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Comparison of Bolus Phenylphrine and Mephentermine for Maintainance of Arterial Blood Pressure during Spinal Anaesthesia in Cesarean Section

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Abstract **Original Research Article**

This prospective randomized study was conducted in 90 singleton pregnant patients scheduled for elective caesarean section who developed hypotension after spinal anaesthesia. They were randomly allocated to Group P-Phenylphrine use (n=45) and Group M-Mephentermine use(n=45) of ASA grade I and II in the age group of 20 -30 years .Both groups were compared with respect of systolic and diastolic blood pressure, heart rate,spo2 and neonatal Apgar score. We conclude that Mephentermine (bolus 3mg/ml) is better than phenylephrine (bolus 50µg/ml) as it was able to sustain a higher rise in systolic blood pressure and bring it to baseline values with fewer repeat dose requirements and fewer incidences of hypotension compared to phenylephrine. But phenylephrine was able to decrease the heart rate back to baseline levels and maintain it at that level, while Mephentermine further raised it. Neonatal Apgar score was same in the two different groups.

Keywords: Bolus phenylephrine, mephentermine, arterial blood pressure.

INTRODUCTION

Caesarean section is generally performed under spinal anaesthesia that is associated with hypotension (30-40% of cases) and bradycardia (10-15% of cases). Hypotension is more common and profound in pregnant population, with an incidence more than 80% without prophylactic management [1]. Hypotension results in dizziness, nausea and vomiting. In severe cases it may result in unconsciousness, pulmonary aspiration, apnea, and neonatal depression [2]. Careful positioning with left uterine displacement and volume preloading with crystalloids or colloids has been used to prevent it, but these are not complete measures and vasopressor is required to correct hypotension quickly [3]. This study was done to compare the effectiveness of bolus injections of two drugs - Phenylephrine hydrochloride at dose of 50µg/ml and Mephentermine sulphate at dose of 3mg/ml for management of hypotension that develops due to spinal anaesthesia for caesarean section and their risk for adverse neonatal outcome.

MATERIALS AND METHODS

90 singleton full term pregnant patients, who were undergoing elective as well as emergency Caesarean sections and developed hypotension after spinal anaesthesia were divided into two groups of 45 each as Group M-Mephentermine 3mg/ml(n=45) and group P- Phenylephrine 50 µg/ml (n=45). The study was prospective and randomized one. Ethical clearance was taken, written informed consent was taken from patients of both groups. Each patient received Inj. Ranitidine 50mg i.v. and Inj. Metoclopramide 10mg i.m. one hour before surgery. All patients were administered Ringer's Lactate, 10ml/kg body weight, rapidly prior to administration of spinal anaesthesia. Pulse oximeter, ECG electrodes, non-invasive sphygmomanometer were applied to the participants. Foetal heart rate was monitored by stethoscope. Spinal anaesthesia was given at L3-L4 region or L4-L5 region under strict aseptic condition and left lateral position with 26G Quincke's spinal needle. After establishing free flow of CSF through the needle, 2.2 ml of hyperbaric bupivacaine was injected into the subarachnoid space, for all participants with height greater than 150cms. For those with height between 141-150 cms, 2ml was used, and volume further decreased by 0.2 ml for every 5cm decrease in height, to maintain equality in block height [4]. Participant were then placed in supine position, with 15° wedge under right hip. Oxygen was administered by simple face mask at 6L/min. Inj. oxytocin 10U in 5% dextrose were given i.v after clamping the cord. Systolic blood pressure (SBP), diastolic (DBP), mean (MAP) and heart rate (HR) were recorded every 3 minutes till 15 minutes and then every 5 minutes till 30 minutes from onset of hypotension. When hypotension developed, time of

onset was noted, and first dose (1ml of drug) was administered. Further bolus doses of drugs were administered when SBP did not rise above 80% of baseline value. Patient was continued to be monitored beyond the study period, in the operating room and in the post-operative recovery room till 2 hours after administration of spinal anaesthesia .In case of severe sustained hypotension, the patients were excluded from study. Neonatal Apgar score was recorded at 1 and 5mins.Inappropriate bradycardia was treated with Inj. Atropine Sulphate 0.3mg i.v. bolus. Shivering during surgery was treated with Inj. Tramadol hydrochloride 0.5mg/kg i.v. bolus and intra operative nausea or vomiting was treated with Inj. Ondansetron hydrochloride 4mg i.v. bolus.

