Section: Anaesthesiology

Original Research Article

A RANDOMIZED DOUBLE BLINDED PLACEBO-CONTROLLED COMPARATIVE STUDY OF THE FIXED RATE INFUSION REGIMENS OF PHENYLEPHRINE IN PREVENTING POST SPINAL HYPOTENSION AND ITS EFFECTS ON FETAL ACID BASE STATUS DURING ELECTIVE CAESAREAN SECTION

Bhavya Reddy H A[1], Shwetha Odeyar S[2], Shruti R Rao[3], Shanmathi devi K[4], Niveditha B[5]

[1]Associate Professor, Department of Anaesthesiology, BGS Global Institute of Medical Sciences, #67, BGS Health and Educational City, Uttarahalli Main Road, Kengeri, Bengaluru 560060, India.
[2]Professor, Department of Anaesthesiology, BGS Global Institute of Medical Sciences, #67, BGS Health and Educational City, Uttarahalli Main Road, Kengeri, Bengaluru 560060, India.
[3]Assistant Professor, Department of Anaesthesiology, BGS Global Institute of Medical Sciences, #67, BGS Health and Educational City, Uttarahalli Main Road, Kengeri, Bengaluru 560060, India.
[4]Post Graduate Student, Department of Anaesthesiology, BGS Global Institute of Medical Sciences, #67, BGS Health and Educational City, Uttarahalli Main Road, Kengeri, Bengaluru 560060, India.
[5]Post Graduate Student, Department of Anaesthesiology, BGS Global Institute of Medical Sciences, #67, BGS Health and Educational City, Uttarahalli Main Road, Kengeri, Bengaluru 560060, India.

Received : 08/01/2023
Received in revised form : 11/02/2023
Accepted : 25/03/2023

Keywords:
Subarachnoid Blockade, Hypotension and Phenylephrine.

Corresponding Author:
Dr. Shruti R Rao,
Email: drshrutirrao@gmail.com

DOI: 10.47009/jamp.2023.5.2.248

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2023; 5 (2); 1170-1174

Abstract

Abstract: Internationally Obstetric anaesthesia guidelines recommend regional anaesthesia over general anaesthesia for caesarean sections because of the risk associated with anticipated difficult airway and risk of aspiration. Subarachnoid block is associated with maternal hypotension which can cause side effects such as nausea, vomiting, light headedness in the mother and if severe, can impair utero-placental perfusion which can lead to neonatal depression, fetal bradycardia and acidosis. Current evidence supports co-loading with intravenous fluids in conjunction with the use of vasopressors to prevent and treat hypotension. Aims and Objectives of the study: To assess the effectiveness of phenylephrine infusion in preventing maternal hypotension and fetal acidosis after subarachnoid block. **Methodology:** Parturients who were posted for elective caesarean section were randomly allocated to receive normal saline (control group) or Phenylephrine 50 mcg/min immediately after subarachnoid blockade. Heat rate and blood pressure were recorded every minute for the first 10 minutes and every 3 minutes thereafter. Continuous monitoring of electrocardiography, respiratory rate, oxygen saturation (Spo2) was done. APGAR score was recorded in 1st and 5th minute and sample from umbilical cord was sent for arterial blood gas (ABG) analysis. **Results:** Out of 70 patients there was no hypotension noted in patients receiving phenylephrine 50 mcg/min, whereas in control group 15 episodes of hypotension was noted, which was statistically significant. Fetal umbilical cord pH and APGAR scores at 1st and 5th minute were comparable in both the groups. **Conclusion:** Patients receiving prophylactic phenylephrine infusions had better hemodynamic outcomes with lesser requirement of additional vasopressors. There was no significant difference in fetal outcomes when compared between the groups.

