IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 14, Issue 1 Ver.VII (Jan. 2015), PP 80-85
www.iosrjournals.org

A Comparative Study of Phenylephrine, Ephedrine and Mephentermine for Maintainance of Arterial Pressure during Spinal Anaesthesia in Caesarean Section

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Abstract: *Hypotension following spinal anaesthesia for Caesarean section is the commonest serious problem encountered by anaesthesiologists. Numerous methods have been tried to minimize hypotension which include fluid preloading, left uterine displacement and use of vasopressor drugs. This study was aimed at comparing the efficacy of three drugs Phenylephrine, Ephedrine and Mephentermine for maintenance of arterial blood pressure during spinal anaesthesia in caesarean section. 60 patients between the age group of 18-35 years undergoing elective as well as emergency caesarean section under spinal anaesthesia who developed hypotension after subarachnoid block(SAB) were selected and randomly allocated into 3 groups of 20 each to receive Group P -Phenylephrine 50mcg, Group E – Ephedrine 6 mg, and Group M –Mephentermine 6 mg as bolus IV and repeated as required. Comparability of groups were analysed with Analysis of Variance (ANOVA) test. All the 3 drugs effectively controlled SBP & DBP. On intergroup comparision rise of SBP and DBP in phenylephrine group was more than in other two groups. Tachycardia was significantly less in Group P after administration of the study drug. Phenylephrine causes reduction in heart rate, which may be advantageous in cardiac patients and patients in whom tachycardia is undesirable.*

Keywords: *Caesarean section, Subarachnoid block, Hypotension, Vasopressor*.

I. Introduction

The delivery of the infant into the arms of a conscious and pain free mother is one of the most exciting and rewarding moments in medicine(Moir D D). With the increasing incidence of Caesarean section[1], the anaesthesiologist has to take a decision about the type of anaesthetic technique to be employed which guarantees the safety of both the mother and fetus.

In caesarean section under spinal anaesthesia hypotension has been reported in as many as 85% of the patients.[2] Maternal hypotension is associated with symptoms like dizziness, nausea, vomiting and may also interfere with surgical procedure and also can cause fetal bradycardia [3] and acidosis[4] Careful positioning and volume preloading with crystalloid or colloids have been used to prevent it, but these are not complete measures [5,6] and a vasopressor is frequently required to correct hypotension quickly[7]. Mephentermine and ephedrine are routinely used.

The aim of this prospective study is to compare the efficacy of mephentermine, ephedrine and phenylephrine for maintenance of blood pressure effectively in caesarean sections under spinal anaesthesia.

II. Methodology

This comparative study was done on parturients coming for elective as well as emergency lower segment Caesarean section conducted under spinal anesthesia in R.L .Jalappa Hospital and Research Centre, Tamaka, Kolar. After approval from our institutional ethics committee, sixty parturients aged between 18-35 years, with ASA I and II scheduled for elective as well as emergency Caesarean section who developed hypotension after subarachnoid block (SAB) were studied.

Patients with gross spinal abnormality, localized skin sepsis, hemorrhagic diathesis, neurological involvement / diseases, known hypertensive patients, diabetic mellitus, cardiac, pulmonary, hepatic or renal disorders, toxaemias of pregnancy, having inadequate subarachnoid blockade and who are later supplemented by general anaesthesia and patients who do not develop hypotension during caesarean section under spinal anaesthesia, were excluded from the study.

Hypotension is defined as fall in systolic pressure >20% from the baseline or a value less than 90mmHg. Patients were randomly allocated to one of the three groups to receive an I.V bolus of the following.

Group “P” -Inj Phenylephrine 50mcg i.v

Group "E"- Inj Ephedrine 6mg i.v

Group "M"- Inj Mephentermine 6mg i.v

Under aseptic precautions , patients were administered subarachnoid (SA) block in lateral position in L_{2-3} or L_{3-4} space with 2ml of 0.5 % hyperbaric bupivacaine. Patient was turned to supine position and a wedge was given under the right hip. They were all preloaded with 15 ml/kg RL solution. Oxygen was administered by facemask to all patients until umbilical cord is clamped .Inj. Oxytocin 15U in 5% dextrose was given after clamping the cord.