RESULTS

The participants in the two groups were statistically similar in their distribution of age with p value of 0.521, height with p value 0.406 and weight with p value 0.654, showing that the participants in both the groups were similar to each other.

Table-1: Showing the variation of age, height, weight of subject in the two groups

variable	DRUG		p Value
	Group M	Group P	
Age	23.78 ± 2.98	24.33 ± 3.39	0.521
Height (cm)	145.53 ± 9.84	143.7 ± 8.82	0.406
Weight (kg)	61.56 ± 7.46	62.02 ± 7.7	0.654

The participants in both the groups were similar in their baseline hemodynamic variables.

Table-2: Compares the baseline basic hemodynamic parameters of participants in the two groups

variables	DRUG		p Value
	Group M	Group P	
Baseline SBP (mmHg)	124.16 ± 8.73	123.5 ± 7.43	0.422(NS)
Baseline DBP (mmHg)	72.39 ± 7.12	73.91 ± 8.11	0.383(NS)
Baseline MAP (mmHg)	89.65 ± 4.65	90.44 ± 6.14	0.806(NS)
Baseline Heart Rate (/min)	84.98 ± 15.37	89.16 ± 11.27	0.061(NS)

Participants in both groups received similar amounts of local anaesthetic for spinal anaesthesia.

Table-3: Compares the average volume of local anaesthetic administered for spinal anaesthesia (Bupivacaine heavy, 0.5%, 8% dextrose)

variable	DRUG		p Value
	Group M	Group P	
	Mean ± Std. Deviation	Mean ± Std. Deviation	
Spinal DrugVolume	1.98 ± 0.24	1.95 ± 0.22	0.461(NS)

The events of delivery of baby, onset of 1st episode of hypotension, occurred at similar time intervals after administration of spinal anaesthesia in both the groups. The time taken for completion of surgery was also similar in both the groups.

Table 4: compares the average time interval from administration of spinal anaesthesia to delivery of baby, onset of first hypotension, and completion of surgery

variable	DRUG		p Value	Significance
	Group M	Group P		
	Mean ± Std. Deviation	Mean ± Std. Deviation		
Time S-Baby delivery	8.62 ± 3.11	8.87 ± 3.44	0.594	Not Significant
Time S-1st Hypotension	11.22 ± 5.43	10.11 ± 4.32	0.338	Not Significant
Time S-Completion	37.76 ± 6.56	37.84 ± 6.22	0.749	Not Significant

Both groups had similar blood pressure at the onset of hypotension. After initial administration of vasopressor, difference of both systolic and diastolic blood pressure in both the groups was not significant.

At 3 and 6 minutes Mephentermine increased systolic blood pressure more than Phenylephrine but diastolic blood pressure was significantly higher in Phenylephrine at 3 minutes. At 9 minutes, both groups had statistically similar systolic blood pressure. Beyond 9 minutes, systolic blood pressure increased in both groups, steadily till the end of observation at 30 minutes, with average values statistically greater in case of Mephentermine. From 6 minutes to 30 minutes difference in diastolic blood pressure was not significant between two groups. Mephentermine, thus increased the blood pressure significantly more compared to phenylephrine.

Table-5: compares the variation in average SBP from onset of hypotension to 30 minutes with respect to baseline values

variable	DRUG		p Value	Significance
	Group M	Group P		
	Mean ± Std. Deviation	Mean ± Std. Deviation		
SBP Baseline	124.16 ± 8.73	123.5 ± 7.43	0.422	Not Significant
SBP 0	93.4 ± 5.49	91.28 ± 6.28	0.101	Not Significant
SBP 3	115.38 ± 6.97	110.27 ± 8.1	0.006	Significant
SBP 6	115.84 ± 6.4	109.38 ± 9.7	0.001	Significant
SBP 9	112.07 ± 10.46	107.44 ± 12.34	0.064	Not Significant
SBP 12	115.18 ± 10.87	107.62 ± 12.56	0.001	Significant
SBP 15	114.38 ± 10.91	107.33 ± 12.25	0.005	Significant
SBP 20	118.64 ± 10.2	113.6 ± 8.95	0.015	Significant
SBP 25	119.64 ± 11.24	115.62 ± 7.96	0.011	Significant
SBP 30	123.22 ± 9.63	115.76 ± 8.01	<0.001	Significant

