

Research Article

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# Prophylactic bolus dose of Nor-Epinephrine versus Phenylephrine bolus for Management of post- spinal Hypotension among patients undergoing Elective Caesarean Section. A Prospective Cohort Study

Yisehak Wolde\*, Sintayehu Samuel, Gediwon Gebrehiwot, Teketel Abebe, Mitiku Desalegn

Department of Anaesthesia, College of Medicine and Health Science, Wachemo University, Hosanna, Ethiopia

## Article Info

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### \*Correspondence:

\*Dr. Yisehak Wolde, Department of Anaesthesia, College of Medicine and Health Science, Wachemo University, Hosanna, Ethiopia; Email: yisehakwolde140@gmail.com

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### Keywords

Postspinal Hypotension

Phenylephrine

Norepinephrine

Caesarean Section

## Abstract

**Background:** Cesarean section (CS) is the preferable procedure to preserve life when spontaneous vaginal delivery poses a risk to the mother and child. Since spinal anesthesia for CS offers superior neonatal and mother outcomes than general anaesthesia, its acceptability has grown significantly. However, there are drawbacks to spinal anaesthesia for Cs. Hypotension (a decrease in systolic blood pressure below 20% of baseline) is the most frequent complication, with an incidence ranging from 7.4% to 74.4%. The most frequent mechanism underlying the hypotension linked to spinal anesthesia is the predominance of vasodilation over vasoconstriction. After spinal anaesthesia, the mechanism for vasodilation is caused by the preganglionic level blocking of sympathetic nerve fibers.

**Method:** An institutional-based prospective cohort study was conducted on 60 pregnant women undergoing elective caesarean section. Based on the responsible anaesthetist's post spinal hypotension management plan, patients were divided into two groups. patients who received Phenylephrine are grouped into PE,  $n=30$  group, and patients who received nor-epinephrine are grouped under the nor-epinephrine group (NE,  $n=30$ ) by data collectors. After the aseptic technique, spinal anaesthesia was administered with 0.5% (3 ml) bupivacaine using a 23G spinal needle. During spinal anaesthesia, a prophylactic bolus dose of 100  $\mu\text{g}$  (4 ml) Phenylephrine and 32  $\mu\text{g}$  (4 ml) NE was given based on the management plan of the shift anaesthetist. Mean arterial pressure (MAP), the heart rate (HR), number of boluses of vasopressor used, incidence of nausea and vomiting, and the Apgar score of babies at 1 and 5 min between the groups were recorded.

**Results:** The nor-epinephrine group had a statistically significant higher MAP compared to the Phenylephrine group in the first 10 and 15 min ( $p>0.05$ ) of the study period. thereafter, there was no statistically significant difference in heart rate between the groups until the end of the study period ( $p > 0.05$ ). The nor-epinephrine group required a lower bolus number of vasopressors compared to the Phenylephrine group to maintain blood pressure( $p<0.05$ ). Apgar scores of all babies at 1 and 5 min were greater than seven. Significant differences regarding maternal complications (nausea and vomiting) between the groups were not detected (nausea, and vomiting,  $p=0.092$ ).

**Conclusion.** Intraoperative hypotension is common after spinal anaesthesia for Caesarean section. Inadequate treatment may lead to significant maternal, fetal, or both adverse outcomes. Consensus guidelines for the management of hypotension during Caesarean section has recommended a standard approach and includes detailed guidance on how to introduce phenylephrine infusions into practice. Other agents with a preferable adrenergic profile may be the focus of further. For a pregnant woman who underwent an elective caesarean section under spinal anaesthesia, nor-epinephrine can be administered in place of phenylephrine to maintain the mother's blood pressure without having a side effect on the mother and fetus.

## Introduction

### Background

Spinal anaesthesia is frequently used during Caesarean section due to its quickness, dependability, low placental drug transfer, and the benefits of the mother remaining awake during the operation. However, compared to epidural anaesthesia, spinal anaesthesia induces more severe and frequent hypotension, which can lead to negative outcomes for both the mother and the foetus if not treated or prevented<sup>1</sup>.

Caesarean section (CS) is the preferred type of procedure to preserve life when spontaneous vaginal delivery poses a risk to the mother and child<sup>2,3</sup>.

