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Intravenous bolus phenylephrine, ephedrine and mephentermine for maintenance of blood pressure during spinal anaesthesia in caesarean section: a comparative study

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ABSTRACT

Objective: To study the efficacy of intravenous bolus Phenylephrine, Ephedrine and Mephentermine for maintenance of Blood Pressure during Spinal Anesthesia in patients undergoing emergency Caesarean Section. **Materials and Methods:** One hundred twenty, ASA type 1 and 2 patients scheduled for emergency caesarean section under spinal anaesthesia who developed hypotension were allocated into 3 groups of 40 each. Group P received Phenylephrine 0.1mg, Group E received Ephedrine 6 mg, and Group M received Mephentermine 6 mg in 1 ml as bolus IV. **Results:** The rise of diastolic blood pressure at 2, 4, and 6 minutes post study drugs were significantly less in Ephedrine and Mephentermine group as compared to the Phenylephrine group ($p<0.05$). Similarly elevation of systolic blood pressure in Phenylephrine group was significantly higher as compared to other two groups for first 6 minutes. Thereafter the differences narrowed off. No significant differences were observed between changes in systolic and diastolic blood pressure of Ephedrine and Mephentermine group at any point of time. In Phenylephrine group, post study drug values of heart rate decreased significantly from the values at onset of the hypotension till the end of the surgery when compared to other two groups ($p<0.001$). Neonatal Apgar score at 1 and 5 min were >7 in all three groups. **Conclusion:** Phenylephrine group had quicker control of blood pressure compared to the other two groups. However, as the time elapsed all drugs achieved comparable control of blood pressure. Phenylephrine did show some advantage over others with regard to reduction in heart rate.

Key words: bolus, ephedrine, mephentermine, phenylephrine

INTRODUCTION

Anaesthesia 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 the fetus. With the increasing incidence of caesarean section[1], the anesthesiologist is trapped in a delicate web of decision making over the type of anaesthetic technique to be employed which guarantees the safety of both the mother and the fetus. In the recent decades, there has been a worldwide shift in obstetric anesthesia practice in favour of regional anesthesia, with spinal anaesthesia being the most popular among them[2]. Spinal anaesthesia was introduced into clinical practice by German surgeon Karl August Bier in 1898.[3] Its popularity is due to the advantages it confers – relative simplicity, rapidity, certainty, duration, low failure rates, minimal side effects, an awake mother, least exposure of mother and fetus to anaesthetic drugs and circumvention of life threatening complications like aspiration, failed intubations and depressed neonate.

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But, like any other anaesthetic technique, it is not devoid of complications, the most common being hypotension which may adversely affect both mother and fetus.[4] In caesarean section under spinal anaesthesia, hypotension has been reported in as many as 85% of patients.[5] Hypotension may be detrimental to the mother and fetus. As is rightly said "A stitch in time saves nine", the most important question that seeks attention is the timely recognition and appropriate management of maternal hypotension. One of the mainstays in management of hypotension is the use of vasopressor agent[6], but those currently available are not perfect and there has been a controversy for years regarding the ideal vasopressor.

Ephedrine, an indirect acting synthetic non-catecholamine is the most widely used agent for this purpose but causes maternal tachycardia due to its non-selective action on both alpha and beta adrenergic receptors. It is difficult to titrate and also exhibits tachyphylaxis.

Phenylephrine is a directly acting sympathomimetic agent with selective alpha 1 adrenergic activity. It is easy to titrate and maintains maternal blood pressure without producing undue tachycardia. Moreover, the administration of phenylephrine is reported to be associated with lower incidence of fetal acidosis than with ephedrine.

Mephentermine is an indirect acting synthetic non-catecholamine that stimulates alpha and beta adrenergic receptors. Mephentermine is readily available and is the most commonly used vasopressor in India to treat spinal anaesthesia induced hypotension, but not many workers have studied and compared it with other vasopressors regarding its safety and efficacy.

One of the mainstays in management of hypotension is the use of vasopressor agent, but those currently available are not perfect and there has been a controversy for years regarding the ideal vasopressor. Hence there is a need to find a suitable drug for the treatment of hypotension, which lacks the fore mentioned maternal side effects and also does not cause any detrimental effect on the fetal pH.

