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Comparison of Bolus Phenylephrine, Ephedrine and Mephentermine for the Management of Hypotension during Spinal Anaesthesia in Caesarean Section: A Clinical Study

Tejaswini Tadooru[1], Nama Nagarjuna Chakravarthy[2]

[1]Assistant Professor, Department of Anaesthesiology, Government Medical College, Mahabubnagar, Telangana 509001, India.
[2]Associate Professor, Department of Anaesthesiology, Gandhi Medical College, Secunderabad, Telangana 500003, India.

Abstract

Background: 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. To compare the efficacy of vasopressors by measuring Systolic and Diastolic blood pressure, Heart rate, Nausea and Vomiting, Neonatal APGAR scores in all Three Groups. *Methods:* A Prospective comparative clinical study was conducted in 30 patients coming for elective lower segment Cesarean section. Parturients were divided into 3 Groups (P, E, M) of 30 each as per the study drugs. Patients meeting the criteria were incorporated into the study. Randomization achieved by sealed envelope technique. Patient's height and weight were measured during the preanesthetic visit. Baseline values for maternal systolic blood pressure, diastolic blood pressure and heart rate were recorded. Epi-info 7 was used for analysis. *Results:* No statistically significant differences were found in all the 3 Groups with regards to baseline heart rate, baseline systolic blood pressure and baseline diastolic blood pressure. There was significant statistical difference in the total dose of Phenylephrine, Ephedrine and Mephentermine used ($p < 0.05$). No Significant differences were observed between heart rate changes in Ephedrine and Mephentermine group. *Conclusion:* Phenylephrine, Mephentermine and Ephedrine effectively maintained arterial blood pressure during spinal anesthesia for cesarean section. Phenylephrine has quicker onset and peak effect in comparison to ephedrine and mephentermine and its predictable carotid sinus reflex effect causes reduction in heart rate, which may be advantageous in cardiac patients and patients in whom tachycardia is undesirable.

Keywords: Phenylephrine; Mephentermine; Ephedrine; Cesarean section; Vasopressor.

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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. With the increasing boom in the incidence of cesarean section,[1] the anesthesiologist is trapped in a delicate web of decision making over the type of anesthetic technique to be employed which guarantees the safety of both the mother

Corresponding Author: Nama Nagarjuna Chakravarthy, Associate Professor, Department of Anaesthesiology, Gandhi Medical College, Secunderabad, Telangana 500003, India.
E-mail: drnag.cn@gmail.com
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and fetus. However, in the recent decades there has been a worldwide shift in obstetric anesthesia practice in favor of regional anesthesia with spinal anesthesia being the most popular among them.[2] Spinal anesthesia was introduced into clinical practice by German Surgeon Karl August Bier in 1898.[3] In cesarean section under spinal anesthesia hypotension has been reported in as many as 85% of the patients.[4] Maternal hypotension is associated with distressing symptoms like dizziness, nausea, vomiting and may also interfere with surgical procedure and can cause fetal bradycardia[5] and acidosis. The rationale behind the study was bolus Phenylephrine, Ephedrine and Mephentermine for the management of hypotension during spinal anesthesia in Cesarean section. Compare the efficacy of vasopressors by measuring heart rate, nausea and vomiting, neonatal APGAR scores in all three groups.

Materials and Methods

Study design:

Prospective comparative clinical study.

Study population:

Parturients coming for elective lower segment Cesarean section.

Study settings:

Gandhi Medial College and Hospital, Secunderabad.

Sampling Technique:

Simple random sampling: Parturients were divided into 3 groups of 30 each as per the study drugs. Patients meeting the criteria were incorporated into the study. Randomization achieved by sealed envelope technique.

Sample size: After approval from the Institutional ethics committee, ninety parturients ASA I and II scheduled for elective cesarean section who developed hypotension after Subarachnoid block (SAB) were studied. All parturients were at term, had uncomplicated singleton pregnancy with cephalic presentation and did not weight more than 70 kg.

Inclusion criteria:

- Patients scheduled for elective lower segment Cesarean section;
- Aged between 20–35 years;
- Patients with ASA Class I and II;
- Baseline systolic blood pressure between 100–140 mm Hg and diastolic blood pressure between 70–89 mm Hg.

Exclusion criteria:

Patients with medical complications like diabetes mellitus, cardiovascular diseases, severe anemia, and cerebrovascular diseases;

Patients with obstetrical complications like antepartum hemorrhage, 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.

Methodology:

Parturients were divided into 3 Groups of 30 each as per the study drugs:

Group P: Phenylephrine 100 μg (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.

The protocol was explained to all patients in detail in their own language and informed written consent was taken.

