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PREVENTION OF OXYTOCIN INDUCED HYPOTENSION BY CO- ADMINISTRATION OF DIFFERENT DOSES OF PHENYLEPHRINE WITH OXYTOCIN IN LOWER SEGMENT CAESAREAN SECTION UNDER SUB ARACHNOID BLOCK: A RANDOMIZED COMPARATIVE STUDY

Anaesthesiology

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ABSTRACT

Objective: This study was designed to evaluate the efficacy of two prophylactic infusion dose of phenylephrine (50 and 75 µg) along with oxytocin to prevent oxytocin induced hypotension in parturients undergoing caesarean section. **Material and Method:** With institutional Ethical committee (IEC) clearance and informed written consent, 420 term parturients undergoing elective caesarean section under SAB were randomly allocated to 3 groups of 140 each. Group C (3 IU oxytocin with normal saline) Group PE50 (3 IU oxytocin with phenylephrine 50µg) Group PE75 (3 IU oxytocin with phenylephrine 75µg) diluted to 10ml with normal saline and infused over 5 min after baby delivery. No of episode, incidence, duration of hypotension, rescue vasopressors requirement and any adverse effect observed. **Results:** In present study, total 67(47.85%), 50 (35.71%) and 26 (18.57%) patients developed hypotension (P= 0.000) and total 110, 65 and 31 episodes (1.64±0.79, 1.30±0.54, 1.19±0.40 per patient) (P= 0.000) in group C, PE50 and PE75 respectively, total duration of hypotensive episode were 349, 217and 107 mins in three groups, and it consumed 131,75, 35 doses (50 µg each) of phenylephrine (1.95±1.13, 1.50±0.81,1.34± 0.48 dose Per patient) (P= 0.005) and total 97.76±56.69µg, 75 ±40.72 µg , 67.30 ±24.25 µg (p= 0.003) phenylephrine per patient as rescue vasopressors in group C, PE50 and PE75 respectively. **Conclusion:** The prophylactic co-administration of 75µg phenylephrine with oxytocin effectively reduced the incidence of oxytocin induced hypotension in term parturients undergoing caesarean section under subarachnoid block compared to 50µg phenylephrine.

KEYWORDS

Sub Arachnoid Block, Phenylephrine, Oxytocin, Hypotension,

INTRODUCTION

Hypotension remains a major drawback following subarachnoid block (SAB) for caesarean section. Hypotension is also common in the parturients due to aorto-caval compression by foetal head and higher level of sympathetic blockade owing to increased spread of local anaesthetic in the cerebrospinal fluid[1] in spite of having 40-50% of more blood volume at term compared to nonpregnant patients. Other factor contributing to maternal hypotension is the administration of oxytocin which causes clinically significant hypotension, reflex tachycardia[2] and myocardial is chemia in a dose dependent manner[3] by acting on oxytocin receptors present on heart wall and large vessels.[4] Prophylactic measures to prevent this includes preloading with crystalloid, colloids, use of vasopressors like ephedrine and phenylephrine. Phenylephrine, a short acting α-1 agonist is now a preferred vasopressor because it maintain utero-placental blood flow better than ephedrine[5] and in titrated doses blunts the effect of oxytocin induced hypotension, tachycardia and increases cardiac output,[6] but at higher doses it causes reflex bradycardia and decreased cardiac output.[7] Doses, route of administration of oxytocin, vary widely in clinical practice and many clinicians are not aware of all the adverse effects of oxytocin. There are a few studies recommending minimum effective dose of phenylephrine for co-administration with oxytocin under spinal anaesthesia to compensate cardiovascular effects of oxytocin. This study was conducted to compare the effectiveness of prophylactic infusion dose of 50µg and 75µg of phenylephrine along with oxytocin at the time of baby extraction to prevent oxytocin induced hypotension in parturients with the primary objective to measure incidence of oxytocin induced hypotension and rescue vasopressor requirement, along with magnitude of hemodynamic changes and side effects.

