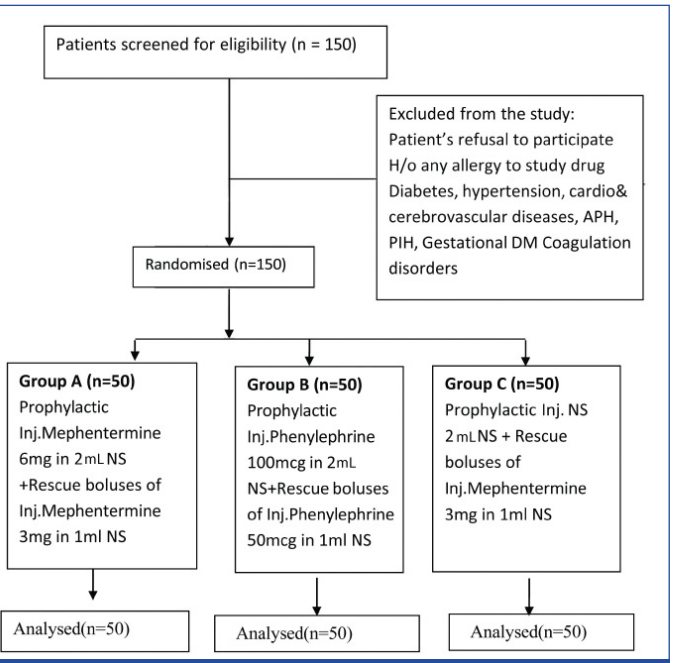
This double-blinded randomised control trial was conducted in the Department of Anaesthesiology, Jawaharlal Nehru Institute of Medical Sciences, Imphal, Manipur, India. Institutional Ethical Committee (IEC) had approved the study (Protocol No. 181/4/PGT-2019). Patients undergoing elective caesarean section under spinal anaesthesia were enrolled.

Inclusion criteria: Patients having American Society of Anaesthesiologists (ASA), physical status II, aged 18- 40 years were included in the study after giving written informed consent.

Exclusion criteria: Those patients with history of any allergy to study drugs, known case of uncontrolled diabetes, hypertension, cardiovascular diseases, severe anaemia, cerebrovascular diseases, Body Mass Index (BMI) >30 kg/m^2, obstetric complications like antepartum haemorrhage, pregnancy-induced hypertension, gestational diabetes mellitus, foetal malformations and malpresentations, cord prolapse, patients with autonomic neuropathy, spinal deformities, neurological diseases, skin sepsis in lumbar area, coagulation abnormalities, hypovolaemia due to any cause were excluded from the study.

Sample size calculation: Based on a published study [14], the mean systolic blood pressure of three study groups were considered as- 120.3±13.5 mm Hg, 111.9±11 mm Hg and 114.9±10.0 mm Hg. At an estimated effect size at the power of 90% and α value of 0.05, the calculated sample size was found to be 46 in each group. Finally, 50 participants were enrolled in each group.

A total of 150 patients were randomised in the trial and allocated to three groups to receive the study drugs: A, B and C of 50 patients each, following a restricted block randomisation with a block size of 6 [Table/Fig-1].



[Table/Fig-1]: CONSORT flowchart.
Inj.: Injection; NS: Normal saline; H/o: History of; APH: Antepartum haemorrhage; PIH: Pregnancy-induced hypertension; DM: Diabetes mellitus

Study Procedure

Preanaesthetic check-up was done in all the patients. Detailed history, physical examination and baseline investigations were done. All patients were kept nil per oral for atleast 8 hrs before the surgery. Premedication given with Tablet (Tab) Ranitidine 150 mg the night before surgery. An 18 Gauge (G) cannula was secured in non-dominant hand and preloaded with intravenous (i.v.) Ringer lactate solution at 20 mL/kg over 15 minutes (mins). Heart Rate (HR), Systolic and Diastolic Blood Pressure were recorded thrice and the middle value was taken as baseline value before giving spinal anaesthesia in operation theatre. Standard monitoring was done with Non Invasive Blood Pressure, Continuous Electrocardiography (ECG) and Pulse oximetry. Intravenous injection (inj.) Ondansetron 4 mg was given. Subarachnoid block was performed under strict aseptic precautions using a 25G Quinke Babcock needle at Lumbar (L)3-L4 interspace in left lateral position using a standard midline approach. Once free flow of cerebrospinal fluid is obtained, hyperbaric Inj. Bupivacaine 0.5% 2 mL was injected over 10-15 seconds (secs). Patient turned supine and a wedge was placed under the right flank.

