

Efficacy of Bolus Administration of Ephedrine and Phenylephrine for Maintenance of Blood Pressure during Spinal Anesthesia

MUHAMMAD YOUNIS, MAZHAR IQBAL, TAHIR NAZIR

ABSTRACT

Aim: To find out the efficacy of bolus administration of ephedrine and phenylephrine for maintenance of systolic blood pressure during spinal anesthesia in patients undergoing elective caesarean section. Spinal anesthesia is a popular technique used for caesarean section associated with hypotension in a significant number of patients which are managed by colloids, vasopressor, light ephedrine and phenylephrine. To assess the efficacy of phenylephrine and ephedrine, a randomized controlled study was carried out on 200 patients [100] in each group. Over 6 months' i.e. from September 2001 to March 2012, undergoing caesarean section. When hypotension occurred group received ephedrine 5mg and group two received phenylephrine 100µgm. Systolic blood pressure was recorded at 2, 4 and 6 minutes interval. 6 minutes recording was taken as final. Chi. Square test was applied for comparison of two groups for efficacy in term of maintenance of systolic blood pressure p-value ≤ 0.05 was considered as significant. Efficacy was found in group-I in 46 patients [46%] and in group –II in 77 patients [77%]. Results were statistically significant ($P < 0.001$). It is concluded that phenylephrine is more effective in maintenance of systolic blood pressure with reduction in heart rate, especially useful in cardiac patients in whom tachycardia is undesirable.

Keywords: Efficacy, ephedrine, phenylephrine, spinal anesthesia, hypotension.

INTRODUCTION

Spinal anesthesia is a popular technique used for caesarean section. The advantages of this technique are simplicity, rapid onset, reliability, dense motor block, and avoidance of the potential airway complications associated with general anesthesia for caesarean section. The quoted incidence varies depending on the patient's status and technique but has been estimated to be as high as 85%². Hypotension occurs in a significant number of patients receiving spinal anesthesia. Hypertension is defined as 20% reduction in baseline systolic blood pressure. Maternal hypotension can be associated with severe nausea or vomiting which can pose serious risks to the mother (unconsciousness, pulmonary aspiration) and baby hypoxia, acidosis and neurological injury)³.

While interventions such as colloids, crystalloids, ephedrine, phenylephrine can reduce the incidence of hypotension^{3,4}. Pre-loading with a colloid or crystalloid solution has been a popular method to prevent the incidence of hypotension during spinal anesthesia, but it does not always provide complete prevention. Vasopressor agents are required to treat the hypotension during preoperative with a rush of colloid or crystalloid solution^{4,5}. Ephedrine, the most commonly used vasopressor agent, has

disadvantage of tachycardia. It's a non-catecholamine adrenergic agonist which acts upon α_1 , β_1 and β_2 receptors. It's because of its strong affinity to β_1 receptors, it causes tachycardia. Other adverse effects include CNS stimulation, raised MAC requirement and tachyphylaxis⁵.

Phenylephrine is a non-catecholamine adrenergic agonist which predominantly has direct α_1 agonist activity. Its primary effect is peripheral vasoconstriction and rise in systemic vascular resistance and arterial blood flow⁷. Thus the use of Phenylephrine instead of ephedrine may be beneficial to prevent and treat hypotension without having a risk of tachycardia. Bhattaral B, with his colleagues, in their study found that rise of blood pressure was significantly higher in case of phenylephrine in case of phenylephrine group in first six minutes, after the bolus, there was significant reduction in the heart rate in phenylephrine group, but there was tachycardia following administration of bolus ephedrine⁸. Mahajan with his colleagues stated that Phenylephrine provided better maintenance with less incidence of hypotension i.e., 0-5% with Phenylephrine compared to 4.2% with ephedrine following spinal anesthesia⁹. Sahu in his comparative study concluded that 80% of patients with Phenylephrine group require single bolus dose where only 45% were maintained with single dose in ephedrine group¹⁰.

Department of Anesthesiology & intensive care. Services Hospital Lahore

Correspondence to Dr. Muhammad Younis Assistant Professor. Cell: 03334543269; email: dryounisshl@gmail.com.

MATERIALS & METHODS

Efficacy was taken as maintenance of systolic blood pressure within 20% of the baseline in first 6 minutes after a single bolus administration of the drug under study. A randomized controlled study was designed at department of Anesthesia Services Hospital /SIMS, Lahore. This study was carried out over a period of six months from 28-09-2011 to 27-03-2012. Sample size of two hundred cases, (100 in each group) was calculated with 80% power of test, 1% level of significance and taking expected percentage of efficacy (as per operational definition) in both groups i.e., 80% in Phenylephrine group versus 45% in ephedrine group during spinal anesthesia in patients undergoing elective caesarean section. The sampling technique was non- probability purposive sampling. All patients between 20-35 years, female parturient scheduled to undergo elective and emergency caesarean section, ASA (American Society of Anesthesiologists) physical status I & II were included. Patient with preoperative systolic pressure less than 100Hg, Patient having diagnosed cardiac (CCF, ischemic heart disease, cardiomyopathy, mitral stenosis or any other uvular heart disease) or diagnosed respiratory disease (COPD, Asthma) and diagnosed twin pregnancy (ultrasound) were excluded from the study.