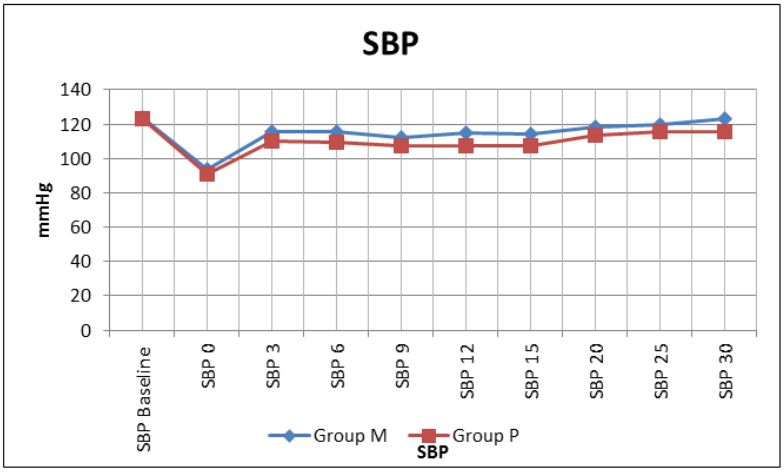

Fig-1: comparative trend of SBP between the two groups

Table-6: comparison of trend of average diastolic blood pressure between the two groups

variable	DRUG		p Value	Significance
	Group M	Group P		
	Mean ± Std. Deviation	Mean ± Std. Deviation		
DBP Baseline	72.39 ± 7.12	73.91 ± 8.11	0.383	Not Significant
DBP 0	60.82 ± 12.9	60.67 ± 7.32	0.462	Not Significant
DBP 3	63 ± 12.62	71.04 ± 11.82	0.006	Significant
DBP 6	67.22 ± 7.06	68.56 ± 10.74	0.324	Not Significant
DBP 9	69.22 ± 6.04	67.2 ± 10.57	0.111	Not Significant
DBP 12	67.71 ± 8.53	65.36 ± 11.48	0.106	Not Significant
DBP 15	66.49 ± 7.96	64.2 ± 9.15	0.130	Not Significant
DBP 20	70.67 ± 7.18	70 ± 8.89	0.707	Not Significant
DBP 25	69.38 ± 9.45	71.51 ± 8.2	0.277	Not Significant
DBP 30	71.89 ± 8.3	73.02 ± 8.96	0.448	Not Significant

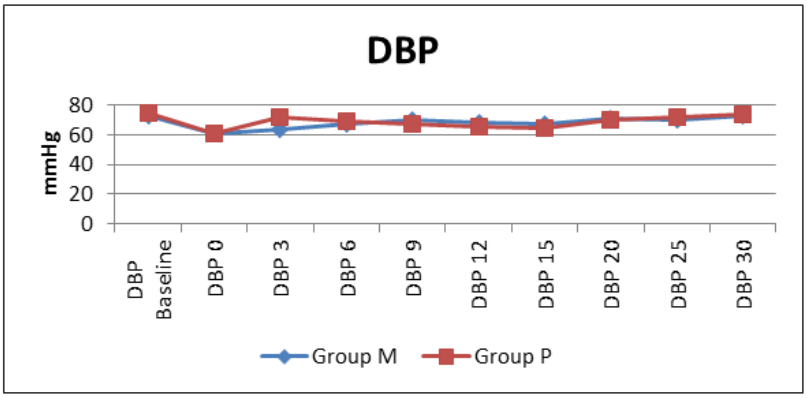

Fig-2: Shows the trend of average diastolic blood pressure between the two groups

Mean arterial pressures were statistically similar between the groups at baseline; and at time 0 minutes when participants developed hypotension. After administration of vasopressor at time 0 minute, the mean arterial blood pressure increased in both groups. There are significant differences in average mean arterial blood pressure between the two groups at time points of 9, 12, 15 minutes, more in favor of group M. The differences in average mean arterial pressure decreased to become statistically not significant from time 20 minutes onwards.

