

Comparison of Bolus Phenylephrine, Ephedrine and Mephentermine for Maintenance of Arterial Pressure during Spinal Anaesthesia in Caesarean Section

ANILKUMAR GANESHANAVAR, AMBI UDAY S., SHETTAR ADARSH E., KOPPAL RAMESH, R. RAVI

ABSTRACT

Introduction: Hypotension following spinal anaesthesia for Caesarean section one of the common problem encountered by an anaesthesiologist. This study was aimed at comparing the efficacy of IV bolus Phenylephrine, Ephedrine and Mephentermine for maintenance of arterial blood pressure during spinal anaesthesia in caesarean section.

Materials and Methods: Ninety American Society of Anesthesiologists (ASA) type 1 and 2 patients scheduled for elective as well as emergency caesarean section under spinal anaesthesia who developed hypotension were selected. These were allocated into 3 groups of 30 each to receive Group P-Phenylephrine 100 microgram, Group E- Ephedrine 6 mg, and Group M-Mephentermine 6 mg in 1 ml as bolus IV.

Results: On intergroup comparison rise of diastolic blood pressure at 2, 4, and 6 minutes post study drugs were

significantly less in Ephedrine group and Mephentermine group as compared to the Phenylephrine group ($p < 0.05$). Similarly elevation of systolic arterial pressure in Phenylephrine group was significantly higher 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 time. In Phenylephrine group, post study drug values of heart rate were decreased significantly from the values at onset of the hypotension till the end of the surgery when compared to other two groups ($p < 0.001$).

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: Hypotension, Anaesthesia, LSCS

INTRODUCTION

With the increasing incidence of Caesarean section [1], the anaesthesiologist 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 fetus. In the recent decades there has been a worldwide shift in obstetric anaesthesia practice in favour of regional anaesthesia 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 drug 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. The usual approach to use vasopressors in this clinical setting is reactive rather than proactive, spinal anaesthesia induced maternal hypotension is allowed to develop and then treated accordingly. Current study aimed to compare the efficacy of IV bolus Phenylephrine, Ephedrine and Mephentermine for maintenance of arterial blood pressure following spinal anaesthesia for elective as well as emergency caesarean section.

MATERIALS AND METHODS

This comparative study was done on parturient coming for elective as well as emergency lower segment Caesarean section conducted under spinal anaesthesia in S.N. Medical College and H.S. Hospital Bagalkot, Karnataka, India in Nov. 2010–August 2011. After approval from the institutional ethics committee, ninety parturients ASA I and II scheduled for elective as well as emergency Caesarean section and who developed hypotension after subarachnoid block (SAB) were included.

All parturients were at term, had uncomplicated singleton pregnancy with cephalic presentation and did not weigh more than 70 Kg. The protocol was explained to all patients in detail in their own language and informed written consent was taken. Following criteria's were adopted for selecting parturients. Inclusion Criteria: Patients scheduled for elective as well as emergency lower segment Caesarean section; Aged between 20-35 years; Patients with ASA Class I and II; Baseline systolic blood pressure between 100-140 mmHg and diastolic blood pressure between 70-89 mmHg; And developed hypotension during the operation. Hypotension was defined as fall in systolic pressure $>20\%$ from the baseline value or a value less than 90 mmHg [4].

Parameter	Study Groups	N	Mean	SD	F* Value	p Value
Age (yrs)	Group P	30	23.17	2.51	0.66	0.51
	Group E	30	22.73	2.32		
	Group M	30	22.53	1.59		
Height (cms)	Group P	30	153.20	4.26	1.3	0.27
	Group E	30	151.83	4.66		
	Group M	30	151.43	4.33		
Weight (kg)	Group P	30	54.33	3.07	0.26	0.76
	Group E	30	54.93	4.62		
	Group M	30	54.27	3.81		
Pulse Rate	Group P	30	90.13	7.47	2.4	0.09
	Group E	30	88.33	7.93		
	Group M	30	92.97	8.90		
Systolic BP	Group P	30	123.47	4.98	2.1	0.11
	Group E	30	124.20	5.86		
	Group M	30	121.13	6.80		
Diastolic BP	Group P	30	78.80	3.18	2.9	0.059
	Group E	30	78.40	4.46		
	Group M	30	76.33	4.90		

[Table/Fig-1]: Patients Pre-operative data (Mean \pm SD)

* Oneway ANOVA Test.