One of the study drugs was injected intravenously soon after giving spinal anaesthesia as specified in the group allocation mentioned as follows:

- Group A- prophylactic intravenous bolus of Mephentermine 6 mg in 2 mL NS immediately after intrathecal block and intermittent rescue boluses of 3 mg Mephentermine in 1 mL NS,
- Group B- prophylactic intravenous bolus of Phenylephrine 100 mcg in 2 mL NS immediately after intrathecal block and intermittent rescue boluses of 50 mcg Phenylephrine in 1 mL NS,
- Group C- prophylactic intravenous bolus of normal saline 2 mL immediately after intrathecal block and intermittent rescue bolus of Mephentermine 3 mg in 1 mL NS.

Rescue boluses (therapeutic) of Mephentermine and Phenylephrine were given intravenously, whenever there was a fall in systolic blood pressure <90 mm Hg or fall more than 20% of baseline. All the study drugs were prepared by the chief investigator in a 2 mL syringe with equal volume. To double-blind the study, the anaesthesiologist and the patients who participated in the study were blinded to the study drug.

Heart rate, systolic and diastolic blood pressure, and peripheral oxygen saturation (SpO_2) were recorded immediately after spinal anaesthesia (0 min), then at every 3 mins for maximum up to 15 mins, and then every 5 mins till the end of the surgery. Whenever hypotension occurred, one of the study drugs was given i.v. as rescue boluses as per the group allocation. The total number of rescue boluses, and the time at which the first rescue bolus was given were noted. Whenever bradycardia (HR <60/min) occurred, Inj. Atropine 0.3 mg i.v. was given. After delivery of the baby, Inj.Oxytocin 10U slow IV in 500 mL Ringer lactate and 10U Intramuscular (IM) was given. The Appearance, Pulse, Grimace, Activity, and Respiration (APGAR) scores of the baby at 1 min and 5 min after delivery was assessed and umbilical arterial blood sample from a segment of clamped umbilical cord in heparinised syringe was taken and analysed using a blood gas analyser. Occurrence of any adverse effects on the mother and foetus was noted particularly bradycardia, nausea and vomiting.

STATISTICAL ANALYSIS

The data collected was then analysed using Statistical Package for Social Sciences (SPSS) Incorporation (Inc.). Chicago 2, United States of America (USA) window based version 22.0, and interpreted using one-way Analysis of Variance (ANOVA) test. All tests were considered significant at p<0.05.

RESULTS

The demographic profile including age and weight were similar among all the three groups [Table/Fig-2].

Primary outcome measures: Baseline SBP, Diastolic Blood Pressure (DBP), Mean Arterial Pressure (MAP) and HR were comparable among all the three groups. The rise of systolic blood pressure,

Parameters	Group A	Group B	Group C	p-value
	Mean±SD			
Age (in years)	29.22±4.29	29.78±4.76	29.88±4.67	0.740
Weight (in kg)	60.82±7.61	64.38±10.27	61.92±5.54	0.080

[Table/Fig-2]: Demographic profile: N=50 in each group.

diastolic blood pressure and mean arterial pressure after prophylactic study drug injection were all lesser in Group C as compared to Group A and B at 3 min with p<0.001 (one way ANOVA). On intergroup comparison (post hoc), Group B had higher mean SBP, DBP and MAP compared to Group A, but found to be statistically insignificant at 3 min. Though statistically insignificant, mean value of all the arterial pressures remained comparatively higher during the initial time period after subarachnoid block and prophylactic study drug injection (upto 9 mins) in Group B [Table/Fig-3-5].

