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Original Research Paper

Comparitive Study Between Phenylephrine Vs Ephedrine in Controlling Spinal Hypotension in Caesarean Section

Medical Science

KEYWORDS : Phenylephrine, Ephedrine, Spinal hypotension, Cesarean section

Dr.Shringarpure Swapnaja S	Department of Anaesthesia, Raigad Hospital and Research Center, Diksal, Tal-Karjat, Dist- Raigad, Maharashtra.
Dr.Mathai Kusuma	Department of Anaesthesia, Raigad Hospital and Research Center, Diksal, Tal-Karjat, Dist- Raigad, Maharashtra.
Dr.Nishkala C	Department of Anaesthesia, Raigad Hospital and Research Center, Diksal, Tal-Karjat, Dist- Raigad, Maharashtra.

ABSTRACT

OBJECTIVE *: The aim of this study was to compare efficacy of bolus ephedrine Vs Phenylephrine for maintainance of arterial pressure during spinal anaesthesia in cesarean section and also to not any adverse effects of them in mother or the foetus.* **MATERIALS AND METHODS** *: A double blind prospective randomized control study was carried out on 100 Female patients with singleton, full term, pregnancy undergoing elective as well as an emergency Caesarean section of ASA PS 1 and 1 'E' in the department of Obstetrics at Southern Railway Headquarters Hospital, Permabur, Chennai between January 2008 to December 2011. Using computer generated random numbers they were divided into 2 groups - Group 1(n= 50)patients receiving 6 mg ephedrine as bolus dose for correction of spinal hypotension . Group 2(n= 50) patients receiving 50 mcg of phenylephrine as bolus dose for correction of spinal hypotension . Whenever hypotension (fall in systolic BP more than 20-30%of baseline or BP less than 90 mmHg) occurs the prefixed (1ml) dose of study drug was administered by I.V. bolus. Number of boluses & time taken to revert hypotension (B.P. > 90 mm of hg) recorded & were analysed with different statistical methods and tests.* **RESULTS** *: All the continous data were presented by mean with standard deviation and it was analysed with the help of Independent t-test.* **CONCLUSION** *: We found that both the vasopressors namely phenylephrine and ephedrine are equally effective in IV bolus form in maintenance of maternal arterial pressure within 20% limit of baseline values, though phenylephrine group required less number of boluses. Phenylephrine caused reactive hypertension which was statistically significant in our study, so it is prudent to take precautionary measures in an already hypertensive patient while using phenylephrine as a vasopressor. Both the vasopressors had no significant adverse effects on neonatal outcomes.*

INTRODUCTION

Anesthesia to a parturient is not only unique but also requires highest degree of care because the anaesthesiologist has to look after two individuals, the mother and foetus. In elective caesarean section under spinal anesthesia, hypotension has been reported in as many as 85% of patients. Hypotension during spinal anesthesia for caesarean section delivery can have detrimental effects on both mother and neonate . These effects include decreased uteroplacental blood flow, impaired foetal oxygenation with asphyxia stress and foetal acidosis and maternal symptoms of low cardiac output such as nausea , vomiting, dizziness and decreased consciousness.Therefore there has been much attention in the literature to methods of preventing and treating hypotension in obstetric anesthesia. Careful positioning with left uterine displacement and volume preloading with crystallods or colloids has been used to prevent it , but these are not complete measures and vasopressor is required to correct hypotension quickly. Vasopressors like Ephedrine, Mephentermine, Phenylephrine, Metarminol and Methoxamine are used for treating the hypotension. In this study we compare the efficacy of Ephedrine and Phenylephrine in treating the hypotension for caesarean section and their undesirable side effects.

AIMS AND OBJECTIVES

1. To study the effect of bolus ephedrine Vs Phenylephrine for maintenance of arterial pressure during spinal anaesthesia in cesarean section.
2. To compare efficacy of bolus ephedrine Vs Phenylephrine for maintenance of arterial pressure during spinal anaesthesia in cesarean section.
3. To study adverse outcomes or side effects if any of bolus Ephedrine vs bolus Phenylephrine in cesaraen section on baby and mother.

