

Original Research Article

A randomized control trial: To evaluate the effect of continuous infusion of low dose vasopressors in elective Cesarean section under spinal anesthesia

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Abstract

Introduction: A lot of researches have been done to support the role of vasopressors in elective Cesarean section to prevent hypotension in patient under spinal anesthesia resulting in better hemodynamic control in mother and fetus. This study was conducted to compare the effect of low dose ephedrine (60 mg) and phenylephrine (2 mg) on hemodynamic stability and fetal acid base profile in patient posted for elective caesarean section under spinal anesthesia.

Materials and methods: Ninety three patients were enrolled in this study and randomly divided into three groups. Group C received ephedrine infusion; group B received phenylephrine infusion while group A were preloaded with crystalloid. Maternal vital signs (blood pressure, heart rate, and arterial oxygen saturation) and fetal APGAR score and acid-base status were recorded.

Results: Hypotension was significantly recorded in crystalloid group as compared to phenylephrine and ephedrine group. Apgar scores in newborns were above 8 in all three groups. Umbilical cord blood pH was higher in phenylephrine and ephedrine groups in comparison to crystalloid group.

Conclusion: Prophylactic low dose phenylephrine and ephedrine infusion were more effective than crystalloid preloading in prevention of hypotension and fetal acidosis during spinal anesthesia for elective Cesarean section.

Key words

Phenylephrine, Ephedrine, Spinal anesthesia, Cesarean section, Hypotension.

Introduction

Safe anesthesia to a parturient is unique as it requires taking care of two lives at once. Neuraxial anesthesia is being used extensively in elective caesarean section due to certain advantages over general anesthesia like requiring minimal drug usage, causing lesser blood loss, comparatively lesser incidence of deep vein thrombosis, also maintaining adequate levels of consciousness during operation which is favorable for preventing aspiration and attaining better pain control in postoperative period for several hours depending on the technique being used [1]. However, hypotension, resulting from sympathectomy is associated with distressing symptoms like dizziness, nausea, vomiting and may also interfere with surgical procedure and can cause fetal bradycardia and acidosis. So we aimed to compare the effect of prophylactic infusion of low dose phenylephrine (2 mg) and ephedrine (60 mg) versus crystalloid preloading in the prevention of hypotension in mother and fetal acidosis after spinal anesthesia in elective Cesarean section.

Materials and methods

Institutional ethical committee approval was taken and all the participants gave written informed consent for this prospective, randomized, double-blind study. Ninety three, ASA I - II females, aged beyond 18 years, with gestational age > 36 weeks and planned for elective lower segment Cesarean section under spinal anesthesia were enrolled. Patients with Medical complications (like Diabetes, Cerebrovascular disease, Cardiovascular disease), obstetric complications like placenta previa, or placental abruption, cord complications (nuchal cord or cord prolapse), pregnancy induced hypertension, fetal malformations.), Patients with autonomic neuropathy, spinal deformities, infectious in the lumbar area, coagulation abnormalities, hypovolemia due to any cause were excluded.

After detailed pre-anesthetic check-up and routine investigations all patients were given ranitidine (150 mg) and metoclopramide (10 mg) per orally a night before and on the morning of surgery. All patients fasted for at least 8 hours prior to surgery. Using computer generated permuted block randomization, patients were divided into three groups A, B and C. group A preloaded with crystalloid 15 ml/kg lactated Ringer Solution over 15 min., group B received I.V. Inj. Phenylephrine 2mg in 40 ml saline solution while Group C received I.V. injection ephedrine 60 mg in 40 ml saline solution. Spinal anesthesia was performed in the sitting position with a 25 gauge whitacre needle, using a midline approach at L4-5 inter space. Once free flow of CSF had been recognized the intrathecal anesthetic solution (12 mg of 0.5% bupivacaine) was injected over 15 seconds. After intrathecal injection, the patients were turned in supine position with left uterine displacement. Surgery was started when a sensory block up to T5 dermatome was obtained. HR, ECG, SpO₂, and end tidal carbon dioxide (EtCO₂) were monitored continuously and NIBP was measured at 1-minute interval till first 10 minutes and at 5-minute interval thereafter till the mother was shifted to the postoperative room. APGAR score for baby is noted at 1 and 5 min. and cord blood sampling done for fetal acid-base status.