Since spinal anaesthesia for CS offers superior neonatal and mother outcomes than general anaesthesia, Its acceptance rate has grown significantly. However, there are some side effects to spinal anaesthesia for Cs<sup>2</sup>. Definitions of hypotension in research studies use a decrease in the absolute value of systolic arterial pressure (SAP; usual threshold between <80 and <100 mmHg), a decrease compared with a baseline value, or a combination<sup>1</sup>. The incidence varies from 7.4% to 74.4%<sup>1</sup>. The most frequent mechanism underlying the hypotension linked to spinal anaesthesia is the predominance of vasodilation over constriction. After spinal anaesthesia, the mechanism for vasodilation is caused by the preganglionic level blocking of sympathetic nerve fibres<sup>3</sup>.

Hypotension is common during the delivery of spinal anaesthesia for caesarean section. If not promptly treated, a decrease in blood pressure (BP) can have deleterious effects, which include maternal nausea, vomiting, dizziness, and cardiovascular instability as well as decreased uteroplacental blood flow with resultant fetal acidosis, hypoxia, and bradycardia<sup>2,4</sup>.

In the previous decade, the  $\alpha$ -agonist phenylephrine (PE) has been the vasopressor of choice for the prevention and treatment of spinal-induced hypotension. Although showing a favourable side effect profile when compared with ephedrine, PE is associated with a baroreceptor-mediated bradycardia and thus causes a subsequent reduction in cardiac output (CO)<sup>5</sup>.

With an incidence of up to 30% reported in the literature, bradycardia and thus reduction in CO are of particular concern to the obstetric anaesthesiologist<sup>6</sup>.

Research suggested that in adult patients who underwent non-cardiac surgery, intraoperative hypotension is alone linked to postoperative 30-day mortality, major adverse cardiac events (MACEs), particularly myocardial infarction, and acute kidney injury (AKI). Another study discovered that longer exposure

times ( $\geq 10$  minutes) to mean arterial blood pressure (MAP) < 80 mm Hg and shorter exposure times (< 70 mm Hg) during the intraoperative phase were associated with an increased risk of end-organ injury<sup>7-9</sup>.

Different approaches were applied to prevent postspinal hypotension, such as leg compression, preloading with crystalloid or colloids, co-loading with crystalloid, and the use of a variety of vasopressors<sup>1,10</sup>. Nor-epinephrine is one of the most commonly used vasopressors used for the management of postspinal anaesthesia for parturient undergoing caesarean sections; its main mode of action is attained by agonising  $\alpha_1$  adrenergic receptors. A recent "International consensus statement on the management of postspinal hypotension recommends the use of a vasopressor<sup>4,11</sup>.

Evidence shows that the occurrence of intraoperative hypotension is associated with multiple intraoperative and postoperative complications. The use of fluid for the prevention of postspinal hypotension is unsatisfactory for many anaesthetists. Phenylephrine and NE are the widely practised and accepted choices of vasopressor for the management of post-spinal hypotension during caesarean section. However, optimum bolus dosing is not yet established<sup>2,7</sup>.

Automated infusion systems are recommended for the administration of measured doses of drugs, but their accessibility in developing countries is low so the establishment of an optimum bolus dose of vasopressor is warranted. Hence, the primary outcome of this study is to compare MAP between groups. During caesarean delivery, a common maternal complication is postspinal hypotension 1. Almost 60% of women get postspinal hypotension during cesarean delivery if a prophylactic vasopressor is not used; therefore, routinely preventing postspinal hypotension during cesarean delivery using a vasopressor is strongly advised<sup>4,12</sup>.

The commonly utilised vasopressors after cesarean delivery are Phenylephrine and ephedrine. Phenylephrine is sometimes associated with maternal cardiac depression; this limits its use in mothers with cardiac comorbidities<sup>2,13</sup>.

Nor-epinephrine seems to be a new attractive alternative to PE with less cardiac depression; however, the proper dose of nor-epinephrine needs more investigation, We suggest that PE is the preferred vasopressor in managing PSH, especially in mothers with heart rates more than 60 bpm and with good cardiac reserve<sup>14</sup>.

