Original article

The efficacy of oral ephedrine in prevention of hypotension following spinal anesthesia in LSCS

T Bajracharya, BP Sah, TR Rahman
Dept of Anesthesiology and Citical Care KISTMCTH, Lalitpur, Nepal, Dept of Anesthesiology and Critical Care BPKIHS, Dharan Nepal

Abstract

Background: Systemic hypotension is seen frequently after spinal anesthesia in obstetric population and if untreated can lead to maternal and fetal complications. Ephedrine, via various routes, has been used both as prophylaxis and treatment of this hypotension. Oral ephedrine has been found to be effective in prevention of hypotension in non obstetric patients after neural block. **Objective:** To study the efficacy of oral ephedrine in prevention of hypotension following spinal anesthesia in LSCS and to assess the neonatal outcome**. Methods:** It was a randomized, controlled double blinded study involving 100 parturients undergoing LSCS. Total duration of study was two years. A preformed structured proforma was used to record the data incidence of hypotension and neonatatal APGAR score were the main outcome variables. This study was carried out in 100 ASA physical status I and II patients admitted for emergency and elective LSCS. Fifty patients received placebo and 50 patients received prophylactic ephedrine orally, before spinal anesthesia. The two groups were compared in respect of their incidences of hypotension and maintenance of SBP and neonatal outcome. **Results**: The incidence of hypotension was much higher in patients who received placebo than who received prophylactic ephedrine orally (19 vs. 6). APGAR score for assessment of neonatal wellbeing was similar in two groups. **Conclusions**: The prophylactic oral ephedrine 30 mg, given 30-45 minutes before LSCS, is a simple and effective measure to prevent hypotension following spinal anesthesia and it does not have any adverse effect on neonatal outcome.

Keywords: LSCS, oral ephedrine, spinal anesthesia.

Introduction

The use of spinal anesthesia for cesarean section has increased due to its overall maternal and fetal safety. However, systemic hypotension is one of the conditon which is seen most frequently (about 33%) [1] and immediately after spinal anesthesia. Intravenous and intramuscular use of ephedrine has been used both as prophylaxis and treatment of hypotension subsequently to neuroaxial block, however the literature describing the use of oral ephedrine in preventing hypotension associated with spinal anesthesia in cesarean section could not be found.

Thus, the purpose of this study was to determine the efficacy of oral ephedrine in preventing hypotension associated with spinal anesthesia in ceserean section and to the assess fetal outcome.

Address for correspondence:
Dr Tamanna Bajracharya
Lecturer, Dept of Anesthesiology and Critical Care
KIST Medical College and hospital, Imadol, Lalitpur, Nepal
Email: drtamannabaj@gmail.com

Methods

This study was a randomized, double blinded controlled study. It was conducted on 100 parturients. Approval of this study was obtained from the B.P Koirala Institute of Health Sciences

ethical committee and informed written consent was obtained from the patients for the procedure.

Patient of ASA Physical Status I and II undergoing emergency or elective cesarean section for cephalopelvic disproportion, breech presentation and previous lower regment section cesarean section (LSCS) and full term uncomplicated singleton gestation under spinal anesthesia were included in the study. Patients with severe fetal distress as manifested clinically by change in heart rate and rhythm, thick meconium stained liquor, severely dehydrated and exhausted patient with or without per vaginal bleeding, patient with pre-eclampsia and eclampsia, and patient requiring general anesthesia after subarachnoid block for any reason were excluded from the study.

Patient were randomized by computerized random number generation technique into two equal groups namely Ä"and "B". Group "A", the control group (n= 50) were given placebo (vitamin B complex tablet looking alike ephedrine). Group "B", the study group (n=50) were given Tab ephedrine 30 mg.

As soon as the decision was taken for cesarean section in the emergency room, or delivery room, or in the elective cases, preanesthetic check up was done in the patient. Then, 30 minutes prior to entering the operation theatre, patient was given the study drug (orplacebo) with a sips of water orally as per randomization. Preloading with lactated Ringer solution 10ml/kg body weight over 10-15 minutes was done, prior to spinal block in both the groups. With the patient in left lateral position or sitting position, a 25-G Quincke-Babcock needle was inserted at L3-4 or L4-5 interspinous space and 0.5% heavy bupivacaine 2.2ml was injected intrathecally after ascertaining free flow of the cerebrospinal fluid (CSF). Then the patient was positioned in the left modified supine position with at least 15 degree of left lateral tilt.

NIBP, MAP, and HR were recorded at 2.5 minutes interval for 15 minutes and 5 minutes interval thereafter till the completion of the surgery and then at 15 minutes interval for 1 hour in the recovery room.

