International Journal on Science and Technology (IJSAT)
E-ISSN: 2229-7677 ● Website: www.ijsat.org ● Email: editor@ijsat.org

Comparison of bolus ephedrine, mephentermine and phenylephrine for maintenance of arterial pressure during caesarian section, a double blind study

Sujith Panasseril Jayapradeep

Consultant Anesthesiologist
MBMM hospital kothamangalam

Abstract:

Context: Hypotension has been observed in more than 80 % of caesarian sections done under spinal anesthesia. Crystalloids, colloids and positioning of the patient are used to circumvent the fall in BP. But for a quicker response, vasopressors has to be used. We aim to study the effect of giving standard bolus doses of the most commonly used vasopressors viz mephentermine, ephedrine and phenylephrine to prevent the initial hypotension after spinal anesthesia in patients undergoing elective and emergency caesarian sections.

Aims:

The aim of this study is to compare the hemodynamic effects of bolus doses of phenylephrine N(100mcg), mephentermine (6 mg) and ephedrine (6mg) in patients undergoing caesarean section under spinal anesthesia.

Settings and design: a prospective randomized double blind study

Methods and material:

After ethical clearance, a prospective, double blind, randomized study was conducted on sixty patients after obtaining written informed consent. Patients with ASA I or II grading were included in the study. Patients unwilling to participate, history of allergy to any of the drugs used in the study, infection at the lumbar puncture site, patients with history of bleeding disorders or abnormal coagulation profile, patients with neuro muscular disorders, patients with diabetes mellitus or hypertension, patients with cognitive impairment or psychiatric diseaseswere excluded from the study

Statistical analysis used:

ANOVA was used for comparision of numerical variables. Categorical variables were compared using chi-square test/ Fisher's test. $p < 0.05$ was taken as statistically significant.

Results:

Phenylephrine, ephedrine and mephentermine are equally efficient in maintaining systolic blood pressure in the test subjects. Phenylephrine has better hemodynamic profile with less tachycardia comparing the other two.

Conclusion:

A 100 mcg phenyleprine bolus is superior in maintaining systolic blood pressure when compared to ephedrine and mephentermine in patients undergoing caesarian section under spinal anesthesia. Tachycardia is also comparatively less with phenyleprine.

Key Words: Post-spinal hypotension, caesarian section, phentermine,phenylephrine,ephrdrine.

1. Introduction

Spinal anesthesia also called subarachnoid block is a form of regional anesthesia and a kind of neuraxial block involving injection of opiods, local anesthetics or other permissive drug into the subarachnoid space. [1,2] Hypotension is one of the most common side effect of spinal anesthesia. Uncorrected hypotension during spinal anesthesia can lead to morbidity and mortality. Careful positioning and volume preloading with crystalloid or colloids have been used to prevent it, but these are not complete measures.[3]Vasopressor is required to correct hypotension quickly[4]. Different drugs like phenylephrine, ephedrine, metaraminol and mephentermine are used as bolus doses during post-spinal hypotension or as a continous infusion.

Phenylephrine:

It is a sympathomimetic amine. It is a selective α1 receptor agonist and β agonist action is only seen at much higher doses.[5] It is frequently used in obstetric anesthesia to counteract the hypotension after spinal anesthesia due to marked arterial vasoconstriction caused by its α1 agonist action.[6] An intravenous dose of phenylephrine has immediate onset and duration of action of 5-10 min[7]. The optimum regimen for administration of phenylephrine has not yet been defined[8]. A dose of 40-100 mcg bolus dose remains the common clinical practice.[9]

Ephedrine:

It is a sympathomimetic amine that has both direct α and β agonist action, but indirect action is more prominent due to the “release of norepinephrine from sympathetic neurons”.[10] It increases the blood pressure by β1 receptor stimulation with increased heart rate and cardiac contractility, whereas the α agonist action causes peripheral vasoconstriction[11,12] As a rescue vasopressor, 5-15 mg intravenous boluses are most commonly advocated for the treatment of hypotension following neuraxial anesthesia. Its clinical effect is primarily due to its indirect action of releasing norepinephrine from postganglionic nerve endings. The drug not only has delayed onset of action, it also has a longer duration of action of about 60 min. Depletion of presynaptic norepinephrine stores also lead to tachyphylaxis.[13]

