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Comparison Of Two Methods Of Administration Of Phenylephrine For The Prevention And Treatment Of Hypotension In Caesarean Section Under Spinal Anaesthesia

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ABSTRACT

Background & Aim: Phenylephrine induces maternal bradycardia in 50% of mothers when used for prevention and treatment of spinal anaesthesia-induced hypotension during caesarean delivery. Rapid fluid administration immediately after initiation of the spinal block (co-loading) may have a vasopressor sparing effect. Even though phenylephrine infusion was active as a vasopressor, there was a fall in heart rate occasionally as a reflex action, but it was not statistically significant. There was no incidence of bradycardia or change in rhythm. Aim of the study is to assess the efficacy of prophylactic and therapeutic phenylephrine when administered by different methods as a vasopressor.

Method: 60 mothers scheduled for elective caesarean section were recruited in this randomized controlled trial. The primigravida included in the study were divided into two groups; group 1 (n = 30) received intravenous prophylactic phenylephrine infusion at 100 micrograms/min for 3 minutes immediately after subarachnoid block and group 2(n = 30) received phenylephrine as boluses of 100 microgram for the treatment of hypotension following subarachnoid block. Vital signs (blood pressure, heart rate, and arterial oxygen saturation) were recorded throughout the surgery. Maternal and neonatal perioperative complications were also controlled and recorded.

Results: There was an insignificant difference in demographic data between the groups. In Group I, only 6.7% incidence of hypotension episodes, whereas in Group II, 96.7% incidence of hypotension episodes were seen, indicating phenylephrine infusion was more effective in preventing hypotension episodes. In both, the groups had similar pre-induction systolic blood pressure, but the mean systolic blood pressure was higher in the infusion group and was statistically significant. In both groups DBP was higher in the infusion group and was statistically significant. Mean arterial pressure pre-induction was similar in both the groups, but mean arterial pressure was higher in the infusion group and was statistically significant. Phenylephrine does much higher in Group I (infusion group) when compared to Group II (bolus group), which was statistically significant (P-value <0.001).No significant side effects were observed in the study (nausea, vomiting). There was no significant difference between the two groups in APGAR score.

Conclusion: Administration of prophylactic phenylephrine infusion is more effective as vasopressor compared to therapeutic Boluses in elective caesarean section done under subarachnoid block. Prophylactic phenylephrine infusion was associated with lower heart rates occasionally when compared to bolus doses. There is no significant reduction in APGAR scores at 1st and 5th min in both groups. Prophylactic infusion of phenylephrine can effectively decrease spinal anesthesia related hypotension without any significant complication for mother or her fetus.

Keywords: hypotension, spinal anesthesia, phenylephrine, maternal bradycardia

1. INTRODUCTION

The delivery of a baby by Caesarean section has become increasingly common. Several factors account for the increased section rate. The widespread use of electronic and biochemical fetal monitoring before and during labour has made it easier to identify a fetus in jeopardy and promptly deliver the baby by the abdominal route. Spinal Anaesthesia appears to be the preferred technique [1]. Although the spinal block offers several advantages like sensory block, muscle relaxation, minimal risk of aspiration, and a well awake patient to assess the clinical condition, it is often associated with significant adverse effects like hypotension. Hypotension is one of the most frequent problems following spinal anaesthesia for Caesarean section, potentially endangering both mother and child. Measures to decrease incidence and severity of maternal hypotension include left uterine displacement, fluid preload, prophylactic vasopressors, Trendelenburg position, and leg compression [2].

This prospective study aims to assess the efficacy of prophylactic and therapeutic phenylephrine when administered by different methods as a vasopressor in elective cesarean sections, under subarachnoid block.

2. MATERIALS AND METHODS

After getting approval from the institutional ethical committee and written and informed consent, a prospective study was conducted in 60 primigravidas undergoing an elective cesarean section. The primigravida included in the study were divided into two groups:

Group I: primigravidas who received intravenous prophylactic phenylephrine infusion at 100 micrograms /min for 3 minutes immediately after subarachnoid block.

