



Anaesthesiology

COMPARISON OF NOREPINEPHRINE AND PHENYLEPHRINE BOLUSES FOR THE TREATMENT OF HYPOTENSION DURING SPINAL ANAESTHESIA FOR ELECTIVE CAESAREAN SECTION- A PROSPECTIVE INTERVENTIONAL STUDY

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ABSTRACT **Background and Aim:** Hypotension following Spinal Anaesthesia (SA) in Lower Segment Caesarean Section (LSCS) can be deleterious to the parturient and the fetus. The choice of the most effective management strategy for Spinal Anaesthesia Induced Hypotension (SAIH) during Caesarean Section (CS) continues to be one of the main challenges in obstetric anaesthesia. Many non-pharmacological and pharmacological techniques like using various vasopressors such as Mephentermine, Ephedrine and Phenylephrine were tried. The primary aim was to evaluate the effectiveness between 4mcg of norepinephrine and 50 mcg of Phenylephrine boluses doses in treating intraoperative hypotension following SA in elective LSCS. **Methodology:** The parturient who are under ASA class II are randomly divided into two groups using Sheffield shield opaque envelope technique each of 30 parturient. Group N received 4mcg (1ml) of norepinephrine as IV boluses and Group P received 50mcg (1ml) of Phenylephrine as IV boluses for the treatment of hypotension following SA. Maternal Parameters like heart rate, blood pressure was noted every 2 minutes till 10 minutes and every 5 minutes till the end of surgery. APGAR score was noted at 1 minute and 5 minute after birth. **Results:** The number of intermittent boluses of vasopressors required to treat hypotension was significantly lower in group N (2 ± 1.14) than in group P (2.3 ± 1.11) with $P = 0.026$. The heart rate was lower in group P, but this difference was not statistically significant. Maternal complications such as nausea and vomiting and shivering were the foetal parameters like APGAR score were also comparable between the two groups. **Conclusion:** Intermittent boluses of norepinephrine are more effective in the management of spinal-induced hypotension during caesarean section than Phenylephrine. The neonatal outcomes were similar in both groups. Norepinephrine boluses can be considered as an alternative to Phenylephrine boluses.

KEYWORDS : Caesarean Section, Spinal anaesthesia, Hypotension, Noradrenaline, Phenylephrine

INTRODUCTION:

Caesarean section in parturient is conventionally done under spinal anaesthesia or sub- arachnoid block considering the advantages of regional anaesthesia over general anaesthesia for the mother as well as the fetus. Regional anaesthesia decreases the foetal drug transfer which is bound to occur during general anaesthesia¹. Spinal anaesthesia induced hypotension (SAIH) is a known consequence in spite of preloading the patients with intravenous fluids.¹ The symptoms associated with this spinal induced hypotension include nausea, vomiting, dizziness and can cause decreased uterine blood flow in turn leading to foetal hypoxia and acidosis². Various pharmacologic measures like vasopressors have been used to treat hypotension. In pregnancy women become more sensitive to local anaesthetics, less responsive to vasopressors and have lower mean arterial pressure (MAP) at term³. Hence, parturient are susceptible to develop profound hypotension following central neuraxial blockade in the lower segment caesarean section.⁴ The alpha agonists have been considered the first-choice vasopressors in treating hypotension for caesarean section. In Noradrenaline as it has weak beta agonist property it has less effect in decreasing the heart rate and thus it maintains better cardiac output.⁵

METHODS:

Following approval from the Institutional Ethical Committee, informed and written consent was taken from 60 parturient of American Society of Anesthesiologists Physical status (ASA) class II undergoing elective lower segment caesarean section under spinal anaesthesia.

A thorough pre anesthetic evaluation was done 24 hours prior to the procedure. The study included parturient posted for elective caesarean section. Standard monitoring with electrocardiography (ECG), automated noninvasive blood pressure (NIBP) and pulse oximetry (SpO₂) using multiparameter Philips Intellivue MP20/MP30 monitor was used for baseline values and intraoperative monitoring.

The 60 parturient are randomly divided into two groups using Sheffield shield opaque envelope technique.

- **Group N** – 30 parturient received 4mcg of norepinephrine as IV boluses for the treatment of hypotension following SA.
- **Group P** - 30 parturient received 50mcg of Phenylephrine as IV boluses for the treatment of hypotension following SA.

All the parturient were pre-loaded with 10ml/kg of lactated ringer's solution. Subarachnoid block (at L3- L4 or L4- L5 level) with 2ml of 0.5% hyperbaric bupivacaine using 25 G quincke's spinal needle in sitting position. The patients were then turned supine with wedge under the right buttock to prevent aorto - caval obstruction after giving spinal anaesthesia and the baseline hemodynamic status was recorded in the supine position.