Pulse rate, systolic and diastolic arterial pressures was recorded for baseline values. Then same parameters was recorded after subarachnoid block, then at every 2 mins for 20 min and thereafter every 5 mins till the end of the surgery. Whenever hypotension (fall in systolic pressure >20% from the baseline value or a value less than 90mmHg) occur, the study drug was given i.v bolus and repeated whenever required. The number of boluses was noted.

If the patient developed bradycardia (pulse rate of <60/ min),it was treated with atropine 0.6 mg i.v. The skin incision to delivery time and uterine incision to delivery time was recorded. The Apgar score of neonate at 1min and 5min was recorded.

Descriptive and inferential statistical analysis has been carried out in the present study. Analysis of variance (ANOVA) has been used to find the significance of study parameters between three or more groups of patients.

A. Significant figures

+ Suggestive significance (P value: $0.05<P<0.10$)

* Moderately significant (P value:$0.01<P \leq 0.05$)

** Strongly significant (P value : $P \leq 0.01$)

III. Results

All the three groups were comparable in demographic profile and baseline parameters. Three groups were comparable in skin incision to delivery time, uterine incision to delivery time and APGAR at 1 and 5 mins.

3.1 Systolic blood pressure (Table1, Graph 1)

Baseline systolic blood pressure for all the three groups were statistically similar. There was statistically significant decrease in blood pressure at onset of hypotension. There was significant rise in blood pressure after administration of the drug. On intergroup comparison, systolic blood pressure in phenylephrine group was higher than in other groups.

3.2 Diastolic blood pressure (Table2 , Graph 2)

No statistically significant differences were found in all the 3 groups with regards to baseline diastolic blood pressure.There was also significant rise of diastolic blood pressure post administration of the drug but rise was more in phenylephrine group than in ephedrine and mephentermine group. There was no significant difference in the change in blood pressure between ephedrine and mephentermine group.

3.3 Heart Rate (Table 3 , Graph 3)

Baseline heart rate in all the three groups were not statistically similar. Heart rate was raised in all the three groups during hypotension, which was significant, but post drug administration there was significant drop in heart rate in phenylephrine group as compared to Ephedrine and Mephentermine group (there was a rise in heart rate post administration of the drug). No significant differences were observed between heart rate changes in Ephedrine and Mephentermine group.

3.4 Number Of Bolus (Table 4, Graph 4)

The mean and standard deviation of no of bolus in group P was 4.00±1.16 , in group E was 2.45±0.99 and in group M was 2.55±1.46. There was significant statistical difference in the total dose of Phenylephrine, Ephedrine and Mephentermine used ($p<0.05$). Number of boluses are significantly more in Group P with P = <0.001**.

IV. Discussion

Although, Caesarean section is one of the oldest operations in recorded history, anaesthesia for Caesarean section is just a century old and is not bereft of controversies. On one hand, anaesthetic techniques like local anaesthesia have been scoffed at, by both anaesthesiologists and obstetricians. While, on the other hand, the obstetric airway with its ensuing complications have instilled fear into the anaesthesiologists. Thus general anaesthesia for parturients was approached with great degree of caution and decision making.

Amidst this chaos, regional anaesthesia especially spinal anaesthesia proved to be the most preferred technique for Caesarean section.[8] The reason being, the unique potential of spinal technique to provide anaesthesia with a blend of low degree of physiologic trespass and with profound degrees of sensory denervation and muscle relaxation. Thus, the safety of spinal anaesthesia is of dual nature; pharmacological as well as physiologic. The only flaw with this technique is the troublesome and persistent incidence of hypotension especially in gravid parturients.

Hypotension is the commonest serious problem endangering both the mother and the child.[9] But, the degree of hypotension that requires treatment has been controversial. There has been no universal consensus among various authors on the definition of hypotension. Some authors have defined hypotension as decrease in systolic arterial pressure to less than 100 mmHg or decrease in systolic arterial pressure to 80% of base line value.[10,11,12]

Others have defined hypotension as a decrease of 30% or more below baseline values or <90 mmHg arterial pressure. [13]For the purpose of our study, hypotension was defined as a decrease in arterial pressure greater than 20% from the baseline systolic pressure. [14]

Dinesh Sahu and colleagues found that maternal hypotension during spinal anaesthesia for Caesarean delivery was a persistent problem in approximately 85% of cases.[14] Other studies quote an incidence of 50-80%. Differing definitions of "significant" hypotension are partly responsible for the wide variation in incidence of hypotension reported in literature.This high incidence and severity of maternal hypotension following spinal anaesthesia could be attributed to various factors as mentioned below. [15]

