

## ORIGINAL ARTICLE

# A Comparative Study of Ephedrine and Phenylephrine in Averting Hypotension during Cesarean Section under Spinal Anesthesia

SHAHID ADALAT CHAUDHRY<sup>1</sup>, MUBASHAR IQBAL<sup>2</sup>, MUHAMMAD NADEEM KHAN<sup>3</sup>, AUROOJ FATIMA<sup>4</sup>, HINA ZUBAIR<sup>5</sup>, MADIHA HAROON<sup>6</sup>

<sup>1</sup>Assistant Professor of Anesthesiology, Mohtarma Benazir Bhutto Shaheed Medical College and DHQ Teaching Hospital Mirpur, Azad Kashmir

<sup>2</sup>Associate Professor of Anaesthesia, Mohi-ud-din Islamic Medical College and Mohi-ud-din Teaching Hospital Mirpur, Azad Kashmir

<sup>3</sup>Associate Professor of Anaesthesia, Mohtarma Benazir Bhutto Shaheed Medical College and DHQ Teaching Hospital Mirpur Azad Kashmir

<sup>4</sup>Associate professor, Gynae/Obs, Mohtarma Benazir Bhutto Shaheed Medical College Mirpur A.K

<sup>5</sup>Associate Professor, Gynae/Obs, Mohtarma Benazir Bhutto Shaheed Medical College Mirpur A.K

<sup>6</sup>Senior Registrar Gynae/Obs, Mohtarma Benazir Bhutto Shaheed Medical College Mirpur A.K

Corresponding author: Dr. Shahid Adalat Chaudhry, Email: [shahidadalat1971@gmail.com](mailto:shahidadalat1971@gmail.com), Mob.0344-5163749

## ABSTRACT

Maternal haemodynamic variations are communal during caesarean section by spinal anesthesia. Several measures are adopted to treat hypotension. The aim of this study is to compare the effectiveness of phenylephrine and ephedrine in treating and preventing hypotension during C-section by spinal anesthesia and its outcome on the condition of the fetus.

**Place and Duration:** In the Anesthesia department of Divisional Headquarter teaching Hospital Mirpur Azad Kashmir for six-months duration from July 2021 to December 2021.

**Methods:** 120 total ASA grade-I patients with normal single pregnancy over 36 weeks who endured planned caesarean-section under spinal-anesthesia were randomized into 2 groups equally. Group I was given 5 mg rescue bolus and 10 mg prophylactic bolus dose of ephedrine intravenously during intrathecal block. Group II received 50 µg of rescue bolus and 100 µg of an intravenous dose of prophylactic phenylephrine bolus during intrathecal block. Haemodynamic variables such as heart rate and blood pressure were documented after every 2-mins until birth and every 5-minutes thereafter. The neonatal score was measured using the 1- and 5-minute Apgar scale and the pH value of the neonatal blood in the umbilical cord.

**Results:** There were no differences in the treatment of hypotension among the 2 groups. The bradycardia incidence was greater in the group of phenylephrine. The variances in Apgar score, birth weight and umbilical cord pH amid the 2 groups were not statistically significant.

**Conclusions:** Ephedrine and phenylephrine are similarly operative in the treatment of hypotension during elective caesarean section given spinal anesthesia. No statical variance in the occurrence of true fetal acidosis between the two vasopressors was noticed. Both groups have good neonatal outcome.

**Key words:** Fetal acidosis, ephedrine, phenylephrine, hypotension and spinal anesthesia.

## INTRODUCTION

For C-section; Spinal anesthesia is extensively used and is safe and effective. The hypotension incidence during C-section under spinal anaesthesia was 82-91% or higher contingent on the used of definition<sup>1-2</sup>. In the case of the maternal signs, hypotension is particularly related with vomiting and nausea and severe cases have danger of pulmonary aspiration, reduced consciousness, cardiac arrest and respiratory depression<sup>3-4</sup>. May have harmful impacts on the new-born, including fetal acidosis, hypotension, impaired fetal oxygenation through asphyxia stress and decreased uteroplacental flow<sup>5</sup>. Since hypotension can be related with equally neonatal and maternal morbidity, numerous approaches have been considered, either singly or in grouping, for together treatment and prevention<sup>6</sup>. It is recognised that displacement of the uterine in left reduces the effects of aorto-caval-compression. Simply lifting the legs has little effect to decrease the hypotension incidence. Pre-hydration or pre-loading is common practice, but with debateable outcomes<sup>7</sup>. Due to the ineffectiveness of non pharmacological methods to efficiently control decreased blood pressure, often a vasopressor is vital during caesarean section under spinal anesthesia<sup>8-9</sup>. A number of factors should be considered in selecting the suitable vasopressor in gynae, including effectiveness in preserving

