

TO COMPARE THE EFFICACY OF TWO DIFFERENT DOSES OF NOREPINEPHRINE AND MEPHENTERMINE IN MANAGEMENT OF HYPOTENSION CAUSED DUE TO SPINAL ANAESTHESIA IN LOWER SEGMENT CAESAREAN SECTION SURGERIES

Atul Kumar Singh¹, Sanjay Kumar Bhasker², Neelesh Anand³, Shikha Sachan⁴

Received : 16/08/2023
Received in revised form : 25/09/2023
Accepted : 07/10/2023

Keywords:

Caesarean section, Mephentermine, Norepinephrine, Spinal Anaesthesia.

Corresponding Author:

Dr. Atul Kumar Singh,
Email: atulksingh84@gmail.com

DOI: 10.47009/jamp.2023.5.5.346

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

Int J Acad Med Pharm
2023; 5 (5); 1765-1767



¹Associate Professor, Department of Anaesthesiology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, Uttar Pradesh, India.

²Senior Resident (PDCC-Neuroanaesthesiology), Department of Anaesthesiology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, Uttar Pradesh, India.

³Senior Resident (PDCC-Critical Care Medicine), Department of Anaesthesiology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, Uttar Pradesh, India.

⁴Associate Professor, Department of Obstetrics and Gynaecology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, Uttar Pradesh, India.

Abstract

Background: Spinal Anaesthesia induced hypotension (SAIH) in one of the commonest adverse effects encountered during regional anaesthesia. The aim is to compare two different doses of Norepinephrine with Mephentermine to manage the hypotension after administration of spinal anaesthesia. **Materials and Methods:** The present double-blind, prospective, randomized study was conducted in a tertiary care teaching hospital after approval from the Institutional Ethics Committee and registration in Clinical Trial Registry of India (CTRI/2022/ 08/044813). 90 parturients were enrolled for the study meeting the inclusion and exclusion criteria. The parturients were equally divided into three groups and intraoperative hemodynamic events were recorded and compared. **Result:** The frequency of administration of Norepinephrine was more as compared to Mephentermine for management of hypotension. Tachycardia was more commonly associated with Mephentermine as compared to Norepinephrine. **Conclusion:** The advantage of using directly acting sympathomimetics such as Norepinephrine results in early response and less side effects as compared to indirectly acting sympathomimetics like Mephentermine.

INTRODUCTION

Spinal anaesthesia (a type of neuraxial regional anaesthesia) is used as an inexpensive, safe, reliable and rapidly effective method of providing anaesthesia for Caesarean section in parturients, but a common complication of spinal anaesthesia is hypotension. This complication is more common in parturient. The criteria for Hypotension is defined as '20-30% decrease in blood pressure from baseline that develops after a spinal puncture, occurs or worsens less than fifteen minutes after neuraxial blockade.^[1,2]

The factors responsible for Hypotension (defined as systolic blood pressure <90 mm Hg) to occur are peak block height greater than or equal to T5, age older than or equal to 40 years, baseline systolic blood pressure less than 120 mm Hg, combined Spinal and General anaesthesia, spinal puncture at

or above the L2-L3 interspace, and the addition of phenylephrine to the local anaesthetic.^[2]

Mephentermine (a mixed sympathomimetic with mainly indirect β stimulation) is one of the most commonly used drugs in our Institute and India. It has been shown to be as effective and safe as Ephedrine for SAIH.^[3,4] It produces both cardiac stimulation and vasoconstriction by directly activating α and β receptors as well as by releasing norepinephrine. Cardiac output, systolic and diastolic blood pressure are increased. AV conduction and refractory period of AV node is shortened with an increase in ventricular conduction velocity. It dilates arteries and arterioles in the skeletal muscle and mesenteric vascular beds, leading to an increase in venous return. The direct positive chronotropic effect on heart is generally counter balanced by vagal stimulation due to rise in mean blood pressure.