Maternal bradycardia (defined as heart rate less than 60 beats per min) was treated with 0.5 mg of intravenous atropine. Severe hypotension was defined by a systolic blood pressure less than 90 mmHg.

Results

Ninety three pregnant women were entered in this study. However, three patients were excluded as they underwent emergency LSCS for fetal bradycardia. Demographic data were summarized in **Table - 1**. There was no significant difference in demographic data.

Indications for caesarean section were repeated caesarean in 66 (73.3%) patients, other obstetrical indications for caesarean (cephalo-pelvic disproportion, breech or other abnormal presentations) in 24 (26.1%).

On comparing control group with study group (group B and C) the mean arterial blood pressure was found statistically significant difference at 1, 3 and 4 minutes ($p < 0.05$) while highly significant ($p < 0.001$) from 5 to 45 minutes time interval. On comparing phenylephrine and ephedrine groups the mean BP difference was found statistically insignificant at all the time intervals i.e. 1 to 45 minutes ($p > 0.05$). (Figure – 1)

On comparing control with study groups the mean pulse rate was found statistically insignificant ($p > 0.05$) up to 3 minutes while significant difference was found at 4 minutes ($p < 0.05$) and highly significant difference was found at 5 to 45 minutes interval. On comparing phenylephrine and ephedrine groups the mean pulse rate, statistically significant difference was found at 3 and 4 minutes ($p < 0.05$) while highly significant ($p < 0.001$) from 5 to 45 minutes time interval. (Figure – 2) While comparing mean SpO_2 at difference time intervals, the difference was found statistically insignificant ($p > 0.05$) when comparing all the three groups at 2 to 45 minutes.

Table -1: Demographic Data

	Group A	Group B	Group C	P value
Age	25.53±3.10	25.73±2.53	25.93±2.68	0.51
Weight (kg)	56.7±12.5	51.9±9.5	54.5±19.5	0.48
Height (cm)	155.9±7.4	158.9±7.4	157.9±7.4	0.41
Hb (gm%)	9.69±0.73	9.76±0.77	9.52±0.58	0.37

Figure - 1: Mean Blood Pressure in between Groups.

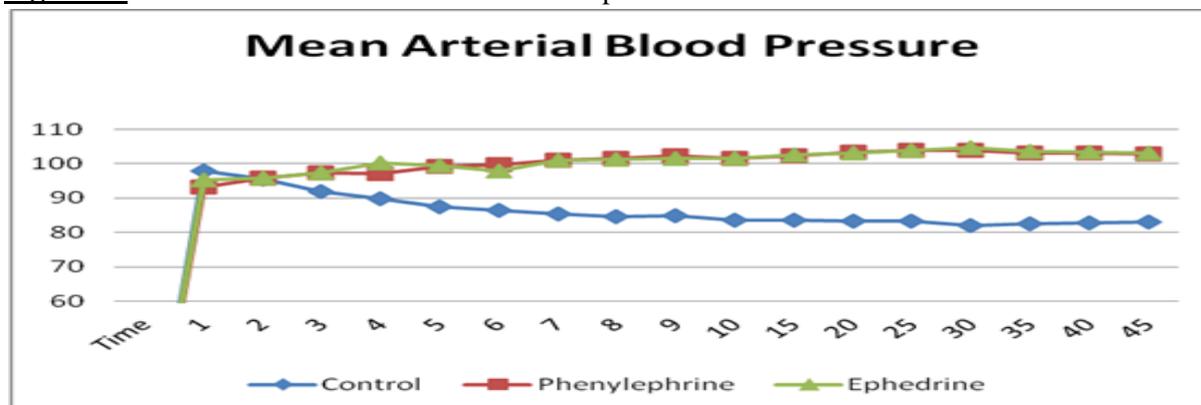
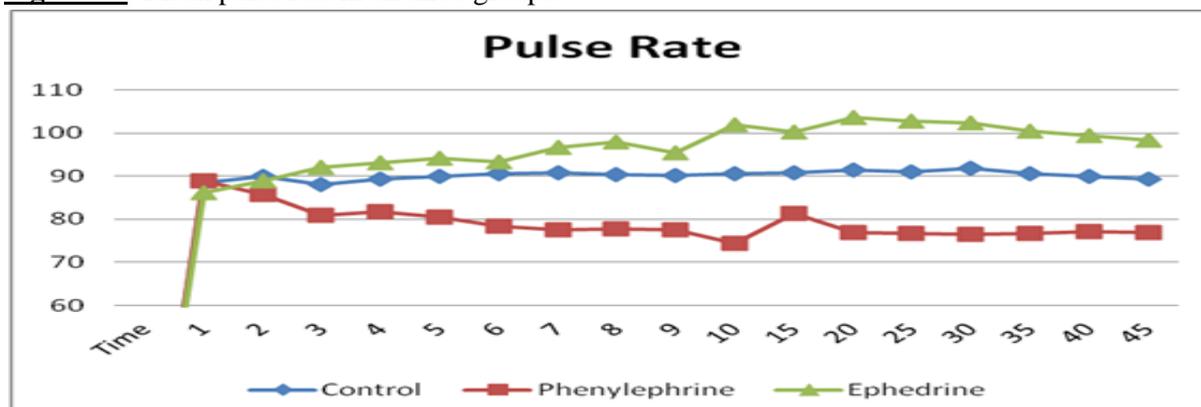