After approval from local research and ethical committee, 200 patients fulfilling the criteria were enrolled in this study from inpatient department. After an informed consent, patients were allocated randomly using random numbers table to one of the two groups comprising 100 patients each (Group I: ephedrine 5mg and group II: Phenylephrine 100µg). All patients were at fast for at least 6 hours before induction of anesthesia. All patients were monitored with ECG, heart rate, non invasive blood pressure and oxygen saturation (SpO₂) in operating room. After intravenous access with 18 G IV cannula, all patients were preloaded with Ringer Lactate solution @10ml/kg. Baseline heart rate and arterial blood pressure was noted by the researcher. Spinal anesthesia was administered in sitting position at L4-5 inter-space with 0.75%, 15mg hyperbaric bupivacaine using 25G spinal needles. Patient was then immediately turned supine and wedge placed under right flank. Oxygen was given at 4L/min with face mask. When hypotension occurred, the study drug was given as single i/v bolus. The systolic blood pressure was recorded at 2, 4 and 6 minutes interval by the researcher. The 6 minute recording of systolic blood pressure was taken as final reading. The whole information was collected through Performa (attached). Efficacy was labeled as per operational definitions.

All the collected information was entered and analyzed using SPSS version 12.0. The age was presented as mean±SD. Chi square test was applied for the comparison of two groups for efficacy in terms of maintenance of systolic blood pressure. P-value ≤0.05 was considered as significant.

RESULTS

A total of 200 cases (100 in each group) were included in this study during the study period of six months from 28-09-2011 to 27-03-2012. Regarding age distribution of patients, 53 patients (55.3.0%) in group-I and 57 patients (57%) in group II were between 20-25 years old. 29 patients (29%) in group I and 27 patients in group II were 26-30 years of age, while 18 patients (18%) in group –I and 16 patients (16%) in group-II were between 31-35 years old. Mean age was 26.9±4.3 and 25.8±4.1 in group I and Group II respectively (Table I). Efficacy was found to be from group I in 46 patients (46%) and from group-II in (77%). Results were statistically significant between two groups (P<0.001) (Table 2).

Table 1: Distribution of cases by age

Age	Group-I (Ephedrine 5mg)		Group-II (Phenylephrine 100µg)	
	No.	%	No.	%
20-25	53	53.0	57	57.0
26-30	29	29.0	27	27.0
31-35	18	18.0	16	16.0
Mean±SD	26.9±4.3		25.8±4.1	

Table 2: Distribution of cases by Efficacy

Efficacy	Group-I (Ephedrine 5mg)		Group-II (Phenylephrine 100µg)	
	No.	%	No.	%
Yes	46	46.0	77	77.0
No	54	54.0	23	23.0

Chi square=20.29

Df= 1

P-values ≤ 0.001

DISCUSSION

Caesarean section is one of the oldest operations in recorded history; however anesthesia for Caesarean section is just a century old. Over time, regional anesthesia especially spinal anesthesia proved to be the most preferred technique for Caesarean section¹¹.

The reason being the unique potential of spinal technique to provide anesthesia with a blend of low degree of physiologic trespass and with profound degrees of sensory de-nerivation and muscle relaxation. Thus, the safety of spinal anesthesia is of dual nature, pharmacological as well as physiologic. However one main hurdle with this technique is the

troublesome and persistent incidence of hypotension especially in gravid parturient. Hypotension is the commonest serious problem endangering both the mother and the child¹².

Hypotension after spinal block for caesarean section is a common clinical problem, with an increase in maternal and fetal morbidity¹³.

The sympathetic blockade causes a reduction in blood pressure as a result of the fall in systematic vascular resistance with a reduction in venous return leading to a fall in cardiac output and occasionally heart rate¹⁴.

The fall in blood pressure has immediate maternal and fetal repercussions. Maternal symptoms include nausea, vomiting, and feeling of impending doom due to a reduction in cerebral reperfusion, and inadequate treatment of hypotension can lead to loss of consciousness and cardiac arrest. The fetus is affected immediately because uterine flow depends on maternal blood pressure¹⁵. An isolated method that prevents hypotension during caesarean section does not exist¹⁶.

The use of crystalloids before spinal block is practically ineffective because, despite the previous volume expansion, 85% of the patients develop hypotension. This happens because crystalloids are rapidly redistributed and induce the secretion of natriuretic peptide, leading to peripheral vasodilatation and extravagation of fluid to the third space. Administration after the spinal block can be useful because it increases the intravascular fluid during the period of maximal risk of hypotension and facilitate the rapid circulation of the vasopressor. It is important to fully understand the hemodynamic responses to choose properly, the vasopressor and clinical dose¹⁷.