MATERIALS AND METHODS : After receiving approval from the Hospital ethics committee a double blind prospective randomized control study was carried out on 100 Female patients with singleton, full term, pregnancy undergoing elective as well as an emergency Caesarean section of ASA PS 1 and 1 'E' in the department of Obstetrics at Southern Railway Headquarters Hospital, Permabur, Chennai between January 2008 to December 2011.

INCLUSION CRITERIA -

All pts who are selected are in American Society Of Anaesthesiologists (ASA) Gr I .and Gr. 1 'E'.

EXCLUSION CRITERIA -

1. Patients contraindicated for spinal anaesthesia.
2. Patient's age less than 20 yrs and more than 35 yrs.
3. Patient's refusal for spinal anaesthesia.
4. Patients having fetal distress or/with maternal complication(s) eg. Hypotension, bradycardia etc.as an indication for caesarean section.

100 patients who fit the inclusion criteria were selected .With the help of computer generated random number, the patients were distributed in two groups by computer generated random numbers -

Group 1: 50 pts receiving 6 mg ephedrine as bolus dose for correction of spinal hypotension .

Group 2: 50 pts receiving 50 mcg of phenylephrine as bolus dose for correction of spinal hypotension .

The study was done by double blind technique in which both the patient and administrator were blind about the nature of the drug to be used for the correction of spinal hypotension. A fixed bolus dose , for ephedrine 6 mg and for phenylephrine 50 mcg was made by the investigator and labelled as group 1 and 2 for the administrator. The admin-

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istrator and the patient were unaware about the nature of the drug. Informed consent was taken from each patient.

Data collection technique and tools –
Results according to set proforma were filled up by the administrator and later analysed by the investigator. After preloading(RL@10ml/kg), pulse rate, systolic and diastolic arterial pressure was recorded thrice when middle value was taken as baseline value. Same parameters was recorded immediately after subarachnoid block. Then at every 2 min for 20 min, BP and pulse was recorded and thereafter every 5 min till the end of surgery. Whenever hypotension (fall in systolic BP more than 20-30%of baseline or BP less than 90 mmHg) occurs the prefixed (1ml) dose of study drug was administered by I.V. bolus. Number of boluses & time taken to revert hypotension (B.P. > 90 mm of hg) recorded & were analysed with different statistical methods and tests.

Statistical analysis -
All the continous data were presented by mean with standard deviation and it was analysed with the help of Independent t-test. Categorical datas were presented by frequency and it was analysed by Chi-square and Fisher exact test. All the analysis was done by using SPSS 14.0, P value less than 0.05 was considered as significant.

OBSERVATIONS AND RESULTS

100 patients were included in this study.

Table No.1 : Age distribution in the two groups.

	Drug	N	Mean	Std. deviation	P value
Age	Ephedrine	50	26.24	3.889	0.743
	Phenylephine	50	26.00	3.387	

The variation in the mean distribution of cases by age in group 1 was 26.24 years while that in group 2 was 26.0 years , which was not statistically significant.

Table no.2: Number of boluses required in the respective groups

	Drug	N	Mean	Std.deviation	P value
No. of Boluses	**Ephedrine**	**50**	**1.84**	**0.738**	**0.397**
	Phenylephrine	**50**	**1.72**	**0.671**	

No.of boluses crosstabulation

		No. of boluses				
		1	2	3	**Total**	**P value**
Drug	Ephedrine	18	22	10	50	**0.551**
	Phenylephrine	20	24	6	50	
Total		38	46	16	**100**	

The mean number of boluses in Group 1 and 2 were 1.84 and 1.72 respectively which was not statistically significant.

Table No. 3 – Comparison of the time required for correction of hypotension in the respective groups.

	Drug	N	Mean	Std.deviation	P value
Time required (min)	Ephedrine	50	5.52	2.667	**0.714**
	Phenylephrine	50	5/74	3/294	

The mean time required for the correction of hypotension in groups 1 & 2 were 5.52 & 5.72 minutes respectively which was not statistically significant (p value- 0.714).

