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Original Research Article

Comparison of norepinephrine with phenylephrine for maintenance of fetal acid-base balance in cesarean deliveries

Ranju Singh[1], Surbhi Saini[1]*, Ratna Biswas[2]

[1]Department of Anaesthesiology and Critical Care, [3]Department of Obstetrics and Gynecology, Lady Hardinge Medical College and Associated Shrimati Sucheta Kriplani Hospital, Connaught Place, New Delhi, India

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***Correspondence:**
Dr. Surbhi Saini,
E-mail: surbhisaini14@gmail.com

ABSTRACT

Background: Currently phenylephrine (PE) is recommended to treat hypotension after spinal anesthesia for cesarean delivery (CD). Recently low dose norepinephrine has been proposed as effective alternative with advantage of less depression of maternal heart rate and cardiac output.
Methods: This was prospective observational study in women scheduled for CD under spinal anesthesia, patients received either PE 100 µg (group PE) or norepinephrine 8 µg (group NE). Primary objective was to study the difference in umbilical artery pH with use of both drugs. The secondary objectives were to compare maternal hemodynamics, number of boluses required and neonatal outcome.
Results: Total 593 patients were enrolled and 226 patients who developed post-spinal hypotension were analysed, 106 patients received PE and 120 patients received norepinephrine. Umbilical artery pH was similar in both groups ($p=0.199$) but in fetal distress, pH was acidotic in both groups with a greater dip with PE than norepinephrine ($p<0.001$). Incidence of bradycardia was significantly higher with PE ($p<0.001$) and number of boluses was greater with norepinephrine. No difference observed in episodes of hypotension and neonatal outcome.
Conclusions: Fetal pH was maintained within normal range with both drugs but in fetal distress, fetal pH was acidotic in both groups, however better maintained with norepinephrine than PE. Norepinephrine was as effective as PE for post-spinal hypotension, with lower incidence of bradycardia and similar neonatal outcome. Norepinephrine is recommended to prevent hypotension in CD, particularly in fetal distress. However, further research is needed to confirm this.

Keywords: Spinal anaesthesia, C-section, Norepinephrine, PE, Umbilical artery pH, Hypotension

INTRODUCTION

The most common complication of spinal anesthesia (SA) during CD is hypotension, with a reported incidence of up to 80%.[1] Severe and sustained maternal hypotension can result in fetal acidosis and neonatal depression due to decreased uterine and intervillous blood flow and impaired fetal oxygenation.[2,3] The commonly practiced non-pharmacological methods of maintaining maternal blood pressure (BP), such as preloading and leg raising, have proven to be largely unsuccessful.[4] And vasopressors now form the basis for managing post-spinal hypotension in CD.

Different vasopressors have been used with varying degrees of success.[5] Mephentermine prevents maternal hypotension with no adverse effect on neonatal outcome but tachyphylaxis to its pressor action develops rapidly.[6] Ephedrine was the preferred vasopressor in the past, but it has a delayed onset and a longer duration of action of about 60 min.[7] Recent evidence demonstrates that PE is effective in maintaining BP during CDs under SA and is associated with a lower rate of fetal acidosis compared to

ephedrine.[8,9] PE has been established 1st-line vasopressor for prevention and treatment of maternal hypotension in last decade.[6,10,11] However, its use is often associated with dose-related bradycardia, leading to a decrease in cardiac output (CO).[12] This has clinical significance in patients with unstressed fetuses, and potential for further harm in fetal distress.[12,13] Norepinephrine is now being investigated for its safety and efficacy as a vasopressor for post-spinal hypotension, with less tendency to decrease HR and CO compared with PE.[14]

The choice of vasopressors used for post-spinal hypotension during CD in our hospital is at the discretion of the attending anesthesiologist with no definitive guidelines. We compared the PE and NE for umbilical artery pH, maternal hemodynamics with the number of episodes of hypotension, hypertension or bradycardia; total dose and number of boluses required to maintain systolic BP, maternal nausea and vomiting episodes, and neonatal outcome in both groups by measuring Apgar scores at 1 and 5 minutes, development of hypoxic ischemic encephalopathy (HIE).