BP, ease of use, maternal non-cardiovascular effects, indirect and direct impacts on the fetus, availability and cost<sup>10</sup>. Vasopressors commonly used during spinal anesthesia to prevent hypotension include metaraminol, phenylephrine and ephedrine<sup>11</sup>. The obstetric use of ephedrine in patients is reinforced by animal analysis showing that the blood flow to uteroplacental is well preserved when ephedrine is given to increase maternal BP<sup>12</sup>.

Phenylephrine is a direct-acting alpha-agonist and potent. Relatively high doses of phenylephrine may be required during pregnancy due to the overall decrease in the response of pressor to exogenous and endogenous vasoconstrictors<sup>15</sup>. Though, no fetal acidosis was verified when there is widely use of phenylephrine to avert symptoms and preserve maternal BP<sup>16</sup>. The aim of this study is to compare the effectiveness of phenylephrine and ephedrine in treating and preventing hypotension during C-section by spinal anesthesia and its outcome on the condition of the fetus.

## MATERIALS AND METHODS

This prospective double blind randomized controlled study held in the Anesthesia department of Divisional Headquarter teaching Hospital Mirpur Azad Kashmir for six-months duration from July 2021 to December 2021.

After procurement of the appropriate and the written informed consent, the study included 120 ASA 1st degree patients with normal single pregnancy > 36 weeks, who underwent elective caesarean section under spinal anesthesia. Patients with diabetes mellitus, hypertension related with pregnancy, history of cerebrovascular and cardiovascular diseases, contraindications for spinal anesthesia and fetal abnormalities were omitted from the study. The patients were randomly divided into two groups of 60 people. Group I was given 5 mg rescue bolus and 10 mg prophylactic bolus dose of ephedrine intravenously during intrathecal block, provided that mother systolic BP was below 90-mmHg. Group II received 50 µg of rescue bolus and 100 µg of an intravenous dose of prophylactic phenylephrine bolus during intrathecal block, provided maternal systolic BP was below 90-mmHg.

To uphold blinding, the anaesthesiologist given solutions of vasopressor in the same syringes or non-patient investigator. Each patient was premedicated with 150 mg ranitidine the night before and 2 hours before surgery. Upon advent in the operating room, blood pressure (NIBP), heart rate (ECG), arterial blood saturation (SaO<sub>2</sub>) and respiratory rate were checked. All patients started the saline infusion and preloaded with 10-ml / kg-saline. Patients were placed in sitting or lateral position conferring to their needs. 25-gauge Quincke needle was used for lumbar puncture and inserted in the intervertebral space of L3-L4. After the cerebrospinal fluid was able to flow freely, 0.5% 2.5 ml bupivacaine was given for ten-fifteen seconds. The injection time of the drug was recorded and the volunteer was immediately positioned in a supine posture with 15 to 20 degrees left lateral tilt. The 5 L / min oxygen was given pending the clamping of the umbilical cord. The diastolic blood pressure, systolic blood pressure and heart-rate were recorded immediately after induction of spinal anesthesia. One minute later the intrathecal injection, patients were administered intravenously with 100 µg of phenylephrine or 10 mg of ephedrine. Haemodynamic variables such as heart rate

and blood pressure were documented after every-2-mins until birth and every 5-minute thereafter. When the systolic blood pressure dropped below 90 mmHg, vasopressor ephedrine 5 mg or phenylephrine 50 µg was administered. Atropine 0.3 mg was administered intravenously when the mother's heart rate had fall below 60 beats/minute. The neonatal score was assessed after 1 and 5 minutes using the Apgar scale and the pH value of the neonatal umbilical cord blood was checked. The umbilical cord is clamped at birth and a 1 ml blood sample is drawn into a heparinized syringe for acid-base analysis. A pH <7.2 in the umbilical artery indicates asphyxia.