So the present study was carried out to find out a better drug for prevention of post spinal hypotension in terms of better hemodynamic control and least maternal and fetal side effects.

A safe, secure and certain control of maternal blood pressure is one of the many requirements for ensuring "the perfect experience" for the mother having her baby delivered by cesarean section under regional blockade. In this study three drugs are being evaluated, each having its own pharmacological properties. The present study was undertaken to compare the efficacy of IV bolus phenylephrine, ephedrine and mephentermine for maintenance of blood pressure following spinal anesthesia for elective as well as emergency caesarean section.

MATERIALS AND METHODS

This prospective, randomized, double blind study was carried out after approval of institutional ethical committee. A sample size of 120 patients of age group of 20–35 years, ASA Grade I & II, were randomly allocated into three groups of 40 each. Group P received i.v bolus phenyl ephrine 0.1mg in 1ml; group E received i.v bolus ephedrine 6 mg in 1ml; group M received i.v bolus mephentermine 6 mg in 1ml. Patients informed/ written consent was taken. After shifting the patient to operating room (OR) routine monitors including noninvasive blood pressure, pulse oximeter and electrocardiogram were attached and baseline vital parameters including systolic & diastolic blood pressure, heart rate (HR), respiratory rate (RR) and SpO_2 were recorded. An intravenous access with 18G cannula was secured. All patients were preloaded with 10 ml/kg ringer lactate and were pre-medicated with iv. ranitidine 50 mg and metoclopramide 10 mg. Under all aseptic precautions subarachnoid block was performed in sitting position at L3-L4 interspace with 25G Quinke spinal needle. After establishing free flow of CSF, hyperbaric inj. bupivacaine 0.5% 2 ml was injected intrathecally and then immediately the patient was turned to supine position. Oxygen was administered at a rate of 3 litre per minute by a face mask to all the patients until the umbilical cord was clamped. Injection oxytocin 10 IU was administered in infusion after clamping the cord.

Vital parameters were recorded just after administration of subarachnoid block, at every 2 min for next 20 min and thereafter at every 5 min till the end of the surgery. Whenever hypotension (fall in systolic pressure >20% from the baseline value or less than 90mmHg) occurred the study drug was given as IV bolus. The hemodynamic effect of study drugs, number of boluses required to recover from hypotension, neonatal Apgar scores and adverse effects (nausea, vomiting, bradycardia, and tachycardia) were noted. Bradycardia (HR < $60min^{-1}$) was treated with i.v atropine 0.6mg. All the recorded results were expressed as mean ± SD. Comparability amongst groups were analyzed with Analysis of variance (ANOVA) test. P value <0.05 was considered significant. Graphpad instant software was used to calculate the statistics.

RESULTS

All the three groups were demographically comparable. There was no significant difference in level of sensory block, degree of motor block, SAB-hypotension time, SAB-delivery time and duration of surgery. (Table 1)

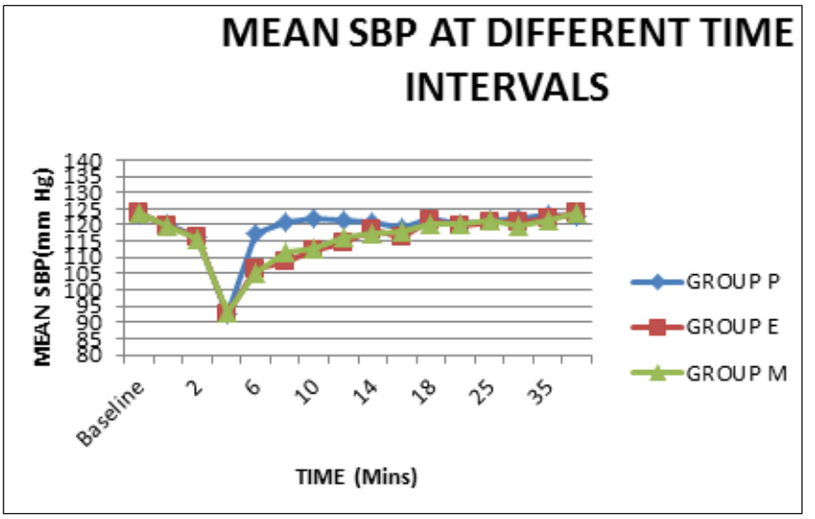

Figure 1. Graphical comparison of changes in mean systolic blood pressure.