Group II: primigravidas who received phenylephrine as boluses of 100microgram for the treatment of hypotension following subarachnoid block.

Inclusion criteria was full-term primigravida posted for elective caesarean section, and age between18-30yrs, and ASA Grade-II.

Exclusion criteria was primigravidas above 30 yrs and below 18yrs, primigravida with preeclampsia, eclampsia, hyperthyroidism, primigravidas with neurological, cardiovascular, renal, cerebrovascular, metabolic, psychiatric disorders, primigravidas with glaucoma, occlusive vascular disorder, known hypersensitive to local anaesthetics and any

contraindications to spinal anaesthesia or having identified fetal abnormalities, and fetal distress.

3. PROCEDURE:

All the primigravidas were preloaded with ringer's lactate solution at the rate of 15 ml/kg over 15 mins after securing intravenous line with 18g cannula and continued at 15ml/min.

A 25G quincke needle was inserted at L2-L3 intervertebral space, and hyperbaric 0.5% bupivacaine 2.0ml was injected intrathecally after confirming the needle position by CSF visualization. After subarachnoid block with 0.5% Bupivacaine upper sensory level of the sympathetic block was assessed by using the alcohol swab and motor block was assessed by Modified Bromage scale.

Immediately after completion of subarachnoid block phenylephrine infusion was started In Group I with a syringe pump that was connected to iv line via a three-way stop cock and was continued for a minimum of 3 minutes at a rate of 1ml/min (100µg/min).After which the infusion was either stopped or continued according to the protocol based on hemodynamic parameters (SBP).

In Group II, phenylephrine bolus at 100µg/each bolus dose was given following a drop in systolic blood pressure of <20% of baseline after giving subarachnoid block.

APGAR score was assessed. All the hemodynamic parameters were recorded at 1^{st} min, 2^{nd} min, 3^{rd} min, 5^{th} min, 15^{th} min, 30^{th} min, 45^{th} min, 60^{th} min, and 90^{th} min.

Chi-square ($\chi 2$) test was used for the association between two categorical variables. The difference between the means of analysis variables between two independent groups analysed by unpaired t-test. If the p-value was < 0.05, statistically significant. Data were analyzed using SPSS software v.23.0.

4. RESULTS

TABLE 1:

DEMOGRAPHICS BETWEEN BOTH THE GROUPS.

AGE(YRS)	Group I	Group II	p-value
	N(%)	N(%)	
≤20	1(3.3%)	0(0.0%)	0.360
21-25	20(66.7%)	23(76.7%)	
26-30	7(23.3%)	7(23.3%)	
>30	2(6.7%)	0(0.0%)	
Total	30(100.0%)	30(100.0%)	

PT AGE (Yrs)-Mean ± SD	24.5 ± 4.2	24.0 ± 2.6	0.579
PTWT- Mean ± SD	64.2 ± 6.1	64.9 ± 2.2	0.557
PT HT- Mean ± SD	157.3 ± 4.5	155.6 ± 2.7	0.074
HR- Mean ± SD	90.7 ± 7.1	92.4 ± 3.5	0.254
SBP- Mean ± SD	124.0 ± 8.8	124.4 ± 6.3	0.840
DBP- Mean ± SD	74.3 ± 4.5	72.4 ± 5.1	0.125
MBP- Mean ± SD	90.7 ± 5.1	89.5 ± 4.7	0.366

TABLE 2:
MEAN HR BETWEEN BOTH THE GROUPS

HR	Group I	Group II	p-value
	Mean ± SD	Mean ± SD	
BASELINE	90.7 ± 7.1	92.4 ± 3.5	0.254
1min	88.9 ± 7.6	94.4 ± 5.8	0.003*
2min	89.1 ± 7.6	94.3 ± 6.4	0.006*
3min	89.6 ± 6.8	91.8 ± 5.0	0.175
5min	88.6 ± 6.8	91.5 ± 3.9	0.053
15min	88.3 ± 5.4	90.9 ± 7.0	0.112
30min	87.0 ± 6.9	90.3 ± 4.7	0.033*
45min	87.9 ± 6.5	90.7 ± 3.6	0.041*
60min	87.7 ± 7.0	90.9 ± 6.3	0.064
90min	85.7 ± 10.2	90.8 ± 7.4	0.029*