Table-7: comparison of mean arterial pressures between the two groups

variable	DRUG		p Value	Significance
	Group M	Group P		
	Mean ± Std. Deviation	Mean ± Std. Deviation		
MAP Baseline	89.65 ± 4.65	90.44 ± 6.14	0.806	Not Significant
MAP 0	71.68 ± 8.3	70.87 ± 5.37	0.939	Not Significant
MAP 3	80.46 ± 8.69	84.12 ± 9.46	0.042	Significant
MAP 6	83.43 ± 4.99	82.16 ± 9.52	0.821	Not Significant
MAP 9	83.5 ± 5.03	80.61 ± 10	0.030	Significant
MAP 12	83.53 ± 6.41	79.44 ± 11.26	0.007	Significant
MAP 15	82.45 ± 6.34	78.58 ± 9.59	0.010	Significant
MAP 20	86.66 ± 6.81	84.53 ± 6.85	0.160	Not Significant
MAP 25	86.13 ± 7.79	86.21 ± 6.25	0.932	Not Significant
MAP 30	89 ± 6.61	87.27 ± 7.2	0.229	Not Significant

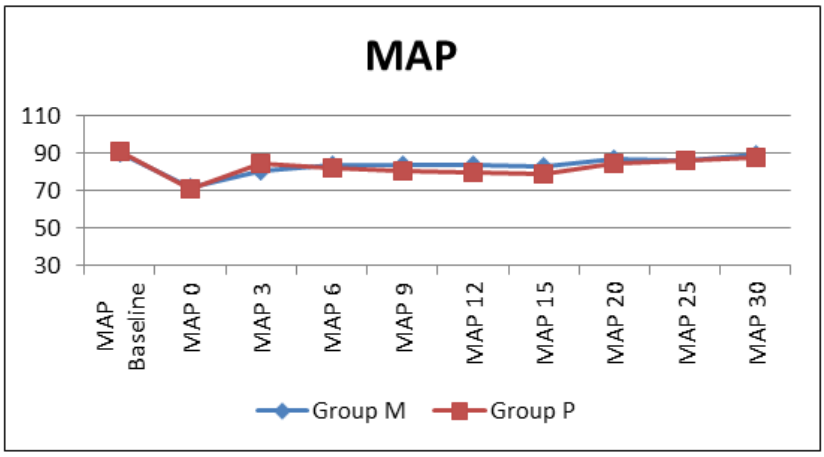

Fig-3: Comparison of the average means arterial pressures between the two groups

Heart rate rose above baseline values upon onset of hypotension at time 0. But the heart rate difference between the two groups was not statistically significant. After administration of vasopressor at time 0, the heart rate rose further in group M while it fell in group P. The difference in average heart rate was statistically significant between the groups at all times till the end of observation at time 30 minutes.

Table-8: compares the average heart rate between the two groups

variable	DRUG		p Value	Significance
	Group M	Group P		
	Mean ± Std. Deviation	Mean ± Std. Deviation		
Heart Rate Baseline	84.98 ± 15.37	89.16 ± 11.27	0.061	Not Significant
Heart Rate 0	98.62 ± 11.37	101.42 ± 10.46	0.379	Not Significant
Heart Rate 3	100.91 ± 8.36	84.84 ± 13.82	<0.001	Significant
Heart Rate 6	103.58 ± 14.28	86.29 ± 13.9	<0.001	Significant
Heart Rate 9	102.38 ± 16.53	86.8 ± 14.16	<0.001	Significant
Heart Rate 12	96.29 ± 15.98	86.8 ± 12.1	0.011	Significant
Heart Rate 15	100.27 ± 14.72	85.33 ± 10.54	<0.001	Significant
Heart Rate 20	104.69 ± 14.52	87.58 ± 15.32	<0.001	Significant
Heart Rate 25	104.2 ± 14.21	88.07 ± 13.68	<0.001	Significant
Heart Rate 30	102.93 ± 12.8	89.67 ± 13.21	<0.001	Significant

