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COMPARATIVE EVALUATION OF HAEMODYNAMIC CHANGES ON USING PROPHYLACTIC INFUSION OF EPHEDRINE ALONE VERSUS EPHEDRINE PLUS PHENYLEPHRINE IN CAESAREAN SECTION UNDER SPINAL ANAESTHESIA

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ABSTRACT: PURPOSE: Prophylactically administered Ephedrine either in bolus doses or by infusion helps to counteract hypotension following subarachnoid block during caesarean section. Clinical experience suggests that Phenylephrine added to Ephedrine increases the α/β -agonist activity ratio; there by preventing spinal anaesthesia induced vasoplegia. Hence we took up this study to compare the effect of prophylactic IV infusion of Ephedrine alone versus Ephedrine plus Phenylephrine in caesarean section under spinal anaesthesia for preventing maternal hypotension, nausea, vomiting and neonatal outcome using APGAR score. **METHODS:** In a randomized double blind fashion, 60 parturient with ASA grade I-II, scheduled for caesarean section were preloaded with ringer lactate of 15 ml/kg. Subarachnoid block was performed with 10 mg hyperbaric Bupivacaine, infusion started with 2mg/min Ephedrine alone (Group-E) or in combination with 10 μ g/min Phenylephrine (Group-E+P) Haemodynamic variables were recorded at regular intervals. The infusion rate was controlled using a predefined algorithm. Hypotension was treated with Ephedrine bolus doses. **RESULTS:** Incidence of hypotension were less in the Group (E+P) 10% as compared to Group (E) 33.66% with a P-value of <0.05. Total requirement of ephedrine was more in group (E) (42.73 $\pm$ 4.40mg) as compared to Group (E+P) (24.2 $\pm$ 4.09mg) which was statistically significant (P<0.001). Incidence of nausea and vomiting were less in group (E+P) with P-value of 0.04. APGAR scores were comparable in both the groups. **CONCLUSION:** Phenylephrine added to Ephedrine infusion decreases the incidence of hypotension, nausea & vomiting.

KEYWORDS: Ephedrine, Phenylephrine, Hypotension, Nausea & vomiting.

INTRODUCTION: Delivering safe anesthesia with highest degree of care is a challenging task for an anesthesiologist. We must ensure safe conduct of anaesthesia for both mother and foetus. Spinal anaesthesia is the most preferred technique for caesarean section among anaesthesiologists because of its ease of performance and reliability. However, occurrence of hypotension following subarachnoid block produces unpleasant maternal symptoms like nausea, emesis and light headedness^{1,2} which is exacerbated in pregnancy by gravid uterus.

Various methods followed to prevent post spinal hypotension in caesarean section are, left uterine displacement, leg elevation, compression bandage, intra vascular volume expansion by preloading with fluids – colloids, crystalloids and vasopressors.^{3,4} The vasopressors have been found to be effective in preventing and treating post spinal hypotension. The various vasopressors used are Ephedrine, Phenylephrine, Mephentermine, Metaraminol, Methoxamine, Dopamine, Dobutamine and Adrenaline, though Ephedrine and Phenylephrine are the most commonly used.

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Phenylephrine used alone may be accompanied by maternal bradycardia^{4,5} and has not yet become popular, particularly for prophylactic use. Clinical experience suggests that Phenylephrine may be useful in addition to Ephedrine when the latter fails to correct hypotension.⁵ The physiologic rationale for adding Phenylephrine to Ephedrine is to increase the α/β -agonist activity ratio⁶. This should help to better counteract spinal anaesthesia induced sympathetic blockade, which impedes venous return and decreases cardiac output.

We thus designed a randomized double-blind prospective study to compare the effectiveness of infusions of Ephedrine plus Phenylephrine versus Ephedrine alone for preventing hypotension during scheduled caesarean delivery. Previously studies have used Ephedrine in bolus doses^{7,8}. In this study we used prophylactic infusion which is unique. In addition, we measured APGAR scores to evaluate neonatal outcome.