METHODS

The study was a prospective observational study conducted in the department of anaesthesiology, Lady Hardinge medical college and associated Shrimati Sucheta Kriplani hospital, after approval by the institutional ethical committee (IEC). The study was registered at clinical trials registry India (CTRI/2019/01/017159) and carried out from November 2017 to March 2019 in term pregnant patients carrying a singleton pregnancy (American society of anesthesiology grade I and II) scheduled to undergo CD under SA. Written informed consent was obtained from all the participants. The study was conducted in accordance with the declaration of Helskinki and good clinical practice.

Exclusion criteria were ASA grade III and IV, patients who refused SA, had a history of drug allergy, had any contraindication to SA, in whom SA was inadequate for conduct of surgery, known fetal abnormality detected antenatally, obstetric complications like placenta previa, placental abruption or cord prolapse, hypovolemia due to any cause and systolic BP <100 mmHg at the time of anesthesia induction.

After the detailed pre-anesthetic check-up and investigations, all patients received appropriate antacid prophylaxis. On arrival in the operating room, standard monitors including non-invasive BP, electrocardiography (ECG) with HR and pulse oximetry (SpO_2) were attached and baseline readings recorded. Fetal heart rate was monitored until the time of surgical preparation. Under all aseptic precautions SA was given with a disposable 25-gauge Quincke's needle and hyperbaric 0.5% bupivacaine 1.8 -2 mL with 25 µgm fentanyl injected. BP was measured at 2-min intervals beginning 1 min after spinal injection until delivery of the baby, thereafter BP was recorded every 5 min until the end of surgery. A blood sample from the umbilical artery (UA) was obtained from a double clamped segment of the umbilical cord. Patient's HR, ECG and SpO_2 were continuously monitored and recorded. The attending neonatologist assessed the Apgar score at 1 and 5 min and subsequently assessed the baby for any features suggestive of hypoxic ischemic encephalopathy (consciousness level/ seizures/ respiratory difficulty/ decreased tone) till 24 hours.

Hypotension was defined as fall in SBP ≥20% below baseline or SBP ≤100 mmHg and vasopressor (either PE or NE) was administered as per anesthesiologist decision. The patients in group PE received an IV bolus of PE 100 µg (100 µg/mL), and those in group NE received an IV bolus of NE 8 µg (8 µg/mL). Bradycardia was defined as HR <50/min and treated with IV atropine 0.6mg administration. Injection ondansetron 4 mg was administered intravenously to treat nausea and vomiting. Hypertension was defined when SBP >120% of baseline.

The primary objective was the difference in UA acid-base balance with the use of PE or NE. The secondary objectives were to compare maternal hemodynamics (number of episodes of hypotension, hypertension, and bradycardia), total dose and number of boluses of either drug required to maintain SBP, the incidence of maternal nausea and vomiting or neonatal outcome (Apgar score/development of HIE).

The sample size was determined based on UA pH with the use of different vasopressors. With reference to previous studies, we defined a difference of 0.05 in umbilical arterial pH as clinically significant. Thus, with the sample size of at least 84 patients in each group, there was 90% power with an effective size of 0.50 at an alpha 0.05 to detect a difference of 0.05 between two groups. Assuming a 20% loss in sample processing, 101 patients in each group needed to be recruited.

Statistical testing was conducted with the statistical package for the social science system (SPSS) version 22.0. The comparison of continuous variables between the groups was performed using Student's t test. Nominal categorical data between the groups were compared using the Chi-squared test or Fisher's exact test as appropriate. Non-normal distribution continuous variables were compared using the Mann Whitney U test. For all statistical tests, a p value less than 0.05 was taken to indicate a significant difference.

RESULTS

A total of 605 patients fulfilled the inclusion criteria and were enrolled in our study. Out of these, in 5 patients SA was converted to general anesthesia and in another 7 patients UA blood sample could not be analysed, therefore these patients were excluded from the study. Thus, 593 patients were included in our study and 226 patients (38%) had at least one episode of hypotension

before delivery of the baby and hence were analysed. Out of the 226 patients, 106 patients received PE (group PE) and 120 patients received norepinephrine (group NE) for treatment of post-spinal hypotension.

The maternal demographic characteristics, gestational age and the height of spinal block at 5 minutes did not differ significantly between the PE group and the NE group (Table 1). The indications of CD in group PE and group NE were comparable (Figure 1). Indications of CD for fetal distress in group PE and group NE were also comparable (Figure 2).

Table 1: Maternal characteristics.