1. Amount of local anaesthetic injected was found to produce a higher level of anaesthesia in pregnant term females than in pregnant females.
2. Factors causing hypotension after spinal anaesthesia which are common to both pregnant and non pregnant females like sympathetic blockade leading to vasodilatation and consequent decrease in preload and cardiac output.
3. Additional factors that may accentuate the cardiovascular response to sympathetic denervation include

i. Large amounts of blood present in uterus.
ii. Weight of uterus impairs venous return from extremities during spinal anaesthesia, especially in supine position, thus decreasing cardiac output.
iii. "Bearing down" of patient causes abdominal muscle contraction which further decreases venous return to heart.

Thus, there has been a constant ongoing search by anesthesiologists to recognize this dangerous haemodynamic instability and correct it promptly.

Careful positioning and volume preloading with intravenous crystalloid solution or colloid solution have been standard practice for prevention of hypotension, but these are not complete measures. As vasodilatation is the primary cause of arterial pressure reduction, it seems logical to use vasopressor to correct it. 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.

The place of IV vasopressors for treatment of hypotension during caesarean section is well established. Ephedrine and mephentermine have got a mixed action directly as well as indirectly on alpha and beta receptors, whereas phenylephrine has pure alpha receptor activity. Although phenylephrine reduces uterine blood flow, studies proved that it does not affect fetal outcome and can be used safely during spinal anaesthesia for caesarean section.

In this study all the three vasopressor effectively maintained arterial pressure within 20% limit of baseline value though phenylephrine maintained better as compared to ephedrine and mephentermine. This may be due to that, phenylephrine has peak effect within one minute, whereas ephedrine has 2-5 minutes and mephentermine has 5 minutes.

Moran and Colleagues gave ephedrine 10 mg or phenylephrine 80 mcg IV bolus to maintain systolic arterial pressure above 100 mmHg. They concluded that phenylephrine is as effective as ephedrine and when used in small incremental bolus injections, it appears to have no adverse neonatal effects in healthy, non laboring parturient. [16]

In our study cardiovascular stability was better with phenylephrine. It caused significant reduction in heart rate after the bolus dose, which is a consistent effect in phenylephrine treated women in their studies also. In ephedrine and mephentermine group the heart rate increased compared to preoperative values which we found as statistically significant consistent with the study by Dinesh Sahu.[14] It may be due to beta adrenergic effect of ephedrine and mephentermine which the phenylephrine lacks.

There was no significant effect of vasopressor on fetus in terms of Apgar score at 1 and 5 minutes which correlated well with the study by Dinesh Sahu. In our study we found only nausea and vomiting as side effects.

V. Conclusion

Based on the present clinical comparative study, the following conclusions can be made: All three vasopressors effectively maintained arterial blood pressure during spinal anaesthesia for caesarean section.Phenylephrine has quicker peak effect , but more bolus doses were required to control the hypotension in our study. Phenylephrine caused significant reduction in heart rate than ephedrine and mephentermine. All drugs did not have any adverse effects on the fetus or the mother. Thus it can be concluded that IV Phenylephrine, Ephedrine and Mephentermine can be safely used during spinal anaesthesia for caesarean section for treatment of hypotension.

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Tables And Graphs

Table 1 : Comparison of Systolic BP (mm of Hg) in three groups of patients studied

SBP(mm Hg)	Group P	Group E	Group M	Overall P value	Significance		
					P-E	P-M	E-M
0 minute	114.85±7.29	112.9±10.00	117.1±10.70	0.378	0.791	0.733	0.344
2 minutes	102.65±9.94	102.4±12.78	96.35±12.36	0.168	0.998	0.216	0.243
4 minutes	113.05±3.73	102.45±13.95	102.05±13.98	0.005**	0.015*	0.011*	0.993
6 minutes	113.35±4.86	105.45±14.58	105.3±14.37	0.065+	0.108	0.100	0.999
8 minutes	113.35±11.09	107.55±13.92	107.75±16.69	0.282	0.339	0.364	0.999
10 minutes	99.9±11.61	111.75±11.69	113.35±19.11	0.009**	0.034*	0.014*	0.936
12 minutes	102±11.57	111.75±12.95	113.4±15.39	0.019*	0.064+	0.025*	0.920
14 minutes	100.15±10.59	110.85±12.18	106.95±13.86	0.026*	0.021*	0.195	0.577
16 minutes	101.1±6.88	110.55±10.43	106.65±13.65	0.025*	0.019*	0.236	0.485
18 minutes	103.5±6.04	109±11.20	106.85±15.14	0.315	0.288	0.625	0.823
20 minutes	105.45±11.09	107.8±10.17	106.7±13.57	0.818	0.801	0.939	0.952
25 minutes	104.55±9.51	109.95±9.15	107.7±10.25	0.215	0.189	0.560	0.742
30 minutes	105.4±6.60	111.05±7.59	107.8±9.25	0.084+	0.069+	0.604	0.399