2. Mephentermine:

It is a sympathomimetic amine**.** It has a mixed α and β receptor agonist action with both direct and indirect effect due to release of norepinephrine and epinephrine[14] Tachyphylaxis to the pressor action of mephentermine develops rapidly[15] While there is immediate onset of action peaking at 5 min and lasting 15-30 min after an intravenous dose, an intramuscular dose starts acting after 5-15 min and has a variable duration of action from 1-4 h. It is commonly used as a 3-5 mg intravenous bolus or intravenous infusion of 2-5 mg/min.[16]

The aim of this study is to compare the hemodynamic effects of bolus doses of phenylephrine N(100mcg), mephentermine (6 mg) and ephedrine (6mg) in patients undergoing lower limb surgeries under spinal anesthesia.

3. Subjects and Methods:

The study was approved by the institutional ethics committee and written informed consent was obtained from all the patients before participation. Sixty patients [American Society of Anesthesiologists (ASA) physical status I and II], scheduled for elective and emergency caesarean section under spinal anesthesia will be included in the study.

Sampling method: Random sampling

Study design : Random double blind control study

The sample size was calculated based on previous studies as well as approximate availability of number of cases in the above mentioned duration satisfying inclusion and exclusion criteria in our college. Size of patients in each group was arrived at with 90% power at an alpha value of 0.05 to detect a 25% difference in the parameters studied.

Sixty patients who fulfill the above criteria will be selected for the study and will be randomized into three groups of 20 patients each using computer generated random table method.

Study groups	E	M	P
IV Bolus Drug Dose	6 mg	6 mg	100 mcg

E : Ephedrine group , M : Mephentermine group , P : Phenylephrine group

- **Brief description of procedure**

All patients selected for the study will undergo basic pre anesthetic check up and necessary investigations prior to surgery. All patients will be explained about the study procedures and written informed consent will be obtained. 18 G IV cannula is secured in all patients and Ringer lactate solution at 10 ml/kg body weight is given as pre load.

Patients will be shifted to the operation table and electrocardiogram (ECG), non invasive blood pressure monitor (NIBP) and pulse oxymeter (SpO2) probe are connected and basal readings recorded. Then patients are put to lateral recumbent position and sub arachnoid block at L2-L3 or L3-L4 is given with 2.2ml 0.5% bupivacaine heavy using 23 G Quinke Babcok needle. Midline approach will be followed for the block. Immediately after the block, patients will be repositioned to supine position and a prophylactic bolus dose of the respective drug is given IV. Vitals are recorded every 5 min for the first 30 minutes then every 10 minutes till the end of the surgery. Whenever hypotension (fall in systolic pressure >20% from the baseline value or a value less than 90mmHg) occurred the study drug will be given IV bolus. The number of boluses and time taken to develop hypotension will be noted. Bradycardia i.e. a pulse rate of 50/min or less was treated with atropine 0.6mg IV. Patients complaining of pain during surgery will be converted to general anesthesia and will be excluded from the study.

After the surgery , patients will be shifted to PACU(Post Anaesthesia Care Unit) and vitals are monitored every 15 min till modified Bromage score of 0.

