ORIGINAL ARTICLE

Phenylephrine for Blood Pressure Control under Sub-arachnoid Block in Elective Caesarean Section: Prophylactic vs Therapeutic Approach

Anand Thakur[1], Amit Sharma Bhattarai[2], Binita Acharya[3]

[1] Consultant Anaesthesiologist, Grande International Hospital, Tokha Road, Kathmandu - 44600, Nepal.
[2] Assistant Professor, Department of Anaesthesiology, Tribhuvan University teaching Hospital, Maharajgunj Medical Campus, Institute of Medicine, Maharajgunj Road, Kathmandu - 44600, Nepal.
[3] Department of Anaesthesiology, Tribhuvan University Teaching Hospital, Maharajgunj Medical Campus, Institute of Medicine, Maharajgunj Road, Kathmandu - 44600, Nepal.

Corresponding Author

Binita Acharya
Department of Anaesthesiology,
Maharajgunj Medical Campus, Tribhuvan University Teaching Hospital, Institute of Medicine,
Maharajgunj Road,
Kathmandu - 44600,
Nepal.
Email: binitaacharya@gmail.com

Keywords

APGAR, Caesarean section, Hypotension, Phenylephrine

Online Access

DOI: 10.3126/mjsbh.v22i2.66355

Date of submission - 2024 Feb 07
Date of acceptance - 2024 May 17

Abstract

Introduction: Hypotension after spinal anaesthesia is common during Caesarean section with incidence of 50 - 80%. There are various methods to prevent maternal side effects like hypotension, nausea and vomiting and fetal outcome by preloading or co-loading with crystalloids, left tilt and vasopressors like phenylephrine. In this study we hypothesized that prophylactic phenylephrine offers better hemodynamic control than therapeutic doses in elective Caesarean section after subarachnoid block.

Methods: A comparative, prospective, randomized double blind study was conducted in 104 patients scheduled for elective Caesarean section. 52 patients each were assigned into either prophylactic (P) or therapeutic (T) group. Baseline data, hemodynamics, nausea and vomiting and APGAR score were collected. Hemodynamics were analyzed using 2-tailed student's t-test for intergroup and paired t-test for intragroup comparison. Nominal categorical data such as gender was also analyzed with Chi-square test.

Results: Systolic, diastolic and mean arterial pressure were significantly lower in therapeutic group as compared to prophylactic group. The overall incidence of hypotension was 53% in group T and 21% in group P. Similarly, nausea and vomiting were significantly higher in group T (46%) compared to group P (11%) at 15, 20 and 30 mins.

Conclusion: Prophylactic dose of phenylephrine significantly prevents hypotension and nausea and vomiting in patients undergoing elective Caesarean section.

INTRODUCTION

Spinal anaesthesia is commonly used in Caesarean sections due to faster onset of sensory and motor blockade and reduction in the risk of local anaesthetic toxicity.[1] It avoids the risk of general anaesthesia and the rapid and profound block provided also results in reduced need for supplemental intravenous analgesia.[2,3] The incidence of hypotension after spinal anaesthesia is high and is more pronounced in pregnant population.[4,5] Hypotension is attributed to factors like contracted subarachnoid space, aortocaval compression, sympathetic blockade and maternal physiological changes. The resulting hypotension may lead to maternal nausea, vomiting, cardiovascular collapse, loss of consciousness and fetal bradycardia and acidosis.[6,7] The strategies to correct hypotension during spinal anaesthesia involves slight tilt to the left side avoiding aortocaval compression and volume preloading with crystalloids 15 ml / kg. These measures alone may not be able to counteract hypotension and often large doses of vasopressors like phenylephrine and mephentermine are required. [8-11]

Recently phenylephrine has been drug of choice for maternal hypotension during Caesarean delivery for effectively reducing severity of hypotension and nausea.[12] There are no evidence of adverse effects of

100 mcg phenylephrine on maternal variables and fetal parameters. Similarly, prophylactic phenylephrine infusion is an effective method for prevention of maternal hypotension during spinal anaesthesia for Caesarean section with no adverse effects on neonatal outcome.[13] Fetal acid-base status might be improved with the use of phenylephrine in terms of higher umbilical artery pH and base excess. It has been shown to decrease maternal cardiac output, however, such changes do not appear to affect normal healthy mothers.[14] Phenylephrine maintains arterial pressure better in first six minutes of bolus dose as compared to ephedrine and mephentermine as it has peak effect within one minute, whereas ephedrine takes two to five minutes and mephentermine takes five minutes to peak.[15]

In this study we compared the efficacy and safety of bolus versus infusion of phenylephrine in patients undergoing elective Caesarean section under subarachnoid block.

