International Journal of Medical and Pharmaceutical Research
Website: https://ijmpr.in/ | Print ISSN: 2958-3675 | Online ISSN: 2958-3683
NLM ID: 9918523075206676
Volume: 4 Issue:3 (May-June 2023); Page No: 545-551

Original Article

Randomized Clinical Study to Compare the Efficacy of Phenylephrine Bolus and Infusion for Maternal Hypotension and Neonatal Outcome during Lower Segment Cesarean Section under Spinal Anesthesia

Dr Gowtham S[1], Dr Aashik P[1], Dr Poornima Shivanna[2], Dr P Saraswathi Devi[3]

[1] Final Years Post Graduate, Dept of Anaesthesia, The Oxford Medical College, Hospital & Research Centre
[2] MBBS MD, Assistant Professor, Dept of Anaesthesia, The Oxford Medical College, Hospital & Research Centre
[3] Professor and HoD, Dept of Anaesthesia, The Oxford Medical College, Hospital & Research Centre

ABSTRACT

Introduction: Phenylephrine is the ideal vasopressor for spinal anesthesia in lower segment ceasearen section, this study was undertaken to compare the bolus doses of 50µg of Phenylephrine with a prophylactic fixed infusion rate of 50µg/min of the same drug.

Methodology: A prospective randomized, comparative study of 60 parturients scheduled for elective or emergency ceasearean section Patients were randomly assigned into two groups by sealed envelope method (bolus/infusion) group. After recording the baseline vital parameters and preloading with 500 ml Ringer lactate, spinal anaesthesia will be administered .Group A received injection Phenylephrine 50 µg bolus if systolic blood pressure is <20% basal value, bolus was repeated if necessary. Group B were given Phenylephrine 50 µg/min infusion started immediately after spinal anesthesia and continued for 2 minutes and subsequent adjustment was made, Hemodynamic monitoring will be done every minute till extraction of the baby.

Results: The present study showed that the mean fall in SBP, DBP, MAP were less in infusion group ($p<0.001$)compared to bolus group however the fall in HR is more in bolus compared to infusion group ($p<0.001$) .

Conclusion: We conclude that prophylactic phenylephrine infusion leads to a significantly better control of post spinal hypotension compared to Phenylephrine bolus dose.

Key Words: *Phenylephrine, hypotension, bradycardia, subarachnoid block, caesarean section*

***Corresponding Author**
Dr Gowtham S
Final Years Post Graduate, Dept of Anaesthesia, The Oxford Medical College, Hospital & Research Centre

INTRODUCTION

Spinal anesthesia is the technique of choice for lower segment cesarean section However this is accompanied by maternal hypotension which has a very high incidence. Hypotension after Spinal Anesthesia is defined when the systolic blood pressure decreases to 20% less than baseline readings [1].

Vasopressors used for prophylaxis and treatment of hypotension should fulfill the following criteria i.e., high efficacy, ability to use liberal doses to maintain maternal blood pressure near normal preventing hypotension induced fetal academia [2].

Hypotension has traditionally been managed by measures such as fluid preloading, prophylaxis and therapeutic vasopressor along with left uterine displacement throughout the surgery [2].

Phenylephrine is the vasopressor that most closely meets the criteria for the ideal vasopressor in obstetrics. It is a short acting alpha agonist and increases maternal blood pressure with a transient reactive bradycardia, responsive to atropine. It can be administered by bolus as well as by infusion, in titrated doses as per the blood pressure response [3].

The present study is undertaken to reduce the risk of hypotension during spinal anesthesia in lower segment caesarean section by administration of an initial bolus dose followed by infusion of phenylephrine along with their effects on neonatal outcome

AIM AND OBJECTIVES OF THE STUDY

Aim

1) To compare reactive bolus doses of 50 µg of phenylephrine and with a prophylactic fixed infusion rate of 50 µg/min of the same drug given

2) To study the neonatal outcome APGAR SCORE 1st and 5th minute and side effects with the two regimes

Objectives

1) The primary objective of this study is to compare bolus doses of 50µg of Phenylephrine with a fixed prophylactic infusion rate of 50 µg/min of the same drug given for maternal hypotension during cesarean section under spinal anesthesia
2) The secondary objective is to study the neonatal outcome (APGAR SCORE 1st and 5th minute) and side effects with the two regimes.