EXCLUSION CRITERIA

Patients with medical complications like diabetes mellitus, cardiovascular diseases, severe anaemia, and cerebrovascular diseases; wt more than 70 kg; Patients with obstetrical complications like antepartum haemorrhage, pregnancy induced hypertension, cord complications (nuchal cord or cord prolapse), fetal malformations or malpresentations; Patients with autonomic neuropathy, spinal deformities, other neurological diseases, infections in the lumbar area, coagulation abnormalities and hypovolemia due to any cause.

Ranitidine 50 mg and Metaclopramide 10 mg were given intravenously as a routine practice before surgery. Patients were divided into three groups of 30 each. First 30 cases which satisfied the inclusion criteria were assigned to the Phenylephrine group and next 30 to Ephedrine group and last to mephentermine group. This was an open label study.

Dose: Group P: Phenylephrine 100 microgram (0.1 mg) in 1 ml as IV bolus Group E: Ephedrine 6 mg in 1 ml as IV bolus and Group M: Mephentermine 6 mg in 1 ml as IV bolus was used as indicated.

Hyperbaric bupivacaine 0.5% was used for establishing spinal anaesthesia. After preloading, pulse rate, systolic and diastolic arterial pressure were recorded thrice when middle value was taken as a base line values. The same parameters were recorded after subarachnoid block, then at every 1 min for 20 min and thereafter every 5 min till the end of surgery. Whenever hypotension occurred the study drug was given IV. The number of boluses and time taken to recover from hypotension were noted. The bradycardia i.e. a pulse rate of 60 min⁻¹ or less was treated with Atropine 0.3 mg iv.

Results were expressed as mean \pm SD. Comparability of groups were analysed with Analysis of Variance (ANOVA) test. Student's two-tailed 't' test was applied to analysed parametric data. P value <0.05 was considered significant. SPSS software 13 version was used to calculate the statistics.

RESULTS

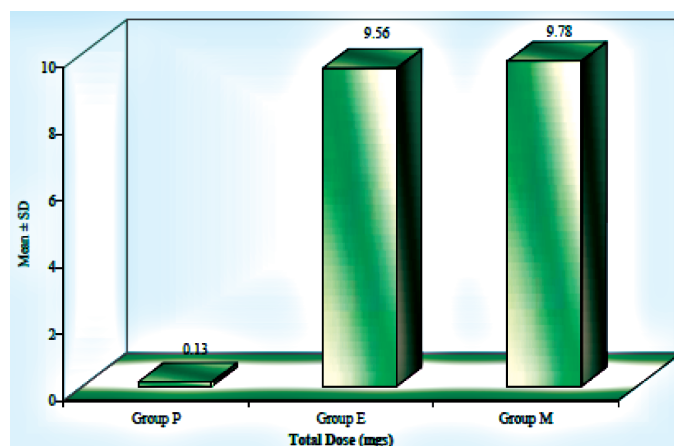
Base line demographics were comparable and are presented in the [Table/Fig-1].

The mean value with standard deviation of total Phenylephrine dose in Group P, total Ephedrine dose in Group E and total Mephentermine dose in Group M were 0.13 \pm 0.05, 9.56 \pm 4.62 and 9.78 \pm 4.01 respectively. There was significant statistical difference in the total dose of Phenylephrine, Ephedrine and Mephentermine used (p<0.05) [Table/Fig-2].

No statistical significant difference were found between 3 groups with regards to level of thoracic sensory block at the onset of surgery (p>0.05).

On intergroup comparison rise of systolic blood pressure and diastolic at 2, 4 and 6 minutes post study drugs were significantly less in Ephedrine group and Mephentermine group as compared to Phenylephrine group (p<0.05) [Table/Fig-3].

In Group P, 77% required single bolus dose while 17% two and 6% three to maintain systolic pressure within 20% limit of basal value.