Note: * significant at 5% level of significance ($p<0.05$)

TABLE 3:
MEAN SYSTOLIC BLOOD PRESSURE (SBP) BETWEEN BOTH THE GROUPS

SBP	Group I	Group II	p value
	Mean ± SD	Mean ± SD	

BASELINE	124.0 ± 8.8	124.4 ± 6.3	0.840
1min	125.8 ± 8.1	127.5 ± 9.7	0.446
2min	124.4 ± 9.4	117.9 ± 13.1	0.032*
3min	125.8 ± 7.7	104.4 ± 13.8	<0.001*
5min	124.4 ± 7.8	100.1 ± 12.6	<0.001*
15min	124.5 ± 9.4	102.8 ± 12.6	<0.001*
30min	123.6 ± 10.1	104.8 ± 8.8	<0.001*
45min	126.3 ± 9.8	108.9 ± 8.8	<0.001*
60min	125.5 ± 9.7	108.9 ± 8.5	<0.001*
90min	123.8 ± 11.8	108.6 ± 7.6	<0.001*

* significant at 5% level of significance (p<0.05)

TABLE 4:
MEAN DIASTOLIC BLOOD PRESSURE (DBP) BETWEEN BOTH THE GROUPS.

DBP	Group I		Group II		p-value
	Mean	SD	Mean	SD	
BASELINE	74.3	4.5	72.4	5.1	0.125
1min	75.3	6.1	74.4	6.8	0.619
2min	74.4	6.2	72.0	7.1	0.166
3min	74.6	5.3	67.9	7.0	<0.001*
5min	73.7	8.0	66.1	7.8	<0.001*
15min	73.3	7.6	66.4	8.9	0.002*
30min	72.5	7.4	67.5	5.7	0.005*
45min	72.8	6.4	69.8	7.7	0.108
60min	74.2	6.4	68.3	4.8	<0.001*
90min	72.3	8.9	68.1	5.0	0.026

* significant at 5% level of significance (p<0.05)

TABLE 5:
MEAN ARTERIAL PRESSURE (MBP) BETWEEN BOTH THE GROUPS.

MBP	Group I	Group II	p-value

	Mean ± SD	Mean ± SD	
BASELINE	90.7 ± 5.1	89.5 ± 4.7	0.366
1min	91.9 ± 5.8	92.0 ± 7.2	0.988
2min	90.9 ± 6.6	87.1 ± 8.3	0.058
3min	91.5 ± 5.3	79.9 ± 8.8	<0.001*
5min	90.4 ± 6.7	77.3 ± 9.1	<0.001*
15min	90.2 ± 7.7	78.4 ± 9.7	<0.001*
30min	89.4 ± 7.9	79.8 ± 6.3	<0.001*
45min	90.5 ± 6.7	82.7 ± 7.1	<0.001*
60min	91.2 ± 6.8	81.7 ± 5.3	<0.001*
90min	89.3 ± 9.2	81.5 ± 5.5	<0.001*

* Significant at 5% level of significance (p<0.05)

TABLE 6:
MEAN DOSAGES OF PHENYLEPHRINE (µG) USED IN BOTH THE GROUPS AND MEANTIME INTERVAL BETWEEN SKIN INCISION TO BABY DELIVERY IN BOTH THE GROUPS.

