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A study on effect of two different doses of phenylephrine with oxytocin on oxytocin induced hemodynamic changes in caesarian section under subarachnoid block

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Abstract

Aim: Administration of phenylephrine can prevent oxytocin induced hypotension during caesarean section under spinal anesthesia.Our aim was to compare the effects of co-administration of two different doses of phenylephrine on oxytocin-induced hypotension during caesarean section under subarachnoid block.

Methods: 90 parturient undergoing caesarean section under spinal anesthesia were randomly divided into three groups. Group A received oxytocin 3U and normal saline. Group B received oxytocin 3U andphenylephrine 50 μg. Group C received oxytocin 3U and phenylephrine 75 μg.Study drug was administered IV over 5 min after baby delivery. The primary outcome was incidence of hypotension and secondary outcome were effect on HR and MAP.

Results: The incidence of hypotension in the parturient in group Band A was significantly higher compared to group C.No of dose and total rescue vasopressor requirement were significantly lower in Group C compared to group A and B without any side effects.HR,SBP,DBP and MAP was higher in group C compared to group A and B.

Conclusion: Co-administration of phenylephrine 75 μg with oxytocin 3U reduces the incidence of oxytocin-induced hypotension compared to phenylephrine 50 μg with oxytocin 3U during caesarean section under subarachnoid block(SAB).

Keywords: Caesarean section, hypotension, oxytocin, phenylephrine, subarachnoid block

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Introduction

The most common cause of postpartum hemorrhageis the postpartum atony of the uterus. Oxytocin is commonly used to prevent it.However, the use of oxytocin is associated with certain side-effects.When administered, it not only acts on the uterus but also exerts action onthe heart and blood vessels. This leads to the development of hypotension aswell as reflex tachycardia.[1] Though so many vasopressors have been used to prevent it, none has been found ideal.Phenylephrine, a directly acting α-1 adrenergic agonist with a short duration of action, is the first line choice of vasopressor for preventing and treating maternal hypotension in parturient. [2] It offers various advantages over other vasopressors, such as better ability to maintain uteroplacental blood flow, better maintenance of MAP during spinal anesthesia due to its quick peak effect within one minute, absence of fetal acidosis, and suitability in situations where tachycardia is undesirable as it can cause baroreceptor mediated reflex bradycardia and decreased cardiac output. [3] When co-administered with oxytocin in titrated doses as an infusion, phenylephrine blunts the effects of oxytocininduced hypotension and reflex tachycardia.[4]Though few studies recommended a minimum effective dose of phenylephrine as 75 mcg for co-administration with oxytocin during LSCS under spinal anesthesia to prevent oxytocin-induced hypotension, search for ideal dose still goes on. The current study compares the effectiveness of coadministering two different dosages of phenylephrine with oxytocin in reducing the incidence of oxytocin-induced hypotensionduring caesarean section under subarachnoid block.

Methods

This prospective double-blind study was done after obtaining approval from Institutional Ethical Committee at a tertiary care hospital.Parturient posted for elective and emergency lower segment caesarean section (LSCS) were included in the study.Parturients with an increased risk of atony or excessive bleeding (known placenta praevia, multiple gestation, abnormal presentations, prolonged labour, more than 2 previous LSCS), cardiovascular instability, pre-eclampsia, essential hypertension, gestational diabetes, those with systemic illnesses such as severe anaemia, bleeding diathesis and cardiovascular disease, parturient with height <150 cm were excluded from the study. A total of 90parturient were randomized into three groups using numbers generated from randomization table and allocation concealment was made by sealed opaque envelope. The envelope was opened by theinvestigator who prepared the study drug accordingly. Group A received oxytocin 3U and normal saline diluted to 10cc infusion over 5 min.Group B received oxytocin 3U and phenylephrine 50 μg diluted to 10cc with normal saline to 10cc infusion over 5 min. Group C received oxytocin 3U and phenylephrine 75 μg dilutedas an infusion over 5 min.The parturient and the anesthesiologist involved in the an anesthetic management of the parturient were unaware of study drug administered.Pre-anesthetic evaluation of all the parturient was done and an informed written consent was taken. In the operation theatre, electrocardiogram, non-invasive BP and pulse oximeter were connected and basal parameters recorded. Intravenous (IV) access with 18G