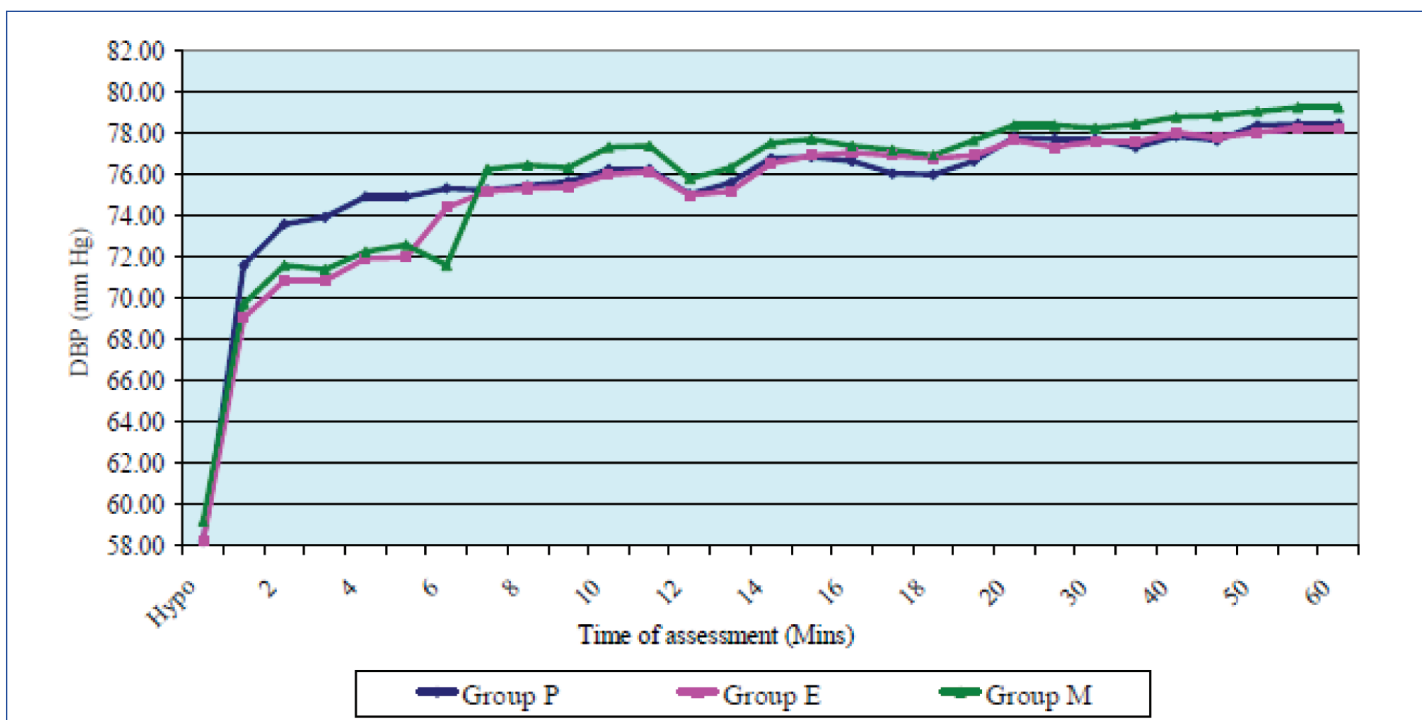
[Table/Fig-2]: Total Dose (mgs)

Time of Assessment	Mean Diff with Hypotension			P* Value
	Group P	Group E	Group M	
1	15.53	11.00	10.73	p<0.001
2	22.47	19.67	19.27	p<0.001
3	22.60	19.73	19.93	p<0.05
4	24.53	22.20	22.00	p<0.05
5	25.40	22.47	22.87	p<0.05
6	26.67	24.20	23.93	p<0.05
7	24.40	24.47	24.73	p<0.05
8	26.73	26.67	26.20	p<0.05
9	26.60	26.67	26.33	p<0.05
10	27.40	27.27	27.33	p<0.05
11	27.53	27.33	27.00	p<0.05
12	27.53	27.00	27.00	p<0.05
13	27.87	27.33	27.93	p<0.05
14	28.40	28.13	28.33	p<0.05
15	27.80	28.00	27.60	p<0.05
16	28.93	28.63	28.60	p<0.05
17	29.00	28.93	28.67	p<0.05
18	30.67	29.07	28.87	p<0.05
19	30.87	29.67	28.27	p<0.05
20	31.80	29.87	29.40	p<0.05
25	30.80	29.87	29.00	p<0.05
30	30.27	30.07	29.27	p<0.05
35	30.20	30.73	28.67	p<0.05
40	30.20	31.13	28.40	p<0.05
45	30.87	31.27	28.93	p<0.05
50	32.20	32.33	32.27	p<0.05
55	33.20	33.13	33.00	p<0.05
60	33.47	33.13	33.07	p<0.05