This study aims to compare the effectiveness of nor-epinephrine intermittent bolus dose (32 micrograms) versus Phenylephrine bolus 100 micrograms) to prevent postspinal hypotension.

## Method and Materials

### Study Design and Setting

An institution-based prospective cohort study was conducted from December 20, 2023, to March 30, 2024, during the study period, after obtaining approval from the local ethical committee. Each pregnant woman provided informed written permission. This investigation was conducted following Helinisk's declaration. Confidentiality was maintained during the study. The study comprised patients in the American Society of Anaesthesiologists (ASA) class II who were between the ages of 18 and 35. We excluded pregnant women with preeclampsia/eclampsia, baseline hypertension (systolic blood pressure > 140 mmHg), body mass index (BMI) > 30 kg/m<sup>2</sup>, foetal abnormality, failed spinal anaesthesia converted to general anaesthesia, contraindication for spinal anaesthesia, and mother with cardiovascular, renal, or hepatic disease, as well as endocrine disease such as uncontrolled diabetes.

### Sample Size and Sampling Technique

The sample size is calculated as follows sample size was calculated by Open Epi version 7.2 by adjusting a power of 80%, confidence level of 95%, and margin of error of 5%. The primary outcome variable of our study was to compare the number of intravenous bolus doses of nor-nor-epinephrine or Phenylephrine required to treat spinal hypotension in cesarean patients which was estimated from the previous study conducted by Nitu Puthenveetil, Swetha N Sivachalam<sup>6</sup>.

$$\text{Sample size (n)} = \frac{(\sigma_1)^2 + (\sigma_2)^2 \times (Z_{1-\beta} + Z_{1-\alpha/2})^2}{d^2}$$

d = difference in means of two groups (effect size)

$\sigma_1$  = SD of Group 1

$\sigma_2$  = SD of Group 2

$Z_{1-\beta}$  = It is the desired power

$Z_{1-\alpha/2}$  = Critical value and a standard value for the corresponding level of confidence.

(At 95% CI it is 1.96 and at 99% CI, or 1% type I error, it is 2.58).

$\sigma_1$  = 0.557

$\sigma_2$  = 1.061

Mean of N= 1.4

Mean of P= 2.28

Effect size(d)= 0.6

$$\text{Sample size (n)} = \frac{(0.557)^2 + (1.06)^2 \times (0.84 + 1.96)^2}{(0.6)^2}$$

n= 26.8 approximately = 27 (adding 10% drop out)

n= 29.7 nearly= 30 study subjects for each group.

According to hospital analysis, 330 elective cesarean sections are performed within three months.

N= 330, =60

K= N/n.....330/60=5

The sampling fraction was 5 and the first participant was taken by using the lottery method for daily elective patients.

### Data Collection

After providing training to the data collectors, data were collected using pretested questionnaires. Data collectors assigned each selected participant to either group depending on the responsible anaesthetists' treatment strategy (whether they received a Phenylephrine bolus dose or nor-epinephrine bolus. Following pre-anaesthetic evaluation, through an 18-gauge cannula, crystalloid solution was infused at the rate of 10 ml/kg in the pre-operative room and IV injection of Metoclopramide 10mg was administered as pre-medication for both groups. By recording baseline vital sign, spinal anaesthesia was done in the sitting position after an aseptic technique with 2 ml -2.5 ml (10 mg - 12.5 mg) of 0.5% isobaric bupivacaine by using 23 gauge needles and above was used to administer the local anaesthetics at the level of L3-L4 for all parturient This is continued until the desired sample was obtained for each group. MAP, HR, the number of boluses of vasopressor used, and Apgar score at 1 and 5 min in each group were recorded.

Incidence of nausea and vomiting and episodes of bradycardia (HR < 60 bpm) were recorded and informed to the assigned anaesthetist for treatment. MAP and HR were recorded every 5 minutes, up to 50 minutes, and till the end of surgery.

For this study, some terms are defined in the following way. Then after, patients were immediately turned to a supine position with slight head elevation using a pillow. Sensory and motor blocks were evaluated by a sense of coldness and the Modified Bromake Scale (0 no motor block; 1, inability to raise an extended leg, 2, inability to flex the knee, and 3, inability to flex the ankle and foot), respectively, within 5 min of intrathecal injection. During spinal anaesthesia, a bolus dose of 100 micrograms of phenylephrine (2 ml) or 32  $\mu$ g (2 ml) NE was given based on the preference of the shift anaesthetist.