MATERIALS AND METHODS

Source of Data:

The study was conducted as a prospective randomized, comparative study of 60 physical status ASA Classes I and II patients are scheduled for elective or emergency Cesarean Section under subarachnoid block in the, Tertiary care centre, Bangalore. The study was conducted between the period of march 2021 to September 2022 after approval by the ethics committee of the institution and informed consent.

Study Site- The Tertiary care centre Bangalore.
Study Duration- The study was done between01-03-2021 to 31-09-2022 18 months
Design of Study- A randomized controlled clinical study.

Sample Size

A total of 60 patients are enrolled in the study. We included 30 patients in each group. Patients are classified as per American Society of Anesthesiologists (ASA) classes I and II. The patients are randomly allocated into two groups of 30each.

METHOD OF COLLECTION OF DATA:

Inclusion criteria:

- Patients who gave written informed consent. (Annexure I)
- Patients aged between 18 to 40 years.
- Patients belonging to ASA Grade I and Grade II.

Exclusion criteria:

- Patients who refuse for the procedure and written informed consent.
- Pre existing or pregnancy-induced hypertension
- Prenatal fetal distress,
- Patient with history of significant cardiovascular, respiratory, neurological, and coagulation disorders

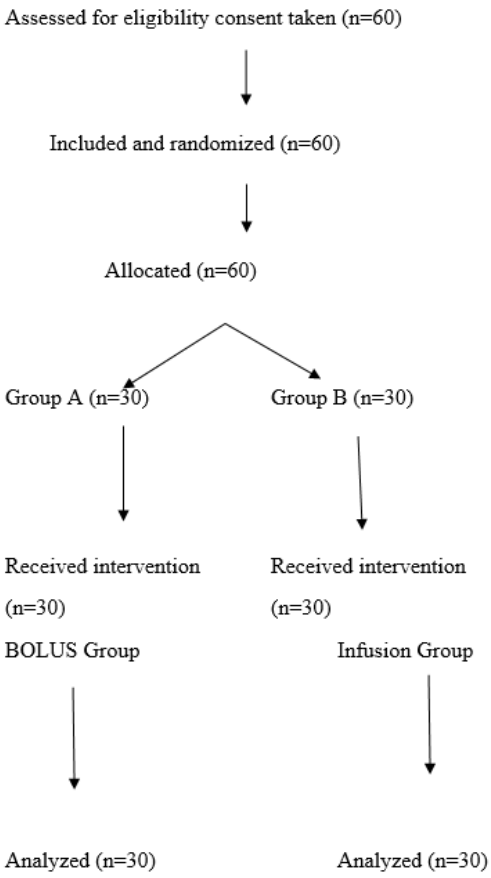
Sampling method:

$$n = \frac{(Z\_(1-\alpha/2) + Z\_(1-\beta))2(\sigma\_1\hat{}2 + \sigma\_(2/r)\hat{}2)}{(\mu\_1 - \mu\_2)2}$$

$$n = \frac{(1.96+0.84)2((6.35)2 + 〚(4.15)〛\_(/1)\hat{}2)}{(5.56 - 1.66)2}$$

Alpha (α)=0.05
Beta (β)=0.2
Mean in group 1(μ_1) = 5.56
Standard deviation in group 1(σ_1) = 6.35
Mean in group 2(μ_2) = 1.66
Standard deviation in group 2(σ_2) = 4.15
Ratio (Group 2/Group 1) = 30/30 = 1
The mean value μ_1 μ_2 and standard deviation value
σ_1 σ_2 is taken from reference study Choudhary et al [4]
Total samples =60
Z=critical value and a standard value for the corresponding level of confidence
At 95% confidence interval or 5% level of significance (type-I error) it is 1.96 and at 99% confidence interval it is 2.58
N=60 samples
Group-1=30 samples
Group-2=30 samples