METHODS

The comparative, prospective, randomized double blind study was designed and ethical approval from Institutional Review Committee (IRC) was obtained. We recruited 52 patients in each group (total sample size of 104). The procedure was explained thoroughly to each patient enrolled in the study and written informed consent was obtained. ASA PS II patients with term singleton pregnancy indicated for elective Caesarean section were included. Patients with heart rate of < 60, hypertension, cardiovascular diseases, fetal anomalies, hypersensitive to study drug and ASA PS III and IV were excluded. The patients were explained about 3 point ordinal scale for nausea and vomiting (0 - none, 1 - mild nausea, 2 - severe nausea and retching and 3 - vomiting).[16] In the operating room, the patients were placed in supine position with left lateral tilt and 18 G intravenous cannula was secured. Subarachnoid block was performed in the sitting position in L_3 - L_4 space with 25 G Quincke's spinal needle and 0.5% hyperbaric bupivacaine 2.2 ml was given. Co-loading was done with infusion of Ringer's lactate at the rate of 15 ml / kg for next 15 minutes. The patients were randomized based on sequentially numbered opaque sealed envelope (SNOSE) technique into two groups, group P who received 50 mcg of phenylephrine and group T who received 1 ml of normal saline. Rescue phenylephrine 50 mcg was administered intravenously in case of hypotension. In case of failure of spinal anaesthesia, the case was converted to general anaesthesia and excluded. Heart rate, SBP and DBP were recorded immediately after performance of subarachnoid block (time 0) then every 2 minutes for next 20 minutes, then every 5 minutes till the surgery was over. APGAR score of the newborn was documented at 1, 5 and 10 minutes. In case of nausea and / or vomiting inj. ondansetron 4 mg was given intravenously. In cases of bradycardia with HR < 60 and hypotensive, inj. mephentermine 6 mg was given. If the patient developed bradycardia with HR < 45 bpm, inj. atropine 0.6 mg was used to increase the heart rate. Statistical analysis was done using statistical package for social sciences (SPSS) software version 17 (SPSS Ltd, Chicago, IL, USA). Values are presented as mean (SD) or number. Hemodynamic data were analyzed using 2-tailed student's t-test for intergroup comparison and paired t-test for intragroup comparison. Nominal categorical data such as gender was also analyzed with Chi-square test. For all determinations p value of < 0.05 was considered significant.

RESULTS

The total number of patients was 104 with 52 in each group with age ranging from 20 to 39 years. Mean age of patients in group P (Prophylactic dose of Phenylephrine) and T (Therapeutic dose of Phenylephrine) were 29.19 and 28.31 years respectively. Regarding ASA-PS classification, there was similar distribution between two groups. Both systolic and diastolic blood pressures in group T were significantly lower than group P at 4, 6 and 8 minutes after performing subarachnoid block (P < 0.001). While at the other times during surgery there were no differences found (Tables 1 and 2).

Table 1: Comparison of systolic blood pressure between two groups

Time interval (SBP mmHg)	Group P		Group T		P value
	Mean	SD	Mean	SD	
Baseline	108.55	9.59	108.25	8.74	0.869
0 min	107.22	5.29	109.69	7.52	0.057
2 min	103.75	2.18	103.08	4.32	0.326
4 min	100.00	7.03	93.79	9.68	< 0.001*
6 min	103.12	4.40	96.98	9.55	<0.001*
8 min	103.86	6.84	98.67	8.99	0.001*
10 min	98.65	7.68	96.69	8.22	0.216