SBP at different time intervals in minutes	Mean±SD (mm Hg)			p-value (ANOVA)
	Group A	Group B	Group C	
Baseline SBP	124.38±8.69	123.94±11.44	124.14±10.59	0.977
SBP0	125.90±9.76	123.32±11.72	123.64±12.49	0.468
SBP3	119.80±4.56	124.18±14.22	100.68±14.87	**<0.001***
SBP6	108.34±3.98	123.18±21.57	118.62±88.53	0.363
SBP9	106.88±8.89	112.30±9.05	107.74±12.71	0.066
SBP12	106.62±1.04	108.20±8.72	105.22±7.47	0.272
SBP15	104.60±11.13	106.34±10.07	105.14±9.29	0.683
SBP20	108.04±6.55	107.80±10.41	107.96±10.57	0.992
SBP25	110.42±5.20	109.92±10.78	108.84±9.73	0.802
SBP30	110.10±0.66	109.98±14.98	110.04±9.58	0.999
SBP35	111.00±6.86	112.00±10.82	110.36±11.16	0.822
SBP40	108.92±7.97	110.33±15.58	108.80±12.89	0.963
SBP45	103.00±3.08	103.33±6.68	102±0.00	0.911

[Table/Fig-3]: Systolic Blood Pressure (SBP) among the groups.
SBP0 is at the time of injection: bold p-value is significant.
*Significant p-value; A vs B =0.134, A vs C =<0.001, B vs C =<0.001 (Post hoc at 3 min); N=50 in each group

DBP at various time intervals in minutes	Mean±SD (mm Hg)			p-value (ANOVA)
	Group A	Group B	Group C	
Baseline_DBP	77.46±7.13	77.42±9.49	74.32±11.71	0.177
DBP0	77.94±7.29	77.70±9.16	74.68±10.95	0.149
DBP3	73.70±12.89	77.20±11.39	60.40±11.52	**<0.001***
DBP6	65.48±12.84	71.12±14.04	65.76±13.75	0.067
DBP9	63.42±10.57	66.70±11.73	62.74±8.82	0.132
DBP12	63.62±13.25	64.34±8.74	62.88±8.67	0.784
DBP15	60.38±8.27	61.40±9.67	59.82±10.19	0.697
DBP20	62.62±7.52	63.30±9.31	62.20±12.99	0.862
DBP25	63.54±10.62	66.36±11.43	62.16±12.07	0.174
DBP30	65.40±9.92	67.52±12.13	62.08±12.67	0.066
DBP35	65.73±7.86	66.30±8.44	65.27±8.97	0.906
DBP40	63.75±10.10	68.00±13.19	61.90±11.01	0.572
DBP45	57.00±4.79	58.67±5.77	55.00±0.00	0.619

[Table/Fig-4]: Diastolic Blood Pressure (DBP) among the groups.
*DBP0 is Diastolic Blood Pressure at the time of injection; N=50 in each group; *Significant p-value; A vs B=0.145, A vs C=<0.001, B vs C=<0.001 (Post hoc at 3 min); N=50 in each group;* bold p-value is significant

MAP at various times in minutes	Mean±SD (mm Hg)			p-value (ANOVA)
	Group A	Group B	Group C	
Baseline MAP	93.08±6.53	92.62±9.84	90.94±10.65	0.473
MAP0	93.88±6.92	92.22±9.65	90.90±10.43	0.265
MAP3	89.04±12.77	92.86±12.05	73.84±12.06	**<0.001***
MAP6	79.80±12.58	88.48±15.82	83.38±33.31	0.158
MAP9	77.82±9.35	81.55±10.09	77.56±9.33	0.071
MAP12	77.93±11.63	78.68±8.09	76.41±7.95	0.468
MAP15	75.10±7.82	76.12±9.00	74.98±8.84	0.766
MAP20	77.62±6.65	77.82±9.86	77.46±11.89	0.983
MAP25	79.00±11.86	80.68±10.84	77.76±10.67	0.422
MAP30	80.28±9.18	81.86±11.79	78.04±11.08	0.206
MAP35	80.79±7.19	81.53±7.82	80.27±8.76	0.843
MAP40	78.67±9.41	82.17±13.59	77.50±11.01	0.707
MAP45	72.20±3.03	73.67±5.13	71.00±0.00	0.636