### Data Processing and Analysis

#### Data Quality Assurance

After giving training for to anaesthetists who collect

data, under the established format, all gathered data was checked once a week for its completeness, clarity, consistency, and accuracy by the principal investigator.

### Data Analysis

This Data used Epi Info version 7.2 to code, edit, and enter data, then exported to Statistical Package for Social Sciences (SPSS) software version 26.0 quantitative data were described in terms of mean, SD for parametric and median (interquartile range) for non-parametric data. Frequency and percentage were used to describe categorical data. The Shapiro–Wilk test was used to test for normal distributions of data, while equality of variance between the groups was assessed using Levene’s test. Comparisons of quantitative data between the study groups were carried out using an unpaired Student’s *t*-test for parametric data and the Mann–Whitney *U* test for non-parametric data. Comparisons using the student *t*-test or the Mann-Whitney *U* test as appropriate. Nominal data were compared using the  $\chi^2$  test. The incidence and timing of hypotension were analyzed using Kaplan–Meier survival analysis, with differences between groups compared using the log-rank test.

### Operational Definition

Baseline value: Measurement taken before induction.

Hypotension: It is defined as a decrease in SBP  $\geq$  20% of the baseline value.

Post-spinal Hypotension: Hypotension occurs after the administration of spinal anaesthesia.

Sensory Block: It is defined as the inability to sense pinprick sensation at T-10 (umbilicus).

Motor Block: It is defined as the inability to move the hips, knees, or toes.

### Preoperative and Intraoperative Procedure

The decision to administer vasopressor prophylaxis before spinal anaesthesia and the management of anaesthesia, including intraoperative treatment of hypotension, were made at the discretion of the anaesthetist assigned to each case. We, the researchers, were not involved in the perioperative management of the patients. Since the study site did not allow experimental study, rather patients were randomly divided into two groups Norepinephrine group( $n=30$ ) and Phenylephrine group ( $n=30$ ) based on assigned data collector from elective waiting list. Those patients who received 100microgram (2 ml) of prophylactic phenylephrine during induction of spinal anesthesia were considered as the phenylephrine group, and patients who received 32 $\mu$ g(4ml) of prophylactic Norepinephrine were considered as the group by the assigned data collector.

In our research, we hypothesised that administering prophylactic norepinephrine during spinal anaesthesia for elective Caesarean section would better maintain maternal MAP compared to prophylactic phenylephrine without having adverse effects on the mother or the baby.

Phenylephrine ampoules (in 2 ml(100microgram); the product of “Misr Company for Pharmaceuticals,” Egypt), diluted in 10 ml of normal saline (20microgram/ml) and norepinephrine ampoules (NE) (8 mg/ ml, the product of “EgyPharma Company, diluted in 500 ml of normal saline (8  $\mu$ g/ml) were the usual preparation used in our routine practice.

The study site follows the following routine procedure during Caesarean section under spinal anaesthesia.

All patients were assessed before the procedure with a history, clinical examination, and routine laboratory investigation (complete blood count, liver function, renal function, and coagulation profile), and baseline blood pressure with a non-invasive blood pressure monitor and heart rate with pulse oximetry were recorded. On arrival to the operating room, two 18-gauge IV cannula needles are secured on bilateral arms. Patients were premedicated with metoclopramide 10 mg IV bolus before induction of anesthesia and preloaded with normal saline (NS).

Finally, this paperwork has been reported in line with STROCCS criteria<sup>15</sup>.

### Result

A total of 60 pregnant women were enrolled in the study that fulfilled inclusion criteria and were randomly divided into two groups of 30 patients: the nor-epinephrine group and the phenylephrine group.

A general 60 patients were included in the study. Two patients in group 1 and 2 patients in group 2 were excluded because the spinal anaesthesia block failed and was converted to GA.