**Statistical analysis:** Parametric data was stated as mean ± SD, so two groups' comparisons were performed using Student's t-test. The two-sided test was used for the p-value significance. P-value below 0.05 was taken significant. The data analysis was done with SPSS 22.0.

## RESULTS

120 total patients participated for this analysis was randomized equally into 2 groups. Both groups were paralleled according to body weight and age [Tab-I] and the length of the operation.

The variance in the baseline mean systolic and diastolic blood pressure and heart rate among the 2 groups was statistically unimportant [Tab-II]. Patients receiving phenylephrine experienced bradycardia more frequently than patients receiving ephedrine.

The variance in mean blood pressure and systolic, diastolic BP among the 2 groups before and afterwards birth at all time points was not statistically significant. Generally, 39/60 (65%) subjects in the group of phenylephrine and 37/60 (61.7%) subjects in the group of ephedrine had one or more hypotension episodes and need one or above bolus doses of vasopressor. The rescue doses number needed in Groups-I and II was insignificant statistically [Tab. III-VI]

Characteristics	Group 1 (n=60) Mean± SD	Group 2 (n=60) Mean± SD	P-value	Significance
Age (years)	29.85±0.61	30.30±0.44	0.15	NS
Weight (kg)	60.41±7.95	68.61±8.09	0.07	NS

Characteristics	Group 1 Mean± SD	Group 2 Mean± SD	t-value	P-value	Significance
Heart rate	91.30±15.20	85.76±11.93	1.02	0.3	NS
Systolic blood pressure	121.01±11.58	122.98±10.21	0.91	0.9	NS
Diastolic blood pressure	79.88±10.10	77.20±9.41	1.01	0.3	NS
Mean blood pressure	91.31±11.10	90.21±8.10	0.64	0.5	NS

Parameter	Heart rate (bpm*)			Systolic blood pressure (mmHg)			Diastolic blood pressure (mmHg)		
till delivery	Group 1 mean± SD	Group 2 mean± SD	P	Group 1 mean± SD	Group 2 mean± SD	P	Group 1 mean± SD	Group 2 mean± SD	P
Immediately after S. A	90.39±20.10	84.14± 11.54	0.06	106.87±15.64	105.70±11.87	0.83	70.85± 10.95	70.98± 11.20	0.95
2 min	98.7±21.21	85.88± 16.35	0.002	120.46±21.49	111.13±14.74	0.070	76.77± 10.21	71.41±11.01	0.054
4 min	96.71±20.30	83.90± 17.01	0.002	109.97±19.41	108.65±18.85	0.09	72.99± 10.20	73.20± 11.74	0.78
6 min	92.78±14.10	81.87±17.88	0.005	107.85±18.10	104.86±15.90	0.4	75.90± 14.21	75.72± 11.66	0.62
8 min	94.10±13.45	86.10±16.44	0.022	111.14±13.98	103.65±11.95	0.08	77.98± 10.77	72.10± 10.99	0.52
10 min	91.91±16.65	4.30±14.11	0.04	110.98± 12.94	101.98±13.60	0.089	78.62± 12.27	74.90± 9.80	0.6
12 min	92.22±16.71	84.68±14.23	0.06	12.97±13.51	110.91± 11.37	0.071	78.99± 9.30	79.20± 9.01	0.61
14 min	96.57± 3.45	95.21±5.34	0.23	114.8±4.70	111.88± 5.88	0.089	71.70± 10.40	71.10± 13.31	0.91

Table 4: Comparison of mean pulse rate, systolic blood pressure and diastolic blood pressure between group-I and II after delivery