INTRODUCTION

Subarachnoid blockade is the technique of choice of anaesthesia for caesarean sections, as it avoids the risks associated with general anaesthesia including difficult intubation and aspiration of gastric contents.[1] There is also decreased postoperative morbidity and mortality with regional anaesthesia when compared with general anaesthesia.[2] Though subarachnoid blockade is technique of choice in

caesarean section, it is associated with fall in maternal blood pressures which can produce unpleasant maternal symptoms such as nausea, vomiting, light headedness and if severe and sustained, can reduce uterine and intervillous blood flow which can cause fetal hypoxia, acidosis and neonatal depression. Thus, it is important to maintain maternal hemodynamics and uteroplacental perfusion following subarachnoid blockade for caesarean section.[3] Current evidence supports co-loading with i.v fluids along with the use of vasopressor as the most effective way to prevent and treat maternal hypotension. Recent data supports the use of α-agonist such as phenylephrine to maintain maternal arterial blood pressure following subarachnoid blockade during caesarean section. Phenylephrine is highly efficacious; it can be titrated to maintain arterial pressure over wide range of values.[4] Phenylephrine is the accepted vasopressor of choice in the parturients.

In our study, we are going to compare the effects of different concentrations of phenylephrine infusion and its control over the maternal hemodynamics and fetal outcomes.

MATERIALS AND METHODS

Source of Data

Parturients posted for elective caesarean section at Bgs Global Institute of Medical Sciences, Bengaluru.

Methods of Collection of Data

Study Design

A Randomized double blinded placebo-controlled comparative study.

Study Period 18 months

Place of Study

Parturients undergoing elective caesarean section at operation theatre of BGS Global Institute of Medical Sciences, Bengaluru.

Sampling Technique

Systematic random sampling from computer generated tables.

Sample Size

The sample size is 70 (35 in each group), for an outcome variable on post- delivery hypotension minimum difference of proportion of 35.0% derived from previous literature, with 90% statistical power, 5% level of significance, in three group comparative study, Sample size is 70(35 in each group).

Inclusion Criteria

- ASA physical status II patients.
- Patients not in labour posted for caesarean section under subarachnoid block.
- Singleton pregnancy.
- Gestational age of more than 36 weeks.

Exclusion Criteria

- Patients with hypertension (SBP >140 mmHg, DBP> 90 mmHg).
- Diabetes mellitus.
- Cardiovascular disease, cerebrovascular disease.
- Known fetal anomalies.
- Contra-indications to spinal anaesthesia.
- Signs of onset of labour.
- BMI >45 kg/m2
- Induction-delivery interval of >10 minutes.

Methodology

After obtaining the clearance and approval of institutional ethical committee, 70 parturients posted for caesarean section under subarachnoid block, who fulfilled inclusion and exclusion criteria were randomly selected and were allotted to one of the two groups (Group A and Group B).

A through pre anaesthetic examination was done for all the parturients on the previous day of surgery. Risks and benefits associated with the study, surgery and type of anaesthesia was explained. Standard protocol for NPO guidelines was followed. Informed consent was obtained on the day of surgery for anaesthesia along with a separate consent for the enrolment in the study.

Two peripheral i.v lines were secured with 18G and 20G cannulas. Through the 18G cannula, preloading was done with crystalloids at 15 ml/kg before subarachnoid block and through the 20G cannula study drug infusion was started immediately after the subarachnoid block through the syringe pump.

Patients received aspiration prophylaxis with inj. pantoprazole 40 mg i.v, and inj.metaclopramide 10 mg i.v 30 minutes before the surgery. Non-invasive blood pressure and heart rate were measured using standard noninvasive monitoring devices after patient rests in left lateral position for 10 minutes. Mean of the three readings were taken as the baseline value. Hypotension is defined as systolic blood pressure <20% of the basal value or <90 mmHg. Systolic blood pressure >20% of basal value was considered as reactive hypertension. Heart rate <20% of basal value or <50 beats/min was considered as bradycardia. Heart rate >20% of basal value was considered as tachycardia.