4. RESULTS

1. The groups were comparable in physical characteristic.

Patient Demographic			
	Phenylephrine	**Ephedrine**	**Mephentermine**
Maternal age (Mean±SD) yrs	24.5±3.1	24.2±3.9	26.2±4.1
Maternal wt (Mean±SD) kgs	62.7±1.7	63±1.26	62.7±1.3
Maternal ht (Mean±SD) inches	65.5±4	62±4.8	65.2±6.4

2. All the three groups were similar in sensory block level

Highest sensory level

		GROUP			
		phenylephrine	Ephedrine)	Mephentermine	Total
T2	Count	1	1	1	3
	%	4.8%	4.8%	4.8%	4.8%
T4	Count	8	9	7	24
	%	42.9%	42.9%	33.3%	39.7%
T6	Count	8	7	9	24
	%	38.1%	38.1%	42.9%	39.7%
T8	Count	3	3	3	9
	%	14.3%	14.3%	19.0%	15.9%
Total	Count	20	20	20	60
	%	100.0%	100.0%	100.0%	100.0%

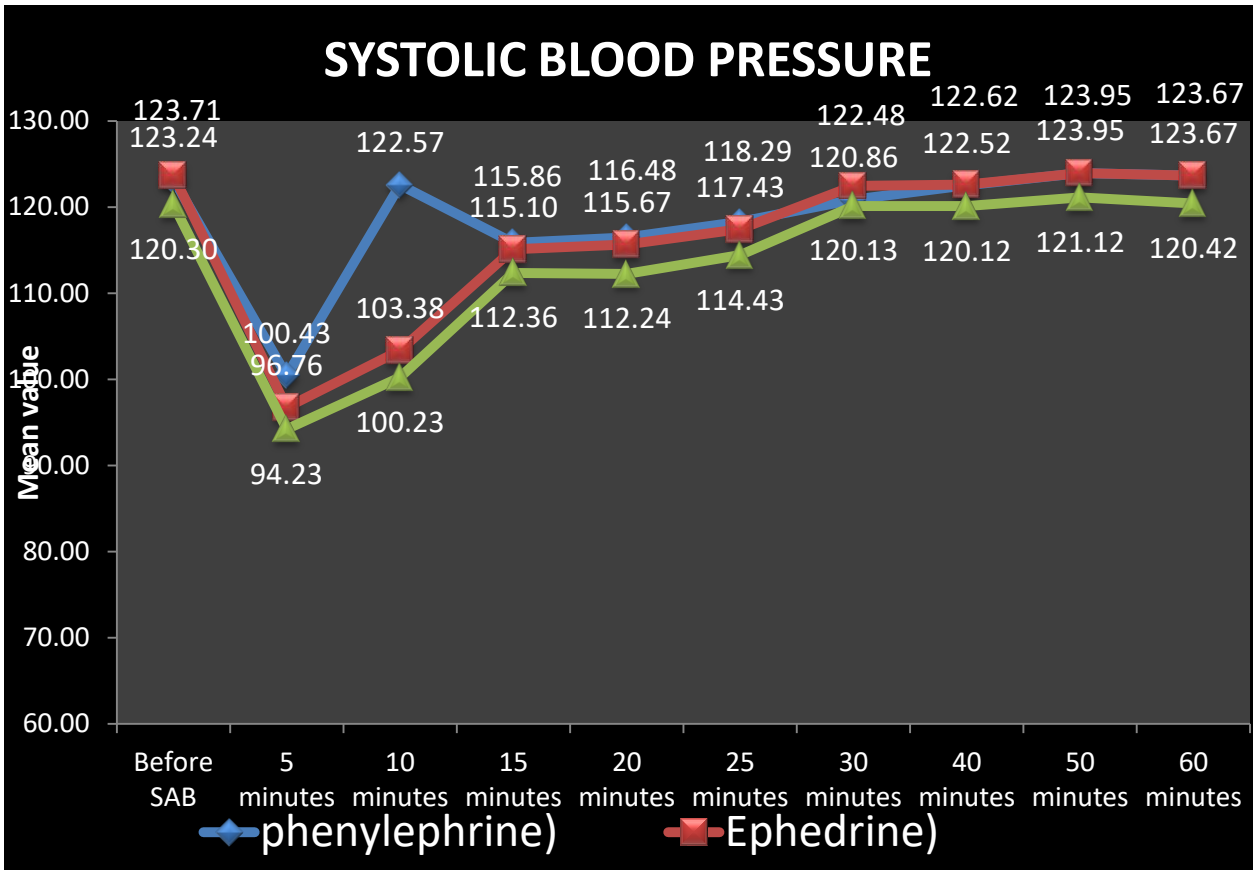
a. x2=0.6 p=0.996 ns

3. The systolic and diastolic arterial pressure were decreased statistically significant (p<0.001) at the onset of hypotension