Maternal characteristic	Group PE, (n=106), Mean ± SD	Group NE, (n=120), Mean ± SD	P value
Age (years)	26.54±4.25	27.24±3.95	0.350
Weight (kg)	66.54±7.30	67.92±6.11	0.054
Heights (cm)	152.88±5.55	152.08±5.47	0.438
Gestational age (weeks)	38.16±1.07	38.17±1.06	0.341
Height of spinal block (After 5 min)	T4 (T4-T5)	T5 (T4-T6)	0.782

Values are mean ± SD, group PE-Group phenylephrine, group NE-Group norepinephrine, Weeks-weeks, min-Minutes.

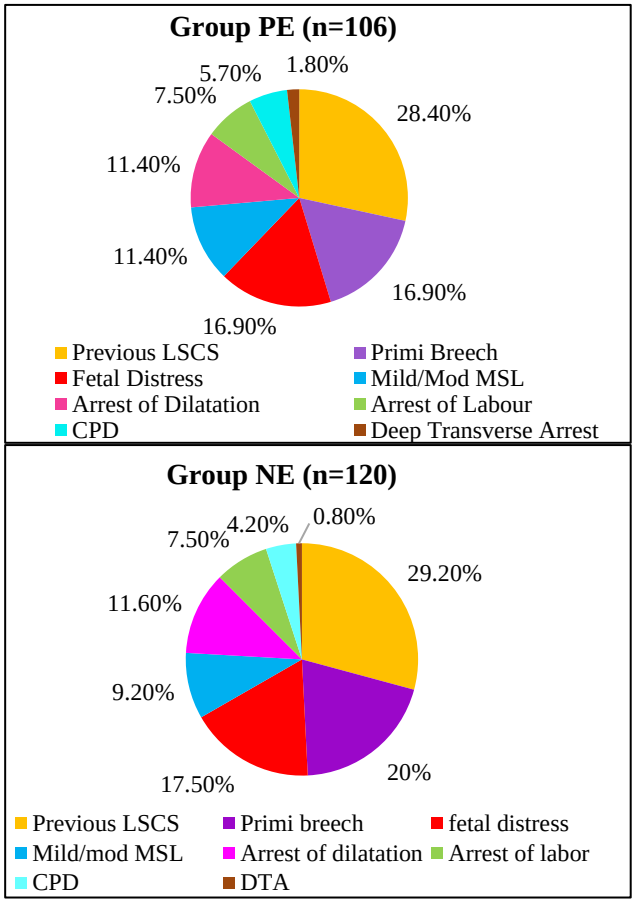

Figure 1: Indications for CD.

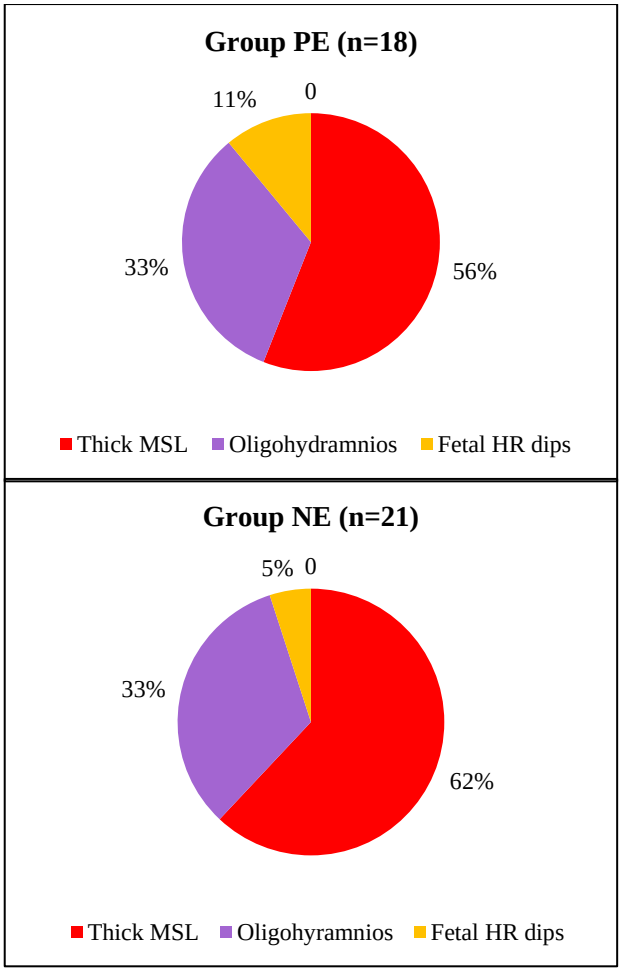

Figure 2: Indications of CD for fetal distress.