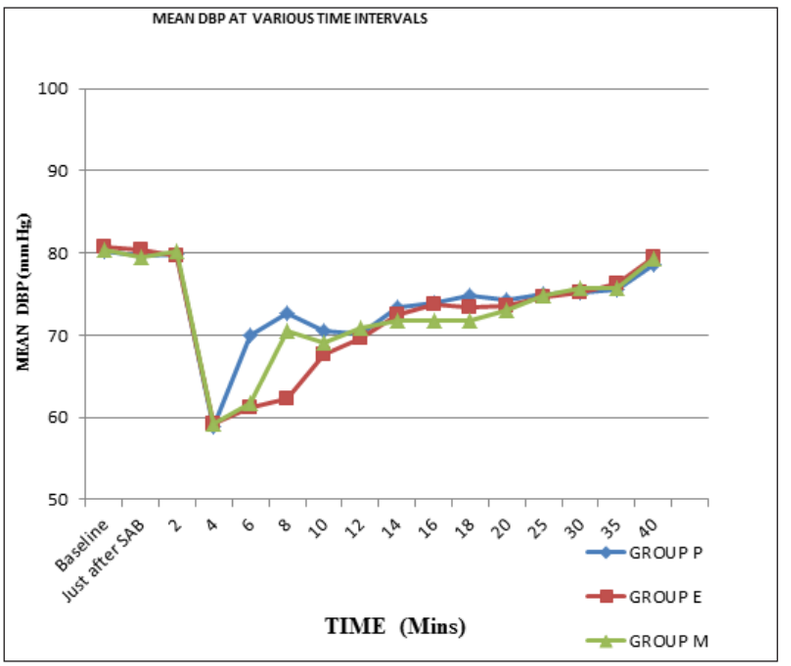

Figure 2. Graphical comparison of changes in mean diastolic blood pressure.

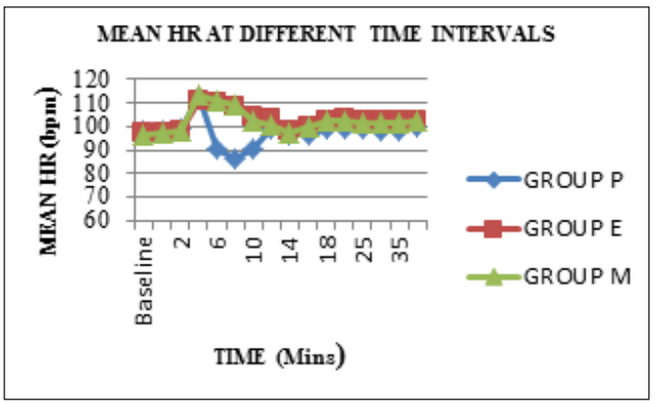

Figure 3. Graphical comparison of changes in mean Heart rate.

The baseline SBP and DBP were comparable in all the three groups. A statistically significant fall in SBP and DBP was noted at 4 min after SAB in all the three groups. A rise in SBP was noted at 2,4, 6 and 8 minutes whereas rise in DBP was noted only at 2,4 and 6 minutes after administration of study drug in all the three groups (Figure 1, 2). This rise in SBP and DBP was statistically highly significant in group P as compared to groups E and M (P<0.0001). But, the difference in rise of SBP and DBP at various time intervals was statistically comparable between groups E and M (p>0.05). Thereafter both SBP and DBP in all the three groups was near baseline level and difference was statistically comparable (p>0.05) (Table 2, 3). The baseline heart rate was statistically comparable in all the three groups. (p>0.05). A significant rise in heart rate was noticed in all the three groups after 4 min of administration of subarachnoid block. The HR was less in group P as compared to group E and group M till 8 minutes after the administration of the study drug and this difference was statistically significant when group P was compared to group E and group M (P<0.05). At all-time intervals after 8 minutes of study drug administration, HR was lesser in group P as compared to group E and group M but the difference was statistically not significant (Figure 3). In group P 77.5% patients required single bolus dose, 15% required two and 7.5% required one bolus dose. In group E 47.5% required one, 42.5% required two and 15% required three bolus doses. In group M 55% required one, 40% two and 05% required three bolus doses to correct hypotension. The difference in mean number of bolus doses required to treat hypotension was statistically significant among groups.