The dermatomal level of sensory loss was determined by pinpricks. All blocks extented up to T6-T4 level before surgery was allowed to start. Patient in whom hypotension [defined as 20% reduction in baseline systolic blood pressure (SBP) or any reduction of MAP to < 50 mmHg] developed was treated by incremental IV boluses of inj ephedrine 3mg at one minute interval till blood pressure returned to normal value.

Data were collected and entered in MS Excel program. Data was analyzed using the statistical package for social science (version 11.5 for windows, SPSS).

Chi square test of proportion, student T test, non parametric tests like KW statistics) were used to analyze the data. Control of measurement bias was done by blinding objective measurement.

Results

The demographic characteristics between the two groups were comparable. The table 1 below shows the technical variables which were comparable between two groups.

Table 1: Technical variables regarding subarachnoid block

Technical variables		Group A (n=50)	Group B (n=50)	P value
No of patients positioned in left lateral decubitus		48	47	0.64
No of patients positioned in sitting		2	3	
No of patients received SAB at L3-L4		4	8	0.21
No of patients received SAB at L4-L5		46	42	
Level of block at 15 min	T6	30	29	0.59
	T4	20	21	

All the values are in number.

There was no statistical difference in baseline mean hemodynamic variables in terms of Systolic blood pressure (SBP), Diastolic blood

pressure (DBP), Mean arterial pressure (MAP), heart rate (HR), between two groups as depicted in table 2 below.

Table 2: Baseline (preblock) mean hemodynamic variables

Parameters	Groups A (n=50)	Groups B (n=50)	p-value
SBP (mmHg)	124.8±10.0	123.7±9.6	0.70
DBP (mmHg)	79.9±9.1	77.6±10.0	0.93
MAP (mmHg)	93.2±93.4	93.4±9.26	0.86
HR/min	91.2±13.9	90.7±15.9	0.55

The values are in mean ± SD.

The mean SBP was higher in group B than group A at all time points intraoperatively which was shown in table 3.

Table 3: Comparison of intraoperative SBP (mmHg) between the groups

Time	Group A	Group B	P- value
0	121.3±10.4	125.2±11.9	0.083
2.5	120.4 ±10.3	123.4±15.6	0.257
5	117.5±12.6	124.2±15.3	0.01*
7.5	113.4±14.4	121.4±16.8	0.013*
10	116.1±16.5	121.6±16.22	0.092
12.5	117.2±14.2	121.8±18.7	0.171
15	113.5±15.4	121.3±14.8	0.011*
20	112.5±13.5	122.1±18.3	0.004*
25	109.3±13.5	121.8±16.8	<0.001**
30	109.9±13.8	121.1±17.5	0.001*
35	110.9±9.2	120.6±19.2	0.002*
40	110.6±12.7	122.1±18.1	0.001*
45	110.7±11.6	125.3±17.9	<0.001**
50	113.8±11.5	125.9±20.3	0.007*
55	116.8±12.4	128.6±18.5	0.017*
60	115.5±7.4	126.8±17.7	0.046*
65	115.8±10.9	128.1±12.5	0.04*
70	121.2±9.8	127.9±9.7	0.215
75	115±9.9	123.1±13.3	0.465
80		131.8±6.3	

The values are in mean ± SD. *statistically significant, ** highly statistically significant.

The changes in MAP in both groups after SAB is shown in table in table 4.

Table 4: Comparision of MAP(mmHg) between the groups

Time	Group A	Group B	P- value
0	90.7±10.6	93.6±12.8	0.218
2.5	88.5±9.8	90.6±15.2	0.414
5	87.4±12.6	89.8±12.4	0.329
7.5	82.7±14.7	87.6±15.5	0.106
10	84.7±13.8	86.9±13.4	0.439
12.5	83.9±11.3	86.8±14.3	0.278
15	82.8±12.5	87.5±16.4	0.115
20	80.8±11.8	85.4±13.7	0.078
25	76.7±13.5	83.6±14.2	0.013*
30	75.9±11.6	82.5±13.2	0.010*
35	75.5±10	81.1±15.8	0.043*
40	74.5±11.5	81.5±15.9	0.016*
45	74.5±12.4	85.0±14.4	0.001*
50	79.4±11.8	86.6±15.8	0.051
55	81.4±12.1	89.3±14.6	0.055
60	79.6±7.5	90.3±16.7	0.047
65	79.4±8.6	92.4±15.7	0.056
70	83.2±3.03	91.5±14.2	0.218
75	86±1.4	91.6±14.1	0.612
80		99±10.5	

The values are in mean ± SD. *statistically significant, ** highly statistically significant.