The mean umbilical artery pH in the PE group and NE group did not differ significantly (Table 2). However, subgroup analysis showed fetal acidosis in the 39 patients who had undergone CD for fetal distress. A significantly greater dip in fetal pH was seen in the PE group as compared to the NE group ($p<0.001$, Table 3). Additionally, some patients undergoing elective CD for non-fetal distress indications were found to have umbilical artery pH<7.2. The number of such patients were comparable (Table 4).

Table 2: Umbilical artery acid-base balance.

Umbilical artery parameters	Group PE, (n=106), Mean ± SD	Group NE, (n=120), Mean ± SD	P value
pH	7.236±0.091	7.248±0.052	0.199
PaO_2	22.07±3.83	21.76±3.51	0.523
$PaCO_2$	47.83±2.12	47.74±2.38	0.775
BE	2.808±0.839	2.676±0.745	0.210
Lactate	2.37±0.89	2.24±0.91	0.276

Values are mean ± SD, group PE-Group phenylephrine, group NE-Group norepinephrine, PaO_2-Partial pressure of oxygen in arterial blood, $PaCO_2$-Partial pressure of carbon dioxide in arterial blood, BE-Base excess.

Table 3: Umbilical artery acid-base balance in the fetal distress subgroup.

Umbilical artery parameters	Group PE, (n=18), Mean ± SD	Group NE, (n=21), Mean ± SD	P value
pH	7.062±0.045	7.183±0.035	<0.001
PaO2	18.07±2.02	18.20±3.50	0.646
PaCO2	49.82±2.33	49.04±3.07	0.119
BE	3.644±1.043	3.048±1.008	0.073
Lactate	3.79±1.19	3.32±1.52	0.156

Values are mean ± SD, Group PE-Group phenylephrine, group NE-Group norepinephrine, PaO_2-Partial pressure of oxygen in arterial blood, $PaCO_2$-Partial pressure of carbon dioxide in arterial blood, BE-Base excess

Table 4: Umbilical artery acid-base balance in CD, and pH<7.2.

Umbilical artery parameters	Group PE, (n=6), Mean ± SD	Group NE, (n=8), Mean ± SD
pH	7.159±0.031	7.179±0.028
PaO_2	19.80±3.62	19.27±1.65
$PaCO_2$	49.30±1.45	51.40±1.97
BE	-2.91±0.45	-3.18±0.16
Lactate	2.37±0.89	2.24±0.91

Values are mean ± SD. Group PE-Group phenylephrine, group NE-Group norepinephrine, PaO_2-Partial pressure of oxygen in arterial blood, $PaCO_2$-Partial pressure of carbon dioxide in arterial blood, BE-Base excess

The mean SBP, DBP, and HR at baseline, immediately after SA, till delivery of the baby and thereafter till end of surgery were comparable in both groups (Figure 3-5).

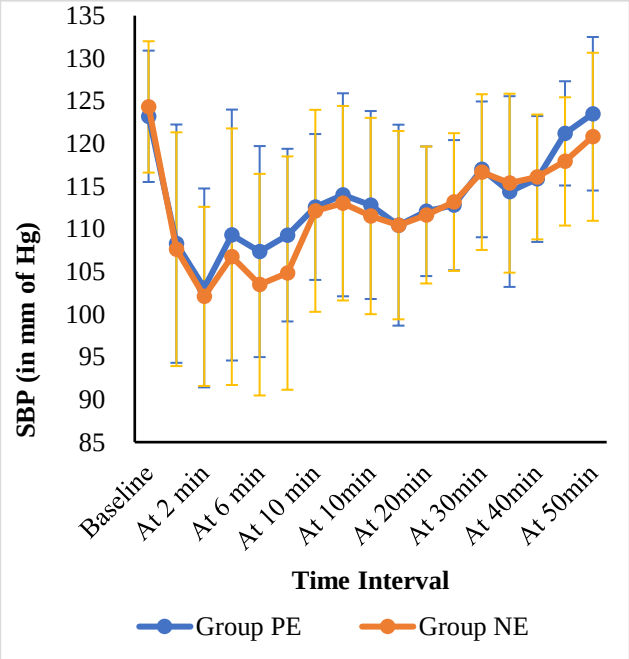

Figure 3: Mean SBP (Systolic blood pressure) after SA (Spinal anesthesia).

