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Clinical Comparative Study of Effect of Two Different Doses of Phenylephrine on Spinal Induced Hypotension during Cesarean Section

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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ABSTRACT

Background and Aims: During Cesarean section, hypotension occurs in the most of parturients, following spinal anesthesia. This prospective observational study was undertaken to determine the efficacy of two different Bolus Doses of Phenylephrine for Prevention of Spinal-Induced Hypotension during Cesarean Section.
Materials and Methods: A total of 120 parturients undergoing cesarean section were divided into two groups of group A and group B with sixty in each group. Group A received phenylephrine 75 mcg IV bolus, while Group B received phenylephrine 100 mcg IV bolus, immediately after giving spinal anesthesia. For the next 20 minutes, systolic blood pressure (SBP), diastolic blood pressure (DSP), mean arterial pressure (MAP), and heart rate (HR) were recorded every 2 minutes, and APGAR scores at 1 and 5 minutes were recorded.
Results: There was no difference between the two groups in terms of preventing hypotension, with 16.6% in Group A and 16.6% in Group B. In the first 2–6 minutes, however, the rise in systolic

pressure in Group B was higher than in Group A. Group B (46.66 %) had a higher rate of bradycardia than Group A (25 %).

Conclusion: Both phenylephrine dosages were equally effective in preventing hypotension following spinal anesthesia. However, Prophylactic bolus dose of phenylephrine 75 mcg was found to be effective for the management of spinal-induced hypotension and should be preferred over 100 mcg which causes significant bradycardia and reactive hypertension.

Keywords: Bradycardia; reactive hypertension; phenylephrine; spine.

1. INTRODUCTION

During Caesarean section, spinal anesthesia - induced hypotension caused by sympathetic neuronal block remains a substantial therapeutic problem [1]. Severe hypotension is commonly accompanied by maternal symptoms such as nausea, vomiting, and dyspnea, and adverse effects on the fetus, including as low Apgar scores and umbilical acidosis, have been linked to the severity and duration of hypotension. Before giving spinal anesthesia, the goal is to maintain the baseline systolic arterial pressure (SAP) at ≥90% and to avoid a baseline decrease of <80% [2]. Because hypotension is frequent, vasopressors should be used routinely and mostly prophylactically.The most appropriate medications for treating or preventing hypotension after spinal anesthesia are alpha-agonist drugs. Currently, phenylephrine is commonly used. Although vasopressors with α1 adrenergic agonist activity have been thought to be the most successful to yet, current research has indicated that adding beta agonist drugs(noradrenaline) may be more beneficial. Phenylephrine has a potent direct α1 adrenergic agonist effect [3]. Postural hypotension result in decrease in blood pressure and stimulating the baroreceptors, thus increasing the heart rate (HR). Low dosage of phenylephrine 20 mcg as determined to be not effective, high doses of around 100 mcg resulted in baroreceptor mediated maternal bradycardia with a consequent reduction in maternal cardiac output [4]. Hypotension (fall in SBP of less than 20% of baseline) was treated with a maximum of two doses (100 mcg) of phenylephrine, and if hypotension persisted or bradycardia developed, another rescue vasopressor (ephedrine 6 mg IV bolus) was given [2]. The goal was to determine the dose of phenylephrine that would maintain hemodynamic stability while without compromising cardiac output. Hence, this randomized study was undertaken to determine the efficacy of two different Bolus Doses of Phenylephrine for Prevention of Spinal-Induced hypotension during Cesarean Section.

2. MATERIALS AND METHODS

After receiving approval from the Institutional research board and written informed consent from the Parturients, a prospective observational study was conducted for 3 months on 120 parturients aged between 20–35 years who were scheduled for elective Caesarean section and had physical status of American Society of Anesthesiologists (ASA) classes I and II.

2.1 Inclusion Criteria

Full-term pregnant women between the ages of 20 and 35 who were scheduled for a caesarean delivery under spinal anesthesia were included in the study.

