Original Article

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Phenylephrine versus Ephedrine during Spinal Anesthesia for Caesarean Section: Prospective Randomized Controlled Trial

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Abstract

Background: Hypotension is a frequent complication during spinal anesthesia for caesarean section which decreases uterine blood flow causing fetal hypoxia, acidosis and neonatal depression. *Methods:* After institutional ethics committee approval and written informed consent taken, 60 parturients (ASA I/II) undergoing elective caesarian section were equally divided into two groups receiving bolus doses of either ephedrine (5 mg, gr.E) or phenylephrine (100 microgram, gr.P) after subarachnoid block (SAB) whenever systolic blood pressure decreased greater than 20% from baseline. Hemodynamic were monitored for 75 minutes following subarachnoid block. All patients received subarachnoid block with 25 G Quincke's needle in left lateral position via midline approach using 0.5% hyperbaric Bupivacaine (2.4 ml) to achieve sensory level of T6 and preloaded with Ringer lactate (10 ml/kg). Umbilical artery blood gas analysis was done within 5 min of baby delivery. Neonatal outcome was assessed by Apgar score at 1, 5 and 10 min. Both groups were compared with respect to the number of vasopressor boluses required, differences in fetal blood gas and complications occurred. *Results:* Number of boluses required to treat hypotension was similar in both groups [2.43±1.13 (E) vs., 2.13±1.17 (P); p=0.23). SBP was higher in gr.P at 12, 14, 16 and 18 min after SAB. But, diastolic blood pressure was higher in gr. E at 35, 40, 45, 50 and 55 min (P<0.05); although the difference remained clinically insignificant. There was no difference in mean blood pressure (MAP). No difference was found in Apgar score at 1, 5 & 10 min. with all neonates having mean Apgar score greater than 8. There was no difference in umbilical arterial blood pH [7.304±0.063 vs., 7.306±0.064 respectively in GROUP P & E; (P=0.66)]. Incidence of vomiting was more in GROUP E [6.67% vs., 0]. Headache for transient period was observed, more in group E [6.67% vs., 3.34%]. *Conclusion:* We conclude that both phenylephrine and ephedrine are safe and effective in maintaining maternal blood pressure within 20% of baseline *without significant differences in fetal blood pH*. However, use of ephedrine is associated adverse effects like tachycardia, vomiting and headache.

Keywords: Ephedrine; Phenylephrine; Caesarian; Spinal anesthesia; Fetal acidosis.

Introduction

Subarachnoid block is the most widely used technique for caesarean section which is relatively safe and advantageous as compared to general and aesthesia [1, 2]. But, hypotension is a frequent complication during spinal anesthesia due to sympathetic blockade [3] and exacerbated by aortocaval compression which may decrease uterine blood flow causing fetal hypoxia, acidosis and neonatal depression [4] apart from maternal symptoms of low cardiac output such as nausea, vomiting and dizziness [5]. The incidence of hypotension during cesarean section under spinal anesthesia has been reported to be 80-90% or greater depending on the definition used [6, 7].

Currently, physical methods such as lateral uterine displacement, leg binders,

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compression stockings [8, 9], intravenous fluid preloading [10] and sympathomimetic drugs [11] are used to prevent/treat this hypotension. But vasopressor is almost always required because of the poor efficacy of these non-pharmacological techniques [12-16]. However, there is a controversy regarding the choice of vasopressor [17] and several studies have demonstrated that umbilical artery pH and base excess are lower with ephedrine as compared to phenylephrine [18-26]. Hence, this study was designed to assess the effectiveness of ephedrine and phenylephrine in treating hypotension during spinal anesthesia for cesarean section and their effect on fetal outcome using umbilical artery blood gas analysis and Apgar scores.

Methodology

This single centered study was done during 2007-08 after approval by institutional Ethics Committee. Sixty ASA grade I and II parturients with uncomplicated singleton pregnancy undergoing elective lower segment caesarean section under spinal anaesthesia were included after taking written informed consent. Patients with pregnancy-induced hypertension, history of diabetes, cardiovascular and cerebrovascular disease, fetal abnormalities, and contraindication to spinal anesthesia were excluded from the study. All parturients were equally divided into two groups (n=30 each). In Group E, parturients received IV ephedrine bolus 5 mg (1 ml) while Group P received IV phenylephrine bolus 100 microgram (1 ml) when hypotension occurred after spinal anaesthesia. Hypotension was defined as decrease in systolic blood pressure (SBP) greater than 20% from baseline or SBP<100 mmHg. All parturients received Ranitidine 150 mg orally evening before surgery and 50 mg IV along with Inj. Ondansetron 4 mg IV in operation theatre. Oxygen supplementation @ 4-6 lit/min via polymask was provided. Preloading with Ringer's Lactate @ 10-15 ml/kg was done in all patients. Under all aseptic precautions, subarachnoid block (SAB) was given in L3-4 interspace in left lateral position via midline approach using 25 Gauge Quincke's spinal needle. The volume of 2.4ml of 0.5% hyperbaric Bupivacaine was given intrathecally after confirming free and clear flow of CSF without blood. Patients were made supine immediately after SAB with a wedge to provide left lateral tilt. Sensory level of T6 was achieved in all patients. An infusion of Ringer lactate solution at 6ml/kg/hr was given intraoperatively in all patients. Injection glycopyrrolate 4mcg/kg IV was administered whenever heart rate fell below 50/min.