Fetal depression was seen in none of the neonates. Apgar score at 1 min and 5 min was 8.075±0.41 and 9.1±0.37 in group P; 8.05±0.38 and 9.1±0.37 in group E and 8.17±0.38 and 9.02±0.35 in group M. The difference in Apgar score at 1 min and 5 min was not statistically significant among the groups.

Nausea, vomiting and bradycardia were the common side effects observed during the study, the incidence of side effects was comparable in all the three groups and was not statistically significant.

Table 1: Patient characteristics & relevant data

Characteristics	Phenylephrine	Ephedrine	Mephentermine
Maternal weight (Mean ± SD) kgs	56.15 ± 3.63	56.28 ± 3.60	55.81 ± 3.69
Maternal height (Mean ± SD) cms	150.68 ± 2.11	150.77 ± 1.88	150.44 ± 1.86
Mean Level of sensory block (T4-T6)	5.1 ± 0.49	5.02 ± 0.53	5.00 ± 0.64
Mean degree of motor block	2.69 ± 0.36	2.72 ± 0.40	2.71 ± 0.33
SAB- Hypotension time (min)	4.01 ± 0.37	4.0 ± 0.34	3.98 ± 0.32
SAB- Delivery time (secs)	596.97 ± 22.13	598.05 ± 24.84	598.97 ± 27.31
Duration of surgery (min)	39.15 ± 3.13	39.65 ± 3.86	39.55 ± 4.08

Table 2: Changes in Systolic Blood Pressure

TIME (mins)	Grp P	Grp E	Grp M	Intergroup comparison		
				P-E	P-M	E-M
Preoperative	122.95±5.67	123.85±5.92	124.00±3.70	0.49	0.33	0.89
Immediate after SAB	120.05±2.28	119.6±2.40	119.85±3.08	0.39	0.74	0.68
2 min	116.05±3.21	116.05±2.69	115.40±3.14	>0.99	0.36	0.32
4 (HP-VP given)	92.35±2.52	92.50±2.28	92.82±2.25	0.78	0.37	0.52
6 min	117.2±2.89	106.25±2.50	105.32±2.35	<0.0001	<0.0001	0.09
8 min	120.85±4.07	108.97±4.48	111.40±4.70	<0.0001	<0.0001	0.20
10 min	122.22±5.09	111.95±3.34	112.8±3.18	<0.0001	<0.0001	0.24

12 min	121.40±4.53	114.57±4.42	116.22±4.62	<0.0001	<0.0001	0.10
14 min	120.75±5.20	118.82±4.75	117.47±4.20	0.08	0.002	0.18
16 min	118.87±4.75	116.22±3.59	117.77±4.30	0.06	0.28	0.08
18 min	122.27±17.25	121.57±4.87	120.22±4.37	0.80	0.46	0.19
20 min	120.30±5.65	119.57±6.01	120.07±5.16	0.58	0.85	0.69
25 min	121.40±5.57	120.90±5.32	121.60±5.28	0.68	0.82	0.51
30 min	121.85±6.12	120.62±5.50	119.80±4.97	0.34	0.10	0.48
35 min	123.22±5.50	122.25±5.58	121.52±5.77	0.43	0.18	0.56
40 min	122.67±4.70	123.80±6.11	123.90±5.45	0.36	0.28	0.93
HP- Hypotension, VP – Vasopressor agents						