2.2 Exclusion Criteria

Parturients below 20 years and above 35 years of age, with height below 150 cm or above 170 cm, weight exceeding 70 kg, resting blood pressure >140/90 mmHg, history of hypertension, preeclampsia/eclampsia, hyperthyroidism, history of any coexisting neurological, cerebrovascular, cardiovascular, renal, metabolic, psychiatric disorder, glaucoma, occlusive vascular disorder, history of hypersensitivity to local anesthetics and any contraindications to spinal anesthesia or having known fetal abnormalities, and fetal distress were excluded from the study.

On the basis of a computer-generated random sample technique, parturients were divided into two groups of group A and group B.After receiving a 9 mg hyperbaric 0.5% bupivacaine intrathecal injection, parturients in Group A received a 75 mcg intravenous (IV) prophylactic phenylephrine bolus. SBP, DBP, MAP, SPO2, and HR were then monitored every 2 minutes for the next 20 minutes. After the intrathecal injection, parturients in Group B received an IV phenylephrine bolus of 100 mcg. SBP, DBP, MAP, SPO2, and HR were then monitored every 2 minutes for the next 20 minutes. After the delivery, the babies' APGAR score were noted in

both groups. Prospective observational study was achieved where anesthesiologist administering the drug and observer recording the parameters.

2.3 Parameters to be Studied

SBP, DBP and HR every 2 minutes for the next 20 minutes following spinal anesthetic induction, as well as the incidence of hemodynamic side effects, nausea and vomiting, and the APGAR score at first 5 minutes.

2.4 Procedure

Inside the operation theatre, parturients were placed in the supine position and given oxygen through a face mask at a rate of 4 L/min, which was maintained until the delivery of baby. Standard monitoring included pulse oximetry, electrocardiogram, and noninvasive blood pressure was monitored using a multi parameter monitor. After establishing an IV line with an 18 G cannula, parturients were preloaded with Ringer lactate solution at a rate of 10 mL/kg for 15 minutes and continued at 10 mL/min. With the parturient in the sitting position, skin infiltration with lidocaine 2% was performed, a 25G Quincke babcocks needle was inserted at the L3–L4 spinal interspace, and hyperbaric 0.5 % bupivacaine 9 mg was administered intrathecally under strict aseptic conditions. After spinal injection, systolic blood pressure , diastolic blood pressure, mean arterial pressure, heart rate and SPO2 were monitored at 2-minute intervals. Hypotension was treated in both the groups by administration of phenylephrine. Immediately after intrathecal injection, parturients in Group A received phenylephrine 75 mcg IV bolus , while parturients in Group B received phenylephrine 100 mcg IV bolus. The number of patients who developed bradycardia (<55 bpm) as a result of phenylephrine was recorded and treated with 0.6 mg of IV atropine. Adverse effects like nausea, vomiting, shortness of breath, and chest pain were recorded. Nausea or vomiting if any was treated with IV ondansetron 0.1 mg/kg.

Block height was measured bilaterally using pin prick method at 5-minute intervals for the first 15 minutes after intrathecal administration of local anesthetic bupivacaine. Slow IV infusions of oxytocin 10 IU in 500 mL lactated Ringers solution were given after birth. In a structured proforma, demographic and obstetric data such as age, weight, parity, gestation week, the total duration of surgery and anesthesia, total fluid needed during surgery, and APGAR scores at 1 and 5 minutes were recorded.

2.5 Statistical Analysis

Unpaired t-tests were used to compare baseline hemodynamic values and post-spinal hemodynamic changes at various time periods. On a categorical scale, the Chi-square test was performed to determine the significance of research parameters. The data was presented as a mean ± standard deviation. P value was used to determine the statistical significance of the difference between Group A and Group B. P <0.05 was considered to be statistically significant, P < 0.01 was considered to be highly significant, P < 0.001 was considered to be very highly significant, and P > 0.05 was considered to be not significant.

3. RESULTS

3.1 Maternal Characteristics

In our investigation, the age, weight, and height of two groups were comparable and determined to be non-significant (P > 0.05).

3.2 Systolic Blood Pressure (SBP) Variations

As indicated in [Table 1], the changes in mean SBP in Group A and Group B following spinal anesthesia were in the range of 114.04 - 129.6 mm Hg and 112.13 - 143.23 mm Hg, respectively.