The mean of MAP was higher in group B than group A at all points of time. In postoperative period, the mean SBP, DBP and MAP were higher in group A than group B and it was statistically significant as shown in the table 5.

Table 5: Postoperative hemodynamic values

Parameters	Ggroup A (n=50)	Group B (n=50)	p-value
SBP (mmHg)	117.7±6.7	124.9±9.9	0.001**
DBP (mmHg)	68.4±7.1	73.5±8.8	0.003**
MAP (mmHg)	84.5±6.5	90.6±8.6	0.001**
HR/min	81.7±10.5	81.4±11.3	0.55

The values are in means (±) SD. *statistically significant, ** highly statistically significant

Overall 19(38%) patients in group A and 6 (12)% patients in group B developed hypotension following SAB.Though APGAR score was higher in groupA compared to group B, it was statistically not significant as shown in table 6.

Table 6:Comparison of neonatal well being as APGAR score between the groups.

APGAR (score)	Group A	Group B	P-value
1 minute	6.5±1.3	6.7±1.0	0.56
5 minute	7.8±1.1	8±0.9	0.50
10 minute	8.9±1.0	9.1±0.7	0.33

The values are in means (±) SD.

Discussion

Subarachnoid block (SAB) is one of the commonly employed techniques for LSCS. Hypotension is the most common side effect of SAB. It is primariliy the result of paralysis of the preganglionic sympathetic fibres that transmit motor impulses to the smooth muscles of the peripheral vasculatures. This results in increased in venous capacitance and pooling of blood in peripheral blood vessels and dimunition of venous return to the heart There is generalized arterial and arteriolar dilatation causing decrease arterial pressure.

In the pregnant women undergoing ceserean section under spinal anesthesia, compression of the inferior venacava by the gravid uterus further impeded venous return to the heart, predisposing to severe hypotension. When hypotension is severe and sustained, it can lead to an impairment of uterine and intervillous blood flow and results in fetal hypoxia, acidosis and neonatal depression.[4] Thus in women undergoing LSCS with SAB, the preservation of maternal normotension is a desirable goal for maternal and fetal well being.

Ephedrine is the most extensively studied vasopressor used to treat hypotension with spinal anesthesia. The effective dose of oral ephedrine is 25-50 mg so we used an average dose of 30mg and it was given 30-45 min prior to SAB as its onset of action is 30-45 minutes after oral administration. [5] However there have been controversies regarding delayed gastric emptying in parturient. But the recent studies have shown that until second stage of labor gastric emptying remains normal in term pregnant ladies. In our study we had included parturient for emergency or elective ceserean section who were taken for surgery before the second stage of labor starts. So assuming that the gastric emptying will be normal, the oral ephedrine was given 30-45 minutes prior to block.

In our study, preloading with 10ml/kg bolus of lactated ringer, 10-15 minutes before the administration of spinal anesthesia, was done. Although the effectiveness of intravenous volume preloading in preventing maternal hypotension has been questioned, the simultaneous use with ephedrine appears to improve cardiac out put and may promote cardiovascular stability [7]. Our result showed that hypotension occured in 19 (38%) women in group A an 6 (12%) women in group B. Minimum SBP and MAP recorded were 86.47±7.17 and 59.11±6.58 mmHg respectively in group A and 87.17±7.78 and 57.00±5.59 mmHg respectively in group B.

Effect of oral ephedrine for prevention of hypotension has been studied by Fusun Eroglu et al [3] and Kafle et al [2] in non pregnant patient. Our finding are comparable with the study conducted by Fusun Eroglu at al [3] in context of prevention of hypotension. They included geriatric group of patient undergoing transurethral prostatectomy, in their study. In their study they found that the incidence of hypotension was halved in study group compared to control group. In our study, incidence of hypotension was more than 3 times halved in the placebo group compared to the study group. Compared to study done by Kafle et al, in our study, the incidence of hypotension was significantly less in study group than placebo group [2].

A study done by Kee et al [8] found that the lowest effective dose of prophylactic iv ephedrine to reduce the incidence of hypotension was 30 mg. The oral ephedrine 30 mg in our study similarly reduced the incidence of hypotension. Thus it was found that equal oral doses of ephedrine against intravenous ephedrine produced similar advantages in preventing the incidence of hypotension. As shown in the study done by Vercauteren MP et al [9], hypotension was

effectively lowered with the use of oral ephedrine in our study. In study done by Kang YG et al [10] in patient given the infusion, SBP didn't change significantly from the base line which was similar to our findings. Thus effect of oral ephedrine was comparable with continous infusion of ephedrine.