Percentage difference from Base to 60 minutes

		N	Mean	Std. Deviation	F	p
MAP	phenylephrine	20	-2.551	8.734		
	Ephedrine	20	-3.948	6.146		
	Mephentermine	20	-7.136	5.852	2.346	.104
SBP	phenylephrine	20	-.932	10.742		
	Ephedrine	20	-.126	3.960		
	Mephentermine	20	-.125	3.964	.093	.911
HR	phenylephrine	20	1.760	14.876		
	Ephedrine	20	-15.619	16.461		
	Mephentermine	20	-15.617	16.464	8.306	<0.001 vhs

4. Comparison of systolic blood pressure over time in the three groups



Heart rate

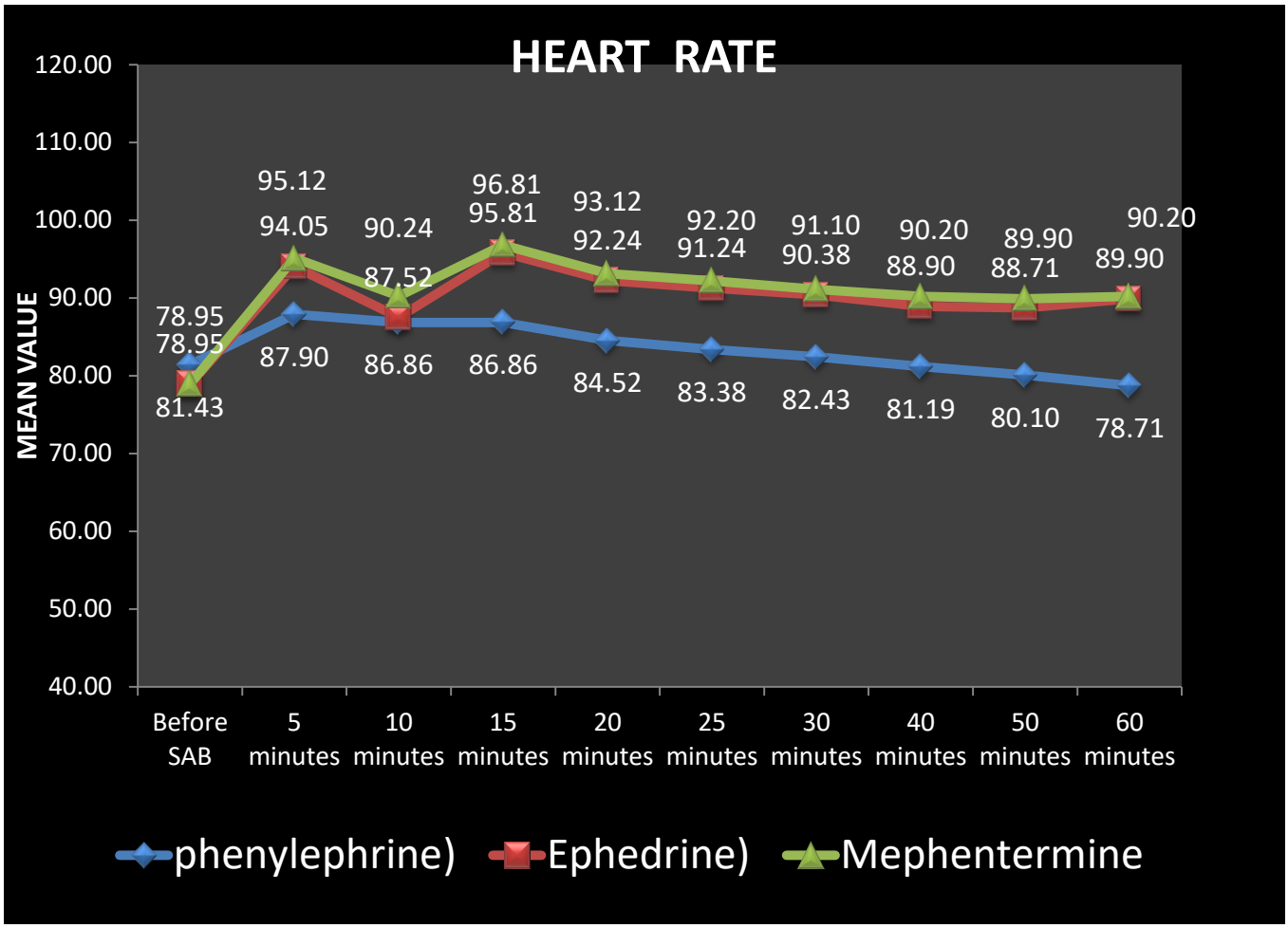
		N	Mean	Std. Deviation	F	p
Hr before SAB	phenylephrine)	20	81.429	10.220		
	Ephedrine)	20	78.952	9.872		
	Mephentermine	20	78.952	9.872	.430	.652
5 minutes	phenylephrine)	20	87.905	6.752		
	Ephedrine)	20	94.048	8.152		
	Mephentermine	20	94.048	8.152	4.440	0.016 sig
10 minutes	phenylephrine)	20	86.857	5.695		
	Ephedrine)	20	87.524	6.242		