Figure - 2: Mean pulse rate in all three groups.



No complication was found in control and phenylephrine groups where as in Ephedrine group flushing was present in 2 cases and nausea + vomiting was present in 2 cases and nausea + vomiting + flushing was present in only 1 patients. On applying chi square test, the difference was found statistically insignificant ($p > 0.05$) (**Table – 2**)

Neonatal outcome was measured in term of APGAR score and umbilical cord ABG. Umbilical arterial blood gas analyses were

summarized in **Table - 3**. Based on the one-way ANOVA test, there was a significant difference in PH and Pco₂ between groups. Using Tukey for Post-hoc test, we found that the difference in PH and Pco₂ was significant between study and control groups. Quantitative evaluation of neonatal acidosis showed that no neonates in group C, 2 in group E (6.66%) and 6 in group P (20.0%) had acidosis. No significant difference was found in APGAR scores in neonates in all three groups.

Complication	Group A		Group B		Group C		Total	
	Control		Phenylephrine		Ephedrine			
	No	%	No.	%	No.	%	No.	%
Flushing			0	-	2	6.7	2	2.2
Nausea+Vomiting			0	-	2	6.7	2	2.2
Nausea+Vomiting+Flushing			0	-	1	3.3	1	1.1
Normal	30	100	30	100	25	83.3	85	94.4
Total	30	100	30	100	30	100	90	100
χ^2	10.588							
P	0.102NS							

	Group A	Group B	Group C	P value
PH	7.2 ± 0.03	7.32 ± 0.01	7.3 ± 0.03	0.031
PCO ₂	50.3±8.6	48.5±10.1	46.5±0.13	0.042
HCO ₃	22.16±1.10	21.90±1.55	21.27±0.97	0.328

(Group A - Control Group, Group B - Phenylephrine Group, Group C - Ephedrine *Mean±Sd)

Discussion

Various previous studies have shown that maintaining a stable hemodynamics and avoiding hypotension intra-operatively results in better utero-placental perfusion and better neonatal acid base status [2-4]. The present study therefore aimed to use prophylactic infusion of vasopressor and compare their efficacy on maternal and neonatal outcomes.

Many studies have compared the effectiveness of phenylephrine and ephedrine in various doses and the route of administrations. A review study of vasopressors in obstetric anesthesia: current perspective done by Nag DS, et al. [5] in 2015.

They evaluated the available evidence on the various vasopressors used in obstetric anesthesia and compared various vasopressors, their effects on maternal and fetal wellbeing and supported the use of phenylephrine as the vasopressor of choice while considering the influence on fetomaternal physiology.

Moslemi F, et al. [6] Compared effect of Prophylactic Infusion of Phenylephrine with Ephedrine for Prevention of Hypotension in Elective Caesarean Section under Spinal Anesthesia. They concluded Prophylactic infusion of phenylephrine can effectively decrease spinal anesthesia related hypotension

without any significant complication for mother or her fetus.

While Megha GH, et al. [7] discussed the effect of Prophylactic Bolus and Infusion of Phenylephrine and Ephedrine for Maintaining Maternal Hemodynamics in Cesarean Section under Spinal Anesthesia After the study they came out with a conclusion that Ephedrine prophylaxis is associated with better overall maintenance of hemodynamics. The incidence of bradycardia was more with phenylephrine. There were no major effects on uterine tone / uterine bleeding/ APGAR score in both groups.