Table 3: Changes in Diastolic blood pressure

TIME (mins)	GROUP P	GROUP E	GROUP M	Intergroup comparison		
				P-E	P-M	E-M
Preoperative	80.27±3.43	80.82±3.55	80.32±3.70	0.48	0.95	0.53
Immediate after SAB	79.62±4.13	80.47±3.85	79.50±4.24	0.34	0.89	0.28
2 min	79.77±3.93	79.72±3.64	80.22±4.07	0.95	0.61	0.56
4 (HP-VP given)	58.8±3.47	59.22±3.34	59.25±3.39	0.57	0.55	0.97
6 min	69.95±3.12	61.22±3.24	61.75±3.63	<0.001	0.79	0.51
8 min	72.72±4.60	62.32±5.11	63.47±5.57	<0.001	0.052	0.47
10 min	70.45±5.01	67.60±4.10	69.10±3.63	0.006	0.17	0.08
12 min	70.22±3.93	69.70±3.92	70.90±4.10	0.55	0.45	0.18
14 min	73.42±5.79	72.52±4.74	71.75±5.85	0.44	0.20	0.51
16 min	73.92±5.41	73.77±5.11	71.85±5.45	0.89	0.09	0.10
18 min	74.77±6.07	73.45±5.37	71.85±5.40	0.30	0.02	0.18
20 min	74.30±5.33	73.57±6.03	73.07±5.94	0.57	0.33	0.70
25 min	74.92±6.15	74.57±5.31	74.85±6.01	0.78	0.95	0.82
30 min	75.10±5.90	75.15±6.17	75.65±5.57	>0.99	0.66	0.67
35 min	75.62±5.04	76.32±4.84	75.80±5.53	0.52	0.88	0.65
40 min	78.57±4.64	79.50±4.67	79.25±4.14	0.37	0.49	0.80

DISCUSSION

Spinal anesthesia has gained popularity in cesarean section because of the advantages it confers – relative simplicity, rapidity, certainty, duration, low failure rates, minimal side effects, an awake mother, least exposure of mother and fetus to anaesthetic drugs and circumvention of life-threatening complications like aspiration, failed intubations and depressed neonate. But, like any other anaesthetic technique, it is not devoid of complications, the most common being hypotension which may adversely affect both mother and fetus. Several methods have been tried for prevention of hypotension during cesarean section, which includes crystalloid preloading, left uterine displacement, leg compression and elevation, prophylactic administration of vasopressors including phenylephrine, ephedrine, and mephentermine, prophylactic angiotensin II infusion and infusion of atrial natriuretic peptide.

Sahu D.[5] and colleagues reported that phenylephrine 0.1 mg is effective as 6mg ephedrine and 6 mg mephentermine for maintaining blood pressure within 20% of baseline value. Thomas and colleagues[7] reported that bolus phenylephrine 100mg is as effective as ephedrine 5mg restoring maternal arterial pressure above 100mmHg. Ganeshvar AK et al[8] also concluded that phenylephrine, ephedrine and mephentermine are effective in IV bolus form for maintenance of arterial pressure within 20% limit of baseline and phenylephrine causes reduction in heart rate compared to ephedrine and mephentermine.

In our study all the three vasopressors effectively maintained blood pressure within 20% limit of baseline value though phenylephrine maintained better in first 6min of bolus dose as compared to ephedrine and mephentermine. This may be due to that, phenylephrine has peak effect within one

minute, whereas ephedrine has 2-5min and mephentermine has 5min.

The HR was less in group P as compared to group E and group M till 8 minutes after the administration of the study drug and this difference was statistically significant when group P was compared to group E and group M ($P<0.05$). HR was reduced in group P due its direct action on α receptors whereas increase in HR was associated with ephedrine and mephentermine due to its indirect action on both α and β receptors.

In group P 77.5% patients required single bolus dose, 15% required two and 7.5% required one bolus dose. In group E 47.5% required one, 42.5% required two and 15% required three bolus doses. In group M 55% required one, 40% two and 05% required three bolus doses to correct hypotension.

Nausea, vomiting and bradycardia were the common side effects observed during the study, the incidence of side effects was comparable in all the three groups and was not statistically significant. Fetal depression was seen in none of the neonates.

CONCLUSION

To conclude our study, phenylephrine, ephedrine and mephentermine are effective in IV bolus form for maintenance of blood pressure during spinal anaesthesia in caesarean section. Phenylephrine has quicker peak effect and better hemodynamic control as compared to both ephedrine & mephentermine and it does not cause increase in heart rate, which may be advantageous in cardiac patients and in patients in whom tachycardia is undesirable.

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