Both groups exhibited similar baseline SBPs; however, Group B's mean SBP was greater and statistically significant at 2 to 6 minutes after the study drug phenylephrine administration.

3.3 Diastolic Blood Pressure (DBP) Variations

As indicated in [Table 2], the changes in mean DBP in Group A and Group B following spinal anesthesia were in the range of 72.91 - 60.92 mm Hg and 84.68 - 63.06 mm Hg, respectively.

Both groups exhibited similar baseline DBPs; however, Group B's mean DBP was greater and statistically significant at 2 to 6 minutes after the study drug phenylephrine administration.

3.4 Mean Arterial Pressure (MAP) Variations

As indicated in [Table 3], the changes in mean of MAP in Group A and Group B following spinal anesthesia were in the range of 91.96 - 78.68 mm Hg and 102.35 - 79.89 mm Hg, respectively.

Table 1. Data statistics

Time	Mean +/- SD		t	P
	Group A	Group B		
Basal	120.73 ± 12.40	116.13±9.46	2.28	0.02
0	119.32 ± 10.72	115.23 ±8.01	2.36	0.019
2	129.6 ± 10.39	141.55 ±6.23	7.64	0.0001
4	129.3 ± 11.03	143.23 ±6.03	8.58	0.0001
6	123.06 ± 9.61	134.81 ±6.91	7.68	0.0001
8	123.08 ± 10.11	127.21 ±5.68	2.75	0.0067
10	118.29 ± 11.17	122.35 ±5.55	2.52	0.013
12	119.61 ± 6.43	119.7 ±5.85	0.08	0.93
14	117.07 ± 6.63	115.03 ±7.37	1.59	0.11
16	116.63 ± 7.99	114.35 ±6.93	1.67	0.09
18	114.08 ± 10.70	112.73 ±6.31	0.84	0.4
20	114.04 ± 9.79	112.13 ±5.02	1.34	0.18

Table 2. Changes in mean DBP in Group A and Group B

Time	Mean +/- SD		*t*	P
	Group A	Group B		
Basal	71.05 ±6.91	69.50 ±5.23	1.38	0.168
0 min	70.12 ±7.06	69.01 ±5.95	0.93	0.35
2 min	72.91 ±9.21	84.68 ±6.01	8.29	0.0001
4 min	71.21 ±9.79	83.11 ±5.96	8.042	0.0001
6 min	68.35 ±8.72	78.19 ±6.19	7.12	0.0001
8 min	68.06 ±10.32	70.63 ±5.63	1.69	0.093
10 min	67.32 ±9.03	68.43 ±4.37	0.85	0.39
12 min	65.41 ±8.85	68.18 ±5.95	2.01	0.04
14 min	66.35 ±9.85	67.95 ±6.28	1.06	0.29
16 min	62.63 ±7.89	64.89 ±7.43	1.61	0.1
18 min	61.99 ±8.79	63.06 ±7.88	0.7	0.48
20 min	60.92 ±8.70	63.68 ±6.95	1.92	0.057

Table 3. Changes in mean of MAP in Group A and Group B

Time	Mean +/- SD		*t*	P
	Group A	Group B		
Basal	87.5 ±7.43	84.8 ±5.21	2.3	0.022
0 min	85.56 ±6.81	83.7 ±6.23	1.56	0.12
2 min	91.96 ±8.39	102.35 ±6.10	7.75	0.0001
4 min	90.11 ±10.49	101.97 ±5.06	7.88	0.0001
6 min	87.5 ±9.23	96.05 ±5.35	6.2	0.0001
8 min	86.89 ±8.56	89.19 ±4.12	1.87	0.06
10 min	83.61 ±9.17	86.63 ±4.70	2.27	0.02
12 min	83.17 ±11.52	85.12 ±6.63	1.13	0.25
14 min	84.79 ±8.07	84.23 ±6.49	0.4	0.67
16 min	80.08 ±8.24	82.10 ±8.28	1.33	0.18
18 min	79.31 ±7.63	80.06 ±6.05	0.590	0.55
20 min	78.68 ±8.68	79.89 ±7.19	0.83	0.4

Both groups exhibited similar baseline MAPs; however, Group B's mean MAP was greater and statistically significant at 2 to 6 minutes after the study drug phenylephrine administration.

