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THE EFFECTIVENESS OF PROPHYLACTIC INTRAVENOUS PHENYLEPHRINE AND EPHEDRINE ON MATERNAL HEMODYNAMICS AND FETAL OUTCOME IN ELECTIVE CESAREAN SECTION UNDER SUBARACHNOID BLOCK

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ABSTRACT

Objective: In this study our goal is to evaluate the effectiveness of prophylactic intravenous phenylephrine and ephedrine on maternal hemodynamics and fetal outcome in elective cesarean section under subarachnoid block. **Method:** This randomized Controlled trial (RCT) study was carried out at Obstetric Operation Theatre Department of Anaesthesia, Analgesia and Intensive Care Medicine, BSMMU for a period of 12 months. A total of 90 parturients admitted for elective caesarean section at Department of Obstetrics and Gynaecology, Bangabandhu Sheikh Mujib Medical Universitywere included in the study, they were divided into two groups, 45 in each. Where Group P was the phenylephrine group and Group E was the ephedrine group. **Results:** During the study period, the mean arterial pressure was statistically significant at 3 minutes, 6 minutes, 9 minutes, 12 minutes before the delivery of the baby and at 20 minutes, 25 minutes, 30 minutes, 35 minutes, 40 minutes, 45 minutes after the delivery. But it was found to be statistically non significant at the baseline, 15 minutes before the delivery of the baby and at 5 minutes, 10 minutes, 15 minutes, 50 minutes after the delivery of the baby.Among all the 90 parturient, 3 parturient in group P and 8 parturient in group E developed hypotension and was subsequently treated with rescue doses of vasopressor. One parturient in group P and 2 parturient in group E developed dizziness. 1 (2.2%) parturient in group P and 8 (17.8%) parturient in group E developed nausea alone and 1(2.2%) parturient in group P and 5(11.1%) in group E had nausea with vomiting which was managed by ondansetron 4 mg. 3 (6.7%) out of 45 parturient in group P developed bradycardia which was managed by atropine 0.5mg .Out of 90 parturients 2(4.4%) parturient in group p and 8(17.8%) parturient developed tachycardia. **Conclusion:** From our study we can conclude that, prophylactic intravenous phenylephrine bolus at the given dose remarkably reduced the incidence of subarachnoid block induced hypotension with fewer adverse maternal effects. The use of phenylephrine was associated with better foetal acid base status, and satisfactory APGAR score.

KEYWORD: Phenylephrine, Subarachnoid block (SAB), anaesthetic technique.

INTRODUCTION

Subarachnoid block is a form of neuraxial regional anaesthesia involving the injection of a local anaesthetic into the subarachnoid space. Subarachnoid block induced hypotension during caesarean section is one of the common complications that has many detrimental effects to the mother and the foetus if left untreated. It is estimated that around 80% of patients undergoing caesarean section under subarachnoid block develop hypotension during the procedure without any prophylactic management.[1] The American Society of Anesthesiologists (ASA) practice guidelines for Obstetric Anaesthesia in 2016 suggests that either intravenous (IV) ephedrine or phenylephrine may be used to treat subarachnoid block induced hypotension.[2] The optimal dosing regimen and optimal method of

administration of phenylephrine is still controversial. Whether to give prophylactic intravenous phenylephrine or an intravenous bolus immediately after subarachnoid administration or to wait and initiate an infusion or give a bolus with the onset of hypotension remains uncertain.[3]

Ephedrine is a non-specific adrenergic agonist and increases blood pressure mainly by increasing cardiac output via stimulation of cardiac β-1 receptors with a smaller contribution from vasoconstriction. Its action is mainly indirect, via stimulating release of norepinephrine from sympathetic nerve terminals; because utero-placental circulation is largely devoid of direct sympathetic innervation, it is relatively resistant to vasoconstrictive effect of ephedrine.[4]

Phenylephrine, a selective alpha 1 adrenergic agonist, which has been used to increase blood pressure. Because of its sympathomimetic effect without β-adrenergic activity, it does not increase contractility force nor the output of the cardiac muscle; it might increase blood pressure resulting bradycardia through vascular baroreceptor stimulation as reflex bradycardia.[5] It is currently considered as the preferred drug of choice for subarachnoid block induced hypotension in caesarean section. In this study our main goal is to evaluate the effectiveness of prophylactic intravenous phenylephrine and ephedrine on maternal haemodynamics and foetal outcome in elective cesarean section under subarachnoid block.

OBJECTIVE

General objective

- To evaluate the effectiveness of prophylactic intravenous phenylephrine and ephedrine on maternal hemodynamics and fetal outcome in elective cesarean section under subarachnoid block.