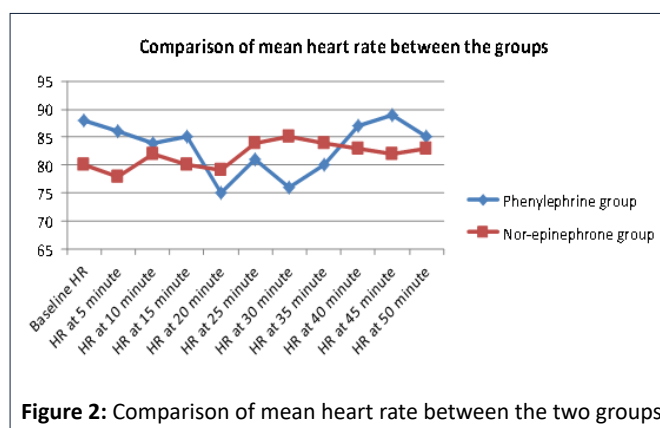
Data were analysed for 30 patients in group 1 and 30 patients in group 2, and a total of 60 subjects. Socio-demographic and Intraoperative Surgical characteristics are shown in Table 1. Serial changes in MAP are shown in Figure 1, and serial changes in HR are shown in Figure 2. Comparison of mean arterial pressure between Phenylephrine and Norepinephrine groups is shown in Table 2. The primary outcomes were significantly different between groups. From the nor-epinephrine group, 15 (53.6%) patients, and the phenylephrine group 19(67.8%) patients had 1 or more episodes of hypotension (uncorrected  $P < .001$ ). MAP was significantly higher in the NE group versus the phenylephrine group, indicating maintenance of systolic BP on average was closer to baseline in group 1 (uncorrected  $P < .0001$ ).

**Table 1:** Socio-demographic and intraoperative characteristics of patients

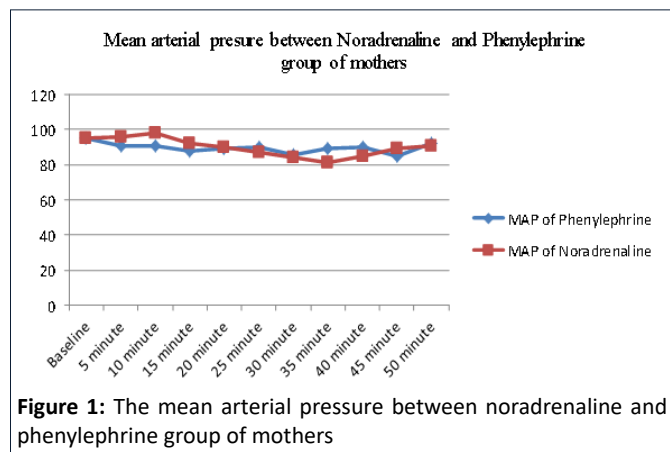
| Variable                          | Group1 NE(N=30) | Group2 PE(n=30) | p-value |
|-----------------------------------|-----------------|-----------------|---------|
| Age (yr)                          | 26.5±6          | 26.1±5          | 0.17    |
| BMI (Kg/m) <sub>2</sub>           | 21.25±3.1       | 22±2.5          | 0.196   |
| Haemoglobin (g/dl)                | 12.3±1.12       | 13±1.23         | 0.32    |
| Skin incision to deliver (min)    | 10.5(5)         | 11(4)           | 0.86    |
| Blood loss (ml)                   | 300(200)        | 350(150)        | 0.165   |
| Fluid infused (ml)                | 2350(1500)      | 2200(1200)      | 0.123   |
| Baseline MAP (mmHg)               | 95.23±11.45     | 95.1±12.12      | 0.91    |
| Baseline Hr (beat/min)            | 75±13           | 75.21±12.3      | 0.45    |
| Duration of surgery (min)         | 60.45±21.4      | 65±20.51        | 0.71    |
| Block height at 5 min (dermatome) | T6(T5-T7)       | T5(T4-T6.5)     | 0.8     |