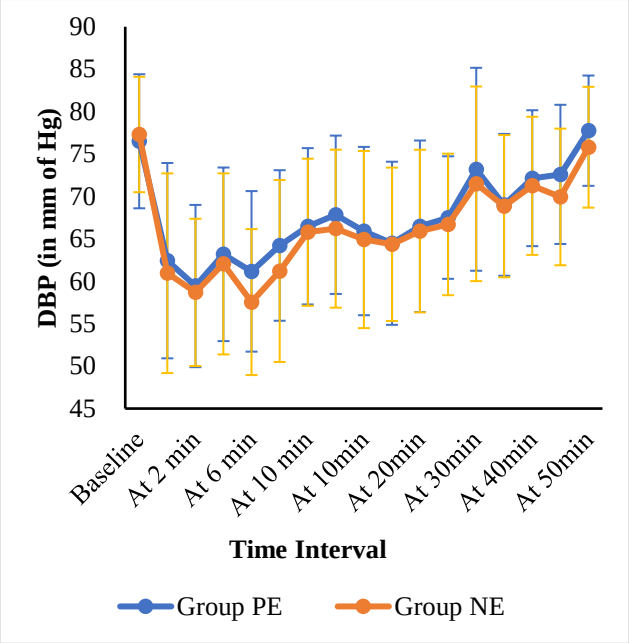

Figure 4: Mean DBP (Diastolic blood pressure) after SA (Spinal anesthesia).

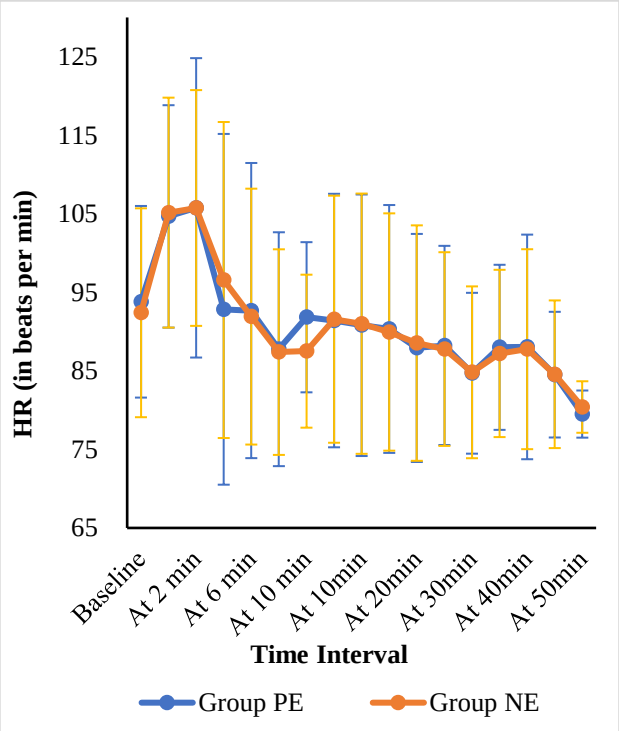

Figure 5: Mean HR (Heart rate) after SA (Spinal anesthesia).

Group PE and group NE were compared for hemodynamic changes in the first episode of hypotension, lowest SBP, lowest DBP, and HR at the time of lowest SBP. These parameters showed no significant difference in the two groups (Table 5). The first episode of hypotension was 2 minutes after giving SA in both groups (Table 6).

Table 5: Systolic BP, diastolic BP, and heart rate measured at critical points.

Groups	SBP, (mmHg) (Mean ± SD)			DBP, (mmHg) (Mean ± SD)			HR, (beats/min) (Mean ± SD)		
	Baseline	At first episode of hypo-tension	Lowest value beforere delivery	Baseline	At first episode of hypo-tension	Lowest value before delivery	Baseline	At first episode of hypo-tension	HR at lowest SBP
Group PE	123.29± 7.73	90.64± 4.97	89.84± 4.7	76.49± 7.88	50.17± 6.93	50.13± 6.85	93.83± 12.25	117.69± 10.69	115.11± 13.07
Group NE	124.30± 7.71	92.35± 6.16	89.72± 5.14	77.33± 6.85	49.77± 5.53	49.38± 5.88	92.40± 13.32	116.29± 10.88	106.57± 17.05

Values are mean ± SD, group PE-Group phenylephrine, group NE-Group norepinephrine, SBP-Systolic blood pressure, DBP-Diastolic blood pressure, HR-Heart rate.