ANOVA and Post –Hoc Tukey test

Graph1 - Comparison in Changes in Systolic Blood Pressure

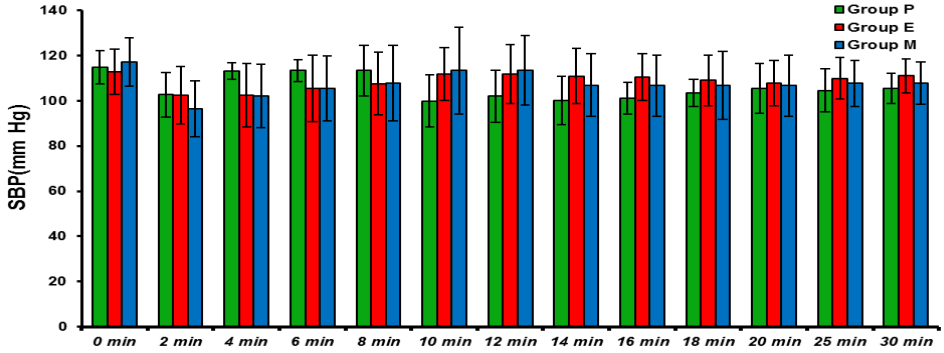

Table 2: Comparison of Diastolic BP (mm of Hg) of three groups of patients studied

DBP(mm HG)	Group P	Group E	Group M	Overall P value	Significance		
					P-E	P-M	E-M
0 minute	71.5±6.25	75.5±5.86	73.6±6.84	0.145	0.122	0.549	0.612
2 minutes	60.25±5.26	62.55±10.36	56.95±11.43	0.176	0.721	0.513	0.153
4 minutes	71.10±9.63	63.35±10.00	61.3±11.12	<0.001**	<0.001**	<0.001**	0.804
6 minutes	73.70±9.65	65.25±11.13	62.1±10.45	0.003**	0.034*	0.002**	0.608
8 minutes	70.45±10.53	65.9±10.51	64.15±13.47	0.216	0.434	0.207	0.882
10 minutes	59.5±8.95	66.6±10.21	66.75±13.06	0.063+	0.106	0.097+	0.999
12 minutes	61.6±10.44	66.6±8.83	64.85±7.39	0.211	0.192	0.491	0.812
14 minutes	59.65±6.99	64.85±7.90	61.2±8.36	0.104	0.096+	0.804	0.306
16 minutes	58.05±7.33	62.95±7.87	60.15±10.16	0.200	0.174	0.718	0.557
18 minutes	58.7±7.74	62.45±9.68	60.8±9.41	0.422	0.390	0.741	0.831
20 minutes	62.4±9.72	59.85±10.15	61.55±8.99	0.697	0.682	0.958	0.843
25 minutes	61.7±8.14	60.6±9.13	64.3±7.17	0.347	0.905	0.577	0.333
30 minutes	64.1±5.27	64.4±4.41	64.5±8.09	0.977	0.987	0.977	0.999

ANOVA and Post –Hoc Tukey test

Graph 2: Comparison of Changes in Diastolic Blood Pressure

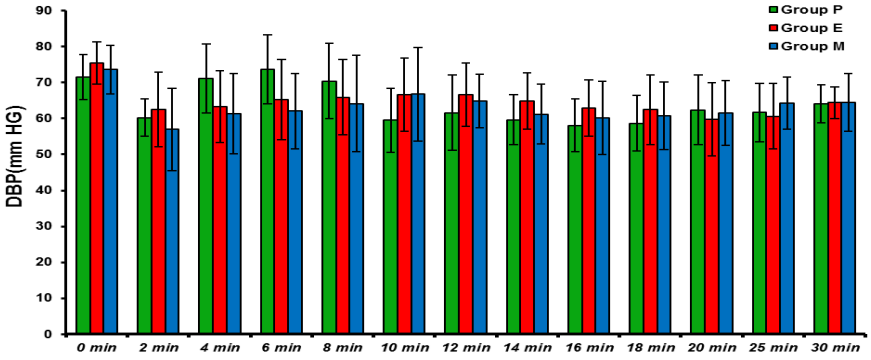

Table 3: Comparison of heart rate (beats per minute) in three groups of patients studied