MATERIAL AND METHODS

This prospective, randomized, double blind case control study was carried out at tertiary care centre with proper institutional ethical committee clearance (IEC) and informed written consent in 420 term pregnant female of 20-35yrs age posted for elective caesarean section under subarachnoid block. All consecutive parturients posted for caesarean section were assesed and randomly divided into three groups of 140 each using opaque sealed envelope technique, Group C (Control) (3 IU oxytocin with normal saline), Group PE50 (3 IU oxytocin with phenylephrine 50µg) and Group PE75 (3 IU oxytocin with phenylephrine 75µg) diluted with normal saline to make 10 ml to be infused over 5 mins. Parturients having emergency indication of caesarean section, coagulation abnormalities or on anticoagulants, having associated systemic illness (hypo/ hyperthyroidism, diabetic, neuromuscular, cardiac, neurological, eclampsia, psychiatric, hematological disorder), having contraindications for SAB, parturients refusal, allergic to local anaesthetic, obesity (weight>100 Kg), short stature (height<140cm) and parturients with fall in mean arterial pressure (MAP) > 25% of baseline following SAB but before oxytocin infusion were excluded from study. Drug was prepared by one anaesthesiologist as per group allocation who was further not involved in the study. Second anaesthesiologist performed all sub arachnoid blocks and recorded all the data and was not aware about the drug regimen been administered to the patient. Patient, surgeon and postoperative ward nurse were also not aware of group allocation. In operation theatre, 20G peripheral I.V. cannula inserted and, preloading with Ringer lactate 10ml/kg prior to SAB was done in all cases. Standard monitoring including non-invasive blood pressure, pulse-oximetry, and electrocardiography were applied. Baseline blood pressure (systolic, diastolic, mean arterial pressure), heart rate and peripheral oxygen saturation on air were recorded. SAB was performed using 25 G Quincke's spinal needle with 10mg of 0.5% bupivacaine (hyperbaric) in left lateral position. Then patient was turned supine, and a wedge under right hip was placed to prevent aortocaval compression. End of spinal injection was taken as time zero for all further data recording. Oxygen at a rate of 5 L/min was administered via a face mask. After baby extraction, study drug solution (10 ml) was administered based on the group allocation over a period of 5 min using a syringe infusion pump. All Vital parameters

were recorded in a proforma every 2 min after the SAB till baby extraction and up to 10 min after the administration of the test drug solution, then every 5 min till the end of surgery. Uterine tone was assessed by obstetricians at the end of uterine closure and was noted as either 'adequate' or 'inadequate'. If uterus is not adequately contracted methylergometrine 0.2mg intramuscular (IM) or prostaglandin (Carboprost) 250µg IM was given on demand of surgeon and noted. Hypotension was defined as the fall in MAP of >25% from baseline value and inj. Phenylephrine 50µg IV bolus was given over 2 min and repeated every 2min till MAP returned to within 25% of baseline. Once MAP return to normal (<25% of baseline) it was considered as 1 episode and its duration was also recorded. If MAP falls again >25% from baseline it was noted as another episode. In this manner the total number of episodes of hypotension and duration were recorded. If MAP did not return even after 3 doses of inj. Phenylephrine, then 1 dose (6mg) of inj. Ephedrine IV was given (upto5 doses). If HR fall to <55 per min along with hypotension at any time, then also inj. Ephedrine 6mg IV was given to treat hypotension. HR < 55 per min was defined as bradycardia and Inj. Atropine 0.4mg IV was given to treat bradycardia. Inj. dopamine, adrenaline, noradrenaline as infusions were considered if needed. Requirement of rescue vasopressor (total number and doses) recorded in each case. If patient or surgeons had complaint about inadequacy of anaesthesia, supplementation was given as fentanyl/ propofol/ midazolam. Time of baby delivery, APGAR score at 1min and 5 min and the condition of baby were recorded. Nausea, vomiting was treated with inj. ondansetron 4mg and any other complications was noted and treated accordingly. Duration of surgery was defined as the time from start of surgery to the end of surgery. If postpartum haemorrhage, or surgical complication occurred, it was treated accordingly and the case was excluded from the study. Any complications postoperatively noted and treated accordingly. To compensate, another case was enrolled for the study.