MATERIAL AND METHODS: After we obtained ethical committee approval and written informed consent. 60 full term parturients, weighing less than 90 kg, height of 152cm or greater, classified as American Society of Anesthesiologists status-I or II, scheduled for elective caesarean section under spinal anaesthesia, were included in the study.

Patients were divided randomly into 2 groups (E group & E+P group) of 30 each. Group E received Ephedrine infusion and Group E+P received Ephedrine and Phenylephrine infusion. Patients were kept NPO according fasting guidelines and premeditated with Tab Ranitidine 150mg PO, previous night and in the morning.

All the parturient were preloaded with Ringer lactate 15ml/kg body weight before the subarachnoid block. Baseline pulse rate, blood pressure, and SpO₂ were recorded. Subarachnoid block was performed in left lateral position, under aseptic conditions with a hyperbaric Bupivacaine 0.5%, 2cc (10mg) using 25 gauge Quincke's (BD, Becton Dickenson, Madrid, Spain) spinal needle in L₃₋₄ intervertebral space.

Prophylactic vasopressor intravenous infusion was started at the end of spinal injection, via an automated syringe (containing 60mg Ephedrine +300 µg Phenylephrine in a total volume of 20ml saline with initial rate of started at 40ml/h that is 0.66ml/min) using infusion pump:-

Group E (n = 30): initially received Ephedrine 2mg/min

Group E+P (n=30): initially received Ephedrine 2mg/min plus Phenylephrine 10µg/min.

Our infusion protocol used a basic 'on-off' algorithm that was designed to be simple and easy to use. This 'on-off' algorithm has previously been used by Kee et al in their previous studies.⁹ The Phenylephrine dosage was chosen taking into account the comparative studies on Phenylephrine versus Ephedrine.^{10,11} These studies suggested a potency ratio of 40–100 mg Phenylephrine to 6 mg Ephedrine,^{10,11} whereas a dose ratio of only 30 mg Phenylephrine to 6 mg Ephedrine should be effective when combining the two drugs. And the series by Taylor and Tunstall.¹²

For the purpose of double blinding, the vasopressor solution was prepared and given in a sealed and coded envelope by the person not involved in the study. The investigator was blinded to the content of envelope and decoding was undertaken at the end of the surgery. After intrathecal injection, upper level of sensory block was assessed by loss of pinprick sensation. Assessment of the block height was made and recorded at the time of skin incision, 5min and 10min. The target level of sensory anesthesia (block height) was up to T-5 segment.

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Blood pressure and pulse rate were measured every minute until the delivery, then every 5 minutes till the end of surgery. The primary outcome variable was the incidence of hypotension, defined as systolic blood pressure (SBP) less than 100mmHg or less than 80% of baseline before delivery.

A predefined algorithm was used to adjust the syringe rate according to systolic blood pressure as follows:

1. The rate was maintained if systolic blood pressure remained within 90 and 105% of baseline.
2. The rate was halved if SBP increased to between 105 and 120% of baseline.
3. The infusion was stopped if SBP increased to more than 120% of baseline (and restarted at 40ml/h or 80ml/h if SBP decreased back to between 90 and 105% of baseline or to <90% baseline, respectively).
4. The rate was doubled (up to 80ml/h) if SBP decreased to between 80 and 90% of baseline.
5. Hypotension (SBP <100 mmHg and <80% of baseline) was treated with 6mg ephedrine bolus dose repeated as needed.

For each subject, the minimum and maximum systolic blood pressure and pulse rate value were observed before the end of surgery. A back up plan was designed to treat several critical situations e.g. severe hypotension (<80% of basal) not responding to Ephedrine bolus doses (treated with Epinephrine), recurrent hypotension despite cumulative Ephedrine bolus doses in excess of 60mg (treated with additional 10µg of Phenylephrine) and extreme tachycardia (>30% of basal, treated by stopping Ephedrine infusion) or bradycardia (<60/min, treated with Inj. Atropine 0.3mg I.V). Any episode of nausea and vomiting was recorded and rated using a four point scale as follows (0= none, 1 = mild Nausea, 2 = Nausea requiring treatment, 3 = Vomiting).