Specific objective

- To detect mean arterial pressure at different time intervalsof the patients.
- To evaluate neonatal birth weight and umbilical arterial blood gas analysis.

METHODOLOGY

Study type

- This study was a randomized Controlled trial (RCT) study.

Place and period of study

- The study was carried out at Obstetric Operation Theatre under supervision of Department of Anaesthesia, Analgesia and Intensive Care Medicine, BSMMU from 12 months.

Sample size

- A total of 90 parturients admitted for elective caesarean section in Obstetric and Gynaecology Department of BSMMU according to the inclusion and exclusion criteria. Patients were randomly divided into two groups using consecutive closed envelopes with random numbers processed by a health care provider who was not involved with the study in any respect. Where Group P was the phenylephrine group and Group E was the ephedrine group. Each group had sample size of 45.

Inclusion criteria

After obtaining the approval of Institutional Review Board and written informed consent 90 female patients of ASA physical status I & II enrolled in this clinical study.

1. Elective caesarean section
2. Normal singleton pregnancy beyond 36 weeks gestation.
3. ASA (American Society of Anesthesiologist) physical status I and II

Data collection procedure

This study was conducted at Obstetric Operation Theatre of Bangabandhu Sheikh Mujib Medical University (BSMMU). After receiving of approval from the Institutional Review Board (IRB), BSMMU and informed written consent from each individual 90 patients were enrolled in this study undergoing elective caesarean section who had fulfilled the inclusion and exclusion criteria. Preoperative evaluation was done with thorough history, physical examination and relevant laboratory investigations. All patients were randomly divided into two groups using consecutive closed envelopes with random numbers processed by a health care provider who was not involved with the study in any respect. Where Group P (n=45): 100 µg phenylephrine and in Group E (n=45): 10 mg Ephedrine was induced.

Demographic and clinical data including age, weight, height, body mass index (BMI) and American Society of Anaesthesiologist (ASA) physical status scores were recorded for all patients. All patients had the standard monitoring including continuous electrocardiography (ECG) (lead II), heart rate (HR), non-invasive blood pressure (NIBP) measured and oxygen saturation via continuous pulse oximetry (SpO2). Intravenous (IV) access with 18G IV cannula was established preferably on the non-dominant hand vein. Injection Ranitidine 50 mg and Metoclopramide 10 mg was given intravenously half an hour before operation.

Data analysis

The statistical analysis was carried out using the Statistical Package for Social Sciences version 23.0 for Windows. Qualitative variables of this study have been expressed as percentage. Quantitative variables are expressed as mean ± standard deviation. Comparison was calculated by Chi-square test for the categorical variables &Unpaired t-test for the continuous variables. P values <0.05 were considered as statistically significant.

RESULTS

In figure-1 shows age distribution of the patients where Group P was the phenylephrine group and Group E was the ephedrine group. Each group had sample size of 45. Most of the patients belong to 21-30 years age group, 64.4% and 73.3%. The following figure is given below in detail:

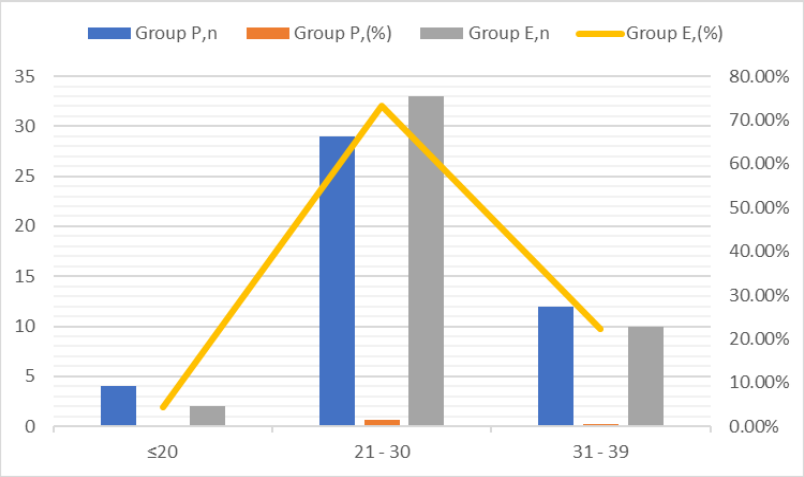

Figure 1: Age distribution of the patients.

Table-1 shows the mean arterial pressure where it was statistically significant at 3 minutes, 6 minutes, 9 minutes, 12 minutes before the delivery of the baby and at 20 minutes, 25 minutes, 30 minutes, 35 minutes, 40 minutes, 45 minutes after the delivery. But it was found to be statistically not significant at the baseline, 15 minutes before the delivery of the baby and at 5 minutes, 10 minutes, 15 minutes, 50 minutes after the delivery of the baby. The following table is given below in detail:

Table 1: Mean arterial pressure at different time intervals between two groups.