**Table 2:** Comparison of mean arterial pressure between the Phenylephrine and Nor-epinephrine groups

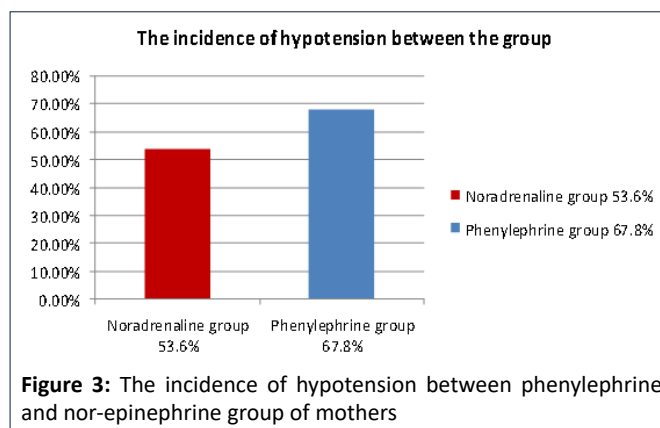
| MAP          | Nor-epinephrine<br>N=30<br>Mean±SD | p-value | Phenylephrine<br>n=30<br>Mean±SD | p-value |
|--------------|------------------------------------|---------|----------------------------------|---------|
| MAP baseline | 95±6.5                             | 0.34    | 95±5.1                           | 0.12    |
| MAP 5        | 96±5.05                            | 0.43    | 91±7.5                           | 0.12    |
| MAP 10       | 98±4.5                             | 0.24    | 91±4.51                          | 0.37    |
| MAP 15       | 92±5.03                            | 0.12    | 88±3.5                           | 0.025   |
| MAP 20       | 90±5.1                             | 0.21    | 89±4.5                           | 0.35    |
| MAP 25       | 87±7.3                             | 0.12    | 90±5.1                           | 0.021   |
| MAP 30       | 84±5.6                             | 0.001   | 86±6.1                           | 0.22    |
| MAP 35       | 81±6.1                             | 0.01    | 89±5.12                          | 0.012   |
| MAP 40       | 85±5.1                             | 0.12    | 90±3.75                          | 0.35    |
| MAP 45       | 89±6.5                             | 0.16    | 85±4.5                           | 0.45    |
| MAP 50       | 91±5.01                            | 0.179   | 92±3.5                           | 0.15    |



**Figure 2:** Comparison of mean heart rate between the two groups



**Figure 1:** The mean arterial pressure between noradrenaline and phenylephrine group of mothers



**Figure 3:** The incidence of hypotension between phenylephrine and nor-epinephrine group of mothers

### The incidence of hypotension between the phenylephrine and nor-epinephrine groups of mothers

Blood pressure was recorded every five minutes starting from the induction of anaesthesia until the end of the operation. The incidence of hypotension was lower for those parturient in the nor-epinephrine group (53.6%) compared to the phenylephrine group (67.8%), and it was statistically significant ( $p < 0.01$ ). After 5 minutes of inducing spinal anaesthesia until 30 minutes of the procedure (MAP)

was significantly higher in the nor-epinephrine group, and the values are presented by bar chart below. (Figure 3)

### Comparison of mean heart rate between Nor-epinephrine and Phenylephrine group of mothers

When we see the trends of heart rate across time, there was no significant difference between the phenylephrine and nor-epinephrine group of mothers from the baseline until the end of the study time, even though nine mothers from the nor-epinephrine group and three mothers from the phenylephrine group experienced the incidence of bradycardia in the time of the study. Concerning palpitation at the time of delivery of both vasopressors,

**Table 3:** Comparison of mean heart rate between the phenylephrine and nor-epinephrine group of mothers (N=60)

| Heart rate    | Nor-epinephrine |         | Phenylephrine |         |
|---------------|-----------------|---------|---------------|---------|
|               | Mean±SD         | p-value | Mean±SD       | p-value |
| Baseline HR   | 80±7            | 0.12    | 88±5.5        | 0.31    |
| HR 5 minutes  | 78±7            | 0.34    | 86±7.1        | 0.04    |
| HR 10 minutes | 82±5            | 0.13    | 84±8.1        | 0.23    |
| HR 15 minutes | 80±6            | 0.15    | 85±6.1        | 0.12    |
| HR 20 minutes | 79±5            | 0.65    | 75±7.1        | 0.025   |
| HR 25 minutes | 84±6.5          | 0.17    | 81±4.5        | 0.06    |
| HR 30 minutes | 85±5.5          | 0.85    | 76±6.1        | 0.5     |
| HR 35 minutes | 84±7.4          | 0.13    | 80±6.41       | 0.45    |
| HR 40 Minutes | 83±3.5          | 0.012   | 87±7.1        | 0.34    |
| HR 45 minutes | 82±5.5          | 0.001   | 89±5.1        | 0.51    |
| HR 50 minutes | 82±7.5          | 0.035   | 85±6.5        | 0.81    |