3.5 Heart Rate (HR) Variations

As indicated in [Table 4], the changes in mean Heart rate(HR) in Group A and Group B following spinal anesthesia were in the range of 88.61 -

72.46 mmHg and 90.11 - 67.7 mm Hg, respectively. Group A and Group B had mean basal HRs of 88.61 and 89.68, respectively, which were not statistically significant. At 4 minutes after study drug phenylephrine administration, the mean HR in Group B was lower and was found to be statistically significant.

3.6 Incidence of Bradycardia

There were 15 out of 60 cases of bradycardia in Group A and 28 out of 60 cases of bradycardia in Group B, respectively. Group A had a 25% and Group B had a 46.66% incidence of bradycardia, respectively.

3.7 Apgar Scores

As indicated in [Table 5], At the 1st minute, Group A and Group B had mean APGAR values of 7.61 and 7.68, respectively, which are statistically not significant.

The mean APGAR scores of at the 5th minute were 9.23 and 9.21, respectively, and are statistically not significant.

4. DISCUSSION

The advantages of the spinal anesthetic for cesarean section approach include its simplicity, rapid onset, low failure rate, low medication dose, and effective muscular relaxation during operation, whereas general anesthesia for cesarean sections has lot of disadvantages and risk factors such as failure of endotracheal intubation and ventilation, aspiration pneumonitis, postoperative nausea and vomiting, delayed lactation and sedation of the newborn etc; [5] To give a sufficient block for cesarean section , spinal anesthetic to the level of T5–T6 is required [6]. Maternal hypotension that is left untreated after spinal anesthesia is harmful to both the mother and the fetus [7]. Parturients undergoing cesarean section should be given prophylactic IV phenylephrine or ephedrine and volume preloading, according to National Institute for Health and Care Excellence (NICE) clinical guidelines, to decrease the risk of hypotension [2]. Furthermore, the American Society of Anesthesiologists (ASA) [8] guidelines for obstetric anesthesia suggests that no delay in administering spinal anesthesia for cesarean delivery to administer a fixed volume of fluid and IV ephedrine or phenylephrine to treat spinal hypotension.

Table 4. Mean HR in Group A and B

Time	Mean +/- SD		*t*	P
	Group A	Group B		
Basal	88.61 ±12.31	89.68 ±9.56	0.53	0.59
0 min	86.10 ±18.08	90.11 ±9.23	1.53	0.12
2 min	76.06 ±12.79	73.2 ±4.11	1.64	0.1
4 min	73.5 ±9.2	67.7 ±4.97	4.29	0.0001
6 min	72.46 ±10.6	69.1 ±8.23	1.93	0.05
8 min	75.9 ±11.43	76.1 ±6.10	0.12	0.9
10 min	77.61 ±12.1	79.06 ±6.06	0.83	0.4
12 min	77.63 ±14.6	80.7 ±7.21	1.46	0.14
14 min	79.35 ±13.8	81.9 ±7.03	1.27	0.2
16 min	80.31 ±11.7	81.23 ±8.99	0.48	0.63
18 min	81.08 ±11.9	83.5 ±9.06	1.25	0.21
20 min	82.32 ±10.61	82.9 ±9.79	0.31	0.75

Table 5. APGAR scores

Time	Mean +/- SD		t	p
	Group A	Group B		
1 min	7.61 ±0.58	7.68 ±0.68	0.6	0.54
5 min	9.23 ±0.43	9.21 ±0.23	0.31	0.75

According to Ngan Kee et al. [8], *various studies conducted by him showed that* ephedrine is not be used for prophylaxis against hypotension, because low doses were ineffective in preventing spinal anesthesia induced hypotension, whereas hypertension occurred with high dose administration of ephedrine and also suggested that prophylactic use of phenylephrine IV bolus was shown to be more successful than other approaches in preventing spinal anesthesia induced hypotension [9].