Mean arterial pressure (mmHg)	Group P (n=45)	Group E (n=45)	p-value
Baseline	86.47 ± 4.43	85.31 ± 4.67	0.232^{ns}
Before delivery			
At 3 minutes	93.09 ± 6.86	82.98 ± 4.58	$<0.001^{***}$
At 6 minutes	92.93 ± 4.81	82.42 ± 5.25	$<0.001^{***}$
At 9 minutes	90.02 ± 4.63	81.00 ± 7.00	$<0.001^{***}$
At 12 minutes	86.02 ± 5.23	79.64 ± 4.95	$<0.001^{***}$
At 15 minutes	82.22 ± 5.68	81.33 ± 3.68	0.637^{ns}
After delivery			
At 5 minutes	79.96 ± 5.66	80.00 ± 4.19	0.966^{ns}
At 10 minutes	78.89 ± 5.83	80.44 ± 3.82	0.138^{ns}
At 15 minutes	79.80 ± 5.72	78.89 ± 2.77	0.338^{ns}
At 20 minutes	80.36 ± 3.64	78.44 ± 3.77	0.016^{*}
At 25 minutes	81.20 ± 4.66	78.22 ± 4.39	0.002^{**}
At 30 minutes	81.42 ± 4.55	78.93 ± 3.52	0.005^{**}
At 35 minutes	82.09 ± 5.43	79.33 ± 3.10	0.004^{**}
At 40 minutes	82.58 ± 4.70	79.78 ± 3.16	0.001^{**}
At 45 minutes	83.89 ± 5.89	79.95 ± 3.96	0.001^{**}
At 50 minutes	81.64 ± 4.82	79.00 ± 2.40	0.153^{ns}

Values are expressed as mean ± SD. P value <0.05 is considered as significant Unpaired t test was done to measure the level of significance
*- significant
**- highly significant
*** - very highly significant
ns- non significant

Table-2 shows the number of parturients requiring rescue doses of vasopressors in two groups. Out of 45 parturient in group E, 6 (13.3%) and 2 (4.4%) parturients required rescue doses of ephedrine before delivery and after delivery respectively and 3 (6.7%) parturients in group P

required rescue doses of phenylephrine after delivery. The following table is given below in detail:

Table 2: Number of parturients received rescue dose in two groups.

Time of rescue dose	Phenylephrine (n=45) n (%)	Ephedrine (n=45) n (%)	p-value
Before delivery	0 (0.0)	6 (13.3)	0.026*
After delivery	3 (6.7)	2 (4.4)	0.999ns

Fisher's exact test was done to measure the level of significance
***- significant, ns- non significant**

Table-3 shows the incidence of maternal complications in both the group. Among all the 90 parturients, 3 parturient in group P and 8 parturient in group E developed hypotension and was subsequently treated with rescue doses of vasopressor. 1 parturient in group P and 2 parturient in group E developed dizziness. 1 (2.2%) parturient in group P and 8 (17.8%) parturient in group E developed nausea alone and 1(2.2%) parturient in group P and 5(11.1%) in group E had nausea with vomiting which was managed by ondansetron 4 mg. 3 (6.7%) out of 45 parturient in group P developed bradycardia which was managed by atropine 0.5mg .Out of 90 parturients 2(4.4%) parturient in group p and 8(17.8%) parturient developed tachycardia. The following table is given below in detail:

Table 3: Incidence of maternal adverse effects in two groups.

Complications	Phenylephrine (n=45) n (%)	Ephedrine (n=45) n (%)	p-value
Hypotension	3 (6.7)	8 (17.8)	0.196ns
Dizziness	1 (2.2)	2 (4.4)	1.000ns
Nausea	1 (2.2)	8 (17.8)	0.029*
Reflex bradycardia	3 (6.7)	0 (0.0)	0.241ns
Nausea+ vomiting	1 (2.2)	5 (11.1)	0.202ns
Tachycardia	2 (4.4)	8 (17.8)	0.044*

Fisher's exact test was done to measure the level of significance
***- significant**
ns- non significant

In table-4 shows neonatal birth weight and umbilical arterial blood gas analysis in two groups. The neonatal birth weight was higher in group E than group P which was found to be statistically not significant. The mean blood pH was statistically higher in group P than group E, which was found to be statistically significant. The mean pO_2 was higher in group P than group E which was statistically significant. The mean pCO_2 was statistically higher in group E than in group P which is statistically significant. The mean HCO_3 was statistically higher in group E than in group P which is statistically not significant. The mean base excessin group P was -2.38 ± 1.17 and in group E was -3.18 ± 1.64 which was found to be statistically significant. The following table is given below in detail:

