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Research Article

COMPARATIVE STUDY OF DIFFERENT DOSES OF BOLUS INTRAVENOUS EPHEDRINE TO CONTROL SPINAL ANAESTHESIA INDUCED HYPOTENSION IN CAESAREAN SECTION

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ABSTRACT

Background: Hypotension following spinal anaesthesia for caesarean section is one of the common problem encountered by anaesthesiologists. A number of strategies for preventing hypotension has been investigated. This study was undertaken to compare the efficacy of different bolus doses of prophylactic ephedrine to prevent spinal anaesthesia induced maternal hypotension during caesarean section.

Methods: This was a prospective, randomized, comparative and interventional study among ninety-six patients who underwent caesarean section under spinal anaesthesia in Kirtipur hospital from September 2017 to August 2018. Total 96 enrolled cases were divided into three groups. Group-I received inj. ephedrine 0.25mg/kg, Group-II 0.5mg/kg, and Group-III normal saline prophylactic IV immediately after administration of spinal anaesthesia. Intra operative hemodynamic changes were recorded and the data was analyzed.

Results: Incidence of hypotension was higher in group III patients receiving inj. normal saline than in group I and II patients receiving 0.25mg/kg and 0.5 mg/kg body weight of inj. ephedrine respectively (25%(n=8) versus 18.8%(n=6) and 3.1%(n=1) respectively). There was a significantly higher incidence of reactive hypertension in group II patients (21.9% (n=7)).

Conclusions: Prophylactic use of 0.25mg/ kg body weight IV ephedrine can reduce incidence of hypotension without adverse effects like reactive hypertension in caesarean section.

Keywords: caesarean section; ephedrine; hypotension; reactive hypertension; spinal anaesthesia.

INTRODUCTION

Karl August Bier introduced spinal anaesthesia into Clinical practice in 1899.[1]In the last five decades it has gained its popularity. Spinal anaesthesia is frequently used for lower abdominal and lower extremity surgeries. It is performed by injecting small amount of local anaesthetic into subarachnoid space at L_{4-5}interspinal level. It is simple to perform and is economical requiring comparatively less time to produce more rapid onset of good quality sensory as well as motor block.[2]

The most common serious adverse effect of spinal anaesthesia for caesarean delivery is hypotension with a reported incidence greater than 80%.[3]Maternal hypotension is an undesirable consequence of spinal anaesthesia for caesarean delivery as it causes detrimental maternal and fetal adverse effects.[4]Various methods have been suggested for preventing hypotension. The use of lateral uterine displacement is a routine procedure to prevent hypotension.[5] Other strategies have included the use of intravenous fluid preload, gravity (leg rising), compression devices on the legs and prophylactic vasopressor.[6]A combination of preloading and vasopressor drugs has maximum efficacy in preventing spinal induced hypotension.[7]Systolic blood pressure more than 20% of baseline after administration of the bolus dose of prophylactic ephedrine within 5 minutes of spinal anaesthesia was considered as reactive hypertension. The prophylactic administration of ephedrine by the intra muscular route is very controversial because its systemic absorption and peak effect are difficult to predict.[8]

Intravenous ephedrine is proven to be more effective for increasing arterial blood pressure with better preservation of uteroplacental blood flow as compared to other vasopressor.[9]It has a predominant beta-effect that causes increase in arterial blood pressure by increasing cardiac output rather than by vasoconstriction.[10] In this study haemodynamic changes were compared with different bolus doses of ephedrine in cases of caesarean section. The aim of this study was to find out an optimal dose of prophylactic ephedrine in Nepalese maternal population to prevent spinal anaesthesia induced maternal hypotension effectively without causing side effect like reactive hypertension.

METHODS

This comparative study was done on parturients who came for elective as well as emergency lower segment caesarean section (LSCS) under spinal anaesthesia in Kirtipur Hospital from 1stSeptember 2017 to 3oth August 2018. After obtaining approval from Institutional Review board, ninety-six women of American Society of Anaesthesiologist (ASA) status I and II, weighing from 50 kg to 70 kg were divided into three groups. Group I received ephedrine 0.25mg/kg body weight, Group II received ephedrine 0.5mg/kg body weight and Group III received normal saline. No randomization was done. Parturients who refused for study were excluded from this study. Besides refusal, parturients with known hypertension, preexisting cardiac and pulmonary disease, spinal pathology, coagulation abnormalities and gestational age less than 37 weeks were also excluded from this study.