Patient's height and weight were measured during the preanesthetic visit. Baseline values for maternal systolic blood pressure, diastolic blood pressure and heart rate were recorded. Before surgery, Ranitidine 50 mg and Metaclopramide 10 mg were given intravenously. Patients were transported to the operating theater in left lateral position with an 18G intravenous cannula in a peripheral vein.

Lumbar puncture was performed under strict aseptic precautions in left lateral position by a midline approach using 23G Quincke Babcock spinal needle inserted at L2-3 or L3-4 vertebral interspace. After establishing a free flow of clear cerebrospinal fluid, 12.5 mg (2.5 ml) of hyperbaric bupivacaine 0.5% was injected.

Statistical Analysis:

Sample size of 30 per group is taken for the study. Data like Age, Weight, Height, Base line BP, Diastolic BP, HR were expressed as mean ± SD. Comparability of groups were analyzed with Analysis of Variance (ANOVA) test to elicit the statistical significance

of variation when 3 variables are taken together Student's two-tailed '*t*' test applied to analyzed parametric data. Nonparametric Chi-square test is used for testing statistical significance for variables measured qualitatively. *p* - value < 0.05 was considered significant.

Results

As per shown in Table 1, hence age, height and weight were comparable in all 3 groups and were found to be statistically not significant. Baseline heart rate, baseline systolic blood pressure and baseline diastolic blood pressure were analyzed. The mean values for baseline heart rate in Group P were 90.13 ± 7.47 per minute, in Group E were 88.33 ± 7.93 per minute and in Group M were 92.97 ± 8.90 per minute. Similarly mean values for basal diastolic blood pressure in Group P, Group E and Group M patients were 78.80 ± 3.18 mm Hg, 78.40 ± 4.46 mm Hg and 76.33 ± 4.90 mm Hg respectively. No

Table 1: Preoperative details of the Study Participants

Parameters	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 2: Clinical Parameters and Characteristics

Parameters	Study Groups	N	Mean	SD	*F* Value	*p* - Value	Significance
SAB Hypotension Time (Mins)	Group P	30	7.00	1.02	0.3	0.73	NS
	Group E	30	7.20	1.00			
	Group M	30	7.13	1.01			
SAB Del Interval (Mins)	Group P	30	9.33	1.21	1.5	0.22	NS
	Group E	30	9.40	0.50			
	Group M	30	9.00	1.29			
UI-Del Interval (secs)	Group P	30	51.50	6.45	2.4	0.095	NS
	Group E	30	46.60	3.78			
	Group M	30	48.80	12.99			
Total dose (mgs)	Group P	30	0.13	0.05	73.38	0.001	HS
	Group E	30	9.56	4.62			
	Group M	30	9.78	4.01			
APGAR 1	Group P	30	8.89	0.58	0.88	0.41	NS
	Group E	30	8.67	0.72			
	Group M	30	8.50	0.77			
APGAR 5	Group P	30	8.78	0.58	0.88	0.41	NS
	Group E	30	8.67	0.72			
	Group M	30	8.50	0.77			

Table 3: Variations in the Heart Rate with Time

Time of Assessment (min)	Mean Diff with Hypotension			*p* - Value	Significance	Significant Pairs
	Group P	Group E	Group M			
1	18.90	-1.47	3.47	$p < 0.001$	HS	P & E, P & M
2	23.97	-2.57	3.47	$p < 0.001$	HS	P & E, P & M
3	24.17	-1.47	4.33	$p < 0.001$	HS	P & E, P & M
4	23.73	4.86	6.87	$p < 0.001$	HS	P & E, P & M
5	23.70	5.46	6.87	$p < 0.001$	HS	P & E, P & M
6	23.30	8.06	6.73	$p < 0.001$	HS	P & E, P & M
7	22.83	7.86	6.33	$p < 0.001$	HS	P & E, P & M
8	22.83	9.60	10.47	$p < 0.001$	HS	P & E, P & M
9	22.97	9.53	10.47	$p < 0.001$	HS	P & E, P & M
10	22.50	9.73	11.20	$p < 0.001$	HS	P & E, P & M
11	22.43	10.06	11.27	$p < 0.001$	HS	P & E, P & M
12	23.30	10.53	11.33	$p < 0.001$	HS	P & E, P & M
13	25.80	10.93	11.53	$p < 0.001$	HS	P & E, P & M
14	22.73	10.93	11.80	$p < 0.001$	HS	P & E, P & M
15	22.73	10.80	11.87	$p < 0.001$	HS	P & E, P & M
16	23.97	11.73	11.93	$p < 0.001$	HS	P & E, P & M
17	23.97	11.60	11.93	$p < 0.001$	HS	P & E, P & M
18	23.70	12.73	11.93	$p < 0.001$	HS	P & E, P & M
19	22.50	12.80	11.93	$p < 0.01$	S	P & E, P & M
20	21.67	12.53	12.27	$p < 0.01$	S	P & E, P & M
25	21.67	13.06	12.67	$p < 0.01$	S	P & E, P & M
30	22.03	13.53	13.33	$p < 0.01$	S	P & E, P & M
35	22.03	14.00	13.67	$p < 0.05$	S	P & E, P & M
40	22.17	14.40	13.87	$p < 0.05$	S	P & E, P & M
45	21.83	15.40	14.13	$p < 0.05$	S	P & E, P & M
50	21.10	16.20	16.33	$p < 0.05$	S	P & E, P & M
55	20.30	17.50	16.53	$p < 0.05$	S	P & E, P & M
60	19.63	17.56	17.06	$p < 0.05$	S	P & E, P & M