[Table/Fig-5]: Mean Arterial Pressure (MAP) among the groups.
bold p-value is significant; *Significant p-value; A vs B=0.112, A vs C=<0.001, B vs C=<0.001 (Post hoc at 3 min); N=50 in each group

Mean heart rate in Group B remained less compared to Group A and Group C till the end of surgery and was statistically significant at 3 mins (p=0.003) [Table/Fig-6].

HR at various time intervals in minutes	Mean±SD (beats/min)			p-value (ANOVA)
	Group A	Group B	Group C	
Baseline HR	93.90±13.40	93.78±11.16	93.82±13.45	0.999
HR0	96.70±12.73	96.36±11.41	95.40±11.76	0.854
HR3	99.34±9.45	90.96±14.83	93.38±11.92	**0.003***
HR6	92.04±10.21	89.08±12.86	91.58±8.87	0.338
HR9	89.64±9.18	87.74±14.60	89.36±11.01	0.688
HR12	87.10±11.45	86.36±9.96	86.48±10.21	0.932
HR15	85.04±10.92	84.52±8.40	83.76±7.24	0.775
HR20	86.32±11.33	85.78±8.79	85.96±8.60	0.960
HR25	86.34±11.18	85.50±7.96	85.94±8.58	0.904
HR30	89.50±10.76	86.34±7.99	87.40±8.61	0.227
HR35	86.81±11.95	85.73±7.96	86.15±8.57	0.919
HR40	86.75±8.83	83.64±9.75	85.89±13.24	0.771
HR45	86.67±10.33	84.83±9.86	85.75±10.99	0.954

[Table/Fig-6]: Comparison of Heart Rate (HR) among the groups.
HR0 is heart rate at the time of injection; *Significant p-value; A vs B=0.001, A vs C=0.007, B vs C=0.371 (Post hoc at 3 min); N=50 in each group

Total volume of rescue boluses used and time at which first rescue bolus given were high and earlier in Group C, when compared to Group A and B (p<0.001) [Table/Fig-7].

Variables	Mean±SD			p-value (ANOVA)
	Group A	Group B	Group C	
Total volume of rescue bolus (mL)	1.53±0.72	1.64±1.75	2.68±1.58	**0.004***
Time to first rescue bolus (mins)	11.63±9.82	16.64±9.13	5.87±4.37	**<0.001***

[Table/Fig-7]: Total volume of drug and time to first rescue bolus.
*Significant p-value in total volume of rescue boluses amongst groups; A vs B=0.800, A vs C=0.003, B vs C=0.012 (Post hoc); *Significant p-value for Time to first rescue boluses amongst groups A vs B=0.066, A vs C=0.013, B vs C=<0.001 (Post hoc)

Secondary outcome measures: On comparison of maternal complications, Incidence of bradycardia (n=8, 16%) was high in Group B but none of them had nausea or vomiting. Incidence of tachycardia (>100 bpm) was higher in Group A (n=42) and nausea or vomiting was found to be higher in Group C (n=10, 20%) when compared among the three groups [Table/Fig-8].

Complications	Group A (n)	Group B (n)	Group C (n)
Bradycardia	0	8 (16%)	0
Nausea/Vomiting	2 (4%)	0	10 (20%)
Shivering	3 (6%)	0	4 (8%)
Tachycardia	42 (84%)	28 (56%)	29 (58%)
Hypotension	15 (30%)	17 (34%)	31 (62%)

[Table/Fig-8]: Maternal side-effects among the three groups (N=50 in each group).
*Hypotension- Absolute value of SBP <90 mmHg

APGAR scores at 1 and 5 min of birth and foetal umbilical cord arterial blood gas values differed insignificantly in all the three groups [Table/Fig-9].