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cannula was established. Parturient were pre-medicated with ranitidine 50 mg IV and metoclopramide 10 mg IV half an hour before the administration of subarachnoid block and pre-loaded with 500 mL Ringer lactate before the administration of SAB.Thesubarachnoid blockwas performed at L_3-L_4/L_4-L_5 interspace using 25G Quincke needle in the left lateral decubitus position and 10 mg of hyperbaricbupivacaine (0.5%). Immediately after the SAB, the patient was repositioned supine with 15° wedge below the right buttock to achieve left uterine tilt. Oxygen was administered through simple face mask at 4 L/min. IV fluid infusion was continued at a rate of 200 mL/10 min throughout the surgery. Heart rate (HR), systolic BP (SBP), diastolic BP (DBP), MAP and peripheral oxygen saturation was monitored every 2 min till baby delivery and up to 10 min after administration of the study drug solution, then every 5 min till the end of surgery.After baby delivery, study drug solutions (10 mL) were administered based on group allocation over a period of 5 min using a syringe infusion pump through a separate IV line. Following this oxytocin infusion at 10U/h was continued up to 4 h. The level of sensory blockade was assessed using cold swab test at 20 min. The APGAR score was recorded for all the neonates at 1 and 5 min.Uterine tone was assessed by obstetricians at the end of uterine closure and noted as either ‘adequate’ or ‘inadequate’. If uterus was not adequately contracted methylergometrine 0.2 mg intramuscular (IM) or prostaglandin F2α 250 μg IM was given. Hypotension was defined as a fall in MAP >20% from baseline and treated with 100 mL IV fluid bolus and rescue dose of phenylephrine 50 μg IV over 2 min. Phenylephrine IV was repeated every 2 min till the MAP increased to within 20% of baseline. A maximum of 4 doses of phenylephrine were administered after which rescue vasopressor was changed to ephedrine 6 mg IV. The requirement of rescue vasopressors was noted. Bradycardia was defined as heart rate <60 beats/min (bpm) and treated with atropine 0.6 mg IV. Adverse effects such as desaturation, nausea, vomiting, headache, bronchospasm, flushing and dysrhythmias if any, during intraoperative period were noted and treated accordingly. All parturient were monitored in the postoperative care unit for 6 h. Based on previous studies[5] to detect a minimum of 50% reduction in the incidence of hypotension between the groups, a minimum of 30 parturient would be required in each group, to attain a power of 80% at alpha error of 0.05, assuming normal distribution of values in all the groups and using Chi-square test for comparison of proportions. Statistical analysis was done using IBM SPSS (statistics package for socialistic sciences) version 20 software. Shapiro Wilk test was done to assess for the normality of the distribution of continuous variables. Chi-square/Fisher's exact test was used to find the significance of study parameters on categorical scale. $P < 0.05$ was considered statistically significant.

Results

Demographic parameters such as age, height, weight, level of sensory block at 20 min and duration of surgery were comparable in all the three groups. The incidence of hypotension was more in Groups A and B compared to Group C. The number of episodes of hypotension

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was significantly higher in Group A compared to Groups C and B. The rescue vasopressor requirement was significantly lower in Group C compared to A and B. Table 1shows the mean heart rate among all three study groups. On analysis, it was seen that post administration of thestudy drug, the heart rate of the parturient in group C was significantly lower compared to group A and Bat 2 mins, 5 mins, and 10 mins respectively.