Table No. 4- Mean number of patients in each group having postoperative nausea & vomiting (PONV) as side –effect of the vasoconstrictor drugs used

Drug		PONV No	PONV Yes	**Total**	**P value**
	Ephedrine	48	02	50	**0.436**
	Phenylephrine	45	05	50	
Total		93	07	**100**	

The number of patients having postoperative nausea & vomiting (PONV) as the side –effect of the vasoconstrictors used in the groups 1 & 2 were 2 & 5 respectively which was not statistically significant(p value-0.436)

Table No.4 – Mean No. of patients having bradycardia as the side-effect of the vasoconstrictor agents in groups 1 & 2.

Drug		Bradycardia No	Bradycardia Yes	Total	**P value**
	Ephedrine	50	0	50	**0.242**
	Phenylephrine	47	3	50	
Total		97	3	100	

The number of patients having bradycardia as the side – effect of the use of the vaso- constrictor agents in groups 1 & 2 were 0 & 3 respectively which was not statistically significant(p- value = 0.242).

Table no. 5 – Number of cases having reactionary hypertension as the side-effect due to the use of vaso-constrictor agents in the respective groups.

Drug		Reactive hypertension No	Reactive hypertension Yes	**Total**	**P value**
	Ephedrine	50	0	50	
	Phenylephrine	46	4	50	**0.041**
Total		96	4	**100**	

Patients in the Phenylephrine (group 2) had reactionary hypertension while none in the Ephedrine group (group 1) which was not statistically significant (p value = 0.041) .

Table no. 6 – APGAR score comparison in both the groups.

	Drug	N	Mean	Std.deviation	P value
APGAR	Phenylephrine	50	9.44	0.501	0.552
	Ephedrine	50	9.50	0.505	

The APGAR scores in group 1& 2 were 9.44 & 9.5 respectively which was not statistically (p value =0

DISCUSSION

After subarachnoid block for cesarean section , hypotension can be minimized by the use of intravenous fluid preload, avoidance of aortocaval compression and judicious use of

vasopressor agent. It has been shown that the percentage decrease in placental perfusion is related to the percentage reduction in maternal arterial pressure and not to the absolute reduction in pressure.

For the purpose of this study,hypotension was defined as a decrease in arterial pressure greater than 20 % from baseline systolic pressure.Ephedrine has got a mixed action directly as well as indirectly on alpha and beta receptors , whereas Phenylephrine has pure alpha receptor activity.

Hemodynamic variables :

Heart rate : In our study there was bradycardia in 3 patients with phenylephrine group and none in the ephedrine group even though this was not statistically significant .

In spinal anaesthesia, since there is a decreased venous return, decreased venous pressure and a decreased right heart pressure thus slowing of the heart Rate is expected on basis of Bainbridge reflex.Bradycardia is also expected in high spinal , probably due to some paralysis of cardioaccelerator nerves.We found that the maternal heart rate was slower with phenylephrine than with ephedrine . This is consistent with the mechanism of action of these drugs that the decrease in heart rate found in phenylephrine group was due to pure alpha receptor activity compared with ephedrine as it has got a mixed action directly as well as indirectly on alpha and beta receptors.Similar results were seen in many studies which was consistent with our study.

In the quantitative systematic review done by Anna Lee et al they found that maternal bradycardia was more likely to occur with phenylephrine than with ephedrine. [(1)]Also Thomas DG etal on comparing the efficacy of bolus ephedrine and phenylephrine , they found that mean maximum percentage in maternal heart rate was larger in the phenylepherine group than the ephedrine group.[(2)] As a consequence atropine was required in eleven out of eighteen women in the phenylepherine group compared with two out of eighteen women in the ephedrine group.In the systematic review by Ngan kee etal , he concluded that Phenylephrine may decrease maternal heart rate and cardiac output.[(3)] In Cooper etal's study on comparing the effects of ephedrine and phenylephrine when administered alone and in combinations they found that the mean heart rate was higher in ephedrine group than in phenylepherine group or the combination. [(4)] In Ngan Kee WD etal's study on comparing the effects of prophylactic infusion and bolus phenylephrine they found that heart rate was significantly slower over time in the infusion group compared with the control group.[(5)] In the study done by Brooker RF etal they found that phenylephrine was associated with a decrease in heart rate and in cardiac output.[(6)] In a study done by Crichley etal ephedrine was accompanied by increase in heart rate in 12 % of cases.[(7)]