Two infusion regimens phenylephrine 50 mcg/min infusion (Group A) and normal saline (Group B) the control group were prepared by an anaesthesiologist who is not involved in the study. Patients who were posted for caesarean section and the investigator doing the study were blinded. Patients were divided into two groups (Group A or Group B) and they will be receiving either of the infusions as per computer generated randomization tables.

Subarachnoid block was performed in left lateral position or sitting position using 25G Quinke's spinal needle at L3-L4 or L4-L5 interspace and 2ml of 0.5% bupivacaine heavy was injected after confirming the clear free flow of CSF. Patients were repositioned in left lateral tilted supine position using a wedge with 10-15 degree. Level of sensory and motor blockade were noted. Patients were given either of the two infusions: normal saline, or phenylephrine 50 mcg/min soon after the subarachnoid block. Infusion was given at the rate of 60 ml/hour by using the standard infusion pump.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Heat rate and non-invasive blood pressure were recorded every minute for the first 10 minutes after subarachnoid block and every 3 minutes thereafter. Continuous monitoring of electrocardiography, respiratory rate and Spo2 were done.

After the extraction of the baby, inj. oxytocin 10U was given in 500 ml ringer lactate slowly and blood samples were collected from the double clamped segment of umbilical cord and sent for pH and ABG analysis immediately, APGAR score was recorded at 1 and 5 minutes.

Study drug was given till 10 minutes after the extraction of baby. Further continuation of the study drug infusion was left to the discretion of the anaesthesiologist. Any episodes of hypotension were noted and was treated with boluses of inj. phenylephrine 50 mcg in all the three groups. Any episode of bradycardia was noted and treated with inj. atropine 0.6 mg i.v bolus. During infusion of the study drug, if there were any episodes of reactive hypertension or bradycardia it was noted and the infusion was stopped immediately and treated. Infusion was restarted only if there were any further episodes of hypotension. If the infusion was stopped for more than 3 times during the study then those patients were excluded from the study.

Nausea and vomiting were noted down and scaled.

Scale 0 – no nausea

Scale 1 – mild nausea

Scale 2 – nausea requiring treatment

Scale 3 – vomiting

Treated accordingly with 0.12 mg/kg of inj. ondansetron i.v

Preparation of the study drug infusion

In our study 10 mg phenylephrine ampule was diluted in 100 ml normal saline to achieve a concentration of 100 mcg/ml. 25 ml of this study drug solution is taken in a 50 ml syringe and double diluted to 50ml with 0.9% normal saline corresponding to 50 mcg/ml

RESULTS

This study includes 70 parturients with 35 in each group. The demographic data comparing age and BMI shows no statistical difference between the groups. [Table 1].

In our study the basal value of the heart rate in Group A is 98.875 ± 11.782 and Group B is 101.25 ± 10.233 and it is not statistically significant. The basal value of systolic blood pressure in Group A is 112.594 ± 6.932 and Group B is 113.031 ± 6.177 and is statistically insignificant. The basal value of diastolic blood pressure in Group A is 63.156 ± 5.131 and in Group B is 64.094 ± 4.761, and it is statistically insignificant. In our study the induction – delivery interval was comparable in both the groups and is statistically insignificant [Table 2].

The incidence of hypotension is higher in Group B where 15 out of 32 parturients (46.88%) had hypotension when compared to Group A where no parturient had hypotension. In our study the number of episodes of bradycardia was higher in Group A (3.12%) when compared to Group B (no episodes of bradycardia). The intraoperative pulse rates were comparable at all-time intervals and was not statistically significant. In our study, nausea and vomiting were scaled from 0-3 and there were no episodes of nausea and vomiting in either of the two groups. In our study the mean value of the umbilical cord pH in Group A is 7.301 ± 0.056 and in Group B it is 7.276 ± 0.04. It is comparable and statistically not significant. The APGAR scores were comparable at 1 and 5 minutes in both the groups and were not less than 7. The fetal umbilical cord and APGAR scores were comparable between the phenylephrine infusion group and the control group [Table 3].