Supplemental oxygen was given through facemask at a flow rate of 5L/min. The highest level of sensory blockade achieved was checked after 5 min of intrathecal injection. Norepinephrine and Phenylephrine were diluted and loaded in an identical coded 10 ml syringe which was either norepinephrine 4 mcg/ml or Phenylephrine 50 mcg/ml. The study drugs was prepared by the same anaesthesiologist who was involved in randomization. Hence the observer and the patient are blinded from the study drugs.

We took into account of the published data by Warwick D. Ngan Kee² where they estimated the relative potency ratio of Noradrenaline: Phenylephrine as 13:1.

The estimated ED₅₀ values (dose giving a 50% response) were norepinephrine 10 µg (95% CI, 6 to 17 µg) and Phenylephrine 137 µg (95% CI, 79 to 236 µg). It was concluded that the estimated dose equivalent to Phenylephrine 100 µg was norepinephrine 8 µg (95% CI, 6 to 10 µg). So, in our study we took that 4mcg of Noradrenaline is equipotent to 50 mcg of Phenylephrine.

Heart rate and blood pressure are monitored every 2 min after SA till 10 min and thereafter every 5 min till the surgery ends. Group P received Phenylephrine 50 mcg as an intravenous bolus dose and group N received 4 mcg of norepinephrine as an intravenous bolus when the systolic blood pressure drops below 20% of the baseline value¹. The duration of sustainability of blood pressure with each bolus for both the drugs were noted.

Once the foetus is delivered 10 IU of oxytocin was administered as intramuscularly as a protocol. Incidence of bradycardia, hypotension, the total doses of vasopressor and intravenous fluids given intra operatively were noted. If the heart rate was less than 60 bpm it was treated with intravenous atropine 0.6 mg. Incidences of nausea, vomiting and dizziness were also noted.

RESULTS:

The demographic parameters like age, height, weight and BMI were measured for the study population and the mean, standard deviation and its comparison with the Noradrenaline and Phenylephrine group. The heart rate, non-invasive blood pressure, number of bolus doses used, APGAR score and side effects like nausea, vomiting were also noted and compared between the two groups.

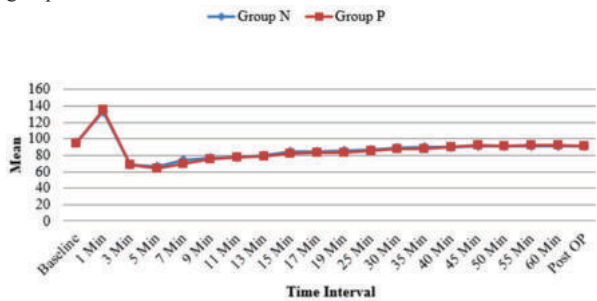
The demographic profile (mean age, mean height, mean weight and mean BMI) were similar in both the groups and were not statically significant.

On comparing the mean heart rate between the two study groups it was observed that the lowest heart rate in Group N was at 13 minutes which was 83.7 and that in Group P was 83 but, there was no statistically significant difference (p-value 1.00) between the trends of the two groups.

On comparing the mean SBP between the two study groups it was observed that the lowest SBP in Group N was at 5 minutes which was 89 and that in Group P was 87.67 but, there was no statistically significant difference (p-value 0.536) between the trends of the two groups.

On comparing the mean DBP between the two study groups it was observed that the lowest DBP in Group N was at 5 minutes which was 54.63 and that in Group P was 51.86 but, there was no statistically significant difference (p-value 0.139) between the trends of the two groups.

On comparing the mean of MAP between the two study groups it was observed that the lowest MAP in Group N was at 5 minutes which was 66.17 and that in Group P was 63.8 but, there was no statistically significant difference (p-value 0.240) between the trends of the two groups.

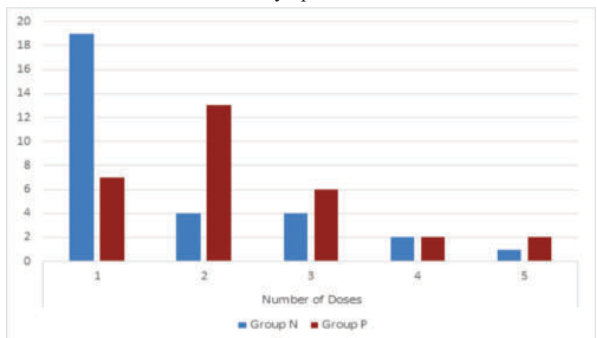


Graph 1: Mean MAP comparison between two groups at different intervals of time

In Group N, 19 (63.33%) parturient received 1 dose of Noradrenaline, 4 parturient (13.33%) received 2 doses, 4 parturient (13.33%) received 3 doses, 2 (6.67%) parturient received 4 doses and 1 (3.33%) parturient received 5 doses. In Group P, 7 parturient (23.33%) received 1 dose, 13 parturient (43.33%) received 2 doses, 6 parturient (20%) received 3 doses, 2 parturient (6.67%) received had 4 doses and 2 parturient (6.67%) received had 5 doses. The maximum parturient (19) in Group N received only 1 dose of the drug where as in Group P maximum parturient (13) received 2 doses.