At delivery	96.30±12.31	90.21± 11.20	0.04	111.21±13.70	107.70±11.93	0.21	71.33± 10.64	78.22± 9.11	0.5	0.76
5 min	92.54±13.78	88.72± 13.23	0.07	117.67±14.14	104.64±13.04	0.69	73.95± 11.33	71.24±10.15	0.08	
10 min	89.31±11.20	85.14± 11.33	0.3	119.74±16.31	114.41±15.01	0.25	74.21± 13.66	70.80± 10.66	0.07	0.41
15 min	91.58±8.74	90.15±14.20	0.00	118.04±13.98	119.94±12.92	0.51	76.84± 8.12	69.41± 11.30	0.16	
min	89.74±4.47	90.22±6.14	0.21	114.00±7.96	108.37±17.64	0.07	72.13± 8.67	71.44± 7.80		
End of surgery	9.21±7.80	81.24±11.88		110.00± 12.64	114.92±11.84	0.89	76.24± 8.11			

Parameter Group 1 Group 2 P Group 1 Group 2 P Group 1 Group 2 P till delivery mean± SD mean± SD mean± SD mean± SD mean± SD mean± SD

Table 5: Comparison of mean blood pressure (mmHg) till delivery between group-I and II

Mean BP (mmHg)	Group 1 Mean± SD	Group 2 Mean± SD	t-value	P-value	Significance
Immediately after SA	80.41±10.70	80.23±10.01	0.034	0.98	NS
2 min	88.32±11.11	84.58±14.00	1.87, 0.33	0.079, 0.78	NS
4 min 6 min 8 min	84.61±10.20	84.22±10.88 91.47±11.95	0.38	0.82	NS
10 min	88.33±11.01	86.01±11.32	0.72	0.42	NS
12 min	87.55±13.71	84.11±8.44 92.44±10.30	0.81, 0.77	0.36, 0.44	NS
14 min	91.54±14.85 87.07±9.10	87.21±11.32	0.11	0.83	NS
	84.64±10.55				NS
					NS

Table 6: Comparison of mean blood pressure (mmHg) after delivery in groups 1 and 2

Mean BP (mmHg)	Group 1 Mean± SD	Group 2 Mean± SD	t-value	P-value	Significance
At delivery	90.16±10.00	90.11±8.51	0.9, 0.4	0.33, 0.70 0.090	NS
5 min after delivery	84.31±10.21	82.28±10.17	1.7, 1.67 1.010	0.11	NS
10 min 15 min	91.41±13.40	84.71±13.50, 81.55±10.04	1.06	0.27	NS
20 min	86.22±8.20	84.34±11.33		0.3	NS
At the end of surgery	83.11±8.00	84.68±7.85			NS
	85.26±8.66				NS

The variance in the birth-weight of new-borns among the 2 groups was not statistically significant [Tab-VII]. No new-born had Apgar score less than seven at one or five mints. The group-I mean pH of neonatal umbilical cord was 7.32±0.03 and 7.33± 0.02 in group-II. Children receiving phenylephrine had high pH of the umbilical cord than children with receiving ephedrine, but the difference was not statistically significant [Tab-VII].

Table 7: Comparison of birth weight cord pH between groups 1 and 2

Parameter	Birth weight (grams)	and umbilical Umbilical cord pH
Group 1	3211±521.0	7.32±0.03
Group 2	3256±410.66	7.33± 0.02
P value	0.81	0.24

## DISCUSSION

The utmost significant physiological spinal anesthesia response is related to the cardiac and respiratory system<sup>16</sup>. The hypotension incidence during C-section under spinal anaesthesia was 82-91% or higher contingent on the used of definition. Low blood pressure can be harmful to both new-born and mother<sup>17</sup>. These effects comprise reduced fetus oxygenation causing asphyxia, decreased blood flow to uteroplacental, fetal acidosis, and mother indicators of decrease cardiac output include vomiting, nausea, decreased consciousness and dizziness. It is recognised that displacement of the uterine in left reduces the effects of aorto-caval-compression<sup>18-19</sup>. Simply lifting the legs has little effect to decrease the hypotension incidence. Pre-hydration or pre-loading is common practice but has provocative consequences<sup>20</sup>. In spite of all precautions, vasopressors are usually essential to avoid hypotension during C-section under spinal anesthesia. All patients in

this study of both groups were parallel in terms of ASA status and age<sup>21</sup>. The baseline parameters difference such as systolic and diastolic BP, heart rate and mean BP among the 2 groups was insignificant, correspondingly. There was no statistically substantial difference between the time of surgery (induction of labor and time from birth to completion of surgery) in Groups-I and II. The bradycardia incidence was higher in subjects who received phenylephrine than people taking ephedrine in this analysis. Lee et al. reported a greater prevalence of bradycardia in phenylephrine given subjects in comparison to the patients given ephedrine for the inhibition of hypotension during C-section in subarachnoid anesthesia<sup>22</sup>.