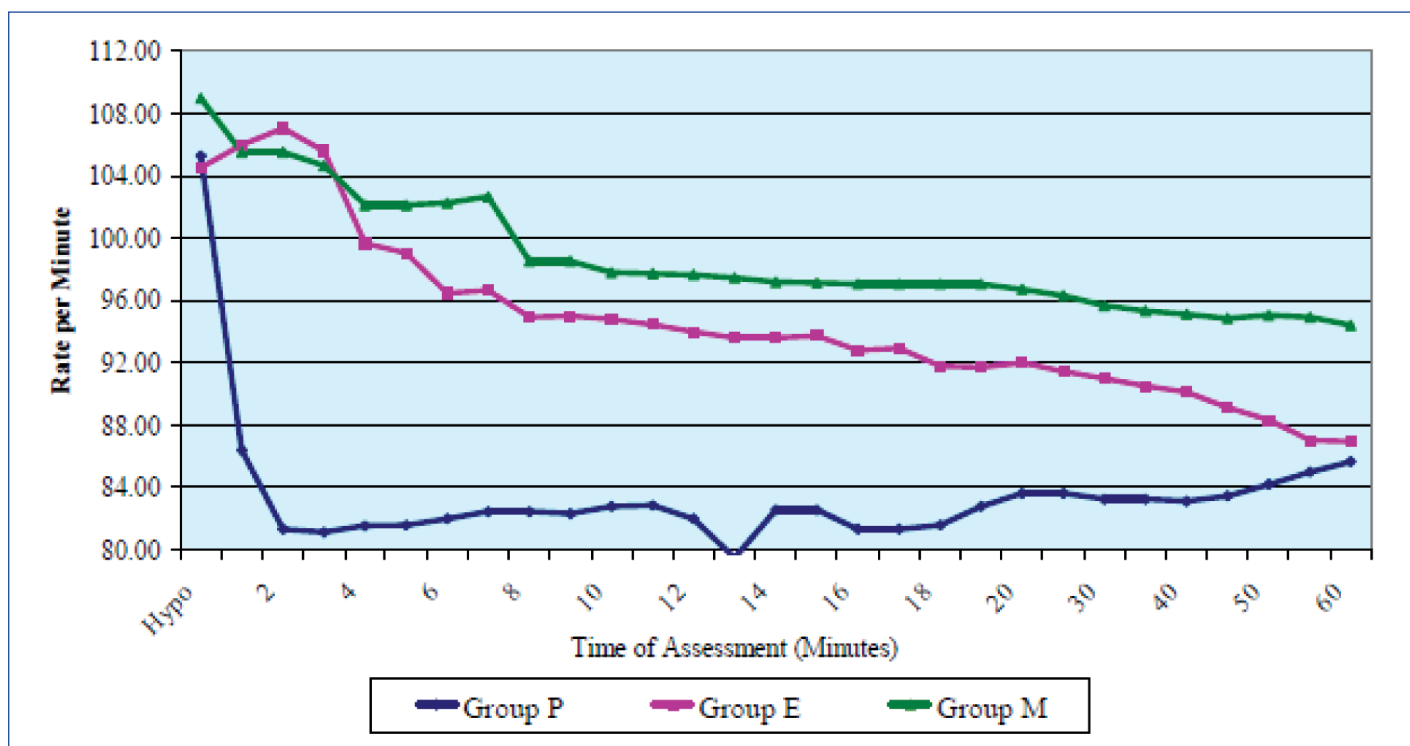
[Table/Fig-3]: Changes in Systolic Blood Pressure (Mean ± SD)

* Oneway ANOVA Test.