Nausea and vomiting with a score of 2 or 3 were treated with IV Metoclopramide if unrelated to hypotension or not corrected by Ephedrine alone. Additional data collection included the time intervals from spinal anaesthesia to incision, from spinal anaesthesia to delivery and from uterine incision to delivery, from spinal anaesthesia to end of surgery, the dose of vasopressor (Ephedrine with or without Phenylephrine) given as an infusion, top up and total dose till the end of surgery, assessment of neonate by neonatal weight, APGAR score at 1 minute and 5 minute.

RESULTS: Inter group comparisons were done using chi-square test, and student t test. Data were expressed in mean $\pm$ standard deviation P value of <0.05 was considered significant. All demographic and anaesthetic data were comparable among both the groups as shown in table no 1. Baseline SBP and maternal pulse rate were comparable between the groups. There was decrease in mean pulse rate (table 2, Fig 1) seen in both the groups up to 5th minute.

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	Group E (n=30)	Group E+P (n=30)	P value
Age ^{NS}	24.80 ± 2.43	24.83 ± 3.17	0.964
Weight ^{NS}	60.23±2.42	60.33±2.63	0.883
Height ^{NS}	157.67±2.02	157.00±1.85	0.791
ASA Grade-1 & 2 ^{NS}	28:2	28:2	1.000
Spinal anaesthesia to Delivery(in minutes) ^{NS}	13.50±1.042	13.83±1.05	0.223
Uterine incision to delivery(in seconds)	169.47±11.5	168±10.8	0.622
Spinal anesthesia to End of Surgery(in minutes) ^{NS}	47.73±3.403	49.20±2.09	0.059
Sensory level at time skin incision(T8:T7:T6) ^{NS}	12:16:2	18:11:1	0.292
Sensory level at 5 th min(T8:T7:T6:T5) ^{NS}	0:9:18:3	2:12:14:2	0.372
Sensory level at 5 th min(T5:T4) ^{NS}	27:3	27:3	1.000

Table 1: Demographic data and subarachnoid block characteristics

NS = p > 0.05; Not Significant.

	E Group	E+P Group	P value
Systolic BP(Basal) ^{NS}	112.27±6.69	112.87±6.23	0.719
Diastolic BP(Basal) ^{NS}	76.33±4.95	75.87±5.27	0.725
Pulse Rate(Basal) ^{NS}	83.40±2.83	83.17±3.57	0.780
Hypotension*	11	3	0.015
Tachycardia*	15	4	0.002
Nausea & vomiting score≥2*	8	2	0.043

Table 2: Hemodynamic Data

NS = p > 0.05; Not Significant; * p < 0.05= significant

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Decrease in pulse rate was more in E+P group but it was not significant. From 6th minute onwards, mean pulse rate was on higher side in Group E suggestive of persistent tachycardia. There was statistically significant difference in the pulse rate between two groups from 6th minute to end of surgery. Mean maximum pulse rate in group (E) was 109 ± 5.35 whereas in group (E+P) was 90.03 ± 4.03 , with a P value of <0.001 . In E group, 15 patients (50%) experienced extreme tachycardia, whereas in E+P group only 4 patients (13.33%) experienced tachycardia, which is statistically significant with p value of 0.002.

Immediately after subarachnoid block mean systolic BP started falling from 1st minute to 5th minute in E group, and from 1st minute to 3rd minute in E+P group with significant difference amongst the groups except at 1st and 2nd minute (Table 2, Fig 3). From 5th minute in E group and from 3rd minute in E+P group, the mean SBP increased gradually till the end of surgery in both the groups with significant difference ($p < 0.05$) except at 25th minute where mean SBP of both the groups were almost equal. Up to 25th minute mean SBP of E group was less than mean SBP of E+P group.