Table 4: comparison of neonatal birth weight and umbilical arterial blood gas analysis in two groups

	Group P (n=45)	Group E (n=45)	p-value
Neonate weight (kg)	2.91 ± 0.39	2.96 ± 0.47	0.575ns
Blood pH	7.34 ± 0.03	7.30 ± 0.04	<0.001***
PO_2	24.40 ± 5.28	20.36 ± 8.16	0.006**
PCO_2	43.51 ± 4.20	49.40 ± 5.45	<0.001***
HCO_3	23.77 ± 1.46	24.18 ± 1.86	0.246ns
Base excess	-2.38 ± 1.17	-3.18 ± 1.64	0.009**

Values are expressed as mean ± SD. P value <0.05 is considered as significant Unpaired t test was done to measure the level of significance.
****- highly significant**
***** - very highly significant**
ns- non significant

In table-5 shows Apgar score at 1st and 5th minute in groups. The mean Apgar score of group P at 1st and 5th minutes are 7.71 ± 0.458 and 9.00 ± 0.00 respectively and of group E at 1st and 5th minutes are 7.71 ± 0.458 and 9.00 ± 0.00 respectively which was found to be statistically not significant. The following table is given below in detail:

Table-5: APGAR score at 1st and 5th minute in both the groups.

APGAR score	Group P (n=45)	Group E (n=45)	p-value
At 1st minute	7.71 ± 0.458	7.71 ± 0.458	1.000ns
At 5th minute	9.00 ± 0.00	9.00 ± 0.00	???

Values are expressed as mean ± SD. P value <0.05 is considered as significant Unpaired t test was done to measure the level of significance, ns- non significant

DISCUSSION

We found that 1(2.2%) parturient in group P and 8 (17.8%) parturient in group E had nausea only. There was significant difference in occurrence of nausea in both the group. Also, the present study shows that there was high incidence of nausea and vomiting occurred together in group E (group P n=1/45 (2.2%), group E n=5/45 (11.1%), (p=0.202). Two studies observed similar result which is consistent with our study.[6-7] However one article reported that parturients receiving phenylephrine had higher incidence of nausea and vomiting compared to those who received ephedrine. They suggested that in all cases who received second dose of vasopressor resulted in increased incidence of nausea and vomiting. These adverse effects developed in those parturient in whom hypotension was observed probably related to decreased cerebral blood flow due to hypotension. It was managed by anti-emetic ondansetron 4 mg.[8]

In the current study, 3 (6.7%) parturient in group P and 8 (17.8%) parturient in group E developed hypotension and required rescue doses of vasopressor. Those 3 parturients in group P had single episode of hypotension after the delivery of baby and were managed by phenylephrine 50µg whereas, among 8 parturients in group E, 6(13.3%) parturient developed hypotension before the delivery of the baby and 2(4.4%) parturient developed hypotension after the delivery of baby and was managed with ephedrine 5 mg. Those parturient in both the group had single episode of hypotension The result of our study is coherent to one study where 11(22%) parturient in ephedrine group and 1(2%) parturient in phenylephrine group required phenylephrine 100 µg as rescue vasopressor which was found to be statistically significant (p=0.002). Parturients in both group were managed by phenylephrine as a rescue drug at given dose.[9]

In this study, there was no difference in the two measurement of the apgar score at one minute and five minutes in group P and group E. Though, the overall episode of hypotension and rescue treatment given for hypotension were significantly higher in group E. In this study, no neonate had as apgar score < 7 at one or at five minutes. This result is coherent with one study which concluded that there was no significant difference between the groups in the first and the fifth minutes apgar score.[10] Another study had reported that neonatal outcome was not affected by the use of prophylactic phenylephrine or ephedrine.[11] One article reported that even high doses of phenylephrine of more than 2000 µg were not associated with adverse fetal effects as determined by apgar score.[12] One article reported that there was no difference in first minute apgar score whereas the fifth minute apgar score seems to be higher in phenylephrine and ephedrine group than in control group. This might be because, prophylactic vasopressors were compared with control group. The difference in birth weight of neonates between group P and group E was statistically non-significant.[13]

CONCLUSION

From our study we can conclude that, prophylactic intravenous phenylephrine bolus at the given dose remarkably reduced the incidence of subarachnoid block induced hypotension with fewer adverse maternal effects. The use of phenylephrine was associated with better fetal acid base status, and satisfactory apgar score.

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