Heart rate	Group P	Group E	Group M	Overall P value	Significance		
					P-E	P-M	E-M
0 minute	92.75±9.87	90.20±19.19	100.20±16.14	0.117	0.863	0.292	0.114
2 minutes	92.30±16.89	91.90±21.04	104.25±17.8	0.067+	0.997	0.115	0.100
4 minutes	93.70±15.84	91.75±20.47	94.80±19.95	0.875	0.943	0.981	0.866
6 minutes	83.60±16.44	97.70±19.70	94.50±21.02	0.059*	0.060+	0.179	0.858
8 minutes	72.20±17.07	98.30±22.76	94.70±16.00	<0.001**	<0.001**	0.001**	0.818
10 minutes	76.70±19.81	99.45±21.30	96.70±19.16	0.001**	0.002**	0.007**	0.902
12 minutes	82.80±16.06	96.55±16.30	93.45±14.66	0.019*	0.020*	0.090+	0.807
14 minutes	82.60±17.01	95.75±15.60	92.70±13.53	0.024*	0.025*	0.106	0.807
16 minutes	76.55±18.63	99.50±13.87	96.35±12.76	<0.001**	<0.001**	<0.001**	0.793
18 minutes	74.60±18.34	100.10±11.52	99.10±10.70	<0.001**	<0.001**	<0.001**	0.972
20 minutes	70.80±17.95	102.85±14.22	99.00±11.95	<0.001**	<0.001**	<0.001**	0.695
25 minutes	71.25±19.43	101.15±15.27	97.15±15.61	<0.001**	<0.001**	<0.001**	0.735
30 minutes	65.65±17.41	96.50±17.81	95.25±14.94	<0.001**	<0.001**	<0.001**	0.970

ANOVA and Post –Hoc Tukey test

Graph 3: Comparison of Changes in Heart Rate

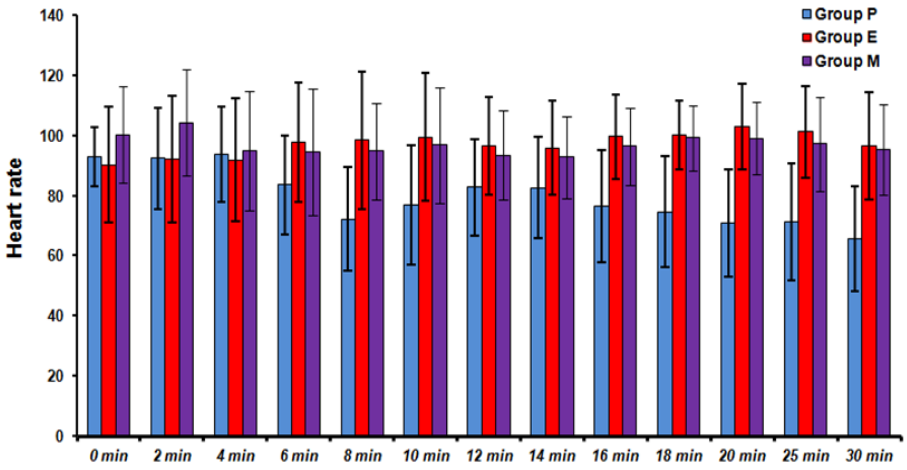

Table 4: Number of bolus in three groups of patients studied

No of bolus	Group P		Group E		Group M	
	No	%	No	%	No	%
1	1	5.0	4	20.0	5	25.0
2	0	0.0	6	30.0	7	35.0
3	5	25.0	7	35.0	4	20.0
4	8	40.0	3	15.0	1	5.0
5 & above	6	30.0	0	0.0	3	15.0
Total	20	100.0	20	100.0	20	100.0
Mean ±SD	4.00±1.16		2.45±0.99		2.55±1.46	

Graph 4– Number Of Bolus