Table 6: Time at the first vasopressor bolus requirement for each group.

Time of bolus dose	Group PE, (n=106) (%)	Group NE, (n=120) (%)
0-2 min	72.6	75.8
3-4 min	20.8	16.7
5-6 min	5.7	5.8
7-8 min	0.9	1.7

Values are in percentage (%). Group PE-Group phenylephrine, Group NE-Group norepinephrine, min-Minute.

Table 7: Maternal intraoperative complications.

Complications		Group PE, (n=106)	Group NE, (n=120)	P value
Bradycardia		14.2%	0.8%	<0.001
Lowest HR, median (IQR), (n=16)		47 (42-49)	49 (49)	
Hypertension		9.4%	6.6%	0.68
Hypertension (mmHg, n=17) (Median)	**SBP**	154	152	
	DBP	94	92	
Nausea and vomiting		43%	43.7%	0.515

Values of bradycardia, hypertension and nausea and vomiting are in Percentage (%). Group PE-Group Phenylephrine, Group NE-Group Norepinephrine, IQR-Interquartile range, SBP-Systolic Blood Pressure, DBP-Diastolic Blood Pressure, HR-Heart Rate, mmHg-Millimetres of Mercury.

Table 8: Number of vasopressor boluses required before delivery, and mean boluses required in each group.

Boluses required	Group PE, (n=106) (%)	Group NE, (n=120) (%)
1	53 (50)	20 (16.7)
2	51 (48.1)	41 (34.2)
3	2 (1.9)	43 (35.8)
4	0 (0)	15 (12.5)
5	0 (0)	1 (0.8)
Required boluses (Mean ± SD)	1.51±0.54	2.46±0.94

Values are in percentage (%) and mean ± SD, group PE-Group phenylephrine, group NE-Group norepinephrine.

No significant difference was observed in the PE group and NE group for the frequency of adverse effects of vasopressors (Table 7). The mean number of vasopressor boluses required and the total dose of vasopressor are shown in Table 8. The neonatal outcomes in both groups were comparable (Table 9).

Table 9: APGAR scores at 1 minute and 5 minutes were comparable in both groups.

Neonatal APGAR	Group PE, (n=106)		Group PE, (n=120)	
	Mean ± SD	Range	Mean ± SD	Range
1 min	8.9±0.14	8-9	8.9±0.46	9-10
5 min	9.7±0.13	8-9	9.7±0.46	9-10
HIE	0		0	

Values are mean ± SD. Group PE-Group Phenylephrine, Group NE-Group Norepinephrine

DISCUSSION

The results of our study show that when used to treat post-spinal hypotension in CD, both PE and NE do not cause any significant difference in the UA pH values. However, on subgroup analysis, it was observed that the lower pH values were seen in patients who underwent CDs for fetal distress with more fetal acidosis observed in patients receiving PE as compared with NE, the difference being statistically highly significant ($p<0.001$). Ours is probably the first study to evaluate UA acid-base values as a primary outcome when comparing intermittent boluses of PE with NE to prevent post-spinal hypotension during CD. Most studies comparing the two drugs have focused on hemodynamic parameters such as bradycardia and hypotension, and commented on the difference in UA acid base values only as a secondary outcome. Therefore, the results of this study have important clinical implications, in that if fetal bradycardia or fetal distress is present, PE may not be an ideal agent for the treatment of post-spinal hypotension in patients undergoing CD. This area needs further research.

We used 100 µgm of PE as a bolus to treat the first episode of hypotension and compared it with 8 µgm of NE. This was as per the estimated dose equivalent

suggested by Ngan Kee et al in a random-allocation, graded dose-response study. The outcome of our study is comparable to this study as the authors reported no change in fetal pH values between the two groups. The pH values in our study are a little lower than observed in their study which could be because we also included patients with fetal distress in our study.[15] Concurrent with our results, the incidence of fetal acidosis (pH<7.2) was found similar with the use of PE and NE.