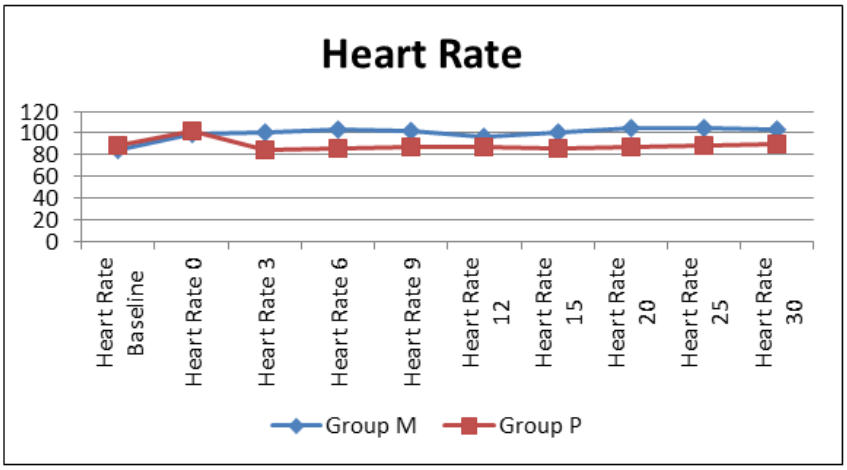

Fig-4: shows the comparison of the average heart rates between the two groups.

Difference of hypotension episodes were more in Group P and it was statistically significant

Table-9: compares the number of episodes of hypotension between the two groups during the study period

variable		DRUG		Total	p Value	Significance
		Group M	Group P			
		No., (%)	No., (%)	No., (%)		
Number of Hypotension	1	28(62.22)	14(31.11)	42(46.67)	0.010	Significant
	2	13(28.89)	26(57.78)	39(43.33)		
	3	4(8.89)	5(11.11)	9(10)		
Total		45(100)	45(100)	90(100)		

At the administered doses, more doses of Phenylephrine were required to treat hypotension due to spinal anaesthesia compared to Mephentermine during the study period.

Table-10: compares the number of doses of vasopressor required to treat hypotension between the groups

variable		DRUG		Total	p Value	Significance
		Group M	Group P			
		No., (%)	No., (%)	No., (%)		
Number of Dose	1	28(62.22)	14(31.11)	42(46.67)	0.007	Significant
	2	13(28.89)	23(51.11)	36(40)		
	3	3(6.67)	8(17.78)	11(12.22)		
	4	1(2.22)	0(0)	1(1.11)		
Total		45(100)	45(100)	90(100)		

The average APGAR scores at 1 minute are 9.64 in group M and 9.71 in group P. The difference in values were not statistically significant. At time 5 minutes, the APGAR score was 10 in both the groups.

Table-11: compares APGAR score between the two groups

variable	DRUG		p Value	Significance
	Group M	Group P		
	Mean ± Std. Deviation	Mean ± Std. Deviation		
APGAR 1	9.64 ± 0.53	9.71 ± 0.51	0.504	Not Significant
APGAR 5	10 ± 0	10 ± 0	1.000	Not Significant

DISCUSSION

Hypotension due to spinal anaesthesia is thought to be due to vasodilation due to loss of sympathetic nerve outflow from sympathetic blockade .It can be minimized using intravenous fluid preload and use of vasopressor agents. Thomas stated in his study that bolus phenylephrine 100µg was as effective as ephedrine 5mg restoring maternal arterial pressure above 100mm Hg [5]. Moran gave ephedrine 10 mg or phenylephrine 80 µg i.v. bolus to maintain systolic arterial pressure above 100mm Hg [6]. Sahu used 100µg phenylephrine, 6mg mephentermine and 6 mg ephedrine bolus doses for treatment of hypotension due to spinal anaesthesia for caesarean section.[7] Bhattarai used 25µg phenylephrine and compared it with 5 mg ephedrine and 6 mg mephentermine and found no difference in their efficacy to treat hypertension except that phenylephrine was better than others at time 6 minutes indicating the difference in time to peak action [8]. In our study, we have found that both phenylephrine at 50µg and mephentermine at 3mg increase blood pressure when administered after onset of hypotension, but mephentermine maintains systolic blood pressure at higher level and is able to bring the pressure to baseline than phenylephrine at the administered doses. Both can raise diastolic and mean arterial pressures equally. Phenylephrine better manages heart rate by bringing them to baseline compared to mephentermine which further raises them.

CONCLUSION

Mephentermine is better than phenylephrine as it is able to sustain a higher rise in systolic blood pressure and bring it to baseline values with fewer repeat dose requirements and fewer incidences of hypotension compared to phenylephrine. But phenylephrine is able to decrease the heart rate - raised due to sympathetic stimulation due to hypotension - back to baseline levels and maintain it at that level, while mephentermine further raises it.

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