Norepinephrine is the endogenous neurotransmitter synthesized and stored in postganglionic sympathetic nerve endings and released with sympathetic nerve stimulation. Norepinephrine is a potent α_1 agonist producing intense arterial and venous vasoconstriction in all vascular beds except for the coronary arteries.^[5] Venous vasoconstriction decreases venous capacitance, thereby increasing venous return to augment stroke volume and cardiac output. Heart rate changes may be minimal as baroreceptor reflex triggered by arterial vasoconstriction are counteracted by β_1 -mediated increase in heart rate. Norepinephrine increases mean arterial pressure primarily by vasoconstriction and to a lesser degree by increasing stroke volume and cardiac output.

With this background the present study was planned to “Study the comparison of two different doses of norepinephrine and mephentermine for management of SAIH in Parturients (18-35 years) undergoing caesarean section”.

MATERIALS AND METHODS

The present double-blind, prospective, randomized study was conducted in a tertiary care teaching hospital after approval from the Institutional Ethics Committee and registration in Clinical Trial Registry of India (CTRI/2022/ 08/044813) within five months duration from March 2022 to October 2022.

After written informed consent to participate in the study, 90 parturients of 18- 35 years of age, 50-100 kg weight, 140-180 cm height, American Society of Anaesthesiologists physical status (ASA)–II and singleton term pregnancy posted for elective CS under Sub-arachnoid block were included in the study. Parturient with pre-existing pregnancy-induced hypertension (eclampsia and pre-eclampsia),

cardiovascular or cerebrovascular disease, hepato-renal disease, diabetes mellitus, allergy to study drugs, intraoperative use of uterotonic other than oxytocin, known foetal abnormality, more than expected blood loss and contraindication to SAB were excluded from the study.

Norepinephrine 5 μ g/ml (Group 1), norepinephrine 10 μ g/ml (Group 2) or mephentermine 5 mg/ml (Group 3) was prepared in three separate 10 ml syringes labelled as vasopressor Group-N5, Group-N10 and Group-M received bolus intravenous norepinephrine 5 μ g/ml, norepinephrine 10 μ g/ml and mephentermine 5mg/ml for the maintenance of intraoperative systolic blood pressure, respectively. Statistical analysis was done by applying Graph-pad in stat software. The numerical variables were compared between the groups by Student's unpaired t-test and within the group by Student's paired t-test. Categorical data were compared between the groups by Chi-square test. P value ≤ 0.05 was considered as significant.

RESULTS

The study carried out with 90 matched Parturients allocated into three study groups. Group 1(N5) contained (n=30) patients who received intravenous bolus dose of norepinephrine 5 mcg/ml, Group 2(N10) contained (n=30) who received intravenous bolus dose of norepinephrine 10 mcg/ml and Group 3 (M5) contained (N=30) patients who received intravenous bolus dose of mephentermine 5 mg/ml. There was no difference in demographic parameters in all the three groups [Table 1]. The number of hypotensive episodes were more in both groups receiving Norepinephrine because it has early onset and short duration of action as compared to Mephentermine [Table 2]. All other intraoperative events were comparable in all the groups.

Table 1: Comparison of Parturients characteristics among the groups

Parturient characteristics	Age (in years)	Height (in cms)	Weight (in kg)	BMI(kg/m ²)	P-value
Group 1	25.60 \pm 2.70	154.90 \pm 2.59	56.00 \pm 4.927	23.39 \pm 1.75	>0.05
Group 2	24.20 \pm 3.85	155.13 \pm 2.75	55.07 \pm 2.62	22.86 \pm 0.79	
Group 3	24.73 \pm 2.72	154.33 \pm 2.66	55.03 \pm 4.56	23.127 \pm 1.94	

Table 2: Comparison of Intraoperative events among groups:

Intraoperative event	Group 1(Mean \pm SD)	Group 2(Mean \pm SD)	Group 3(Mean \pm SD)
Number of hypotensive episodes (SBP<80 mm Hg)	2.73 \pm 0.94	2.20 \pm 0.99	1.33 \pm 0.48
Total number of boluses	2.77 \pm 0.89	2.20 \pm 0.99	1.33 \pm 0.47
Total duration of surgery (min)	50.33 \pm 8.92	50.83 \pm 10.76	50.40 \pm 10.99
Total intraoperative blood loss (ml)	472.67 \pm 84.24	440.67 \pm 70.66	445.67 \pm 64.42
Total i.v. fluid (ml)	1326.67 \pm 152.98	1186.67 \pm 125.21	1220.00 \pm 121.49
Total urine output (ml)	136.83 \pm 30.81	104.67 \pm 17.17	109.00 \pm 15.39