Statistical Analysis

Sample size was calculated on the basis of a previous study by Gangadharaiah R et al (2017)[8] where the incidence of oxytocin induced hypotension was observed as Group A – 90%, Group B – 10%, Group C – 98%, (P = 0.001). A minimum sample size of 132 patients in each group was required to study the difference of 8% in incidence of hypotension following spinal anaesthesia in lower segment caesarean section in three groups, at confidence interval of 95% and power of 80%. We enrolled 140 parturients in each group to compensate for dropouts. Data were entered into MS EXCEL and analyzed using SPSS version 20. Categorical (qualitative) data were presented as number (proportion) and compared using chi-square test. Continuous variable (quantitative) were presented as mean ±SD and compared using Analysis of Variance (ANOVA) test and Post hoc test with Bonferroni correction were also applied as per need. P value < 0.05 was considered as statistically significant.

RESULTS

Table 1: Comparison of demographic data and mean delivery time in three groups

Variable	Group C (n=140)	Group PE50 (n=140)	Group PE75 (n=140)	p value
Age (Yrs.)	27.40 ±2.21	27.28 ±2.62	27.53±2.78	0.714
Weight (Kg)	60.96±5.37	60.37±4.67	60.32±4.78	0.478
Height (Cm)	156.16±3.74	156.53±3.81	156.21±3.94	0.647
Gestational age	37.66±1.19	37.72 ±1.39	37.65±1.16	0.896
Induction to delivery time (in mins)				
Time	10.21 ± 1.19	10.31 ± 1.11	10.30 ± 1.14	0.990
Skin incision to delivery time (in mins)				
Time	5.04 ± 1.16	5.22 ± 1.49	5.33 ± 1.28	0.175

Table-1 shows that all three groups were statistically comparable regarding mean age, weight, height, duration from induction and incision to delivery. (P=>0.05)

Mean heart rate post baby extraction was statistically comparable in all the three groups (P > 0.05). Variation in mean HR was of less than ±10 b/min at all-time intervals. Mean arterial blood pressure post baby extraction was statistically significant at 2, 4, 6 and 35 min intraoperatively (P < 0.05). Lowest value of mean MAP was 80.67±8.90 mmHg at 8 min, 81.75±8.11 mmHg at 10 min and 82.32±7.25 mmHg at 10 min after baby extraction with fall of around 12.13 mmHg (13.07%), 10.81 mmHg (11.67%) and 9.75 mmHg (10.58%) from the baseline in group C, PE50 and PE75 respectively.

Table 2: Hypotensive episodes and rescue vasopressure requirement in three groups

Variable		Group C (n=140)	Group PE50 (n=140)	Group PE75 (n=140)	p value
Incidence of hypotension	Present	67 (47.85%)	50 (35.71%)	26 (18.57%)	0.000
	Not present	73 (52.15%)	90 (64.29%)	114 (81.43%)	
Episode distribution	1 episode	67	50	26	
	2 episode	33	13	5	
	3 episode	7	2	0	
	4 episode	3	0	0	
Total episodes of hypotension	110	65	31		
No. of hypotensive episodes per patient	Mean± S.D	1.64 ± 0.79	1.30 ± 0.54	1.19 ± 0.40	0.000
	Range	0-4	0-3	0-2	
Duration of episodes (Patient distribution)	2 min	18	22	12	
	4 min	12	1	9	
	6 min	16	15	3	
	8 min	13	8	1	
	10 min	4	4	1	
	≥12 min	4	0	0	
Total duration (Mins)	349	217	107		
Duration of hypotension per patient (min)	Mean ± S.D	5.20 ± 3.15	4.34 ± 2.43	4.11 ± 2.26	0.124
	Range	2-15	2-10	2-10	
No. of patient receiving vasopressors	No	73 (52.14%)	90(64.28 %)	114(81.42 %)	
	Yes	67 (47.85%)	50(35.71 %)	26 (18.57%)	
	No of patient received phenylephrine	67	50	26	0.000
	No. of patient received ephedrine	5	0	0	
Patient distribution as per doses of phenylephrine	0 dose	73	90	114	
	1 dose	28	32	17	
	2 doses	25	14	9	
	3 doses	7	1	0	
	4 doses	4	3	0	
	5 doses	2	0	0	
	6 doses	1	0	0	
Phenylephrine requirement	Total no. of doses	131	75	35	
	No. of dose requirement per patient	1.95±1.13	1.50±0.81	1.34±048	0.005
	Total cumulative dose (µg)	6550	6250	3700	