After 25th minute mean SBP of E group increased above the mean SBP of E+P group, with significant difference among both the groups up to 35th minute. ($p < 0.05$) Mean minimum systolic blood pressure in E group was 89.80 ± 7.09 mm of Hg, whereas in E+P group was 99.63 ± 7.63 mm of Hg which is statistically highly significant. ($p < 0.001$) In group E, 11 patients (33.66%) experienced hypotension, whereas in E+P group only 3 patients (10%) experienced hypotension with p value of 0.015. Mean Maximum systolic blood pressure in E group was 147.03 ± 6.92 mm of Hg, whereas in E+P group was 139.50 ± 5.91 mm of Hg. ($p < 0.01$).

Regarding vasopressor requirement (Fig-4), E group received 40.60 ± 4.59 mg Ephedrine through infusion, 0.37 ± 0.49 mg Ephedrine as top up dose and 42.73 ± 4.40 mg Ephedrine as overall total dose. Whereas E+P group received 24.03 ± 4.03 mg Ephedrine through infusion, 0.10 ± 0.30 mg Ephedrine as top up dose and 24.27 ± 3.99 mg Ephedrine as overall total dose, along with 119.50 ± 20.81 µg Phenylephrine, which is statistically significant ($p < 0.001$) In E group 8 patients (26.66%) experienced nausea score ≥ 2 (table 2), where as in E+P group 2 patients (6.66%) experienced nausea score ≥ 2 , which is statistically significant. ($p = 0.043$). Neonatal weights and the APGAR score were comparable between the two groups. ($p > 0.01$)

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DISCUSSION: Spinal anaesthesia has become the preferred technique for scheduled caesarean delivery because of ease of performance and availability of fine-gauge pencil-point needles. However, hypotension remains a major drawback with this technique, despite maternal positioning to avoid aorto-caval compression and various other preventive measures, including crystalloid and colloid infusions.¹³ We found that, compared with Ephedrine alone, the Ephedrine – Phenylephrine combination decreased the incidence of hypotension, abolished maternal tachycardia and decreased the frequency of nausea.

Bradycardia is a common accompanying manifestation apart from hypotension in subarachnoid block. Bradycardia in caesarean section is more frequent than in other surgeries. Treatment of bradycardia is important as it can significantly decrease cardiac output thereby affecting both mother and foetus. In our study immediately after spinal anaesthesia there was decrease in mean pulse rate in both the groups up to 5th minute. There was statistical significance in the pulse rate between two groups from 6th minute to end of surgery. ($p < 0.05$) Also mean maximum pulse rate in E group was 109 ± 5.35 whereas in E+P group was 90.03 ± 4.03 , with significant difference. ($p < 0.05$.)

Thomas et al in 1996 studied the effect of bolus Phenylephrine and Ephedrine in maintenance of maternal arterial pressure and concluded that maternal heart rate was higher in Ephedrine group and patients in Phenylephrine group showed significant bradycardia.¹⁴ In our study decrease in pulse rate was gradual and not significant with Ephedrine-Phenylephrine infusion. Ephedrine is known to cause tachycardia which stimulates both the alpha and beta adrenergic receptors as seen in E group.

In contrast, the addition of Phenylephrine (E+P group) completely abolished the tachycardia and maintained the pulse rate in the normal range. Thus, we believe the Phenylephrine/Ephedrine ratio we used is appropriate. Similar results were observed in the study done by Mercier et al who added Phenylephrine to ephedrine infusion to have better control of maternal pulse rate following spinal anaesthesia.¹⁵

In group E, 11 patients (33.66%) experienced hypotension, where as in E+P group only 3 patients (10%) experienced hypotension, which is statistically significant. ($p < 0.05$) This shows Phenylephrine with Ephedrine controls hypotension better than Ephedrine alone. Also mean maximum systolic blood pressure in E group was 147.03 ± 6.92 mm of Hg, whereas in E+P group was 139.50 ± 5.91 mm of Hg which is statistically significant. ($p < 0.001$) Similar results were found in the study conducted by Mercier et al. where Phenylephrine was added to Ephedrine infusions to have better control of maternal BP following spinal anaesthesia.¹⁵

Various authors have noted the incidence of hypotension following subarachnoid block in elective caesarean section ranging from 70% to 100% ¹⁶. It is well established that in obstetric practice, this hypotension should be treated rapidly as maternal hypotension leads to neonatal acidemia. This is more important in the initial 10 minutes following subarachnoid block to prevent detrimental effects on both mother and foetus.¹⁶