** Bonferroni Test.



[Table/Fig-4]: Comparison of changes in Mean Diastolic Blood Pressure



[Table/Fig-5]: Comparison of changes in Heart Rate

On intergroup comparison rise of diastolic blood pressure at 2, 4, and 6 minutes post study drugs were significantly less in Ephedrine group and Mephentermine group as compared to the Phenylephrine group ($p < 0.05$). No significant differences were observed between changes in systolic and diastolic blood pressure of Ephedrine and Mephentermine group [Table/Fig-4].

In Group E 57% required single, 27% two and 16% three bolus doses, whereas In Group M 47% required single, 43% two, and 10% three doses.

Heart rate raised in all three groups during hypotension. In group P, post study drug values of heart rate were decreased significantly from the values at onset of the hypotension till the end of the surgery when compared to other two groups ($p < 0.001$). No significant differences were observed between heart rate changes in Ephedrine and Mephentermine group [Table/Fig-5].

There was no significant effect of vasopressor on fetus in terms of Apgar score at 1 and 5 minutes.

DISCUSSION

Caesarean section is one of the oldest operations in recorded history, however anaesthesia for Caesarean section is just a century old and is not bereft of controversies. Over time, regional anaesthesia especially spinal anaesthesia proved to be the most preferred technique for Caesarean section [5, 6]. 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. However one main hurdle 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 [5, 7]. Dinesh Sahu *et al* [8] found that maternal hypotension during spinal anaesthesia for Caesarean delivery was a persistent problem in approximately 85% of cases [8]. This high incidence and severity of maternal hypotension following spinal anaesthesia could be

attributed to various factors like the amount of local anaesthetic injected, sympathetic blockade, uterus impairing venous return from extremities in supine position etc [6].

When a drug is used to treat the same many questions arise in mind of the anaesthetist. What level of hypotension should they treat?, what will be effects of hypotension on mother and unborn baby and if treated what effects will the drug have on the duo. Also the degree of hypotension that requires treatment itself is controversial with various authors using different cutoffs [9,10,11]. In this study three drugs were evaluated. Each having its own pharmacological properties. Phenylephrine being a synthetic non-catecholamine primarily stimulating α_1 – adrenergic receptors by a direct action. Ephedrine being an indirectly acting synthetic non-catecholamine, that stimulates α and β adrenergic receptors. Mephentermine is an indirect acting synthetic non-catecholamine that stimulates α and β adrenergic receptors.

All the three vasopressor effectively maintained arterial pressure within 20% limit of baseline value though phenylephrine maintained better in first 6 minutes 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 2-5 minutes and mephentermine has 5 minutes. After this time all three drugs were comparable in their control of blood pressure.

Thomas *et al* reported that bolus phenylephrine is as effective as ephedrine in restoring maternal arterial pressure above 100 mmHg [12]. Similarly, Moran *et al* reached the same conclusion and further concluded that the drug appears to have no adverse neonatal effects [13]. Current study also did not find any significant effect of vasopressor on fetus in terms of Apgar score at 1 and 5 minutes.

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 [13,14,15]. In ephedrine and mephentermine group the heart rate increased compared to pre-operative values. This was alike to an earlier Indian study by Dinesh Sahu [8]. This is probably

due to beta adrenergic effect of ephedrine and mephentermine which the phenylephrine lacks.

Thomas D.G. et al [12] reported a high (58%) incidence of bradycardia (heart rate less than 60 beats /min) when phenylephrine was given as IV bolus after induction of spinal anaesthesia, but in our study the incidence for such extreme hypotension was nil. Selection of patients and different criteria of treating hypotension could have caused the difference. In the current study the only side effects noticed were nausea and vomiting. No extreme hypertension and headache was noticed as found in two cases in the study by Taylor JC et al [16].

CONCLUSION

We have found that phenylephrine, ephedrine and mephentermine are effective in IV bolus form in maintenance of arterial pressure within 20% limit of baseline, though phenylephrine has quicker peak effect in comparison to ephedrine and mephentermine and it causes reduction in heart rate, which may be advantageous in cardiac patients and patients in whom tachycardia is undesirable.

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