DISCUSSION

This study was done to compare the effects of intermittent bolus doses of norepinephrine 5 mcg/ml, norepinephrine 10 mcg/ml and mephentermine 5 mg/ml in the management of spinal anesthesia induced hypotension (SAIH)

during caesarean section. The results of this study shows that both norepinephrine and mephentermine are effective in managing spinal anaesthesia induced hypotension with no detrimental effects on the neonatal and maternal outcome. The number of norepinephrine boluses required to maintain blood pressure was significantly more with norepinephrine

than when mephentermine boluses were used. There was less incidence of bradycardia in the norepinephrine group.

There was significant rise observed in blood pressure (systolic and diastolic) and fall in heart rate were recorded throughout the study period after administration of vasopressors compared to first hypotensive value in both the groups ($p < 0.001$) as per statistics. Although changes in SBP and DBP were comparable between the groups, HR was significantly high compared to baseline after mephentermine administration after 9 mins of hypotension. In addition to, the response percentage of the 1st bolus of norepinephrine was significantly high, though significantly more number of boluses were required to manage SAIH in comparison to mephentermine.

Ngan Kee et al,^[6] in his study compared norepinephrine to phenylephrine for maintaining SBP in Caesarean section induced under spinal anaesthesia with a computer-controlled closed-loop feedback system. He noted higher response% which is well correlated with our finding. The higher response percentage with norepinephrine and frequent boluses requirement in our study may be because of the faster onset of action and shorter half-life of norepinephrine compared to mephentermine.

Onwochei et al,^[7] also conducted a trial in which he compared the effect of different intermittent i.v. boluses of norepinephrine to management SAIH in caesarean delivery. The results obtained were feasible and were not associated with significant maternal or fetal adverse effects that coincide with the results of our study.

There are various limitations to our study like the limited study duration which was till the end of surgery that should be extended till passing off effect of SAB. Neonatal outcomes like lack of monitoring of fetal acid base status was another lacunae in our study. Dilution of drugs to desired strength was another technical difficulty.

CONCLUSION

The study advocates the use of intermittent boluses of norepinephrine in the effective management of spinal induced hypotension during caesarean section. Although the hemodynamic variables are stable with the usage of intravenous boluses of norepinephrine and mephentermine, the number of doses of vasopressor use was found to be significantly more with the use of norepinephrine. In the norepinephrine group, the episodes of tachycardia are significantly less as compared to the mephentermine group.

REFERENCES

1. Neal JM, Barrington MJ, Brull R, et al. The second ASRA practice advisory on neurologic complications in regional anesthesia and pain medicine. *Reg Anes Pain Med.* 2015;40:401–30.
2. Carpenter RL, Caplan RA, Brown DL, et al. Incidence and risk factors for side effects of spinal anesthesia. *Anesthesiology.* 1992;76(6):906–16.
3. Kansal A, Mohta M, Sethi AK, Tyagi A, Kumar P. Randomized trial of intravenous infusion of ephedrine or mephentermine for management of hypotension during spinal anaesthesia for Caesarean section. *Anaesthesia.* 2005;60(1):28–34.
4. Ghaem H, Fakhropour A, Fattahi Z, Zaree S. Maternal and anaesthesia-related risk factors and incidence of spinal anaesthesia-induced hypotension in elective caesarean section: A multinomial logistic regression. *Indian J Anaesth.* 2018;62(1):36.
5. Carvalho B, Dyer RA. Norepinephrine for spinal hypotension during cesarean delivery another paradigm shift? *Anesthesiology.* 2015;122:728–30.
6. Ngan Kee WD. A random-allocation graded dose-response study of norepinephrine and phenylephrine for treating hypotension during spinal anesthesia for cesarean delivery. *Anesthesiology.* 2017;127:934–41.
7. Onwochei DN, Ngan KW, Fung L, Downey K, Xiang YY, Carvalho JC. Norepinephrine intermittent intravenous boluses to prevent hypotension during spinal anesthesia for cesarean delivery: A sequential allocation dose finding study. *Anesth Analg.* 2017;125:212–8.