Flow Chart



METHODOLOGY

Patient fulfilling the inclusion criteria are enrolled in the study. Pre anesthetic checkup is done documenting demographic data, history, general physical examination and a written informed consent is obtained, patients are randomly assigned in to two groups by sealed envelope method (bolus/infusion) group Intraoperatively standard aseptic precautions are followed for the spinal anesthesia after reading the basal vital parameters and preloading with 500 ml Ringer lactate solution.

Group A received injection Phenylephrine 50 µg bolus if systolic blood pressure is <20% basal value, bolus is repeated if necessary.

Group B received injection Phenylephrine 50 µg/min infusion started immediately after spinal anesthesia and is continued for at least 2 minutes subsequent adjustment of infusion is done according to systolic blood pressure.

Hemodynamic monitoring is done every minute till 10 min and then every 3 min till the end of surgery Hypotension are treated with Phenylephrine drug boluses Bradycardia <60beats per minute is given inj atropine 0.6mg Neonatal outcome is assessed as Appearance, pulse, grimace, activity, and respiration (APGAR) score is assessed at 1st and 5th min after the delivery Post operative monitoring assessed for 1 hour.

STATISTICAL METHOD APPLIED

Statistical analysis frequency and percentage are calculated by using descriptive statistics. Normally distributed continuous variables are presented as mean ± standard deviation with 95% confidence interval (CI) of mean and non-normally distributed continuous variables are presented as median (interquartile range) with 95% CI of median. Normality of data will be tested by Kolmogorov–Smirnov test. If the normality is rejected, then nonparametric test is used. Normally distributed quantitative variables are compared using unpaired t- test and non-normally distributed quantitative variables are compared using Mann–Whitney test.

Statistical analysis is performed with The Statistical Package for Social Sciences version 25.0 software (SPSS Inc., Chicago, IL, USA) and P value <0.05 is considered as statistical significance.

RESULTS

Table 4: Age distribution

	Phenylephrine bolous	Phenylephrine infusion
20 – 25	15	16
26 – 30	10	10
31 – 35	3	2
36 – 40	2	2
Total	**30**	**30**
Mean± SD	**26.60 ± 4.81**	**26.43 ± 4.53**

In the present study the mean age of the participants in the phenylephrine bolus is 26.60 ± 4.81and in the phenylephrine infusion group it was 26.43 ± 4.53. thus both the groups are comparable in terms of age.

Table 5: Height

	MINIMUM	MAXIMUM	MEAN ±SD
Phenylephrine bolous	156	170	161.26 ± 3.31
Phenylephrine infusion	156	173	163.80 ± 6.27
T test = 1.96, p=0.06, Not significant			

In the present study the mean height of the participants in the phenylephrine bolus group is 161.26 ± 3.31 and in the phenylephrine infusion group it was 163.80 ± 6.27. in the present study there was no significant difference between both the groups and thus they are comparable.

Table 6: Weight

	MINIMUM	MAXIMUM	MEAN ±SD
Phenylephrine bolous	58	72	64.33 ± 3.59
Phenylephrine infusion	60	69	64.26 ± 2.57
T test = 0.08, p=0.93, Not significant			

The mean weight of the participants in the phenylephrine bolus group is 64.33 ± 3.59 and in the phenylephrine infusion group it is 64.26 ± 2.57, there was no significant difference across the groups and thus the group stand comparable.