All women were premedicated with inj. ranitidine 50mg and metoclopropamide10 mg intravenously one hour before surgery. Baseline heart rate, blood pressure, pulse, electrocardiogram (ECG), and oxygen

saturation were recorded. All patient were preloaded with 500 ml Ringer's lactate solution for 15-20 minutes. After skin infiltration with 2% xylocaine, Spinal anaesthesia was administered in sitting position at the level of L_{3-4}inter space with 2.2ml of 0.5% hyperbaric bupivacaine using 27 gauge whitacre spinal needle. Patients were then turned to supine position with 15 degree left lateral tilt of operation table to prevent aortocaval compression.

Bolus dose of prophylactic study drug was given IV immediately on turning the patient to supine position from a prefilled syringe. All the patients received oxygen 2-3litres/minute by nasal pronge. The level of the sensory block was evaluated by loss of pinprick discrimination at the time to incision and every five minutes. Sensory block to T5 dermatome was considered as adequate for surgery

A systolic blood pressure less than 20% of baseline was considered as hypotension, and systolic blood pressure more than 20% of baseline after administration of the bolus dose of prophylactic ephedrine within 5 minutes of spinal anaesthesia was considered as reactive hypertension.

Parturient who developed hypotension after bolus dose of prophylactic ephedrine, additional rescue bolus dose of 6 mg ephedrine was given and infused Ringer's lactate solution fastly. Haemodynamic changes were noted. Frequency of hypotension, reactive hypertension, bradycardia and tachycardia were also recorded. Changes in maternal SBP, DBP, MAP and heart rate throughout anaesthesia, total dose and the number of bolus of vasopressor (rescue drug), sensory block level and total volume of fluids infused were also noted down.

All the relevant data were recorded on a specially designed proforma and were analyzed by SPSS version 11. Mean and standard deviation of age, weight, parity, baseline heart rate, blood pressure as well as rescue bolus dose of ephedrine were calculated. These variables were compared in three groups. Frequency of hypotension and reactive hypertension were also compared in these three groups. ANOVA and Chi square test were used. P-value less than 0.05 was considered significant.

RESULTS

Ninety-six parturients were included in this study, 32 each in three groups. The groups were comparable in age, weight, duration of surgery, upper sensory level block and total volume infused (Table 1). All parturients had adequate surgical anesthesia. The median upper sensory level 5 minutes after the intrathecal injection was T5 (T3-T6) for all the study groups.

There was no significant difference in baseline pulse, systolic blood pressure, diastolic blood pressure and mean arterial pressure (Table 2). The incidence of hypotension was 18.8% (n=6), 3.1% (n=1) and 25% (n=8) in group I, II and III respectively. The incidence of reactive hypertension was 3.1% (n=1), 21.9% (n=7) and 6.1% (n=2) in group I, II and III respectively. So group II had significant higher incidence of reactive hypertension (Table3). Total dose of rescue drug was significantly less in group II (Table 4,5).

	Group I (n=32)	Group II (n=32)	Group III (n=32)	p value*
Age (years)	27.71 ±4.43	26.38±2.65	26.24±4.14	0.263
Weight (Kg)	62.54±7.56	66.47±8.73	64.42±9.28	0.214
Duration of surgery (minute)	43.57±10.23	44.16±19.39	46.09±22.83	0.855
Upper Sensory Level (Median Range)	T5 (T3-T6)	T5 (T3-T6)	T5 (T3-T6)	
Total Fluid Infused (ml)	1850±120	2050±150	2040±200	

p-value < 0.05 is significant

Table 1: Demographic characteristic of patients (n=96).

	Group I	Group II	Group III	p value*
Pulse	87.39±10.61	87.84±13.07	96.94±22.98	0.042
Systolic blood pressure	120.11±11.51	117.81±12.72	118.55±9.92	0.734
Diastolic blood pressure	75.71±8.01	74.06±6.59	78.97±8.79	0.042
Mean arterial pressure	89.04±8.51	86.91±8.86	92.36±8.68	0.043

p-value < 0.05 is significant

Table 2: Baseline haemodynamicdata (n=96).