Parameters	Mean±SD			p-value (ANOVA)
	Group A	Group B	Group C	
APGAR-1min	8.90±0.36	8.90±0.30	8.94±0.24	0.753
APGAR-5min	8.98±0.14	9.00±0.00	8.98±0.14	0.370
pH	7.32±0.06	7.33±0.55	7.31±0.04	0.442
$PaCO_2$ (mm Hg)	42.23±4.72	42.59±9.24	42.12±7.60	0.947
HCO_3 (mEq/L)	22.61±2.09	24.39±744	22.55±1.27	0.071
Base excess (mEq/L)	-4.31±0.51	-4.32±0.53	-4.22±0.47	0.537
PaO_2 (mm Hg)	18.00±1.29	17.87±1.57	18.02±1.15	0.474

[Table/Fig-9]: APGAR (Appearance, Pulse, Grimace, Activity, and Respiration) scores and foetal umbilical arterial cord blood analysis among the three groups.

DISCUSSION

Haemodynamic changes in the form of hypotension following subarachnoid block during Cesarean section is the most common unwanted finding which, if not appropriately intervened, has hazardous consequences in vital organ perfusion in the parturient and foetal placental perfusion [15,16]. The choice of vasopressors for obstetrics is guided indirectly by foetal acid base status as there is absence of definitive evidence showing absolute clinical benefit of one over the other. Mephentermine and phenylephrine are commonly used vasopressors in obstetric anaesthesia. In this study, with the prophylactic intravenous administration of study drugs after sub-arachnoid block, prophylactic normal saline (group C) had significantly higher incidence of hypotension than prophylactic phenylephrine (group B) and prophylactic mephentermine (group A).

While evaluating the haemodynamic changes among the study groups, mean value of systolic pressure, diastolic pressure and mean arterial pressure showed a decrease from the baseline after subarachnoid block throughout the observation period. However the blood pressures were better controlled in phenylephrine group B (100 mcg prophylactic and 5 mcg rescue bolus) followed by mephentermine group A (6 mg prophylactic and 3 mg rescue bolus) and prophylactic normal saline group C (2 mL normal saline as prophylaxis and mephentermine 3 mg rescue bolus) particularly at third minute observation ($p<0.001$). In a previous study by Lakshmi Mahajan et al., [16]. Phenylephrine group was found to have significantly higher blood pressure and more closely meets the criteria for its use as vasopressor in obstetric anaesthesia.

During the entire observation period, phenylephrine group B had maintained systolic pressure, diastolic pressure and mean arterial pressure than mephentermine group A and prophylactic normal saline group C; especially at the initial time period after prophylactic study drug administration, thereafter all were found decreased during the subsequent observation period. This may be explained by the short onset and duration of action of phenylephrine [17-21]. Thus, prophylactic phenylephrine bolus administration is comparatively superior to mephentermine and normal saline in the present study though both mephentermine and phenylephrine effectively maintained arterial blood pressures after prophylactic intravenous bolus for prevention of maternal hypotension.

Mean heart rate decreased in phenylephrine Group B throughout the observation from baseline and was statistically significant at third minute ($p=0.003$) when compared with mephentermine group A and prophylactic normal saline group C. Mudiganti RKR et al., [21]. reported that the occurrence of reflex bradycardia due to bolus intravenous injection of phenylephrine is dose dependent, which is mostly found to occur in those who received 100 mcg. In the present study, 100 mcg phenylephrine was used and reflex bradycardia significantly in phenylephrine group B (16%) and required atropine administration ($p<0.001$), where phenylephrine was used both as a prophylactic study drug as well as rescue bolus. Lee HM et al., [22] and Kamalakanan M et al., [23] reported the similar occurrence of bradycardia and use of atropine in their studies. As it is reported that the incidence of hypertension and bradycardia are dose-dependent, the use of 100 mcg phenylephrine in the present study did not manifest any harmful clinical outcome. Therefore, considering the variable dose-effects of phenylephrine [24] there still exists the need to study the drug in a large number of subjects to ascertain the dose-effect relationship of this reflex bradycardia, which was of proven benefit among the patients having tachycardia.