Whenever systolic BP decreased more than 20% of the baseline or < 100 mm Hg, either ephedrine or phenylephrine was administered as per group allocation to restore systolic BP. Maternal heart rate and saturation was monitored. The number of boluses needed was noted. After baby delivery and umbilical cord clamping, 1 ml umbilical arterial blood was collected for blood gas analysis. Neonatal outcome was assessed by Apgar score at 1, 5 and 10 minutes. Complications, if any were noted and compared.

Statistical Analysis

All data were analyzed using SPSS software. Differences between groups were compared using unpaired t-test for normally distributed data, while Mann-Whitney test was used to compare non-parametric data. Comparison of proportions was performed using Fisher's exact test. P<0.05 was considered significant. All analyses were two tailed.

Observation and Results

All parturients in both groups were comparable with respect to age, height, weight and ASA status. Both groups were also comparable with respect to the incidence of hypotension and degree of fall in

Table 1: Patients characteristics and relevant data

Parameter	Group P	Group E	P value
Age (yrs)	24.4 ± 2.78	25.6 ± 4.05	0.31
Weight (kgs)	56.8 ± 6.2	57.86 ± 6.42	0.48
Height (cms)	152.26 ± 4.9	152.83 ± 6.3	0.91
SAB–Delievery interval (mins)	17.7 ± 4.6	16.8 ± 4.49	0.44
No. of occasions on which SBP fell >20%(i.e. hypotension occurred)	2.13 ± 1.16	2.43 ± 1.13	0.23
Maximum fall in SBP (%)	27.38 ± 10.91	26.06 ± 6.71	0.96

Graph 1: Comparison of heart rate

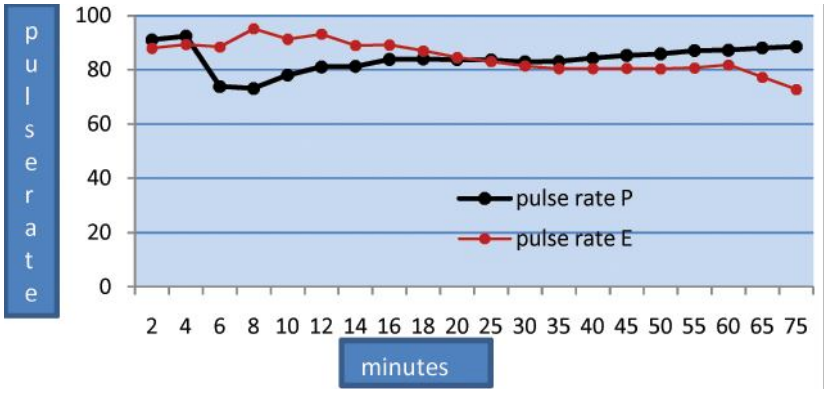
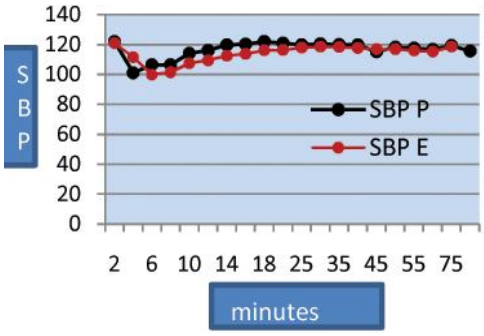


Table 2: Comparison of Apgar score and side effects

	Group P	Group E	P value
No. of boluses of vasopressor required	2.13 ± 1.16	2.4 ± 1.13	0.23
Apgar score at 1 min	8.23	8.5	0.07
Apgar score at 5 min	8.93	9.2	0.11
Apgar score at 10 min	9.63	9.8	0.25
Incidence of nausea/vomiting	0	6.67%	1
Incidence of headache	3.34%	6.67%	1