Table 7: Indication

	Phenylephrine bolous	Phenylephrine infusion
CPD	3	2
Failure to progress	2	4
Foetal distress	9	4
IUGR	1	2
Maternal request	4	3
Non progression of labour	3	3
Previous LSCS	4	6
PROM	4	6
Total	**30**	**30**

Table 8: SBP

	Phenylephrine bolous	Phenylephrine infusion	P value
10’	106.23 ± 10.99	116.03 ± 5.03	<0.001*
12’	104.80 ± 13.64	117.93 ± 5.00	<0.001*
14’	108.40 ± 7.55	116.93 ± 5.19	<0.001*
16’	110.23 ± 8.32	117.10 ± 5.02	<0.001*
18’	112.13 ± 8.25	117.43 ± 5.28	<0.001*
20’	114.00 ± 6.93	117.57 ± 5.29	<0.001*

In the present study a significant difference has been observed in the SBP in the patients who have received phenylephrine bolus and infusions, it is observed that the changes in SBP are significantly lower in the bolus group when compared to the infusions.

Table 9: DBP

	Phenylephrine bolous	Phenylephrine infusion	P value
10’	56.80 ± 6.83	63.37 ± 4.50	<0.001*
12’	56.80 ± 9.62	68.00 ± 4.57	<0.001*
14’	58.53 ± 8.76	66.33 ± 4.51	<0.001*
16’	58.47 ± 9.68	67.87 ± 5.14	<0.001*
18’	59.80 ± 9.88	68.80 ± 4.96	<0.001*
20’	59.70 ± 5.66	63.87 ± 4.55	<0.001*

In the present study a significant difference has been observed in the DBP in the patients who have received phenylephrine bolus and infusions, it is observed that the changes in DBP were significantly lower in the bolus group when compared to the infusions

Table 10: MAP

	Phenylephrine bolous	Phenylephrine infusion	P value
10’	71.43 ± 8.74	80.92 ± 3.21	<0.001*
12’	72.40 ± 10.81	84.64 ± 3.00	<0.001*
14’	74.57 ± 8.50	83.20 ± 3.27	<0.001*
16’	74.70 ± 8.14	84.28 ± 3.65	<0.001*
18’	75.47 ± 8.24	85.01 ± 3.52	<0.001*
20’	76.50 ± 5.44	81.77 ± 3.19	<0.001*

In the present study a significant difference has been observed in the MAP in the patients who have received phenylephrine bolus and infusions, it is observed that the changes in MAP were significantly lower in the bolus group when compared to the infusions

Table 11: HR

	Phenylephrine bolous	Phenylephrine infusion	P value
10’	85.57 ± 16.36	102.17 ± 15.00	<0.001*
12’	86.70 ± 12.58	107.07 ± 15.00	<0.001*
14’	89.07 ± 11.92	104.63 ± 15.02	<0.001*
16’	85.27 ± 19.18	101.63 ± 6.35	<0.001*
18’	88.07 ± 12.84	104.20 ± 6.40	<0.001*
20’	89.37 ± 20.59	98.20 ± 7.66	<0.001*

In the present study a significant difference has been observed in the HR in the patients who have received phenylephrine bolus and infusions, it is observed that the changes in HR were significantly lower in the bolus group when compared to the infusions

Table 12: SPO2

	Phenylephrine bolous	Phenylephrine infusion	P value
10’	99.90 ± 0.31	99.47 ± 0.51	0.001*
12’	99.97 ± 0.18	99.57 ± 0.50	0.001*
14’	99.97 ± 0.18	100.00 ± 0.00	0.16
16’	100.00 ± 0.00	100.00 ± 0.00	-
18’	99.97 ± 0.18	100.00 ± 0.00	0.16
20’	100.00 ± 0.00	100.00 ± 0.00	-

In the present study it is observed that there was a significant difference between the SpO2 across the groups at 10’ and 12’, the mean SpO2 was significantly lower in the infusion group compared to the bolus group.

Table 13: APGAR Score

	Phenylephrine bolous	Phenylephrine infusion
1 min	8.62 ± 0.62	9.0 ± 0
5 min	9.0 0± 0.0	9.0 ± 0

In the present study the mean APGAR score at 1 minute was observed to be 8.62 ± 0.62 and in the infusion group it was 9.0 ± 0 and at 5 mins it was 9.0 0± 0.0 in both the groups.