12 min	103.61	9.20	101.15	9.43	0.184
14 min	102.69	12.43	101.27	12.56	0.566
16 min	102.08	9.11	100.77	9.03	0.466
18 min	109.08	6.52	107.98	6.99	0.412
20 min	109.41	3.40	109.35	3.40	0.922
25 min	113.84	2.28	113.31	2.74	0.290
30 min	109.36	6.60	108.73	5.97	0.614
35 min	107.87	5.08	108.05	4.65	0.866
40 min	105.59	3.86	104.34	4.41	0.216
45 min	105.83	4.45	105.77	2.95	0.963
50 min	105.91	2.70	105.33	2.31	0.743
55 min	102.00		102.00		
60 min	100.00		100.00	8.74	

*Statistically significant

Table 2: Comparison of diastolic blood pressure between two groups

Time interval (DBP mmHg)	GROUP P		GROUP T		P value
	Mean	SD	Mean	SD	
Baseline	68.94	9.62	70.08	8.30	0.522
0 min	73.49	7.78	72.63	7.45	0.570
2 min	74.08	8.13	73.69	8.91	0.819
4 min	73.86	11.25	65.42	13.88	0.001*
6 min	79.49	4.97	72.38	11.80	< 0.001*
8 min	79.61	5.60	73.73	11.53	0.001*
10 min	73.65	4.23	71.69	6.04	0.060
12 min	75.84	4.06	73.88	5.93	0.054
14 min	78.75	1.79	78.35	3.11	0.428
16 min	76.71	3.98	76.23	4.85	0.588
18 min	80.59	7.17	79.79	7.79	0.589
20 min	79.73	4.38	79.65	4.33	0.934
25 min	78.80	2.38	78.63	2.03	0.706
30 min	77.90	6.58	77.81	6.54	0.943
35 min	80.94	5.87	80.88	6.00	0.967
40 min	79.56	4.53	78.67	4.79	0.425
45 min	73.83	4.97	72.71	2.89	0.448
50 min	80.45	9.50	74.67	4.62	0.337
55 min	74.00		74.00		
60 min	74.00		74.00	8.30	

*Statistically significant

Similarly, mean arterial pressure also showed similar trend of decrease at 4, 6 and 8 minutes in group T as compared to group P (Table 3). Incidence of hypotension in group T was 53% and in group P, it was 21%. The heart rates, however, was not significantly different between two groups.

Table 3: Comparison of mean arterial pressure between two groups

Time interval (MAP mmHg)	Group P	SD	Group T	SD	P value
	Mean	SD	Mean	SD	
Baseline	82.06	9.10	82.80	7.86	0.660
0 min	84.60	6.80	84.99	6.48	0.769
2 min	83.54	5.56	83.49	6.88	0.966
4 min	82.52	8.87	74.88	11.73	< 0.001*
6 min	87.40	3.90	80.58	10.76	< 0.001*
8 min	87.72	4.77	82.04	9.87	< 0.001*
10 min	82.12	5.11	80.03	6.38	0.071
12 min	85.20	4.37	82.97	5.95	0.034
14 min	86.80	4.99	85.99	5.65	0.444
16 min	85.54	5.17	84.41	5.75	0.300
18 min	90.04	6.41	89.19	6.99	0.522
20 min	89.64	2.64	89.55	2.30	0.857
25 min	90.82	2.16	90.19	1.50	0.093
30 min	88.51	5.24	88.12	5.12	0.703
35 min	90.28	5.39	89.94	5.28	0.761
40 min	88.59	3.96	86.07	7.72	0.082
45 min	84.68	3.58	81.21	9.37	0.106
50 min	88.67	5.76	84.89	3.85	0.307
55 min	84.00	1.41	83.33		0.766
60 min	83.00		82.67		

*Statistically significant

Table 4: Comparison of nausea and vomiting between two groups

Time (mins)	Group P		Group T		P value
	Mean	SD	Mean	SD	
5	0.00	0.00	0.00	0.00	
10	0.08	0.27	0.12	0.38	0.552
15	0.06	0.31	0.33	0.68	0.010*
20	0.00	0.00	0.19	0.56	0.015*
30	0.00	0.00	0.27	0.74	0.010*
40	0.00	0.00	0.06	0.42	0.320
50	0.00	0.00	0.04	0.28	0.320
60	0.00	0.00	0.00	0.00	0.00

There was a high incidence of nausea and vomiting in group T compared to group P at 15, 20 and 30 minutes which was statistically significant. The incidence of nausea and vomiting in group T was 46% as compared to group P (11%). After 30 minutes, however, there was no significant difference between the two groups (Table 4). There was no significant difference in APGAR score between two groups.