Table 1: Demographic Data

	Group A	Group B	P Value
AGE	26.219±3.489	24.625±2.893	0.196
BMI	27.372±3.494	26.437±3.229	0.631

Table 1: Maternal Hemodynamics and Fetal Outcomes

	Group A	Group B	P Value
No Of Episodes Of Hypotension	0.000	0.656	<0.001
Number Of Boluses OfPhenylephrine	1	21	<0.001
Number Of Episodes OfBradycardia	0.094	0.000	0.203
Nausea And Vomiting	-	-	-
UMBILICAL CORD Ph	7.301±0.056	7.276±0.04	0.118
Apgar At 1st Minute	7.781±0.42	7.625±0.492	0.495
Apgar At 5th Minute	10	10	

DISCUSSION

Subarachnoid blockade is the choice of anaesthesia for caesarean sections allowing the mother to be awake and avoids the risks associated with general anaesthesia such as maternal aspiration syndrome and problems associated with difficult airway. It has been reported that some maternal mortality is attributable to the complications associated with general anaesthesia. However, the hypotension induced by sympathetic blockade can affect utero-placental perfusion and can have adverse effects on

ISSN (O): 2687-5365; ISSN (P): 2753-6556

neonatal outcomes which can be avoided by prophylactic use of vasopressors as we have done in our study.

In our study we have compared phenylephrine 50mcg prophylactic infusion with control who receive normal saline infusion and found that parturients who receive prophylactic phenylephrine infusion have better maternal hemodynamic stability and better fetal outcomes when compared to control group. There was no statistical significance in adverse effects such as nausea and vomiting.

Table 3: Intraoperative Heart Rate

Time	Group A		Group B	
	Mean	SD	Mean	SD
Baseline	98.875	11.782	101.250	10.233
1 min	97.938	16.142	109.031	16.726
2 min	92.250	16.668	114.969	12.280
3 min	82.406	13.550	109.563	11.813
4 min	79.188	12.494	106.875	13.671
5 min	76.063	12.864	103.375	12.435
6 min	74.594	16.559	100.906	9.650
7 min	74.906	16.143	99.438	10.752
8 min	72.969	16.954	99.063	10.540
9 min	72.156	14.303	95.906	9.988
10 min	73.625	15.197	96.219	10.552
13 min	72.500	17.705	95.969	10.117
16 min	74.344	18.709	92.906	10.205
19 min	75.156	19.636	93.250	7.180

Table 4: Intraoperative Mean Arterial Pressure

Time	Group A		Group B	
	Mean	SD	Mean	SD
Baseline	79.635	4.486	78.156	7.839
1 min	79.802	7.875	68.552	7.101
2 min	77.813	6.179	67.323	6.798
3 min	78.562	6.814	70.885	4.583
4 min	80.302	5.579	73.073	4.142
5 min	80.573	7.103	73.917	4.701
6 min	80.731	7.583	74.602	5.451
7 min	79.871	5.950	76.946	4.984
8 min	79.667	5.909	76.495	5.005
9 min	81.860	8.290	77.903	5.479
10 min	81.376	5.649	77.903	4.823
13 min	81.301	5.538	78.634	3.887
16 min	82.215	4.583	78.462	4.587
19 min	82.602	4.791	76.409	3.986

In 2004, Warwick D Ngan Kee et al.[5] conducted a study on comparing phenylephrine boluses of 100mcg with prophylactic phenylephrine infusion of 100mcg/min. when compared to control group infusion group exhibit lower incidence, amplitude and frequency of hypotension and heart rate slowed down noticeably over time. In both the groups umbilical cord blood gas values and APGAR scores were comparable.

In 2010, Terrence K Allen et al.[6] conducted a double blinded placebo-controlled trial on four fixed rate infusion regimens of phenylephrine for hemodynamic support during spinal anaesthesia for caesarean section on 101 patients. Their analysis showed doses of phenylephrine of 25 mcg/min and 50 mcg/min offered better maternal hemodynamic stability and necessitated less medical interventions than the 75 mcg/min and 100 mcg/min infusion rates.