DISCUSSION

Socio-Demographic Characteristics:

The study examined the mean age, height, and weight of participants who received either phenylephrine bolus or infusion. With respect to age, the mean age for the bolus group was 26.60 ± 4.81 while it was 26.43 ± 4.53 for the infusion group, indicating the two groups were statistically comparable.

The mean height was 161.26 ± 3.31 cm for the bolus group and 163.80 ± 6.27 cm for the infusion group. Similarly, the mean weight of the bolus group was 64.33 ± 3.59 kg while that of the infusion group was 64.26 ± 2.57 kg. The absence of significant difference between the groups' height and weight further reinforces their comparability.

Vitals:

Our understanding of the mechanism of hypotension following subarachnoid anesthesia for cesarean sections (SA for CS) has evolved, shifting from dependency on IV fluid preloading to proactive administration of vasopressors, given their direct counteraction of the primary physiological alterations instigated by the sympathetic block. While ephedrine was initially favored, phenylephrine emerged as more efficacious, with less placental transfer and a lower likelihood of depressing fetalpH.

Regarding optimal dosing and administration method for phenylephrine, controversy persists. Intermittent boluses are straightforward, but there is growing interest in titrated continuous infusions. Factors such as body mass index, weight gain during pregnancy, age, preoperative HR, and tests like the supine stress test and orthostatic hypotension, have been identified as predictive for spinal hypotension.

This study revealed significant differences in systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and heart rate (HR) between those who received phenylephrine bolus and infusions. The changes in these parameters were significantly lower in the bolus group. There was also a significant difference in SpO2 at 10 and 12 minutes, with the infusion group exhibiting lower mean SpO2 than the bolus group.

Comparative Analysis:

Several studies have explored the prevention and treatment of hypotension following SA in cesarean sections, adopting various methods and yielding differing observations. Our study, as well as those conducted by Choudhary et al. [4], Saurombe et al. [5], and Vijayakumar et al. [6], suggested that phenylephrine infusion demonstrates better control and results. On the other hand, Patel et al. [7] and Hall et al. [8] showed better outcomes with bolus doses. In our research, phenylephrine infusion was found superior.

APGAR Scores:

The average Apgar scores at 1 and 5 minutes were evaluated for both groups. The mean score for the bolus group at 1 minute was 8.62 ± 0.62 and at 5 minutes was 9.0 ± 0.0. Similarly, the infusion group had a mean score of 9.0 ± 0.0 at both time points. This indicates no significant difference between the groups, a finding corroborated by Choudary et al. [4]. and Patel et al. [7]. This aligns with our study's results, underlining the similar Apgar scores between the groups.

CONCLUSION

The data gleaned from this study substantiate the efficacy of prophylactic phenylephrine infusion as a viable method for mitigating the incidence and severity of hypotension induced by spinal anesthesia during cesarean deliveries. The investigation closely examined and compared the outcomes associated with the use of phenylephrine as an infusion versus a bolus.

Phenylephrine infusion was found not only to significantly diminish the occurrence of hypotension but also its degree when it did occur. This outcome bears crucial clinical implications as it can help in maintaining maternal hemodynamic stability during cesarean procedures, thereby ensuring patient safety.

Furthermore, our findings also provide a reassurance of safety concerning neonatal outcomes. When comparing the effects of the phenylephrine bolus versus infusion methods, there was no significant negative impact observed on the neonates. This was supported by similar Apgar scores observed in both groups, suggesting that the prophylactic phenylephrine infusion regimen does not compromise neonatal wellbeing.

In conclusion, the findings strongly advocate for the implementation of prophylactic phenylephrine infusion as a practical, safe, and effective approach to attenuate the risk of hypotension during cesarean sections performed under spinal anesthesia, without any consequential adverse effects on the neonatal outcome. Therefore, it appears to be a preferable alternative to the usage of phenylephrine in bolus form for this specific clinical setting.

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