According to the findings of this study, the incidence of hypotension was higher in parturients who did not get prophylactic phenylephrine than in those who did receive prophylactic phenylephrine. Patients who received prophylactic phenylephrine had better blood pressure control than those who did not [10].

Hypotension is fall in SBP of less than 20% of baseline [2]. Hence, in order to prevent the spinal anesthesia induced hypotension, in this randomized study, we used two different Bolus Doses of Phenylephrine for Prevention of Spinal-Induced Hypotension During Cesarean Section to determine the efficacy.

4.1 Observations

4.1.1 Blood pressure

In this study, Systolic blood pressure, diastolic blood pressure, mean arterial pressure were higher in group B and were statistically significant at 2 to 6 minutes after the study drug phenylephrine administration. Hypotension was found in 16.66 percent of Group A and 16.66 percent of Group B, respectively. This demonstrates that both groups have steady blood pressure management.This is related to phenylephrine's agonistic effect, which causes veno-constriction and so increases preload. Ngan Kee et al. [9] compared phenylephrine infusions of 100 g/min to bolus injections and found that infusions of phenylephrine are as effective as bolus injections in reducing the incidence and severity of hypotension. Bhattarai et al(2018) examined phenylephrine 25 mcg, ephedrine 5 mg, mephentermine 6 mg as boluses for maintaining arterial pressure and found that on IV administration, all three medications maintained hemodynamics within 20% of baseline [11] These studies corroborated our findings.

4.2 Heart Rate

Except for the 4th minute after study medication administration, when it was considerably lower in Group B, the mean HR in both groups for 20 minutes was comparable. Bradycardia (<55 bpm) was more common in Group B (46.66 %) than in Group A (25%). Atropine 0.6 mg IV was used to treat these occurrences. This is most likely owing to phenylephrine induced reflex bradycardia, which reduced the HR. In comparison to the ephedrine group, Thomas et al. [12] discovered that >50% of women given phenylephrine developed significant bradycardia. Given that cardiac output is the product of HR and stroke volume, phenylephrine appears to restore a larger stroke volume than ephedrine. The higher stroke volume produced by phenylephrine is most likely due to a higher preload than ephedrine, because phenylephrine is devoid of β inotropic effect. Hall et al. [13] reported two incidences of bradycardia in the phenylephrine group, both of which were cured with a bolus dose of atropine. Both of these episodes occurred after numerous phenylephrine doses. There had been no additional cases of bradycardia. These data backed up our findings, implying that phenylephrine produces reflex bradycardia.

4.3 Side Effect

None of the individuals in our study suffered nausea or vomiting after receiving phenylephrine. An increase in vagal tone following preload reduction, according to Cooper et al. could be the cause of nausea and vomiting. Saravanan et al. [6] discovered that phenylephrine performed much better than ephedrine in preventing vomiting in patients with inadequate blood pressure control.

All of the studies cited above found that patients receiving phenylephrine had a lower incidence of nausea and vomiting, which is similar to our findings.

4.4 Neonatal Outcome

At 5 minutes, both groups had similar APGAR scores, which were over 9. Previous research has demonstrated that phenylephrine, either as a bolus or as an infusion, has no adverse effects on neonates [14].

5. CONCLUSION

Both phenylephrine doses were equally effective in preventing hypotension following spinal anesthesia in cesarean section, with the incidence of hypotension being the same in both groups, without any adverse effects on neonatal outcome. However, Prophylactic bolus dose of phenylephrine 75 mcg was found to be effective for the management of spinal-induced hypotension and should be preferred over 100 mcg, because the incidence of bradycardia was higher in 100 mcg group and the reactive hypertension was found.

6. LIMITATION

We were unable to link the individual cardiovascular effects of phenylephrine and oxytocin since the hemodynamic effects of oxytocin were not observed and recorded in this study. Because of the short-acting vasopressor activity of phenylephrine hypotension might reoccur after the preventive IV bolus wears off, necessitating repeated boluses, which was another major drawback of our study.

CONSENT AND ETHICAL APPROVAL

As per international standard or university standard guideline participant consent and ethical approval has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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