**Table 4:** The Total number of boluses of vasopressor used during intervention

|                                      | GroupNE [N=30] | GroupPE [N=30] | p-value |
|--------------------------------------|----------------|----------------|---------|
| The number of boluses of vasopressor | 2.5(1.5)       | 3.6(1.4)       | 0.0012  |

a total 11(18.3%) clients had experienced palpitation immediately after administration. However, brief episodes, from this 7(63.63%) was after delivery of nor-epinephrine and 4(36.37%) for the phenylephrine group. There was no significant electrographic (ECG) trace change on the intervention of both vasopressors on post-spinal hypotension management during study time. (Table 3 & 4)

The nor-epinephrine group required fewer vasopressors than the Phenylephrine group to maintain blood pressure ( $p < 0.05$ ).

## Discussion

The results of this study showed that in patients having spinal anaesthesia for caesarean delivery, a manually controlled norepinephrine titrated prophylactic bolus dose of 32 µg/min by compared with a prophylactic bolus dose of 100µg phenylephrine during caesarean delivery. The result revealed that the nor-epinephrine bolus dose was effective for decreasing the incidence of hypotension and resulted in more stable BP control compared with the phenylephrine bolus to treat hypotension when it occurred. Despite a much greater dose of norepinephrine given to patients who received norepinephrine prophylactic dose, no adverse effect on neonatal outcome was detected.

The current study follows on from a previous study in which we compared norepinephrine with phenylephrine during caesarean delivery and found that norepinephrine had the advantage of causing less depression of HR, which was associated with greater cardiac output compared with phenylephrine<sup>7</sup>.

In contrast, in our investigation, we employed a

simple algorithm to manage the infusion manually. The senior author recently reported on the routine use of norepinephrine after caesarean birth over a year, during which infusions based on our methodology were used in most cases<sup>1,6</sup>.

In this group, rescue intermittent boluses of norepinephrine(32µg) were given as required to treat any episodes of hypotension that occurred.

The purpose of the inclusion of the control group was to provide a baseline comparator to facilitate the evaluation of the efficacy of prophylactic norepinephrine infusion. Of course, the study was not designed to compare the efficacy of infusion versus boluses of norepinephrine. In clinical practice, when an intermittent bolus technique is used, boluses may be given earlier or more frequently and as prophylaxis rather than treatment of hypotension; thus, a lower incidence of hypotension may be achieved than that observed in the control group in our study. Further work is required to compare optimized intermittent bolus dose and infusion techniques for intervention.

The study conducted at Shams University in Cairo revealed that Nor -Nor-Epinephrine group (35.6%) and PE group (46.7%) of patients did not need additional boluses of the vasopressor, but the difference was not statistically significant<sup>13,16</sup>. This result is different from our study result that the NE group had a statistically significantly lower number of boluses than the phenylephrine group. This difference may be attributed to the difference in the bolus dose of the NE used (32µg; NE group) and phenylephrine group(100µg) in the study population in which the study was conducted on patients having spinal anaesthesia lower orthopaedic surgery.

A study conducted to assess the efficacy and safety of bolus administration of NE versus phenylephrine for the maintenance of systolic blood pressure during spinal anaesthesia in coronary artery disease patients undergoing knee arthroscopy showed that efficacy was found in 20 (40%) patients of the group in phenylephrine and 40 (80%) patients of a group of nor-epinephrine. The results were highly significant ( $p < 0.001$ )<sup>2,17</sup>. These results were in line with the results of our study, despite of Nor-epinephrine dose of (32 µg iv) and phenylephrine dose (100µg iv) bolus doses used as prophylaxis.