Table 4 (A): Changes in Systolic Blood Pressure

Time of Assessment (min)	Mean Diff with Hypotension			*p* - Value	Significance	Significant Pairs
	Group P	Group E	Group M			
1	15.53	11.00	10.73	$p < 0.001$	HS	P & E, P & M
2	22.47	19.67	19.27	$p < 0.001$	HS	P & E, P & M
3	22.60	19.73	19.93	$p < 0.05$	S	P & E, P & M
4	24.53	22.20	22.00	$p < 0.05$	S	P & E, P & M
5	25.40	22.47	22.87	$p < 0.05$	S	P & E, P & M
6	26.67	24.20	23.93	$p < 0.05$	S	P & E, P & M
7	24.40	24.47	24.73	$p > 0.05$	NS	-
8	26.73	26.67	26.20	$p > 0.05$	NS	-
9	26.60	26.67	26.33	$p > 0.05$	NS	-
10	27.40	27.27	27.33	$p > 0.05$	NS	-
11	27.53	27.33	27.00	$p > 0.05$	NS	-
12	27.53	27.00	27.00	$p > 0.05$	NS	-
13	27.87	27.33	29.93	$p > 0.05$	NS	-

(Contd.)

Time of Assessment (min)	Mean Diff with Hypotension			*p* - Value	Significance	Significant Pairs
	Group P	Group E	Group M			
14	28.40	28.13	28.33	$p > 0.05$	NS	-
15	27.80	28.00	27.60	$p > 0.05$	NS	-
16	28.93	28.63	28.60	$p > 0.05$	NS	-
17	29.00	28.93	28.67	$p > 0.05$	NS	-
18	30.67	29.07	28.87	$p > 0.05$	NS	-
19	30.87	29.67	28.27	$p > 0.05$	NS	-
20	31.80	29.87	29.40	$p > 0.05$	NS	-
25	30.80	29.87	29.00	$p > 0.05$	NS	-
30	30.27	30.07	29.27	$p > 0.05$	NS	-
35	30.20	30.73	28.67	$p > 0.05$	NS	-
40	30.20	31.13	28.40	$p > 0.05$	NS	-
45	30.87	31.27	28.93	$p > 0.05$	NS	-
50	32.20	32.33	32.27	$p > 0.05$	NS	-
55	33.20	33.13	33.00	$p > 0.05$	NS	-
60	33.47	33.13	33.07	$p > 0.05$	NS	-

Table 4 (B): Changes in Diastolic Blood Pressure

Time of Assessment (min)	Mean Diff with Hypotension			*p* - Value	Significance	Significant Pairs
	Group P	Group E	Group M			
1	13.40	10.87	10.53	$p < 0.05$	S	P & E, P & M
2	15.40	12.67	12.40	$p < 0.05$	S	P & E, P & M
3	15.73	12.67	12.20	$p < 0.05$	S	P & E, P & M
4	16.73	13.73	13.07	$p < 0.05$	S	P & E, P & M
5	16.73	13.80	13.40	$p < 0.05$	S	P & E, P & M
6	17.13	16.20	12.40	$p < 0.05$	S	P & E, P & M
7	17.07	17.00	17.07	$p > 0.05$	NS	-
8	17.27	17.13	17.27	$p > 0.05$	NS	-
9	17.47	17.20	17.13	$p > 0.05$	NS	-
10	18.07	17.80	18.13	$p > 0.05$	NS	-
11	18.07	17.93	18.20	$p > 0.05$	NS	-
12	16.87	16.80	16.60	$p > 0.05$	NS	-
13	17.40	17.00	17.13	$p > 0.05$	NS	-
14	18.60	18.33	18.33	$p > 0.05$	NS	-
15	18.67	18.73	18.53	$p > 0.05$	NS	-
16	18.47	18.87	18.20	$p > 0.05$	NS	-
17	17.87	18.73	18.00	$p > 0.05$	NS	-
18	17.80	18.60	17.73	$p > 0.05$	NS	-
19	18.47	18.73	18.47	$p > 0.05$	NS	-
20	19.60	19.47	19.20	$p > 0.05$	NS	-
25	19.53	19.13	19.20	$p > 0.05$	NS	-
30	19.53	19.40	19.07	$p > 0.05$	NS	-
35	19.13	19.40	19.27	$p > 0.05$	NS	-
40	19.67	19.87	19.60	$p > 0.05$	NS	-
45	19.47	19.60	19.67	$p > 0.05$	NS	-
50	20.20	19.87	19.87	$p > 0.05$	NS	-
55	20.27	20.07	20.07	$p > 0.05$	NS	-
60	20.27	20.07	20.07	$p > 0.05$	NS	-