Sen I, et al. [8] conducted a study on Colloid cohydration and variable rate phenylephrine infusion effectively prevents post spinal hypotension in elective Cesarean deliveries. They concluded that a combination of colloid cohydration and prophylactic phenylephrine infusion initiated at 60 µg/minute maintained maternal hemodynamics and neonatal well-being during Cesarean deliveries requiring minimum interventions by the anesthesiologist.

In another review study done by Ashraf S, et al. [9], on the impact of phenylephrine administration on maternal hemodynamics and maternal and neonatal outcomes in women undergoing caesarean delivery under spinal Anesthesia. They compared various vasopressors in different doses and in form of boluses and infusion, and their effects on maternal and neonatal outcomes and concluded that both ephedrine and phenylephrine are effective in managing spinal anesthesia-induced hypotension. Phenylephrine may be associated with a lower incidence of IONV, and higher umbilical artery pH and base excess compared with ephedrine. Simin, et al. [10], compared the effect of ephedrine and phenylephrine in treatment of hypotension after spinal anesthesia during caesarean section. They found that there was no difference in treatment of hypotension following sympathectomy after spinal block with two drugs. Neonatal outcome was similar in two

groups. There were not significant differences in umbilical arterial values in two groups. They concluded that ephedrine and phenylephrine are both effective vasopressors for treatment of hypotension associated to spinal block during caesarean section without adverse effects on infants/neonates.

Sayasach, et al. [11] compared infusions of phenylephrine, ephedrine and their combination with lower doses for prophylaxis against maternal hypotension following spinal anesthesia. They found that phenylephrine alone is a better choice than ephedrine or combined. In our study, we found that there was no significant difference between ephedrine and phenylephrine in term of their efficacy for managing hypotension but patients with phenylephrine group shown relatively low and stable heart rate. In addition, neonatal outcome was better in study groups. There were no differences in Apgar scores at 1 and 5 minutes of birth and differences between study groups in umbilical artery pH were not significant although true acidosis ($\text{pH} \leq 7.20$) was not seen in any of neonates.

As the uteroplacental perfusion depends directly to the mean BP of mother so prevention and treatment of spinal anesthesia induced hypotension remains the most important intervention for fetal wellbeing, with various mode of management [12-14]. Various previous studies has confirmed that phenylephrine has better umbilical pH profile⁵⁻¹¹ and suggested phenylephrine as the first line drug for preventing maternal hypotension [15-17]. Although both phenylephrine and ephedrine effectively maintain blood pressure, phenylephrine causes reflexes bradycardia and it may reduce cardiac output [18, 19] and so the utero-placental blood flow while ephedrine is associated with tachycardia. For counteracting the cardiac effects of both vasopressors, the combination of these two vasopressors in used different ratios given by infusion and compared with single agent infusion. Ngan Kee, et al. [20] found combination of vasopressors have no advantage compared with phenylephrine alone.

While Loughy, et al. [21] noted that ephedrine alone is better than the combination of two vasopressors.

Current literature supports the use of phenylephrine as the vasopressors of choice while considering the influence on fetomaternal physiology. However, this concept is mostly based on studies conducted in elective Cesarean sections. In another study Ngan Kee, et al. [22], compared the phenylephrine with ephedrine in non-elective caesarean section. They concluded that despite small differences between groups in umbilical cord blood lactate concentration and PO₂, there were no differences in fetal acid-base status or clinical neonatal outcome between the two vasopressors. Our study results relatively conform to the Ngan Kee, et al. [22] study.

The results of this study show that women who underwent spinal anesthesia for elective caesarean section, mean blood pressure and heart rate were better maintained with a prophylactic infusion of phenylephrine and ephedrine as compared to control group. In our study no complication was found in control and phenylephrine groups whereas in Ephedrine group flushing was present in 2 cases and nausea + vomiting was present in 2 cases and nausea + vomiting + flushing was present in only 1 patient. On applying chi square test, the difference was found statistically insignificant ($p > 0.05$). Similarly neonatal condition was better in study groups than control group.

Conclusion

Both phenylephrine (2 mg) and ephedrine (60 mg) maintained BP and heart rate perioperatively. Cord blood pH was better in phenylephrine and ephedrine group but nausea, vomiting and flushing were observed more in ephedrine group. This study observed that both vasopressors in low doses maintained maternal and fetal wellbeing but low dose infusion of phenylephrine provided better maternal hemodynamics without any significant complication for mother or her fetus.

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