At every norepinephrine dosage, the order of beneficial and poor responses in the prior trial, 3, 4, 5, 6, and 7 µg of the dosages were employed. The 8-µg dosage was never administered. Using the truncated DM technique, the estimated bolus ED90 of norepinephrine to prevent hypotension was 5.49 µg (95% CI, 5.15–5.83). At 5.80 µg (95% CI, 5.01–6.59), the isotonic regression estimator of ED90 was determined. At a dose of 6 µg/min, the majority of patients attained the desired outcome. At this dosage

level, the number of boluses required in the successful cases dose ranged from 1 to 13, corresponding to A Total of cumulative norepinephrine dose range of 6 to 78  $\mu\text{g}$  from intrathecal injection to delivery of the fetus<sup>2,7</sup>.

At a dose of 8 $\mu\text{g}$ -24 $\mu\text{g}$ , most of the clients did not attain the desired outcome in a previous study<sup>2</sup>. At dose of 32 $\mu\text{g}$ , the majority of patients had effective responses. The number of boluses required for each consecutive case ranged from 1 to 4, the total cumulative NE and PE doses needed were (32 - 128  $\mu\text{g}$  and (100 $\mu\text{g}$ -300 $\mu\text{g}$ ), from intrathecal injection to delivery of the fetus, respectively. This discrepancy may be attributed to the difference in the bolus dose of the NE used (32 $\mu\text{g}$ ) and the study population which was characterised by low socio-economic status which caused more hemodynamically instability. Finally in our study by using isotonic regression, the optimum dose of nor-epinephrine used to prevent hypotension was 40.43 $\mu\text{g}$  (95%CI, 29.23-53.45), and the phenylephrine used was 160 $\mu\text{g}$  (95%CI; 115-201.3).

Parturient undergoing elective Cesarean section were administered NE at 6  $\mu\text{g}$ /minute or phenylephrine at 50 $\mu\text{g}$ /minute immediately after spinal anaesthesia. Infusion of 6  $\mu\text{g}$ /minute NE presented fewer episodes of tachycardia compared to the phenylephrine group. Our study also demonstrated a lower heart rate for the NE group, although fetal outcome was similar between the groups, with an Apgar score > 7 for all new-borns.

The optimal dose of nor-epinephrine for a patient having a caesarean section was determined by comparing several intermittent NE bolus doses of 3, 4, 5, 6, 7, or 8 $\mu\text{g}$ /min in a prospective, double-blind trial. Intermittent NE IV boluses appear to be a reasonable way to prevent spinal-induced hypotension in elective cesarean-section procedures, and no adverse effects have been reported. In practice, they propose the 90% effective dose of 6  $\mu\text{g}$ /min more research Advocates that is necessary to clarify the relative benefits and risks of alternating IV bolus doses of NE and phenylephrine<sup>2,6,7</sup>.

### Limitation

This was a cohort study; the confounders might not have been adequately controlled.

### Conclusion

Intraoperative hypotension is common after spinal anaesthesia for Caesarean section. Inadequate treatment may lead to significant maternal, fetal, or both adverse outcomes. Consensus guidelines for the management of hypotension during Caesarean section has recommended a standard approach and include detailed guidance on how to introduce phenylephrine in-fusions into practice. Other agents with a preferable adrenergic profile may be the focus of further studies. For a pregnant woman who underwent

an elective cesarean section under spinal anaesthesia, nor-epinephrine can be administered in place of phenylephrine to maintain the mother's blood pressure without having a side effect on the mother and fetus.

### Abbreviations

MAP- Mean Arterial Pressure

PE- Phenylephrine

NE- Nor-Epinephrine

AOR- Adjusted Odd Ratio

CS- Caesarean Section

### Declarations

#### Ethical Approval

Ethical approval was obtained from the College of Medicine and Health Sciences' ethical review committee. Written informed consent was obtained from each patient, and confidentiality was maintained by instructing the data collectors not to record any identification information found.

#### Consent

Written informed consent was obtained from the patient for publication, including accompanying photographs. The patients were informed of the intervention to be performed in their local language. A copy of the written consent is available for inspection by the journal's editor-in-chief upon request.

All the authors were asked to confirm, as part of the submission process, that such consent had been obtained.

#### Availability of Data and Materials

The data sets used and analysed during the study are available from the corresponding author upon reasonable request.

#### Consent for Publication

Not applicable.

#### Competing Interest

There are no conflicts of interest among the participants of the article.

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