	Mephentermine	20	87.524	6.242	.4.455	0.02
15 minutes	phenylephrine)	20	86.857	5.695		
	Ephedrine)	20	95.810	7.789		
	Mephentermine	20	95.810	7.789	10.946	<0.001 vhs
20 minutes	phenylephrine)	20	84.524	5.955		
	Ephedrine)	20	92.238	6.016		
	Mephentermine	20	92.238	6.016	11.588	<0.001 vhs
25 minutes	phenylephrine)	20	83.381	6.029		
	Ephedrine)	20	91.238	5.770		
	Mephentermine	20	91.238	5.770	12.595	<0.001 vhs
30 minutes	phenylephrine)	20	82.429	5.582		
	Ephedrine)	20	90.381	5.635		
	Mephentermine	20	90.381	5.635	14.031	<0.001 vhs
40 minutes	phenylephrine)	20	81.190	4.823		
	Ephedrine)	20	88.905	5.214		
	Mephentermine	20	88.905	5.214	16.096	<0.001 vhs
50 minutes	phenylephrine)	20	80.095	4.437		
	Ephedrine)	20	88.714	5.139		
	Mephentermine	20	88.714	5.139	21.512	<0.001 vhs
60 minutes	phenylephrine)	20	78.714	5.542		
	Ephedrine)	20	89.905	5.186		
	Mephentermine	20	89.905	5.186	31.123	<0.001 vhs