DISCUSSION

Hypotension after subarachnoid block is relatively common clinical problem, with an increase in maternal and fetal morbidity.[13,17-19] The mechanism for hypotension is the sympathetic blockade causing reduction in blood pressure as a result of fall in systemic vascular resistance with reduction in venous return leading to a fall in cardiac output and occasionally heart rate.[13] Crystalloids have been used since a long period of time to counteract the hypotension that occurs after the performance of subarachnoid blockade. Despite this volume expansion, hypotension still occurs because crystalloids are rapidly redistributed to the third space.[19]

The two groups we compared were well matched demographically. The incidence of hypotension that we found (53%) in therapeutic group was comparable to various studies which demonstrated that the incidence of hypotension is 50 - 85%. In the group that received prophylactic phenylephrine the incidence of hypotension was 21% which was 39.62% lower than therapeutic group ($p < 0.001$). We did not use infusion of phenylephrine but rather used prophylactic dose of phenylephrine in our study. One problem associated with phenylephrine infusion is reactive hypertension and bradycardia seen with the infusion.[20] We did not encounter such problem probably due to proper fluid management (preloading) and use of only one small dose of phenylephrine. Although there was a drop in heart rate after administration of phenylephrine in both groups, it was not statistically significant and none of the patients had to be given atropine to treat bradycardia. The incidence of nausea and vomiting was higher in therapeutic group as compared to the prophylactic group. There are studies which demonstrate the similar findings.[1]

In our study, we did not find any significant difference in APGAR score between the two groups. All the newborns had APGAR score of 7 or more at 1 minute and 5 minutes. A study by David W Cooper et al compared fetal and maternal effects of phenylephrine and ephedrine during Caesarean section and found that there was a significantly lower incidence of fetal acidosis in the group receiving phenylephrine infusion.[21] In our study, although we did not analyze umbilical cord blood for acidosis, the APGAR score was found to be similar in both groups.

Ngan Kee et al compared phenylephrine infusion regimens for maintaining maternal blood pressure during spinal anaesthesia for Caesarean section. They noted that phenylephrine decreased hypotension with higher umbilical arterial pH and decrease in incidence of nausea and vomiting. There was no detrimental neonatal outcome in the study.[22] Similarly, Heseen M et al did a systematic review to determine the harm and benefit associated with prophylactic phenylephrine for Caesarean section under subarachnoid block. Phenylephrine reduced the risk of hypotension and nausea and vomiting after spinal doses of bupivacaine generally exceeding 8 mg, but there was no evidence that it reduced other maternal or neonatal morbidities.[23] Similar multiple studies have been done to demonstrate safety and efficacy of phenylephrine in terms of maternal blood pressure, intraoperative nausea and vomiting and fetal outcome in terms of APGAR and umbilical cord pH.[24,25] Because of its short duration of action prophylactic phenylephrine boluses for the prevention of hypotension after spinal anaesthesia may not be adequate throughout the length of the surgery. Prophylactic phenylephrine infusion may provide better haemodynamic stability compared to phenylephrine boluses.

We have to acknowledge few limitations. Umbilical cord pH was not measured in our study which is a routine practice. Neonates were not followed up beyond immediate postnatal period. The study is limited to one center only and hence, generalisation of our findings may not be feasible. The study findings should be validated in larger, multi centric studies in the future.

CONCLUSION

When compared to therapeutic phenylephrine for control of blood pressure after hypotension has occurred following subarachnoid block in elective Caesarean section, prophylactic phenylephrine significantly prevents hypotension, nausea and vomiting without detrimental effects to the neonatal outcome.