Systolic Blood Pressure (SBP)	Group I	Group II	Group III	p value*
>20% SBP	1(3.1%)	7(21.9%)	2(6.1%)	
<20% SBP	6(18.8.%)	1(3.1%)	8(25%)	0.019
Diastolic Blood Pressure (DBP)				
>20% DBP	0 (0%)	1(3.1%)	0 (0%)	
<20% DBP	12 (37.5%)	2(6.2%)	15(46.9%)	0.001
Mean Arterial Pressure (MAP)				
>20% MAP	2 (6.2%)	5(15.6%)	0 (0%)	
<20% MAP	9 (28.1%)	2 (6.2%)	16 (50%)	0.001

p-value < 0.05 is significant

Table 3: Hemodynamics after 5 min of spinal anaesthesia (n=96).

Systolic Blood Pressure (SBP)	Group I	Group II	Group III	p value*
>20% SBP	8(25%)	0 (0%)	8 (25%)	
<20% SBP	0 (0%)	4 (12.5%)	1 (3.1%)	0.005
Diastolic Blood Pressure (DBP)				
>20% DBP	15 (46.9%)	3 (9.4%)	14 (43.8%)	
<20% DBP	0 (0%)	3 (9.4%)	0 (0%)	0.001
Mean Arterial Pressure (MAP)				
>20% MAP	11 (34.4%)	2 (6.2%)	12 (37.5%)	
<20% MAP	0 (0%)	3 (9.4%)	0 (0%)	0.003

p-value < 0.05 is significant

Table 4: Hemodynamics after 10 min of spinal anaesthesia (n=96).

Systolic Blood Pressure (SBP)	Group I	Group II	Group III	p value*
>20% SBP	4 (12.5%)	4 (12.5%)	10 (31.2%)	
<20% SBP	0 (0%)	4 (12.5%)	1 (3.1%)	0.006
Diastolic Blood Pressure (DBP)				
>20% DBP	10 (31.2%)	14v(43.8%)	10 (31.2%)	
<20% DBP	0 (0%)	4 (12.5%)	1 (3.1%)	0.023
Mean Arterial Pressure (MAP)				
>20% MAP	7 (21.9%)	7 (21.9%)	18 (56.2%)	
<20% MAP	0 (0%)	3 (9.41%)	1 (3.1%)	0.003

p-value < 0.05 is significant

Table 5: Hemodynamics after 15 min of spinal anaesthesia (n=96).

Systolic Blood Pressure (SBP)	Group I	Group II	Group III	p value*
>20% SBP	2(6.21%)	2 (6.21%)	8 (25%)	0.016
<20% SBP	1 (3.1%)	6 (18.8%)	2 (6.2%)	
Diastolic Blood Pressure (DBP)				
>20% DBP	17 (53.1%)	12 (37.5%)	14 (43.8%)	0.283
<20% DBP	3 (9.4%)	2(6.2%)	0 (0%)	
Mean Arterial Pressure (MAP)				
>20% MAP	13 (40.6%)	8 (25%)	12 (37.5%)	0.667
<20% MAP	3 (9.4%)	2(6.2%)	2(6.2%)	

p-value < 0.05 is significant

Table 6: Hemodynamics after 20 min of spinal anaesthesia (n=96).

	Group I	Group II	Group III	pvalue
Yes	16 (50%)	2(6.2%)	15(45.5%)	0.001
No	16 (50%)	30(93.8%)	17(54.5%)	
Total	32	32	32	

Table 7: Rescue drug used (n=96).

Total ephedrine used (times)	Group I N=16	Group II N=2	Group III N=15	Total
1	7	1	5	13
2	6	1	8	15
3	3	0	1	4
4	0	0	1	1
Total	16	2	15	

Table 8: Total number of rescue drug used (n=33).