In this study, no variance between phenylephrine and ephedrine in terms of their effectiveness in controlling hypotension succeeding spinal anesthesia in Caesarean section patients in the dose range studied. Adigun et al has the same results like this study<sup>23</sup>.

According to Gundy et al. compared the side effects and effectiveness of vasopressors, phenylephrine and ephedrine used in the management of low BP during planned C-section under spinal anesthesia<sup>24</sup>. As with our findings, they found no difference in the treatment of the hypotension. No alteration in the Apgar scores among the 2 groups was noted. In this study, no child scored <7 Apgar points at one or five mints. The difference in the birth weight of new-borns between the two groups was not statistically significant. In their study, Adigun and Amnaor-Boadu compared intravenous ephedrine with phenylephrine to maintain BP during planned caesarean section under spinal anesthesia<sup>25</sup>. Both groups have similar mean Apgar scores; None of the infants achieved Apgar

score < eight in any group. The outcomes are consistent with this study.

## CONCLUSION

Ephedrine and phenylephrine are similarly operative in the treatment of hypotension during elective caesarean section given spinal anesthesia. No statical variance in the occurrence of true fetal acidosis between the two vasopressors was noticed. Both groups have good neonatal outcome.

## REFERENCES

1. Kee WD, Khaw KS, Ng FF, Lee BB. Prophylactic phenylephrine infusion for preventing hypotension during spinal anesthesia for cesarean delivery. *Anesthesia & Analgesia*. 2004 Mar 1;98(3):815-21.
2. 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 Jul 1;2(2):92.
3. Kee WD, Khaw KS, Ng FF. Prevention of hypotension during spinal anesthesia for cesarean delivery: an effective technique using combination phenylephrine infusion and crystalloid cohydration. *The Journal of the American Society of Anesthesiologists*. 2005 Oct 1;103(4):744-50.
4. Mercier FJ, Riley ET, Frederickson WL, Roger-Christoph S, Benhamou D, Cohen SE. Phenylephrine added to prophylactic ephedrine infusion during spinal anesthesia for elective cesarean section. *The Journal of the American Society of Anesthesiologists*. 2001 Sep 1;95(3):668-74.
5. Cooper DW, Carpenter M, Mowbray P, Desira WR, Ryall DM, Kokri MS. Fetal and maternal effects of phenylephrine and ephedrine during spinal anesthesia for cesarean delivery. *The Journal of the American Society of Anesthesiologists*. 2002 Dec 1;97(6):1582-90.
6. Moran DH, Perillo M, LaPorta RF, Bader AM, Datta S. Phenylephrine in the prevention of hypotension following spinal anesthesia for cesarean delivery. *Journal of clinical anesthesia*. 1991 Jul 1;3(4):301-5.
7. Kee WD, Lee A, Khaw KS, Ng FF, Karmakar MK, Gin T. A randomized double-blinded comparison of phenylephrine and ephedrine infusion combinations to maintain blood pressure during spinal anesthesia for cesarean delivery: the effects on fetal acid-base status and hemodynamic control. *Anesthesia & Analgesia*. 2008 Oct 1;107(4):1295-302.
8. Kee WD, Khaw KS, Lee BB, Lau TK, Gin T. A dose-response study of prophylactic intravenous ephedrine for the prevention of hypotension during spinal anesthesia for cesarean delivery. *Anesthesia & Analgesia*. 2000 Jun 1;90(6):1390-5.
9. Mercier FJ, Augè M, Hoffmann C, Fischer C, Le Gouez A. Maternal hypotension during spinal anesthesia for caesarean delivery. *Minerva Anestesiologica*. 2013 Jan 1;79(1):62-73.