ACKNOWLEDGEMENT Researcher and team would like to acknowledge Department of Anaesthesiology, Tribhuvan University Teaching Hospital, Maharajgunj Medical Campus, Institute of Medicine for the immense support to conduct this study.

FUNDING SOURCE None

CONFLICT OF INTEREST None

CONFLICT OF INTEREST None

REFERENCES

1. Das Neves JF, Monteiro GA, de Almeida JR, Sant'Anna RS, Bonin HB, Macedo CF. Phenylephrine for Blood Pressure Control in Elective Cesarean Section: Therapeutic versus Prophylactic Doses. Rev Bras Anestesiol. 2010;60(4):391-8.
DOI: 10.1016/S0034-7094(10)70048-9
PMID: 20659611

2. Pernoll ML Mandell JE. Caesarean Section.Chapter 30, Principles and Practice of Obstetric Analgesia and Anaesthesia, 2nd ed, Bonica JJand Mc Donald JS, Williams and Wilkins; 1995. 968-1009. ISBN: 0683009303

3. Chestnut DH. Chestnut's Obstetric Anesthesia: Principles and Practice. 5th ed. Elsevier; 2014.

4. Sahoo T, SenDasgupta C, Goswami A, Hazra A. Reduction in spinal-induced hypotension with ondansetron in parturients undergoing caesarean section: A double-blind randomised, placebo-controlled study. Int J Obstet Anesth 2012;21(1):24-8.
DOI: 10.1016/j.ijoa.2011.08.002
PMID:22100822

5. Yu C, Gu J, Liao Z, Feng S. Prediction of spinal anesthesia-induced hypotension during elective cesarean section: a systematic review of prospective observational studies. Int J Obstet Anesth. 2021;47:103175.
DOI: 10.1016/j.ijoa.2021.103175
PMID: 34034957

6. Ebner H, Barcohana J, Bartosheck AK. Influence of postspinal hypotension on the fetal electrocardiogram. Am J Obstet Gynecol [Internet]. 1960;80(3):569-72.
DOI: 10.1016/S0002-9378(16)36516-4
PMID: 13819175

7. Šklebar I, Bujas T, Habek D. Spinal anaesthesia-induced hypotension in obstetrics: prevention and therapy. Acta Clin Croat. 2019;58(Suppl 1):90-95.
DOI: 10.20471/acc.2019.58.s1.13
PMID: 31741565

8. Jackson R, Reid JA, Thorburn J. Volume preloading is not essential to prevent spinal-induced hypotension at Caesarean section. Br J Anaesth. 1995;75(3):262-5.
DOI: 10.1093/bja/75.3.262
PMID: 7547039

9. Karinen J, Rasanen J, Alahuhta S, Jouppila R, Jouppila P. Effect of crystalloid and colloid preloading on uteroplacental and maternal haemodynamic state during spinal anaesthesia for Caesarean section. Br J Anaesth. 1995;75(5):531-5.
DOI: 10.1093/bja/75.5.531
PMID: 7577275

10. McCrae AF, Wildsmith JAW. Prevention and treatment of hypotension during central neural block. Br J Anaesth. 1993;70(6):672-80.
DOI: 10.1093/bja/70.6.672
PMID: 8329261

11. Stewart A, Fernando R, McDonald S, Hignett R, Jones T, Columb M. The dose-dependent effects of phenylephrine for elective cesarean delivery under spinal anesthesia. Anesth Analg. 2010;111(5):1230-7.
DOI: 10.1213/ANE.0b013e3181f2eae1
PMID: 20841418

12. Doherty A, Ohashi Y, Downey K, Carvalho JCA. Phenylephrine infusion versus bolus regimens during cesarean delivery during spinal anesthesia : A double blind randomised clinical trial to assess hemodynamic changes. Anesth Analg 2012;115(6):1343-50.
DOI: 10.1213/ANE.0b013e31826ac3db
PMID: 23011562