Graph 2: Comparison of Systolic Blood Pressure



Graph 3: Comparison of Diastolic Blood Pressure

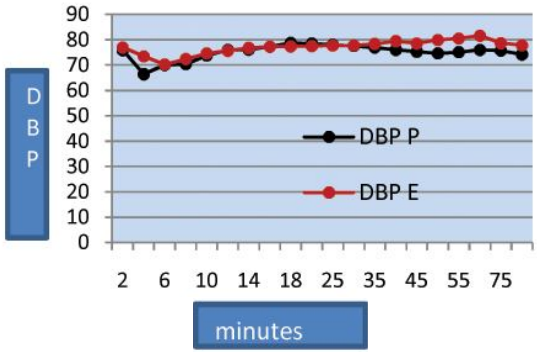


Table 3: Comparison of Umbilical artery blood gases

Umbilical arterial blood gas	Phenylephrine	Ephedrine	P-value
pH	7.304 ± 0.063	7.306 ± 0.064	0.6679
pO2	26.003 ± 7.802	30.316±13.376	0.3291
pCO2	39.763 ±7.423	41.44±9.869	0.4077
B.E.	-4.483 ± 3.666	-4.8±2.789	0.442
HCO3	22.183 ± 4.064	20.78±3.739	0.1693

SBP. Baseline hemodynamic parameters such as HR, SBP & DBP were similar in both groups. Induction to delivery time was also similar.

Use of ephedrine resulted in significant increase in heart rate as compared to phenylephrine, Graph 1. Gr. P showed greater degree of rise in SBP as compared to gr. E. at 12, 14, 16 and 18 min after SAB, Graph 2. But, DBP remained higher in gr.E at 35, 40, 45, 50 and 55 minutes, Graph 3. Blood pressure was comparable during other period in both groups. Number of bolus dose required to restore SBP was also similar in both groups, Table 2.

Mean Apgar score remained above 8 in both groups at 1, 5 & 10 min denoting good fetal outcome. Both groups showed similar umbilical arterial blood gas values,

(Table 3). There was no neurological complication related to SAB. However, few patients in gr.E complained of vomiting and headache which was transient.

Discussion

In this study, patients receiving ephedrine developed more tachycardia than those with phenylephrine. This explains reflex bradycardia (baroreceptor reflex) like effect of phenylephrine. Seven parturients who received phenylephrine developed bradycardia which responded to IV glycopyrrolate. The results of this study were in accordance with the study of Lee *et al*, [27] in which they reported higher incidence of bradycardia in patients receiving phenylephrine as compared with patients receiving ephedrine for prevention of hypotension during spinal anesthesia for cesarean section.

We also found out that, initially phenylephrine produced greater increase in SBP than ephedrine. But the difference was not clinically significant. Hence, we proved that both drugs were efficacious in managing hypotension following spinal anesthesia. Adigun *et al*, [28] also observed similar findings. However, Magalhães *et al* [29] observed that ephedrine was more effective than phenylephrine in the preventing hypotension. The difference can be attributed the lesser dose of phenylephrine used as compared to our study. Use of ephedrine was associated with increased adverse effects like tachycardia, vomiting and headache in our study.

We also found similar mean Apgar score in both groups suggesting good fetal outcome in accordance with similar study [28].

Umbilical arterial blood gas analysis revealed no significant difference in terms of fetal acidosis. No neonate in the study group had pH < 7.2. Since acidotic changes in umbilical artery are sensitive indicators of uteroplacental insufficiency; our study suggests that uterine blood flow is well maintained with both vasopressors similar to Cooper *et al* [30]. However more recent studies [23, 31, 32] in humans have shown that ephedrine is associated with lower values for umbilical arterial pH and more frequent incidence of fetal acidosis compared with alpha agonist phenylephrine. Nagan Lee et al [33] suggested that ephedrine 30 mg was the most effective i.v. bolus dose to prevent hypotension, but at the risk of an increased incidence of reactive hypertension and tachycardia. Increasing dose of ephedrine has been associated with decreasing umbilical artery pH in patients receiving spinal and epidural anaesthesia. Recently, Ngan Kee WD, et al [34] found that umbilical arterial (UA) and venous (UV) pH and base excess were similar between groups but in the ephedrine group, UA and UV lactate concentration was higher and more patients had nausea or vomiting. Advocates of phenylephrine claim better fetal acid-base status and similar efficacy in blood pressure control [20, 23, 32, 35]. Nagan Lee et al [31] in one of their study suggested that, in order to minimize the risk of fetal acidosis, ephedrine should not be used before delivery, uterine incision to delivery time should be as short as possible, and hypotension should be aggressively managed, preferably using alpha agonist phenylephrine.

Conclusion

Phenylephrine and ephedrine both are safe in managing hypotension during spinal anesthesia for elective cesarean section without risk of true fetal acidosis.

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Conflict of interest: Nil

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