Mean – 2 ± 1.142693 for Noradrenaline.

Mean = 2.3 ± 1.118805 for Phenylephrine.

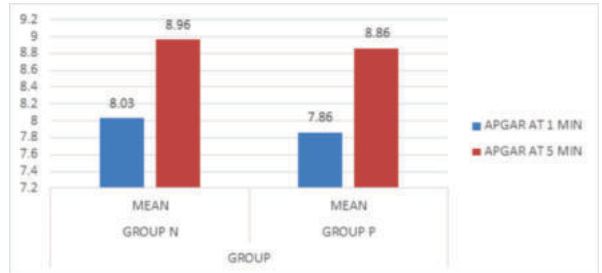


Graph 2: Number of doses of vasopressors used.

There was significant difference in number of doses used between two groups with P-value 0.026.

There was no significant difference (p value of 0.750) in nausea and vomiting between two groups.

The APGAR scores of Noradrenaline and Phenylephrine were compared in 1 min and 5 min and was found out to be statistically not significant with the p values of 0.14 and 0.083 respectively.



Graph 3: APGAR scores at 1 min and 5 min between two groups

DISCUSSION:

The study compared the effects of intermittent bolus doses of norepinephrine and phenylephrine in the treatment of spinal-induced hypotension during caesarean section. The results of the study showed that intermittent boluses of intravenous norepinephrine are effective in managing spinal hypotension with no detrimental effects on the neonatal and maternal outcome. The number of norepinephrine boluses required to maintain blood pressure was significantly less than when phenylephrine boluses were used.

The study by Warwick D. Ngan Kee estimated the relative potency ratio of noradrenaline : phenylephrine as 13:1. The estimated ED₅₀ values (dose giving a 50% response) were norepinephrine 10 µg (95% CI, 6 to 17 µg) and phenylephrine 137 µg (95% CI, 79 to 236 µg). It was concluded that the estimated dose equivalent to phenylephrine 100 µg was norepinephrine 8 µg (95% CI, 6 to 10 µg). So in our study we took that 4mcg of noradrenaline is equipotent to 50 mcg of phenylephrine. In total number of study drug boluses required for the treatment of hypotension or to maintain blood pressure after spinal anesthesia as per protocol were 2 ± 1.14 in noradrenaline group and 2.3 ± 1.11 in phenylephrine group. The mean number of boluses required with phenylephrine were more when compared to noradrenaline and the difference among the groups was statistically significant (p = 0.026). In our study the APGAR scores at 1 min and 5 min after the delivery of the baby were found to be similar. The mean APGAR scores at 1 minute after the delivery of babies were 8.03±0.49 in noradrenaline group and 7.86 ± 0.68 in phenylephrine group with the p value of 0.14 which is not statistically insignificant. The mean APGAR score at 5 minute after the delivery were 8.96 ± 0.18 in noradrenaline group and 8.86±0.35 in phenylephrine group with the p value of 0.083 which is also statistically not significant. The limitations of our study were enlisted as The sample size used in our study groups may not be adequate enough to elicit the actual differences in the outcomes between the groups. To monitor foetal outcome in view of oxygenation or acid base condition the most effective indicator is umbilical cord blood gas analysis. But it could not be performed due financial limitations and ethical issues. In our study we took only the parturient who are in ASA physical class II and who are planned for elective lower segment caesarean section. Further studies should be performed in parturient who are in ASA physical class III and IV. We should have also compared the effect of vasopressors in emergency surgeries.

CONCLUSION:

In our study both the vasopressors, Noradrenaline and Phenylephrine effectively maintained arterial blood pressure during spinal anesthesia for caesarean section. The total number of boluses used to treat hypotension were less in Noradrenaline group when compared to Phenylephrine group and it is statistically significant (p=0.026). Phenylephrine caused mild reduction of heart rate but it is not significant statistically. Both the drugs did not have any statistically significant adverse effects to both mother and foetal outcome. Thus it is concluded that intermittent boluses of Noradrenaline is found to be effective in the management of hypotension after spinal anesthesia for caesarean section.

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