13. Kee WDN, Khaw KS, Ng FF, Lee BB. Prophylactic Phenylephrine Infusion for Preventing Hypotension During Spinal Anesthesia for Cesarean Delivery. Anesth Analg 2004;(6) 98:815-21.
DOI: 10.1213/01.ANE.0000099782.78002.30
PMID: 14980943

14. Habib AS. A Review of the Impact of Phenylephrine Adminstration on Maternal Hemodynamics and Maternal and Neonatal Outcomes in women undergoing Cesarean delivery under Spinal Anesthesia. Anesth Analg 2012;114(2):377-90.
DOI: 10.1213/ANE.0b013e3182373a3e
PMID: 22104076

15. 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 J Nepal Med Assoc. 2010;49(177):23-28.
DOI: 10.31729/jnma.128
PMID: 21180216

16. Yildirim BG, Bombaci E, Atakan Y T, Korucu H, Colakoglu S. Prophylaxis of perioperative nausea and vomiting with subhypnotic dose of propofol and dexamethasone during intradural anesthesia in cesarean section: A-592. Eur J Anaesthesiol. 2005; 22: 155.
DOI: 10.1097/00003643-200505001-00557

17. Tanaka M, Balki M, Parkes RK, Carvalho JCA. ED95 of phenylephrine to prevent spinal-induced hypotension and/or nausea at elective cesarean delivery. Int J Obstet Anesth 2009;18(2):125-30.
DOI: 10.1016/j.ijoa.2008.09.008 PMID: 19162468
PMID: 19162468

18. Macarthur A, Riley ET. Vasopressor Choice for Postspinal Hypotension During Cesarean Delivery. Int Anesthesiol Clin. 2007;45(1):115-32.
DOI: 10.1097/AIA.0b013e31802b8d53
PMID: 17215703

19. Siddik-Sayyid SM, Nasr VG, Taha SK, Zbeide RA, Shehade JMA, Al Alami AA, et al. A randomized trial comparing colloid preload to coload during spinal anesthesia for elective cesarean delivery. Anesth Analg. 2009;109(4):1219-24.
DOI: 10.1213/ane.0b013e3181b2bd6b
PMID: 19641050

20. Siddik-Sayyid SM, Taha SK, Kanazi GE, Aouad MT. A randomized controlled trial of variable rate phenylephrine infusion with rescue phenylephrine boluses versus rescue boluses alone on physician interventions during spinal anesthesia for elective cesarean delivery. Anesth Analg. 2014;118(3):611-8.
DOI: 10.1213/01.ane.0000437731.60260.ce
PMID:24299932

21. 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. Anesthesiology. 2002;97(6):1582-1590.
DOI: 10.1097/00000542-200212000-00034
PMID:12459688

22. Ngan Kee WD, Khaw KS, Ng FF. Comparison of phenylephrine infusion regimens for maintaining maternal blood pressure during spinal anaesthesia for Caesarean section. 2004;92(4):469-74.
DOI: 10.1093/bja/aeh088
PMID:14977792

23. Heesen M, Klohr S, Rossaint R, Straube S. Prophylactic phenylephrine for caesarean section under spinal anaesthesia: Systematic review and meta-analysis. Anaesthesia. 2014;69(2):143-65.
DOI: 10.1111/anae.12445
PMID:24588024

24. Guo L, Xu X, Qin R, Shi Y, Xue W, He L, et al. Prophylactic Norepinephrine and Phenylephrine Boluses to Prevent Postspinal Anesthesia Hypotension During Cesarean Section: A Randomized Sequential Allocation Dose-Finding Study. Drug Des Devel Ther. 2023;17:1547-1555. Published 2023 May 23.
DOI: 10.2147/DDDT.S406671
PMID: 37249928 PMCID: PMC10224683

25. Veeser M, Hofmann T, Roth R, Klohr S, Rossaint R, Heesen M. Vasopressors for the management of hypotension after spinal anesthesia for elective caesarean section. Systematic review and cumulative meta-analysis [published correction appears in Acta Anaesthesiol Scand. 2012 Oct;56(9):1204]. Acta Anaesthesiol Scand. 2012;56(7):810-816.
DOI: 10.1111/j.1399-6576.2011.02646.x
PMID:22313496