The use of 50mg IM ephedrine was found to be associated with higher incidence of hypertension as shown in the study by Rout CC et al [11] and Rolbin SH et al [12] whereas the use of oral ephedrine either 30mg or 50mg was found to be associated with the no incidence of hypertension in study done by Kafle et al [2] and Eroglu et al [3]. In our study we also found that incidence of hypertension (2%) was low. So use of oral ephedrine has advantage over intramuscular ephedrine regarding the occurence of hypertension. Pain on injection is well known disadvantage of IM administration. Thus the oral ephedrine is good alternative to avoid the pain caused by injection of ephedrine for pretreatment. Moreover pressor and cardiac responses to ephedrine persist for up to 3-5 hours after oral admistration while it persists up to 60 minutes with IM administration. So oral ephedrine provides more sustained hemodynamic stability compared to IM ephedrine.

In our study, tachycardia occured in four patient (8%) in group B and none in group A. One patient in group B developed hypertension after 25 minutes of SAB and it was associated with increased with HR. Maximum reading of SBP was 175 mmHg at 30 minutes following SAB. This is in contrast to study by Kafle et al [2] where none had an undesirable rise in blood pressure and tachycardia postoperatively.

Despite the overall 50% incidence of hypotension (12% in ephedrine group and 38% in placibo group) neonatal APGAR scores were similar in all the neonates. For practical reasons we couldnot assess the acid base parameter of umbilical cord blood which is one limitation of our study. However although umbilical blood gases would have been helpful as a measure of neonatal well being, the association between maternal hypotension and adverse neonatal base status has already been well documented. [13]

Conclusion

In conclusion, the prophylactic oral ephedrine 30mg , given 30-45 minutes before LSCS, is a simple and effective measure to prevent ocurrence of hypotension following spinal anesthesia and it doesnot have any major adverse effect on neonatal outcome.

References

1. Carpenter RL, Caplan RA, Brown DL, Stephenson RN, Wu R. Incidence and risk factors for side effects of spinal anesthesia. Anesthesiology 1992;76: 906-916
2. Kafle SK, Malla SM, Lekhak BD. Prophylactic oral ephedrine reduces the incidence pf hypotension after subarachnoid block. Can J anesth 1994 nov; 41:1091-3
3. Eroglu F, Yavuz L, Ceylan BC, Sevin G, Soyupek S. prophylactic effect of systemic oral ephedrine in spinal anesthesia-induced hypotension during transurethral prostatectomy. Scand J Urol Nephrol 2003; 37: 145-150
4. Corke BC, Datta S, Ostheimer GW, Weiss JB, Alper MH. Spinal anesthesia for cesarean section: The influence of hypotension on neonatal outcome. Anesthesia 1982; 37: 658.
5. Hoffman BB. Catecholamine and sympathetomimetics drugs and adrenergic receptor antagonist. In: Jeol GH, Lee EL, Alfred GG editors. Goodman & Gilman's the pharmacological basis of therapeutics. 10th ed. New york: McGrew hill companies, Inc: 2001.p. 237-38
6. Park GE, Hauch MA, Curlin F, Datta S, Bader AM. The effects of varying volumes of crystalloid administration before cesarean delivery on maternal hemodynamics and colloid osmotic pressure. Anesth Analg 1996; 83: 299-303.

7. Wennberg E, Frid I, Haljamae H, Noren H Colloid (3% dextran 70) with or without ephedrine infusion for cardiovascular stability during cesarean section. Br J Anesth 1992; 69: 13-8.
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. Anesth Analg 2000 ; 90(6): 1390-5
9. Vercauteran MP, Coppejans HC, Hoffmann VH, Mertens E, Adriaensen HA. Prevention of hypotension by a single 5mg dose of ephedrine during small-dose spinal anesthesia in prehydrated cesarean delivery patients. Anesth Analg 2000 ; 90(2): 324-7.
10. Kang YG, Abouleish E, Cartis S, Prophylactic intervenous ephedrine infusion during spinal anesthesia for cesarean section. Anesth Analg. 1982 ; 61(10):839-42.
11. Rout CC, Rocke DA, Brijball R, Koovarjee RV. Prophylactic intramuscular ephedrine prior to cesarean section. Anesth Intensive Care. 1992 ; 20(4):448-52.
12. Rolbin SH, Cole AF, Hew EM, Pollard A, Virgint S. Prophylactic intramuscular ephedrine before epidural anesthesia for cesarean section: efficacy and action on the fetus and newborn. Can Anesth Soc J. 1982 ; 29(2):148-53.
13. Littleford J. Effects on the fetus and newborn of maternal analgesia and anesthesia: a review. Can J Anesth 2004; 51: 589-609.