Table 5: Side Effects in Study Participants

Side Effects		Drug		
		Group P	Group E	Group M
Nausea & Vomiting	Count	2	5	5
	%	6.67	16.67	16.67
Nil	Count	28	25	25
	%	93.33333	83.333333	83.33333

Chi-square = 1.730, $p > 0.05$, Nonsignificant

statistically significant differences were found in all the 3 groups with regards to baseline heart rate, baseline systolic blood pressure and baseline diastolic blood pressure.

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 ± 0.05, 9.56 ± 4.62 and 9.72 ± 4.01 respectively. There was significant statistical difference in the total dose of Phenylephrine, Ephedrine and Mephentermine used ($p < 0.05$), shown as in Table 2.

Heart rate raised in all three groups during hypotension. In Group P, poststudy 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, shown in Table 3.

On intergroup comparison rise of systolic blood pressure at 2, 4 and 6 minutes poststudy drugs were significantly less in Ephedrine Group and Mephentermine Group as compared to Phenylephrine Group ($p < 0.05$), shown as in Table 4 (A and B).

Shown in Table 5, side effects observed were only nausea and vomiting. 6% developed nausea and vomiting in Group P, whereas 16% developed in Group E and Group M. APGAR score did not reveal any untoward effect on fetal status, since, all newborn of three groups had APGAR score greater than 7.

Discussion

Regional anesthesia, especially spinal anesthesia, proved to be the most preferred technique for cesarean section.[6] The reason being, the unique potential of spinal anesthesia to provide Subarachanoid block with a blend of low-degree of physiological changes and with profound degrees sensory denervation and muscle relaxation. Thus, the safety of spinal anesthesia is of dual nature, pharmacological as well as physiological, when compared to general anesthesia.

The results of the present study, correlate well with the study by *Dinesh Sahu and colleagues*.[7] They studied 60 patients undergoing elective as well as emergency cesarean section under spinal anesthesia who developed hypotension after subarachnoid block. They were randomly allocated to one of three groups to receive an IV bolus of the following Group P Phenylephrine 100 µg (n = 20), Group E Ephedrine 6 mg (n = 20) or Group M Mephentermine.

Thomas and Colleagues[8] reported that bolus phenylephrine 100 µg is as effective as ephedrine 5 mg in restoring maternal arterial pressure100 mm Hg. More than 50% of women given phenylephrine in their study developed significant bradycardia. But in our study, decrease in heart rate was seen but not below 60 beats/min than with Ephedrine and Mephentermine Groups.

Taylor JC et al.[9] who reported two cases of overdose resulting in extreme hypertension and headache. In one case she developed decreased blood pressure after induction of spinal anesthesia to 110/59 mm Hg and there were symptoms of faintness and nausea. She was given phenylephrine 250 µg IV. These side effects are may be due to larger doses of phenylephrine when compared to the present study where the dose was given in small incremental doses.

Ramanathan and colleagues[10] studied in 127 healthy patients undergoing elective cesarean section under epidural anesthesia. They concluded that transient maternal hypotension does not affect neonatal acid – base status, both ephedrine and phenylephrine do not cause fetal acidosis, when used for treating maternal hypotension.

Casey study[11] showed that 10-point APGAR score as affective as umbilical artery pH measurement to assess the condition and prognosis of new born. Hence, APGAR score was used to predict neonatal outcome in our present study.

Conclusion

Phenylephrine, Mephentermine and Ephedrine effectively maintained arterial blood pressure during spinal anesthesia for cesarean section. Phenylephrine has quicker onset and peak effect in comparison to ephedrine and mephentermine and its predictable carotid sinus reflex effect causes reduction in heart rate, which may be advantageous in cardiac patients and patients in whom tachycardia is undesirable. Thus, it can be concluded that IV Phenylephrine, Ephedrine and Mephentermine can be safely used during spinal anesthesia for cesarean section for treatment of hypotension.

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