Dong et al did not report any significant difference in pH with use of either drug.[16] Patients were randomized to receive prophylactic bolus NE (10 µgm) or PE (50 µgm) immediately after SA. The incidence of bradycardia was significantly lower in the NE group than that in the PE group ($p<0.05$). Cardiac output at 5 min was significantly greater in the NE group than that in the PE group ($p<0.05$). Sharkey et al and Vallejo et al also reported no difference in UA blood gases between PE and NE.[17,18] However, both these studies were in women presenting for elective CD. Similarly, in many of their subsequent studies, the pioneers of NE use in obstetrics, Ngan Kee et al have not reported any difference in the UA blood gases between PE and NE when used in elective CDs.[12,19-20]

Both drugs were equally efficacious in maintaining BP. However, the incidence of bradycardia was higher with the use of PE in our study. It is obvious that fetal wellbeing is compromised leading to fetal acidosis in cases of fetal distress. Any deterioration in maternal hemodynamics can add insult to injury. If a drug like PE is used in these cases, the bradycardia and fall in CO that it causes as a result of its pharmacologic profile only makes the situation more catastrophic. Although it seems logical that PE is to be avoided in fetal distress cases, reports on the use of PE in patients undergoing CD for fetal distress are limited.[21] Similar to our study, high incidence of bradycardia with the use of PE has been reported by Dong et al and Sharkey et al.[16,17] Bradycardia was the primary outcome in the study conducted by Sharkey et al.[17] Patients in the PE group had a higher risk of multiple bradycardia episodes (≥2 episodes) compared to the NE group. No differences were observed between the 2 groups in the incidence of other secondary outcomes. However, results not corroborating with ours were observed by Vallejo et al who reported no difference in the incidence of bradycardia between group PE and group NE, probably because the drugs were used in the potency ratio of 2:1 in their study instead of the usual potency ratio 20:1.[18]

The use of NE was associated with episodes of hypertension, although transient. The majority of the studies regarding NE are dose-finding studies, and there is no mention of hypertension episodes in these studies. The episodes of hypertension could relate to the use of NE as a bolus and using it as a continuous infusion could probably eliminate this adverse effect. Furthermore, a continuous infusion would also reduce the number of intermittent boluses required, which were more with the use of NE as compared with PE. This can be explained on the basis of drug pharmacokinetics, NE being an extremely short acting drug.

Xu et al recently published a systematic review and meta-analysis to compare the efficacy and safety of NE and PE.[22] The authors concluded that NE is a promising alternative to PE, with similar efficacy to manage maternal hypotension as PE; with the added advantage of reduction in certain side effects like bradycardia and nausea and vomiting. Further, they did not observe a difference between the two vasopressors in the incidence of neonatal APGAR scores <7 at 1 and 5 mins or in UV blood gas which is a finding corroborated by our observations too and by many other authors.[14-17,20] However, we were unable to find any published data in which HIE has been used for the assessment for neonatal outcome. Most studies have used the Apgar score to assess neonates at 1 and 5 mins.

The main limitation of our study was that it was an observational study as a randomized control trial is not permitted by our IEC due to the ethical issues related to research on high-risk and emergency obstetric cases. The dose-response analysis was based on the treatment of the first episode of hypotension after induction of SA, and the response may be different after the treatment of subsequent episodes of hypotension. Although we compared 8 µg NE with 100 µg PE but the true potency ratio and hence the comparable doses are still a little uncertain in obstetric patients. Also, could not measure CO directly and recorded HR as surrogate marker.

In conclusion, our study showed that fetal pH was effectively maintained within normal range with both NE and PE used for treatment of post-spinal hypotension in CD. In patients undergoing CD for the indication of fetal distress, fetal pH was acidotic in both groups, but better maintained with the use of NE than PE. Norepinephrine is as effective as PE in preventing post-spinal hypotension, with significantly lower incidence of bradycardia, although it causes transient episodes of hypertension when used as intermittent boluses. The neonatal outcome was similar with both the drugs. Therefore, we recommend that NE be used to prevent post-spinal hypotension in CDs, particularly in parturients with an indication of fetal distress. However, further research is needed to confirm the safety and efficacy of NE in larger groups of obstetrics patients with fetal distress.