10. Loughrey JP, Yao N, Datta S, Segal S, Pian-Smith M, Tsen LC. Hemodynamic effects of spinal anesthesia and simultaneous intravenous bolus of combined phenylephrine and ephedrine versus ephedrine for cesarean delivery. *International journal of obstetric anesthesia*. 2005 Jan 1;14(1):43-7.
11. Mitra JK, Roy J, Bhattacharyya P, Yunus M, Lyngdoh NM. Changing trends in the management of hypotension following spinal anesthesia in cesarean section. *Journal of postgraduate medicine*. 2013 Apr 1;59(2):121.
12. Vallejo MC, Attaallah AF, Elzamzamy OM, Cifarelli DT, Phelps AL, Hobbs GR, Shapiro RE, Ranganathan P. An open-label randomized controlled clinical trial for comparison of continuous phenylephrine versus norepinephrine infusion in prevention of spinal hypotension during cesarean delivery. *International journal of obstetric anesthesia*. 2017 Feb 1;29:18-25.
13. Abbasivash R, Sane S, Golmohammadi M, Shokuhi S, Toosi FD. Comparing prophylactic effect of phenylephrine and ephedrine on hypotension during spinal anesthesia for hip fracture surgery. *Advanced biomedical research*. 2016;5.
14. 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 Nov 1;34:208-15.
15. Lee HM, Kim SH, Hwang BY, Yoo BW, Koh WU, Jang DM, Choi WJ. The effects of prophylactic bolus phenylephrine on hypotension during low-dose spinal anesthesia for cesarean section. *International Journal of Obstetric Anesthesia*. 2016 Feb 1;25:17-22.
16. Saravanan S, Kocarev M, Wilson RC, Watkins E, Columb MO, Lyons G. Equivalent dose of ephedrine and phenylephrine in the prevention of post-spinal hypotension in Caesarean section. *British journal of anaesthesia*. 2006 Jan 1;96(1):95-9.
17. Moslemi F, Rasooli S. Comparison of prophylactic infusion of phenylephrine with ephedrine for prevention of hypotension in elective cesarean section under spinal anesthesia: A randomized clinical trial. *Iranian journal of medical sciences*. 2015 Jan;40(1):19.
18. Dyer RA, Reed AR. Spinal hypotension during elective cesarean delivery: closer to a solution. *Anesthesia & Analgesia*. 2010 Nov 1;111(5):1093-5.
19. Siddik-Sayyid SM, Nasr VG, Taha SK, Zbeide RA, Shehade JM, Al Alami AA, Mokadem FH, Abdallah FW, Baraka AS, Aouad MT. A randomized trial comparing colloid preload to colloid during spinal anesthesia for elective cesarean delivery. *Anesthesia & Analgesia*. 2009 Oct 1;109(4):1219-24.
20. Lee A, Kee WD, Gin T. Prophylactic ephedrine prevents hypotension during spinal anesthesia for Cesarean delivery but does not improve neonatal outcome: a quantitative systematic review. *Canadian Journal of Anesthesia*. 2002 Jun;49(6):588-99.
21. De Diego Pdel R. Ephedrine vs. phenylephrine by intravenous bolus and continuous infusion to prevent hypotension secondary to spinal anesthesia during cesarean section: a randomized comparative trial. *Revista Española de Anestesiología y Reanimación*. 2011 Aug 1;58(7):412-6.
22. 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 Nov 1;111(5):1221-9.
23. Ngan Kee WD. A random-allocation graded dose-response study of norepinephrine and phenylephrine for treating hypotension during spinal anesthesia for cesarean delivery. *Anesthesiology*. 2017 Dec;127(6):934-41.
24. Dusitkasem S, Herndon BH, Somjit M, Stahl DL, Bitticker E, Coffman JC. Comparison of phenylephrine and ephedrine in treatment of spinal-induced hypotension in high-risk pregnancies: A narrative review. *Frontiers in medicine*. 2017 Jan 20;4:2.
25. Ituk US, Cooter M, Habib AS. Retrospective comparison of ephedrine and phenylephrine for the treatment of spinal anesthesia induced hypotension in pre-eclamptic patients. *Current medical research and opinion*. 2016 Jun 2;32(6):1083-6.