Our study was also comparable with Ramanathan et al. who suggested that intravenous bolus doses of Ephedrine and Phenylephrine restored blood pressure similarly during epidural anaesthesia for caesarean delivery by producing a comparable increase in preload only.¹⁷ In present study E group received 40.60 ± 4.59 mg Ephedrine through infusion pump, 0.37 ± 0.49 mg Ephedrine as top up dose and 42.73 ± 4.40 mg Ephedrine as overall total dose. Whereas E+P group received 24.03 ± 4.03 mg of Ephedrine through infusion pump, 0.10 ± 0.30 mg ephedrine as top up dose and 24.27 ± 3.99 mg

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Ephedrine as overall total dose, along with $119.50 \pm 20.81 \mu\text{g}$ Phenylephrine, which is statistically significant. ($p < 0.05$, Fig. 4)

This shows almost half dose of Ephedrine was required along with Phenylephrine to maintain maternal blood pressure in E+P group as compare to E group. Our study was comparable with the study conducted by Lee et al, where $36 \pm 16 \text{ mg}$ Ephedrine plus $178 \pm 81 \mu\text{g}$ Phenylephrine was infused in Ephedrine-Phenylephrine group, whereas $54 \pm 18 \text{ mg}$ Ephedrine was infused in Ephedrine alone group.¹⁸ Cooper and colleagues suggest that a possible explanation for vomiting might be an increase in vagal tone following reduction of preload, which is more likely to occur in the presence of beta stimulation. Phenylephrine, a pure alpha – agonist, provides better vasoconstriction, reducing the decrease in cardiac preload, and diminishing the vagal reflex.¹⁹

This may explain the lower incidence of vomiting in Phenylephrine-ephedrine group. In the present study, E group 8 patients (26.66%) experienced nausea score ≥ 2 , where as in E+P group 2 patients (6.66%) experienced nausea score ≥ 2 , which is statistically significant. ($p < 0.05$, Table 2) They were treated with Inj Metoclopramide 10mg IV. The weight of neonate delivered by parturient in E group was 3.13 ± 0.14 , whereas in E+P group was 3.15 ± 0.17 , with p value 0.573 which was statistically not significant. ($p > 0.05$) There was no small for gestational age neonate, which may affects the APGAR score.

Neonatal wellbeing has been assessed by using various techniques ranging from simple APGAR score to sophisticated techniques such as umbilical cord blood gas assessment and pH measurement.¹⁸ We used APGAR scores in our study as yard stick to assess foetal wellbeing as our center did not have facilities to measure umbilical cord blood gas & pH. In our study the APGAR score at 1 and 5 minute was statistically insignificant. ($P > 0.05$) and was comparable with the study conducted by Cooper et al in which APGAR scores were similar in the both the groups ¹⁹.

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	E Group	E+P Group	P value
Neonatal Weight ^{NS}	3.13±0.14	3.15±0.17	0.573
APGAR at 1min ^{NS}	8.73±0.45	8.80±0.40	0.549
APGAR at 5min ^{NS}	9.67±0.47	9.80±0.40	0.250

Table 3: Neonatal Parameters

NS = p > 0.05; Not Significant

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CONCLUSIONS: From our study we concluded that hypotension following sub arachnoid block for scheduled caesarean delivery remains a common complication despite prophylactic intravenous Ephedrine infusion. We demonstrated that the addition of Phenylephrine to an Ephedrine infusion decreased the incidence of hypotension, abolished tachycardia, and reduced nausea and vomiting. The APGAR scores were similar in both the groups.