Table 1: Comparison of changes in intraoperative heart rate among study groups

Intraoperativehe artrate	Studygroups			p-value
	Group A (n=30) (mean±SD)	Group B (n=30) (mean±SD)	Group C (n=30) (mean±SD)	
Baseline	98.2±6.1	98.6±10.8	99.6±11.5	0.838
2minafterSAB	99.5±10.7	100.9±13.4	101.4±13.5	0.466
5minafterSAB	99.1±8.6	98.5±6.7	100.2±10.3	0.456
Drug administration	99.5±4.6	100.3±6.3	100.6±7.2	0.519
2min	99.8±8.8	94.1±10.4	91.8±10.1	<0.001
5min	100.1±7.6	95.6±12.5	92.7±10.5	<0.001
10min	102.1±7.8	96.2±8.2	94.4±8.2	<0.001
20min	96.2±6.8	98.7±10.2	97.7±8.1	0.361

Table 2 shows that post administration of the study drug, the mean arterial pressure of the participants receiving onlyoxytocin was significantly lower than the participants receivingphenylephrine 50 mcg and 75 mcg at 2 mins, 5 mins and 10 mins respectively. MAPwas more in theparticipants receiving 75 mcg phenylephrine combined with oxytocin.

Table 2: Comparison of changes in intraoperative MAP among study groups

Intraoperative MAP (mean±SD)	Studygroups			p-value
	Group A (n=30) (mean±SD	Group B (n=30) (mean±SD)	Group C (n=30) (mean±SD)	
Baseline	96.2±4.8	96.3±10.7	95.5±5.8	0.904

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2minafterSAB	93.1±7.1	91.9±6.2	89.7±6.9	0.142
5minafterSAB	86.7±5.6	85.8±8.7	85.7±5.8	0.912
Drug administration	85.4±8.9	89.1±12.3	80.6±6.9	0.004
2min	78.3±6.5	81.7±7.2	82.8±8.5	0.072
5min	76.9±5.1	83.5±6.2	92.3±8.1	<0.001
10min	74.8±5.8	77.1±3.4	94.5±7.4	<0.001
20min	76.5±4.8	78.9±3.9	94.1±7.1	<0.001

Table 3 shows that that incidence of hypotensive episodes was significantly higher among participants receiving only oxytocin as compared to those who received phenylephrine 50 mcg or 75 mcg with oxytocin.

Table 3:Comparison of incidence ofhypotensive episodes among study groups

Hypotensive episodes	Studygroups			p-value
	Group A (n=30) n (%)	Group B (n=30) n (%)	Group C (n=30) n (%)	
0	11(36.7)	23(76.7)	27(90)	<0.001
1	15(50)	4(13.3)	2(6.7)	
2	4(13.3)	3(10.0)	1(3.3)	
Total	30(100)	30(100)	30(100)	

Discussion

In our study, wefound that administration of 75 μg phenylephrine with oxytocin reduced the incidence and the number of episodes of oxytocin-induced hypotension whereas 50 μg of phenylephrine did not reduce the incidence of hypotension but reduced the number of episodes of hypotension and rescue vasopressor requirement compared to control.Gangadharaiah R et al. compared two different doses of phenylephrine (50 mcg and 75 mcg) on oxytocin-induced maternal hypotension in 90 parturient undergoing LSCS under spinal anesthesia. They concluded that combined, oxytocin 3 U and phenylephrine 75 mcg significantly reduced the incidence of oxytocin-induced maternal hypotension during LSCS performed under spinal

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anesthesia without producing any unfavorable side effects. [6]Butwick AJ et al in his studies have compared the efficacy of different doses of phenylephrine i.e. 100 μg, 125 μg and 150 μg to treat post-spinal hypotension in elective caesarean section and concluded that there was no significant difference in all the 3 groups.[7]Rumboll CK et al found that IV phenylephrine 50 μg administered immediately before 3 U oxytocin during elective caesarean section, did not prevent maternal hypotension and tachycardia.[8]Mohta M et al[9] suggested more studies to find the optimal dose for co-administration with oxytocin, hence the present study was undertaken to compare co-administration of two lower doses in an effort to minimize phenylephrine-induced side effects. We found that the co-administration of phenylephrine 75 μg with oxytocin 3U had better efficacy compared to phenylephrine 50 μg with oxytocin 3U and was associated with the minimal adverse effect.Phenylephrine causes a significant reduction in heart rate after the bolus dose. There was no incidence of bradycardia in the present study which may be attributed to the administration of phenylephrine as infusion rather than bolus. There is evidence that phenylephrine delivered as an infusion is the most effective method for preventing maternal hypotension and intraoperative nausea or vomiting.[10]Jaitawat S et al., compared the effect of administering two different bolus doses of phenylephrine (75 mcg and 100 mcg) for the prevention of spinal-induced hypotension during LSCS under spinal anesthesia in 120 parturient of ASA grade 1st and 2nd between 18 to 35 years of age. They concluded that prophylactic administration of bolus phenylephrine significantly decreases the incidence of maternal hypotension. A 75 mcg phenylephrine is preferred over 100 mcg phenylephrine, which causes significant bradycardia and reactive hypertension.[11] Estimation of intraoperative blood loss was not done and hence the effect of phenylephrine co-administration on blood loss could not be studied. We have not done pulse waveform analysis (perfusion index) and cardiac output monitoring for our cases which can be a limitation. Cardiac output monitoring is used as a marker of oxygen delivery to tissues. It is used in guiding treatment for fluid resuscitation, and the use of vasoactive and inotropic drugs and hence may require further studies for validation.[12]