DISCUSSION

Regional anaesthesia especially spinal anaesthesiais proved to be the most preferred technique for caesarean section.[11,12] The incidence of hypotension during spinal anaesthesia for caesarean section is reported to be as high as 80% despite fluid preload, lateral displacement and use of vasopressor.[13]In obstetric applications, profound hypotension can potentially lead to serious hypoxia and hypovolemia in the mother and

fetus. As placental blood flow is directly proportional to the maternal blood pressure, the hypotension can lead to placental hypoperfusion and fetal asphyxia.[14]The prevention and treatment or maternal hypotension associated with spinal anaesthesia remains a difficult problem and there was no consensus on its optimal management.

Colloid solutions have also been studied and shown to produce a lower incidence of hypotension. 5% albumin is probably the most effective solution, but is expensive and not easily available. Other colloids are less effective than albumin, but they may cause anaphylactic reaction.[15]

Rout et al[3] demonstrated that incidence of hypotension decreased significantly from 71% to 55% for un preloaded versus preloaded subject respectively. Increasing the crystalloid preload from 10 to 30ml/kg may further reduce the incidence of hypotension. However two studies demonstrated that 1000 ml of crystalloid alone did not appear to be more effective than preloading with 200 ml or no prehydration at all.[16,17]

Phenylephrine is purely alpha stimulant and it is effective in increasing blood pressure due to vasoconstriction. On the other hand it may lead to placental hypoperfusion and reflex maternal bradycardia.[18] Ephedrine has become the drug of choice for more than 30 years in the treatment of maternal hypotension in obstetric anaesthesia. Ephedrine is a sympathomimetic that has mixed alpha and beta adrenoreceptor activity. It maintains arterial pressure mainly by increasing cardiac output (CO) and heart rate as a result of its predominant activity on B1 adrenoreceptor.[19]

Simon et al [20] reported that incidence of hypotension was significantly higher in women who received 10 mg prophylactic dose of ephedrine than in those who received either 15mg or 20mg prophylactic dose of ephedrine. In our study women who received normal saline had higher incidence of hypotension as compared to women who received ephedrine 0.25mg/ kg body weight and 0.5mg/kg body weight.

Loughery JP et al[21] proved in their study that 12 mg prophylactic ephedrine could better counteract spinal hypotension.

Previously Ngan Kee et al [22] suggested that ephedrine 30 mg wa**s** the most effective IV bolus dose to prevent maternal hypotension, but at the expense of an increased incidence of reactive hypertension. Some studies showed that low doses of prophylactic IV ephedrine significantly reduced the incidence of maternal hypotension [21,23].

Chan et al[24] reported that there was a lower incidence of severe hypotension in the ephedrine group as compared to fluid group (35% vs 65%, p=0.04), although the incidence of moderate hypotension was similar. In our study the incidence of hypotension in group I who received 0.25mg/kg ephedrine was less as compared to group III who received inj 0.9% normal saline (18% vs 25%).

Lee et al [25]reviewed studies to determine the dose-response characteristics of prophylactic intravenous ephedrine for the prevention of hypotension during spinal anaesthesia for caesarian delivery. They suggested that, use of larger doses of ephedrine (>14mg) does not completely eliminate hypotension but causes reactive hypertension and a minor decrease in umbilical artery pH.

Iclal et al [26]investigated the effect of intravenous ephedrine given according to maternal weight of

0.5mg/kg after induction of spinal anesthesia for caesarian section to prevent hypotension related to spinal anaesthesia. Their findings demonstrated that prophylactic intravenous ephedrine during spinal anaesthesia for caesarian section prevent hypotension without significant maternal tachycardia and hypertension and also it increases the first rescue ephedrine time.

But in our study, there was a significantly higher incidence of reactive hypertension in group II parturients receiving 0.5mg/ kg body weight of ephedrine.

Shearer et al [27]conducted a study to evaluate the effects of a prophylactic intravenous bolus of ephedrine on the incidence and severity of maternal hypotension and on neonatal outcome. Ninety two women received 10 mg ephedrine as a prophylactic intravenous bolus prior to intrathecal epidural anaesthesia. Their study found that intravenous prophylaxis with ephedrine did not significantly decrease the frequency of hypotension in women receiving regional anaesthesia.

But in our study prophylactic intravenous ephedrine was given just after spinal anaesthesia.

CONCLUSIONS

Ephedrine at the dose of 0.25mg/kg intravenously prevents spinal anaesthesia induced hypotension in Caesarean Section without reactive hypertension.

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