In 2016, Syed N Muzzafer et al.[3] conducted a study exploring novel infusion regimens of phenylephrine during spinal anaesthesia for caesarean section and their effects on maternal hemodynamic control and fetal acid-base status on 90 patients. In order to prevent maternal hypotension during caesarean delivery under spinal anaesthesia, it was determined that a low dose infusion regimen of 60 to 80 mcg/min was more beneficial.

In 2017, Abatneh Feleke Agegnehu et al.[7] conducted a study comparing prophylactic phenylephrine boluses of 50mcg and 100 mcg with non-treatment group. The incidence of hypotension was lower in prophylactic boluses group when compared to non-treatment group. Fetal outcomes were comparable between the groups.

In 2018, Manish Choudhary et al.[2] compared phenylephrine bolus and infusion for maternal hypotension and neonatal outcome during caesarean sections under spinal anaesthesia in 100 patients. They concluded that patients receiving infusion of 50 mcg/min had lesser fall in mean blood pressure and lesser incidence of nausea and vomiting.

CONCLUSION

Prophylactic phenylephrine infusion has shown to maintain the maternal hemodynamics near baseline when compared to control group. Number of episodes of hypotension and requirement of phenylephrine boluses were more in control group. We did not notice any adverse effects such as nausea, vomiting and reactive hypertension. Bradycardia was more in prophylactic infusion of phenylephrine 50mcg/min group but was not statistically significant. When neonatal outcomes are compared, neonatal pH and APGAR scores were better in phenylephrine groups compared to control group but this was not statistically significant.

Hence, we conclude that prophylactic dose of phenylephrine 50 mcg/min infusion is better and safer in maintaining maternal hemodynamics and favourable fetal outcomes.

REFERENCES

1. Habib AS. A Review of the Impact of Phenylephrine Administration on Maternal Hemodynamics and Maternal and Neonatal Outcomes in Women Undergoing Cesarean Delivery Under Spinal Anesthesia. Anesthesia & Analgesia. 2012 Feb;114(2):377–90.
2. Choudhary M, Bajaj J. Study comparing phenylephrine bolus and infusion for maternal hypotension and neonatal outcome during cesarean section under spinal anesthesia. Anesth Essays Res. 2018;12(2):446.
3. Samanta S, Muzaffar S, Jain K, Bhardwaj N, Kumar P. Exploring novel infusion regimens of phenylephrine during spinal anesthesia for caesarean delivery: The effects on hemodynamic control and fetal acid-base status. J Obstet Anaesth Crit Care. 2016;6(2):86.
4. Ngan Kee WD, Khaw KS, Ng FF. Comparison of phenylephrine infusion regimens for maintaining maternal blood pressure during spinal anaesthesia for Caesarean

ISSN (O): 2687-5365; ISSN (P): 2753-6556

section . British Journal of Anaesthesia. 2004 Apr;92(4):469–74.
5. Ngan Kee WD, Khaw KS, Ng FF, Lee BB. Prophylactic Phenylephrine Infusion for Preventing Hypotension During Spinal Anesthesia for Cesarean Delivery: Anesthesia & Analgesia. 2004 Mar;815–21.
6. Allen TK, George RB, White WD, Muir HA, Habib AS. A Double-Blind, Placebo-Controlled Trial of Four Fixed Rate Infusion Regimens of Phenylephrine for Hemodynamic Support During Spinal Anesthesia for Cesarean Delivery. Anesthesia & Analgesia. 2010 Nov;111(5):1221–9.
7. Agegnehu AF, Gebreegzi AH, Lemma GF, Endalew NS, Gebremedhn EG (2017) Effectiveness of Intravenous Prophylactic Phenylephrine for the Prevention of Spinal Anaesthesia Induced Hypotension during Caesarean Section. A Prospective Observational Study. J Anesth Clin Res 8: 779.

ISSN (O): 2687-5365; ISSN (P): 2753-6556