There should be an appropriate timing of hypotension correction by vasopressors in order to avoid adverse physiological insult to parturients and for foetal well-being. In the present study, the time of first rescue vasopressor used was earlier in prophylactic normal saline group C (5.87±4.37 min) after the subarachnoid block which was quite early when compared to prophylactic mephentermine group A and phenylephrine group B ($p<0.001$).There is scarcity of literature data comparing the timing of vasopressor requirement among the study groups.

The amount of vasopressor administered prior to delivery of the baby is an important determinant of cord gases and foetal acidosis [25]. In the present study, prophylactic normal saline group C required more amount of the rescue vasopressor used when compared to prophylactic mephentermine group A and phenylephrine group B. Thus, the total volume or dose of the vasopressor requirement was significantly lesser when the prophylactic intravenous bolus dose of vasopressor (with both phenylephrine and mephentermine) was given immediately after the subarachnoid block.

It is well established that the neonatal outcome can be assessed using Apgar score at 1 and 5 minute and umbilical cord blood pH values at the time of delivery. Vasopressors used to manage spinal anaesthesia induced hypotension may alter metabolic effect of the foetus due to the placental crossing of the drug used. In the present study, Apgar score at 1 and 5 min and the foetal umbilical arterial blood gas values in all the three groups were maintained within the normal range which was similarly reported in the previous studies [26].

Some of the adverse effects like nausea, vomiting and shivering can be seen as findings in caesarean section under subarachnoid block due to hypotension [27,28]. In the present study, these were more common in prophylactic normal saline group C which might be due to the cerebral and gut hypoperfusion following hypotension that stimulated the vomiting centre in the brainstem and causes serotonin release, respectively.

Limitation(s)

Height and habitus of the patient were not considered as a criteria and peri-operative fluid status was not recorded, which may have an impact on haemodynamic parameters.

CONCLUSION(S)

There was a significant improvement of arterial blood pressures and better neonatal outcome when phenylephrine (100 mcg) and mephentermine (6 mg) were given as a prophylactic intravenous bolus dose immediately after subarachnoid block; especially during the initial time period between skin incision and delivery of the baby, which has the advantage of lesser total dose requirement of the vasopressors used and better haemodynamic maintenance till delivery of the baby.

REFERENCES

[1] Lonkar SS, Khatavkar SS, Thatte WS, Santhi N. Comparison between phenylephrine, ephedrine and mephentermine in preventing hypotension during spinal anaesthesia for caesarean section and their effect on fetal outcome. IOSR J Dent Med Sci (IOSR-JDMS). 2016;15(9):52-58.

[2] Nag DS, Samaddar DP, Chatterjee A, Kumar H, Dembla A. Vasopressors in obstetric anesthesia: A current perspective. World Journal of Clinical Cases: WJCC. 2015;16;3(1):58.