	Total dose per patient	97.76	125	142.30	
	Phenylephrine with oxytocin infusion (µg)	0	2500	1950	
	Total Rescue requirement (µg)	6550	3750	1750	
	Rescue dose requirement per patient (µg)	97.76±56.69	75 ± 40.72	67.30±24.25	0.0036
Patient distribution according to	0 dose	135	140	140	
	1 dose	5	0	0	
	2 doses	0	0	0	
Ephedrine requirement	Total no. of doses	5	0	0	
	Total dose (mg)	30	0	0	
	Rescue Vasopressor requirement per patient (mg)	6	0	0	

In our study, group C patients developed more no of patients with hypotension 67 (47.85%), no. of episode (110) and of longer duration (349 min) compared to group PE50 (50, 35.71%, 65 episode of 217 min duration) and PE75(26, 18.57%, 31 episodes of 107 min duration). Patients with hypotension received inj. Phenylephrine 50 µg bolus as a primary rescue vasopressor. Among these 5 (3.25%) patients in Control group and none in group PE50 and group PE75 required additional doses of ephedrine to treat hypotension. A total of 131 doses (6550µg), 75 doses (3750 µg) and 35 doses (1750 µg) of phenylephrine in group C, PE50 and PE75 respectively were administered as a rescue vasopressor. Group C patients received more no of bolus doses (6), per patient rescue dose (1.95±1.13) and total phenylephrine (97.76±56.69µg) compared to group PE50 and PE75. Control group patients received additional 5 doses (total 30 mg, 6mg/patients) of ephedrine to treat hypotension while none of the patients received rescue ephedrine in PE50 and PE75 group. All three groups were statistically comparable regarding mean APGAR score at 1 min (p= 0.951) and 5 min (p= 0.385) of babies delivered. Incidence of nausea and vomiting in Control group (16.42%) was significantly higher than the group PE75 (5%), (p= 0.008), rest adverse effect were comparable in three groups (p>0.05)

DISCUSSION

Prophylactic co-administration of Phenylephrine with oxytocin after baby delivery might improve hemodynamic stability in term parturients undergoing LSCS under SAB, as it counteract hypotension and reflex tachycardia induced by oxytocin.

In present study, compared to previous studies[8,9] Mean heart rate post baby extraction was maximum in Control group while other groups showed minimal fluctuation, suggest that the phenylephrine infusion keeps the heart rate uniform as compared to the boluses where a fluctuation in the heart rate was observed. The magnitude of fall in MAP after oxytocin infusion was highest in control group followed by group PE50 and group PE75. This was even higher in previous study[8] and difference could be attributed to sample size (90 as compared to 420 in present study). Lowest MAP recorded after oxytocin infusion was between 8th and 10th min and was comparable in all the three groups and previous study[10]. The mean SBP, DBP and MAP were consistently higher in the phenylephrine infusion group (50 and 75) when compared to the control group, due to the stimulation of post synaptic α-receptors by phenylephrine resulting in intense arterial and peripheral venoconstriction causing rise in blood pressure and change in blood pressure paralleled the increasing doses of prophylactic phenylephrine.[11] This incidence of hypotensive episodes were comparatively much more in Control group than group PE50 and PE75. Our results are contradictory to previous study[3,8,11] which might be due to a small sample size, 90 -120 parturients as compared to 420 in present study.

Requirement of rescue vasopressors were also higher in control group similar to previous studies.[8,11] Phenylephrine consumption in terms of number of doses and total rescue dose, number of bolus, rescue vasopressor dose per patient, Mean consumption per patient was comparatively more in Control group and also required rescue ephedrine. Our results are different from the past studies[8,11] which might be due to difference in sample size and phenylephrine dose.

The incidence of adverse effects were higher in Control group and no maternal complications occurred in any group patients. All patients had good neonatal outcome. None of the baby had complication in terms of neonatal death.

Limitations of the study:

1) Invasive blood pressure measurement could show beat to beat variation and would demonstrate hemodynamic changes in the three groups more precisely.
2) Umbilical cord blood gas analysis would have been more informative regarding maternal hypotension on neonatal outcome

CONCLUSION

Prophylactic phenylephrine infusion dose of 75µg is better than 50µg for co-administration with oxytocin for prevention of oxytocin induced hypotensive episodes in term parturients posted for elective LSCS under SAB without causing untoward side effects.

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