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REFERENCES

1. Klohr S, Roth R, Hofmann T, Rossaint R, Heesen M. Definitions of hypotension after spinal anesthesia for cesarean section: literature search and application to parturients. Acta Anaesthesiol Scand. 2010;54:909-21.
2. Rasanen, J, Alahuhtat S, Kangas-Saarelat T, Jouppilat R, Jouppila P. The effects of ephedrine and etilefrine on uterine and fetal blood flow and on fetal myocardial function during spinal anesthesia for cesarean section. Int J Obstet Anesth. 1991;1:3-8.
3. Loughrey JPR, 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. Int J Obstet Anesth. 2005;14:43-7.
4. Cyna AM, Andrew M, Emmett Rs, Middleton P, Simmons SW. Techniques for preventing hypotension during spinal anesthesia for cesarean section. Cochrane Database Syst Rev. 2006:CD002251.
5. Ngan Kee WD, Khaw KS, Ng FF, Lee BB. Prophylactic phenylephrine infusion for preventing hypotension during spinal anesthesia for cesarean delivery. Anesth Analg. 2004;98:815-21.
6. Nag DS, Samaddar DP, Chatterjee A, Kumar H, Dembla A. Vasopressors in obstetric anesthesia: A current perspective World J Clin Cases. 2015;3:58-64.
7. Lee A, Ngan 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. Anesth Analg. 2002;94:920-6.
8. 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;97:1582-90.
9. Ngan Kee WD, Lee A. Multivariate analysis of factors associated with umbilical arterial pH and standard base excess after cesarean section under spinal anesthesia. Anesthesia. 2003;58:125-30.
10. American Society of Anesthesiologists Task Force on Obstetric Anesthesia. Practice guidelines for obstetric anesthesia: an updated report by the American Society of Anesthesiologists Task Force on Obstetric Anesthesia. Anesthesiology. 2007;106:843-63.
11. Ngan Kee WD, Khaw KS, Ng FF, Lee BB. Prophylactic phenylephrine infusion for preventing hypotension during spinal anesthesia for cesarean delivery. Anesth Analg. 2004;98:815-21.
12. 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;111:1230-7.
13. Hasanin AM, Amin SM, Agiza NA, Elsayed MK, Refaat S, Hussein HA et al. Norepinephrine infusion for preventing postspinal anesthesia hypotension during cesarean delivery: A randomized dose-finding trial. Anesthesiology. 2019;130:55-62.
14. Carvalho B and Dyer RA. Norepinephrine for spinal hypotension during cesarean delivery: another paradigm shift? Anesthesiology 2015; 122:728-730.
15. 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;127:934–41.
16. Dong L, Dong Q, Song X, Liu Y, Wang Y. Comparison of prophylactic bolus norepinephrine and phenylephrine on hypotension during spinal anesthesia for cesarean section. Int J Clin Exp Med. 2017;10:12315-21.
17. Sharkey AM, Siddiqui N, Downey K, Ye XY, Guevara J, Carvalho JCA. Comparison of intermittent intravenous boluses of phenylephrine and norepinephrine to prevent and treat spinal-induced hypotension in cesarean deliveries: randomized controlled trial. Anesth Analg. 2018.
18. Vallejo MC, Attaallah AF, Elzamzamy OM, Citarelli DT, Phelps AL et al. An open-label randomized controlled clinical trial for comparison of continuous phenylephrine versus norepinephrine infusion in prevention of spinal hypotension during cesarean delivery. Int J Obstet Anesth. 2016;29:18-25.
19. Ngan Kee WD, Lee S, Ng FF, Tan PE, Khaw KS. Randomized double-blinded comparison of norepinephrine and phenylephrine for maintenance of blood pressure during spinal anesthesia for cesarean delivery. Anesthesiol. 2015;122:736-45.
20. Ngan Kee WD, Khaw KS, Tam YH, Ng FF, Lee SW. Performance of a closed-loop feedback computer-controlled infusion system for maintaining blood pressure during spinal anesthesia for cesarean section: a randomized controlled comparison of norepinephrine versus phenylephrine. J Clin Monit Comput. 2016;31:617-23.
21. Jain K, Makkar JK, Subramani VPS, 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. J Clin Anesth. 2016;34:208-15.
22. Xu S, Shen X, Liu S, Yang J, Wang X. Efficacy and safety of norepinephrine versus phenylephrine for the management of maternal hypotension during cesarean delivery with spinal anesthesia. Medicine. 2019;98:5(e14331).

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