[3] Mohta M, Janani SS, Sethi AK, Agarwal D, Tyagi A. Comparison of phenylephrine hydrochloride and mephentermine sulphate for prevention of post spinal hypotension. Anaesthesia. 2010;65(12):1200-05.
[4] Kansal A, Mohta M, Sethi AK, Tyagi A, Kumar P. Randomised trial of intravenous infusion of ephedrine or mephentermine for management of hypotension during spinal anaesthesia for Caesarean section. Anaesthesia. 2005;60(1):28-34.
[5] Kaur D, Khan AL, Pathak A. A comparative study of three vasopressors for maintenance of blood pressure during spinal anesthesia in lower abdominal surgeries. Anesthesia, Essays and Researches. 2018;12(2):333-337.
[6] Singh R, Verma R, Bhatia VK, Chaudhary AK, Chandra G. A comparative study of phenylephrine and ephedrine combination to ephedrine and phenylephrine alone for maintenance of blood pressure for caesarean delivery and their effects on foetal acid base status. Journal of Obstetric Anaesthesia and Critical Care. 2018;8(1):29-34.
[7] Gupta S. Vasopressors and tight control of maternal blood pressure during cesarean delivery: A rocky alliance. Journal of Anaesthesiology, Clinical Pharmacology. 2013;29(1):01-03.
[8] Ganeshanavar A, Ambi US, Shettar AE, Koppal R, Ravi R. Comparison of bolus phenylephrine, ephedrine and mephentermine for maintenance of arterial pressure during spinal anaesthesia in caesarean section. Journal of Clinical and Diagnostic Research. 2011;5(5):948-52.
[9] Nazir I, Bhat MA, Qazi S, Buchh VN, Gurcoo SA. Comparison between phenylephrine and ephedrine in preventing hypotension during spinal anesthesia for cesarean section. Journal of Obstetric Anaesthesia and Critical Care. 2012;2(2):92.
[10] Lee A, Kee WD, Gin T. A quantitative, systematic review of randomized controlled trials of ephedrine versus phenylephrine for the management of hypotension during spinal anesthesia for cesarean delivery. Anesthesia & Analgesia. 2002;94(4):920-26.
[11] McDonnell NJ, Paech MJ, Muchatuta NA, Hillyard S, Nathan EA. A randomised double-blind trial of phenylephrine and metaraminol infusions for prevention of hypotension during spinal and combined spinal-epidural anaesthesia for elective caesarean section. Anaesthesia. 2017;72(5):609-17.
[12] Jain K, Makkar JK, Gander S, Kumar P. A randomized trial comparing prophylactic phenylephrine and ephedrine infusion during spinal anesthesia for emergency cesarean delivery in cases of acute fetal compromise. Journal of Clinical Anesthesia. 2016;34:208-15. Doi: 10.1016/j.jclinane.2016.03.015. Epub 2016 May 12.
[13] Doherty A, Ohashi Y, Downey K, Carvalho JC. Phenylephrine infusion versus bolus regimens during cesarean delivery under spinal anesthesia: A double-blind randomized clinical trial to assess hemodynamic changes. Anesthesia & Analgesia. 2012;115(6):1343-50.
[14] Sahu D, Kothari D, Mehrotra A. Comparison of bolus phenylephrine, ephedrine and mephentermine for maintenance of arterial pressure during spinal anaesthesia in caesarean section-A clinical study. Indian J Anaesth. 2003;47(2):125-28.
[15] Corke BC, Datta S, Ostheimer GW, Weiss JB, Alper MH. Spinal anaesthesia for caesarean section: The influence of hypotension on neonatal outcome. Anaesthesia. 1982;37(6):658-62.
[16] Mahajan L, Anand LK, Gombar KK. A randomized double-blinded comparison of ephedrine, phenylephrine and mephentermine infusions to maintain blood pressure during spinal anaesthesia for cesarean delivery: The effects on fetal acid-base status and haemodynamic control. Journal of Anaesthesiology Clinical Pharmacology. 2009;25(4):427-32.
[17] Cooper DW, Sharma S, Orakkan P, Gurung S. Retrospective study of association between choice of vasopressor given during spinal anaesthesia for high-risk caesarean delivery and fetal pH. International Journal of Obstetric Anesthesia. 2010;19(1):44-49.
[18] Savanth Kumar P, Nikilesh Kumar GS. Comparing effect of phenylephrine and ephedrine in patients undergoing lower segment caesarean section under spinal anaesthesia. MedPulse International Journal of Anesthesiology. 2017;3(1):43-47.
[19] Chaturvedi NK, Panigrahi MR, Mukhopadhyay B, Biswas BK. Efficacy and safety of intravenous phenylephrine and mephentermine for management of hypotension during spinal anaesthesia: A single blind prospective and comparative study among patients undergoing cesarean section. Indian Journal of Clinical Anaesthesia. 2020;7(1):177-81.
[20] Bhattarai B, Bhat SY, Upadya M. Comparison of bolus phenylephrine, ephedrine and mephentermine for maintenance of arterial pressure during spinal anesthesia in cesarean section. JNMA; Journal of the Nepal Medical Association. 2010;49(177):23-28.
[21] Mudiganti RKR, Rajkumar J, Subhash AT. Comparison of bolus intravenous ephedrine and phenylephrine for maintenance of arterial blood pressure in caesarean section during spinal anaesthesia. J Evid Based Med Healthc. 2016;3(19):792-97.
[22] Lee HM, Kim SH, Hwang BY, Yoo BW, Koh WU, Jang DM, et al. The effects of prophylactic bolus phenylephrine on hypotension during low-dose spinal anesthesia for cesarean section. International Journal of Obstetric Anesthesia. 2016;25:17-22. Doi: 10.1016/j.ijoa.2015.08.009. Epub 2015 Aug 15.
[23] Kamalakanan M, Anandhalakshmi D. Comparative effect of ephedrine, mephentermine and phenylephrine during spinal anaesthesia. Annals of International Medical and Dental Research. 2017; 3(3):58-64.
[24] Allen TK, George RB, White WD, Muir HA, Habib AS. A double-blind, placebo-controlled trial of four fixed rate infusion regimens of phenylephrine for hemodynamic support during spinal anesthesia for cesarean delivery. Anesthesia & Analgesia. 2010;111(5):1221-29.
[25] Shah PJ, Agrawal P, Beldar RK. Intravenous norepinephrine and mephentermine for maintenance of blood pressure during spinal anaesthesia for caesarean section: An interventional double-blinded randomised trial. Indian Journal of Anaesthesia. 2020;64(Suppl 4):S235.
[26] Ngan Kee WD, Khaw KS, Lau TK, Ng FF, Chui K, Ng KL. Randomised double-blinded comparison of phenylephrine vs ephedrine for maintaining blood pressure during spinal anaesthesia for non-elective Caesarean section. Anaesthesia. 2008;63(12):1319-26.
[27] Tarkkila PJ, Kaukinen S. Complications during spinal anesthesia: A prospective study. Regional Anesthesia and Pain Medicine. 19911;16(2):101-06.
[28] Balki M, Carvalho JC. Intraoperative nausea and vomiting during cesarean section under regional anesthesia. International Journal of Obstetric Anesthesia. 2005;14(3):230-41.