5.

*‘P’ value <0.05 indicates statistically significant. p< 0.001 is very highly significant(vhs)

Heart rate is significantly on the lower side in phenylephrine group, when compared to mephentermine and ephedrine group.

6. Comparison of heart rate over time in the three groups



Phenylephrine group has lower heart rates when compared to the other two groups.

5. DISCUSSION

This study was mainly to outline the effectiveness of the three commonly used vasopressors viz. ephedrine, mephentermine and phenylephrine in maintaining hemodynamics post spinal in ceaserian section patients. It is inferred from this study that all the three drugs maintained the systolic blood pressure within 20% limit of the baseline value. Mephentermine and ephedrine had very close characterestics in maintaining blood pressure, though phenylephrine maintained systolic blood pressure and mean arterial pressure more effectively in the first 10 minutes. Significantly lower incidence of maternal tachycardia was seen in phenylephrine group.

6. CONCLUSION

• Mephentermine,Phenylephrine and Ephedrine are equally effective in preventing post spinal hypotension in patients undergoing caesarian section.

• Phenylephrine group showed less tachycardia when compared to ephedrine and mephentermine group.

• Phenylephrine is found to be better in maintaining systolic blood pressure in the initial 10 minutes after spinal anesthesia.

• After 15 min the effectiveness of all the three drugs were similar in maintaining systolic blood pressure.

• The cumulative dose required to maintain systolic blood pressure was found to be lower in phenylephrine group.

References

1. Cook TM, Counsell D, Wildsmith JA. Royal College of Anaesthetists Third National Audit Project. Major complications of central neuraxial block: report on the Third national audit project of the royal college of anaesthetists. Br J Anaesth 2009; 102: 179-90
2. Rodgers A, Walker N, Schug S. Reduction of postoperative mortality and morbidity with epidural or spinal anaesthesia: results of overview of randomised trials. BMJ 2000; 321: 1493-7.
3. Jackson R, Reid JA, Thorburn J. Volume preloading is not essential to prevent spinal induced hypotension at caesarean section. Br J Anaesth 1995; 75: 262-5.
4. Sahu, Kothari, Mehrotra. Comparison of bolus phenylephrine, ephedrine and mephentermine for maintenance of arterial pressure during spinal anaesthesia in caesarean section : A Clinical Study. Indian J. Anaesth. 2003; 47 (2) : 125-128.
5. Westfall TC, Westfall DP. Adrenergic agonists and antagonist. Goodman and Gilman's: The Pharmacological basis of therapeutics. 11 th ed. New York: McGraw Hill, 2006: 237-295.
6. Nag, Samaddar, Chatterjee, Kumar, Dembla. Vasopressors in obstetric anesthesia: A current perspective. World J Clin Cases 2015 January 16; 3(1): 58-64.
7. Glick DB. The autonomic nervous system. In: Miller RD, Eriksson LI, Fleisher LA, editors. Miller's Anesthesia. 7th ed. Philadelphia: Elsevier, 2011: 261-304.
8. 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. Anesth Analg 2012; 114: 377-390. [PMID: 22104076 DOI: 10.1213/ANE.0b013e3182373a3e]
9. 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. Anesth Analg 2012; 114: 377-390 [PMID: 22104076 DOI: 10.1213/ANE.0b013e3182373a3e]
10. Westfall TC, Westfall DP. Adrenergic agonists and antagonists. In: Brunton LL, Lazo JS, Parker KL, editors. Goodman and Gilman's: The Pharmacological Basis of Therapeutics. 11 th ed. New York: McGraw Hill, 2006: 237-295.
11. Reidy J, Douglas J. Vasopressors in obstetrics. Anesthesiol Clin 2008; 26: 75-88, vi-vii [PMID: 18319181 DOI: 10.1016/ j.anclin.2007.11.005]
12. Kee VR. Hemodynamic pharmacology of intravenous vasopressors. Crit Care Nurse 2003; 23: 79-82 [PMID: 12961786]
13. Kol IO, Kaygusuz K, Gursoy S, Cetin A, Kahramanoglu Z, Ozkan F, Mimaroglu C. The effects of intravenous ephedrine during spinal anesthesia for cesarean delivery: a randomized controlled trial. J Korean Med Sci 2009; 24: 883-888 [PMID: 19794988 DOI: 10.3346/jkms.2009.24.5.883]
14. Hodge RL, Dornhorst AC. The clinical pharmacology of vasoconstrictors. Clin Pharmacol Ther 1966; 7: 639-647 [PMID: 5334234]
15. Fawaz G, Simaan J. The Tachyphylaxis Caused By Mephentermin And Tyramine. Br J Pharmacol Chemother 1965; 24: 526-531 [PMID: 14320866 DOI: 10.1111/j.1476-5381.1965.tb01742.x]

16. Kansal A, Mohta M, Sethi AK, Tyagi A, Kumar P. Randomised trial of intravenous infusion of ephedrine or mephentermine for management of hypotension during spinal anaesthesia for Caesarean section. Anaesthesia 2005; 60: 28-34 [PMID: 15601269. DOI: 10.1111/j.1365-2044.2004.03994.x]