REFERENCES:

1. Loughrey JP, Walsh F, Gardiner J. Prophylactic intravenous bolus ephedrine for elective caesarean section under spinal anaesthesia. *Eur J Anaesthesiol* 2002; 19(1): 63-68.
2. Tsen LC, Boosalis P, Segal S, Datta S, Bader AM. Hemodynamic effects of simultaneous administration of intravenous ephedrine and spinal anesthesia for caesarean delivery. *J Clin Anesth* 2000; 12 (5): 378-82.
3. Wollmann SB, Marx GF. Acute hydration for prevention of hypotension during spinal anaesthesia for caesarean section. *Anesthesiology* 1968; 29 (2): 374-80.
4. Morgan P. The role of vasopressors in the management of hypotension induced by spinal and epidural anaesthesia. *Can J Anaesth* 1994; 41 (5 pt 1): 404-13.
5. Hall PA, Bennett A, Wilkes MP, Lewis M: Spinal anaesthesia for caesarean section: Comparison of infusions of Phenylephrine and ephedrine. *Br J Anaesth* 1994; 73 (4): 471-4.
6. Riley ET, Cohen SE, Macario A, Desai JB, Ratner EF. Spinal versus epidural anaesthesia for caesarean section: A comparison of time efficiency, costs, charges and complications. *Anesth Analg* 1995; 80 (4): 709-112.
7. Lewinsky RM, Riskin - Mashiah S. Autonomic imbalance in preeclampsia: evidence for increased sympathetic tone in response to the supine pressor test. *Obstet Gynecol* 1998; 91 (6): 935-9.
8. Datta S, Alper MH, Ostheimer GW, Weiss JB. Method of ephedrine administration and nausea and hypotension during spinal anesthesia for caesarean section. *Anesthesiology* 1982; 56 (1): 68-70.
9. Ngan Kee WD, Khaw KS, Ng FF. Prevention of hypotension during spinal anaesthesia for caesarean delivery. *Anesthesiology* 2005; 103 (4): 744-50.
10. Rout CC, Rocke DA. Prevention of hypotension following spinal anaesthesia for caesarean section. *Int Anesthesiol Clin* 1994; 32 (2): 117-35.
11. Thomas DG, Robson SC, Redfern N, Hughes D, Boys RJ: Randomized trial of bolus of Phenylephrine or ephedrine for maintenance of arterial pressure during spinal anaesthesia for caesarean section. *Br J Anaesth* 1996; 76: 61-5.
12. Taylor JC, Tunstall ME. Dosage of Phenylephrine in spinal anaesthesia for caesarean section. *Anaesthesia* 1991; 46 (4): 314-6.
13. Ueyama H, He YL, Tanigami H, Mashimo T, Yoshiya I: Effects of crystalloid and colloid preload on blood volume in the parturient undergoing spinal anesthesia for elective cesarean section. *Anesthesiology* 1999; 91: 1571-6.
14. Thoma DG, Robson SC RN. Randomized trial of bolus phenylephrine or ephedrine for maintenance of arterial pressure during spinal anaesthesia for Ceaserean section. *Br J Anaesth* 1996; 76 (1): 61-65.

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15. Mercier FJ, Riley ET, Frederickson WL, Roger-Christoph S, Benhamou D, Cohen SE et al. Phenylephrine added to prophylactic ephedrine infusion during spinal anaesthesia for elective cesarean section. *Anesthesiology* 2001; 95 (3): 668-74.
16. Cyna AM, Andrew M, Emmett RS, Middleton P, Simmons SW. Techniques for preventing hypotension during spinal anesthesia for cesarean section. *Cochrane Database of Systemic Review* 2007: 1.
17. Ramanathan S, Grant G. J. Vasopressor therapy for hypertension due to epidural anaesthesia for caesarean section. *Acta Anaesthesiol Scand* 1988; 32: 559-565.
18. Lee A, NganKee WD, Gin T. A quantitative, systemic review of randomized controlled trials of ephedrine versus Phenylephrine for the management of hypotension during spinal anaesthesia for caesarean section. *Anesth Analg* 2001; 94(2): 920-26.
19. Cooper DW, Carpenter M, Mowbray P, Desira WR, Ryall DM, Kikri MS. Fetal and maternal effects of Phenylephrine and ephedrine during spinal anaesthesia for caesarean delivery. *Anesthesiology* 2002; 97(6): 1582-90.

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