Parameter	Group I	Group II	p-value
	Mean ± SD	Mean ± SD	
Phenylephrine(mcg)	470.0 ± 262.8	203.3 ± 92.8	<0.001*
TIME INTERVAL	530.0 ± 62.7	528.0 ± 55.5	0.896

* Significant at 5% level of significance (p<0.05)

TABLE 7:
DISTRIBUTION OF APGAR SCORE AT 1MIN BETWEEN BOTH THE GROUP

	Group I	Group II	p value
	N (%)	N (%)	
APGAR SCORES AT 1 MIN			
8	14(46.7%)	5(16.7%)	0.360
9	10(33.3%)	18(60.0%)	
10	6(20.0%)	7(23.3%)	
Total	30(100.0%)	30(100.0%)	

Apgar scores at 1 min-Mean ± SD	8.7 ± 0.8	9.1 ± 0.6	0.077
APGAR SCORES AT 5 MINS			
9	9(30.0%)	8(26.7%)	0.774
10	21(70.0%)	22(73.3%)	
Total	30(100.0%)	30(100.0%)	
Apgar scores at 5 mins-Mean ± SD	9.7 ± 0.5	9.8 ± 0.4	0.779

TABLE 8:
INCIDENCE OF COMPLICATIONS IN PERCENTAGES BETWEEN BOTH THE GROUPS.

COMPLICATIONS	Group I		Group II		p-value
	N	%	N	%	
Nausea/Vomiting	0	0.0%	1	3.3%	0.874
Incidence of Hypotension Episodes	2	6.7%	29	96.7%	<0.001

* Significant at 5% level of significance ($p<0.05$)

5. DISCUSSION

The usual approach to use vasopressors is reactive rather than proactive. Spinal anaesthesia-induced maternal hypotension is allowed to develop and then treated accordingly. We have, instead, studied prophylactic phenylephrine infusion and Spinal anaesthesia has become the preferred technique for cesarean section. Hypotension remains a significant drawback with this technique, despite maternal positioning to avoid aortocaval compression and various other preventive measures, including crystalloid and colloid infusions [3].

For the purposes of this study, hypotension was defined as a decrease in arterial pressure greater than 20% from baseline systolic pressure[4].

Dinesh Sahu et al. found that maternal hypotension during spinal anaesthesia for cesarean delivery was a persistent problem in approximately 85% of cases. This is in spite of pregnant patients having 40-50% of more blood volume at term are more prone to develop hypotension due to the occurrence of aortocaval compression by the fetal head and high level of sympathetic blockade owing to increased spread of local anaesthetic in CSF[5].

Hypotension is better prevented than treated. Blood pressure is usually maintained in the face of vasodilation, caused due to factors other than a central neural blockade, by a reflexive increase in cardiac output cannot increase and is often reduced. The result is

severe hypotension with reduced uteroplacental perfusion, impaired fetal oxygenation, fetal acidosis, and decreased APGAR score.

It has shown that the percentage decrease in placental perfusion is related to the percentage reduction in maternal arterial pressure and not an absolute reduction in weight.

Non-pharmacological method: left uterine displacement to decrease the effect of the aortocaval compression leg elevation, Intravenous pre-hydration with crystalloid solutions is compelling. The use of colloid solutions may be more effective than crystalloids, but the benefits are still limited but with limitations.

It was shown that Joupilla and colleagues that preload maintains placental blood flow despite the moderate reduction in parental pressure, then minimizing fetal acidosis. In our study, we have preloaded with ringer's lactate at the rate of 15ml/kg over 15 minutes so that placental blood flow could be maintained during hypotensive periods lasting longer than 2minutes [6].

Pure α-agonist vasopressors initially were considered contraindicated in obstetrics, because early experimental studies reported a substantial decrease in uteroplacental blood flow linked to their vasoconstrictive properties. However, doses used in these studies were much higher than those needed clinically in humans, although they were appropriate to the species studied to restore spinal anaesthesia-induced hypotension. In addition, a more recent experimental study suggested that pregnancy is associated with an attenuated uterine vascular response to phenylephrine.

Clinical studies in women undergoing scheduled caesarean delivery have confirmed that small (40–100μg) bolus doses of phenylephrine used to counteract hypotension during spinal anaesthesia were effective and as safe as ephedrine bolus doses for the mother and the neonate.

compared it with the control group, which is not receiving prophylactic infusion for, but when hypotension occurred, were treated with phenylephrine.

Vasopressors are often required, and current evidence suggests that phenylephrine is more suitable than ephedrine in obstetrics [7].