PARTICULARS OF CONTRIBUTORS:
1. Postgraduate Trainee, Department of Anaesthesiology and Critical Care, Jawaharlal Nehru Institute of Medical Sciences, Imphal, Manipur, India.
2. Senior Resident, Department of Anaesthesiology and Critical Care, Jawaharlal Nehru Institute of Medical Sciences, Imphal, Manipur, India.
3. Assistant Professor, Department of Anaesthesiology and Critical Care, Jawaharlal Nehru Institute of Medical Sciences, Imphal, Manipur, India.
4. Associate Professor, Department of Anaesthesiology and Critical Care, Jawaharlal Nehru Institute of Medical Sciences, Imphal, Manipur, India.
5. Postgraduate Trainee, Department of Anaesthesiology and Critical Care, Jawaharlal Nehru Institute of Medical Sciences, Imphal, Manipur, India.
6. Postgraduate Trainee, Department of Anaesthesiology and Critical Care, Jawaharlal Nehru Institute of Medical Sciences, Imphal, Manipur, India.
7. Postgraduate Trainee, Department of Anaesthesiology and Critical Care, Jawaharlal Nehru Institute of Medical Sciences, Imphal, Manipur, India.
8. Postgraduate Trainee, Department of Anaesthesiology and Critical Care, Jawaharlal Nehru Institute of Medical Sciences, Imphal, Manipur, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Rakesh Nongthombam,
Associate Professor, Department of Anesthesiology and Critical Care, Jawaharlal Nehru Institute of Medical Sciences, Porompat, Imphal-795005, Manipur, India.
E-mail: kanglanong@gmail.com

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