Blood Pressure : The systolic and the diastolic pressures were decreased statistically significant at the onset of hypotension and increased after the bolus dose of drug in both the groups.The pressures generally remained high in the phenylephrine group when compared with the ephedrine group.The systolic blood pressure was generally highest in the phenylephrine group immediately after the administration.The diastolic blood pressure was also greater in phenylephrine group when compared with ephedrine. This finding is consistent with the onset of action and efficacy of the drug that phenylephrine has quicker onset of action and better maintenance of arterial pressures when compared with the other two drugs.

Laporta etal compared maternal and neonatal catecholamine concentrations, following the use of either bolus phenylephrine or ephedrine to treat drop in maternal blood pressure after spiunal anaesthesia for cesarean section.[(8)] They found that phenylephrine appears to be safe and effective as ephedrine in treatment of a drop in blood pressure in healthy non labouring parturient undergoing LSCS. Ann Lee etal in their systematic review, they found that for the management , prevention and treatment of hypotension, there was no difference between phenylepherine and ephedrine and both effectively . maintained the systolic blood pressure within 20 % of baseline values.[(1)] Thomas DG etal in their study compared the efficacy of bolus ephedrine and phenylephrine for the maintenance of arterial pressure during spinal anaesthesia for caesarean section and found that maternal systolic blood pressure and cardiac output changes are similar in both the groups.[(2)]

Cyna AM etal studied the randomized controlled trials controlled trials comparing the interventions to prevent hypotension during spinal anaesthesia for cesarean section.[(9)] From 75 trials they found that ephedrine was significantly more effective than control or crystalloid in preventing hypotension.There were no significant differences between ephedrine and phenylephrine in treating hypotension.Similiar results were also obtained from our study also. Ram Nathan etal assessed the maternal hemodynamic changes and neonatal acid-base status in 127 healthy patients undergoing elective caesarean section under epidural anaesthesia and concluded that both ephedrine and phenylepherine increase cardiac preload and effectively maintained systolic blood pressure within 20% of baseline values.[(10)]

Cooper etal compared phenylephrine 100 microgm, ephedrine 3mg/ml and phenylephrine 50 microgm/ ml & ephedrine 1.5 mg/ml in combination given by infusion to maintain maternalsystemic arterial pressure at baseline during spinal anaesthesia for LSCS and found that the mean systolic arterial pressure was similar in the three groups.[(4)] In the review done by Warwick D etal they discussed about various measures to prevent and treat hypotension.[(11)] Recent studies support use of alpha-agonists such as phenylephrine .Phenylephrine is more effective and can be titrated more easily than ephedrine as it may be given by boluses (50-100 microgram) or by infusion (50-100 microgram/ min).Brooker RF etal studied sequential infusion of phenylephrine to manage hypotension.In their study also phenylephrine was effective at restoring systolic blood pressure after spinal anaesthesia.[(6)]

Yap JC etal on comparing the efficacy of fluid preloading with two fluid vasopressor regimes , Intravenous ephedrine boluses was more effective in maintaining systolic blood pressure.[(12)]Alahutta S etal studied the effects of ephedrine and phenylephrine to maintain systolic arterial pressure 20% above baseline values during spinal anaesthesia for caesarean section.[(13)] In this study also both the vasopressors restored maternal arterial pressure effectively.