In a systematic review of randomized controlled trials, Lee et al [8]. Showed that ephedrine and phenylephrine have similar efficacy for preventing or treating hypotension, and although ephedrine use was associated with lower umbilical cord blood pH values than phenylephrine, there was no difference in Apgar scores.

In a study conducted by Mercier al, rescue phenylephrine bolus doses appear capable when ephedrine alone fails to correct hypotension [9].

The propensity of ephedrine[10] to cause maternal tachycardia and depress fetal pH and base excess has resulted in suggestions to eliminate or drastically limit its use. Most clinical trials have focused on relatively high-dose prophylactic infusions of vasopressor [10].

Comparative studies suggest that the use of phenylephrine is associated with better fetal acid-base status [11].

In our research, phenylephrine was administered for prevention and treatment of hypotension in the cesarean section during spinal anaesthesia Group-I, 30 pts were given intravenous phenylephrine prophylactically 100mcg/min for 3 minutes immediately after spinal anaesthesia and Group-II, 30 patients received 100µg of bolus phenylephrine for treatment of hypotension episodes.

All the patients were primigravida and between the age group of 18-30 yrs. And a significant number of patients were included between 21-25 yrs of age, which is 20 patients (66.7%) in Group I and 23 patients (76.7%) in Group II, as seen in Table 1. The mean age of both the groups was 24.5yrs and 24 yrs, respectively.

Mean patients weight In Group I was 64.2 and in Group II was 64.9. The mean patient's height in Group I was 157.3, and in Group II was 155.6.

In our study Group, I had fallen in HR than Group II, which was at 1min, 2min, 30min, 45min, 90min periods. A study conducted by Bilal Mohammad et al., also used prophylactic phenylephrine infusion for hypotension showed significant fall in HR in their study group than their control group with ephedrine. This fall in HR was not <50/min. Hence, atropine was not used in any of the cases[12].

In our study, hemodynamic changes showed that Group I showed SBP and MAP were significantly higher, starting from 3 minutes to 90 minutes when compared with Group II, similar to the study conducted by Bilal Mohammad et al. The SBP and MAP were significantly higher in Group I than Group II.

The number of episodes of hypotension higher in Group I out of 30 patients, only two patients (6.7%) had hypotension episodes when compared with 29 patients (96.7%) in Group II, (P <0.001)

The mean dose of phenylephrine used in Group I was 470mcg, and the mean dose of phenylephrine used in Group II was 203.3mcg. The dosage used in Group I, i.e., infusion Group, was significantly higher than Group II (P<0.001).

6. NEONATAL OUTCOME:

The mean APGAR at 1min for Group I was 8.7 and for Group II was 9.1 the mean APGAR at 5 min for Group I was 9.7, and Group II was 9.8.

Of both, the Groups APGAR score at 1 min was categorized into 8,9,10. Of which maximum babies came in APGAR score 8 in Group I 14, i.e. (46.7) and in Group II APGAR score of 9, i.e., 18(60%).

At the end of 5 minutes, the APGAR score of 10 was seen in maximum babies in both groups. That is 21(70%) in Group I and 22(73.3%) in Group II.

In our study incidence of nausea and vomiting, only one patient out of 30 in Group II and none of 30 patients in Group, I have nausea and vomiting. This correlation with the study

was done by cooper and colleagues in which nausea and vomiting were less frequent with phenylephrine.

As per our study, which was done with infusion of phenylephrine in Group I and bolus dose of 100mcg of phenylephrine in Group II there was statistically significant difference in hemodynamic parameters of the Group I that in those given infusion of phenylephrine there was statistically significant difference in SBP and MAP and less incidence of hypotensive episodes in Group I than Group II.

The other parameters, like APGAR, score at 1 and 5 minutes, and nausea and vomiting showed no significance.

7. CONCLUSION

Administration of prophylactic phenylephrine infusion is more effective as vasopressor compared to therapeutic Boluses in elective cesarean section done under subarachnoid block. Prophylactic phenylephrine infusion was associated with lower heart rates occasionally when compared to bolus doses. There is no significant reduction in APGAR scores at 1st and 5th min in both groups. There were no significant maternal side effects seen in both groups.

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