Conclusion

Compared to phenylephrine 50 mcg, the coadministration of phenylephrine 75 mcg with oxytocin 3U reduces the incidence of oxytocin-induced hypotension and the need for rescue vasopressors during caesarean section under subarachnoid block.

References

1. Amy JJ. Severe postpartum haemorrhage: A rational approach. Natl Med J India. 1998;11:86–8.

2. Prendiville W, Elbourne D, Chalmers I. The effects of routine oxytocic administration in the management of the third stage of labour: An overview of the evidence from controlled trials. Br J ObstetGynaecol. 1988;95:3–16.

ISSN:0975 -3583,0976-2833 VOL 15, ISSUE 12, 2024

3. Gutkowska J, Jankowski M, Mukaddam-Daher S, McCann SM. Oxytocin is a cardiovascular hormone. Braz J Med Biol Res. 2000;33:625–33.

4. Anilkumar G, Ambi Uday S, Shettar AE, Koppal R, Ravi R. Maintenance of arterial pressure during spinal anaesthesia in caesarean section. J Clin Diagn Res. 2011;5:948–52.

5. Dyer RA, Reed AR, van Dyk D, Arcache MJ, Hodges O, Lombard CJ, et al. Hemodynamic effects of ephedrine, phenylephrine, and the coadministration of phenylephrine with oxytocin during spinal anesthesia for elective cesarean delivery. Anesthesiology. 2009;111:753–65.

6. Gangadharaiah R, Duggappa DR, Kannan S, Lokesh SB, Harsoor K, Sunanda KM, et al. Effect of co-administration of different doses of Phenylephrine with Oxytocin on the prevention of Oxytocin induced hypotension in caesarean section under spinal anaesthesia: A randomised comparative study. IJA. 2017;61(11):60-66.

7. Butwick AJ, Coleman L, Cohen SE, Riley ET, Carvalho B. Minimum effective bolus dose of oxytocin during elective caesarean delivery. Br J Anaesth. 2010;104:338–43.

8. Rumboll CK, Dyer RA, Lombard CJ. The use of phenylephrine to obtund oxytocin-induced hypotension and tachycardia during caesarean section. Int J ObstetAnesth. 2015;24:297–302.

9. Mohta M, Harisinghani P, Sethi AK, Agarwal D. Effect of different phenylephrine bolus doses for treatment of hypotension during spinal anaesthesia in patients undergoing elective caesarean section. Anaesth Intensive Care. 2015;43:74–80.

10. Sahu D, Kothari D, Mehrotra A. Comparison of bolus phenylephrine, ephedrine, and mephentermine for maintenance of arterial pressure during spinal anaesthesia in caesarean section – A clinical study. Indian J Anaesth. 2003;47:125–8.

11. Jaitawat SS, Partani S, Sharma V, Johri K, Gupta S. Prophylactic administration of two different bolus doses of Phenylephrine for prevention of spinal induced hypotension during caesarean section: A prospective double blinded clinical study. JOACC. 2019;9(2):81-87.

12. Thomas DG, Robson SC, Redfern N, Hughes D, Boys RJ. Randomized trial of bolus phenylephrine or ephedrine for maintenance of arterial pressure during spinal anaesthesia for caesarean section. Br J Anaesth. 1996;76:61–5.

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