Side –effects:

The heart rate remained generally low in the phenylephrine group when compared with the ephedrine group.Three patients developed bradycardia in phenylephrinegroup compared with none in the ephedrine group and they were subsequently treated with injection atropine 0.3mg IV bolus.The incidence of tachycardia is more in ephedrine and Mephenteramine groups than in phenylephrine group.this is due to both direct and indirect actions of ephedrine and mephenteramine compared with phenylephrine which has only direct action on alpha receptors.This direct action of

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phenylephrine is also responsible for the increased incidence of bradycardia as seen in our study.

In the quantitative systematic review of seven clinical trials,Anna Lee etal they found that maternal bradycardia was more likely to occur phenylephrine than with ephedrine.[1]In a review article by Ngan kee etal they found that ephedrine causes maternal tachycardia when compared with phenylephrine which causes decreased maternal heart rate.[3]Cyna AM etal in their review of 75 clinical trials found that high rates or doses of Ephedrine may increase tachycardia incidence.[9]Crithcley LAH etal found that ephedrine ws not a potent vasoconstrictor and systolic arterial pressure was maintained mainly by increases in stroke index and heart rate.[7]

Neonatal outcome – Casey etal in their retrospective analysis found that APGAR score is comparable to umbilical artery pH in predicting neonatal outcome On assessing the APGAR score in our study two neonates had APGAR score of 6 in group I and II and one neonate in group III.[14]At 5 minute, no neonate had an APGAR score less than 7 in all the three groups.Moran etal reported in their study with one neonate with an APGAR score less than 7 in Ephedrine group compared with no neonate in phenylephrine group. [15] However at 5 minutes, no neonate in the ephedrine or phenylephrine group s had an APGAR score less thn 7.In the studies done by Thomas etal[2],Alahutta etal[13], Laporta etal[8] and Ayorinde etal[16] same results were obtained.All the neonates had an APGAR score of more than 7 at 5 minutes in both ephedrine and phenylephrine group.

Dosage requirements- I

In group I (Ephedrine) : 33% of patients required one, 44% of patients required two and 23% of patients required three boluses to maintain systolic pressure within 20% of limit of basal value.

In group II (Phenylephrine): 40% of patients required one , 48% of patients required two and 12% of patients required three bolus doses to maintain systolic pressure within 20% limit of basal value. Phenylephrine was most effective in treating hypotension than ephedrine though this was not statistically significant.

Thomas DG etal concluded that in ephedrine and phenylephrine groups median (range) number of boluses of ephedrine and phenylephrine was similar. [2]Thus both the vasopressors effectively maintained pressures within 25% of baseline values; phenylephrine maintained it effectively with fewer doses than ephedrine.

SUMMARY

This double blind prospective randomized control study was designed to evaluate the efficacy of ephedrine and phenylephrine in treating hypotension during spinal anesthesia for caesarean section. The incidence of undesirable side effects and neonatal outcome in terms of APGAR score were also studied. The following observations were made:

Both the vasopressors maintained the arterial pressure effectively within 20% of baseline values.

The mean value of heart rate was higher in ephedrine group

Phenylephrine group required fewer number of bolus doses when compared to the ephedrine group.

The incidence of reactive hypertension was more in the phenylephrine group compared to the ephedrine group.

The heart rate generally remained low throughout the study period in the phenylephrine group and the incidence of bradycardia was more in the phenylephrine group when compared with the ephedrine group.

The occurrence of nausea and vomiting were similar and comparable in both the groups.

In both the groups no neonate had an APGAr score of less than 9 at the 5 th minute.

CONCLUSION :

In conclusion , we found that both the vasopressors namely phenylephrine and ephedrine are equally effective in IV bolus form in maintenance of maternal arterial pressure within 20% limit of baseline values, though phenylephrine group required less number of boluses.Phenylephrine causes reduction in heart rate, which may be advantageous in patients in whom tachycardia is undesirable. Phenylephrine caused reactive hypertension which was statistically significant in our study, so it is prudent to take precautionary measures in an already hypertensive patient while using phenylephrine as a vasopressor. Both the vasopressors had no significant adverse effects on neonatal outcomes.

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