The ideal vasopressor should have a low cost, be readily available, have a fast onset of action, be reliable, and have favorable effects in maternal heart rate, fetus, and placement perfusion. Phenylephrine is considered the first drug of choice and its efficacy and safety during caesarean section have been thoroughly investigated. This is a synthetic non-catecholamine drug, but its function is similar to that of nor-epinephrine with direct action in the adrenergic receptor. It promotes vasoconstriction especially arterial by increasing systematic vascular resistance, and therefore increasing preload.

In the present study, Group-I, received ephedrine 5mg and group-II, received Phenylephrine 100µg. Thomas et al¹⁸ reported that bolus Phenylephrine 100mg is as effective as ephedrine 5mg restoring maternal arterial pressure above 100Hg.

Moran et al¹⁹ gave ephedrine 10mg or Phenylephrine 80µg IV bolus to maintain systolic

arterial pressure above 100mmHg. They concluded that Phenylephrine is as effective as ephedrine and when used in small incremental bolus injections, it appears to have no adverse neonatal effects in healthy, non laboring parturients. Ramanathan et al²⁰ studied in 127 healthy patients undergoing elective caesarean section under epidural anesthesia. They concluded that transient maternal hypotension does not affect neonatal acid-base status, both ephedrine and Phenylephrine increase cardiac preload and agent like Phenylephrine does not cause fetal acidosis, when used for treating maternal hypotension.

In current study, when Phenylephrine compared with ephedrine, Phenylephrine causes significant increase ($P < 0.001$) in systolic blood pressure during spinal anesthesia in patients undergoing elective caesarean section. Which is consistent effect in Phenylephrine treated women in other studies also²¹. In spinal anesthesia, since there is decreased venous return, decreased venous pressure and a decreased right heart pressure thus slowing of the heart rate is expected on the basis of the Brain-bridge reflex. Bradycardia is also expected in high spinal, probably due to some paralysis of the cardiac accelerator nerve.

Sahu et al found that maternal hypotension during spinal anesthesia for Caesarean delivery was a persistent problem in approximately 85% of cases. This high incidence and severity of maternal hypotension following spinal anesthesia could be attributed to various factors like the amount of local anesthetic injected, sympathetic blockade, uterus impairing venous return from extremities in supine position etc²².

CONCLUSION

It is concluded, that Phenylephrine, is effective in IV bolus form in maintenance of systolic pressure within 20% limit of baseline, through Phenylephrine has quicker peak effect in comparison to ephedrine and it causes reduction in heart rate, which may be advantageous in cardiac patients and patients in whom tachycardia is undesirable.

REFERENCES

1. Cyna AM Andrew M, Emmett RS, Middleton P, and Simmons SW. Techniques for preventing hypotension during spinal anesthesia for caesarean section. *Cochrane Database Syst Rev* 2006; 18:CD002251.
2. Kee WN. Treatment of spinal hypotension : proactive or reactive? *ESA* 2004;6:2009-12.
3. Ngan-Keen WD, Khaw KS, and Ng FF. Prevention of hypotension during spinal anesthesia for cesarean

- delivery: an effective technique using combination phenylephrine infusion and crystalloid cohydration. *Anesthesiology* 2005; 103:744-50.
4. Siddik-Sayyid SM, Nasr CG, Taha SK, Zebeid RA, Sheade JM, Al Alami AA, et al. spinal anesthesia for elective cesarean delivery. *Anesth Analg* 2009; 109:1219-24.
 5. Adigun TA, Amanor-Boadu SD, Soyannwo OA. Comparison of intravenous ephedrine with Phenylephrine for the maintenance of arterial blood pressure during elective caesarean section under spinal anesthesia. *Afr J Med Med Sci* 2010; 39:13-20.
 6. Morgan GE Jr, Mikhail MS, Murray MJ. *Clinical anesthesiology*. 4th ed. Philadelphia: McGraw –Hill Companies, Inc. 2006.p.247-9.
 7. Imran M, Khan FH, Khan MA. Attenuation of hypotension using Phenylephrine during induction of anesthesia with propofol. *J Pak Med ASSoc* 2007; 57:543-7.
 8. Bhattarai B, Bhat SY, Upadya M. Comprison of bolus Phenylephrine, ephedrine and mephentermine for maintenance of arterial pressure during spinal anesthesia in ceasarean section. *JNMA J Nepal Med Assoc* 2010; 49:23-8.
 9. Mahajan L, Anand LK, Gombar KK. A randomized double-blinded comparison of ephedrine, Phenylephrine and mephentermine infusion to maintain blood pressure during spinal anestehisa for cesarean delivery: The effects on fetal acid-base status and haemodynamic control. *J Anesth Clin Pharmacol*2009; 25:427-32.
 10. Sahu D, Kothari D, Mehrotra A. Comparison of Bolus Phenylephrine, Ephedrine, and Mephentermine for maintenance of arterial pressure during spinal anesthesia in caesarean section – a clinical study. *Indian J Anesth* 2003; 47:125-8.
 11. Croke BC, Datta S, Ostheinar GW. Spinal Anesthesia for caesarean section. The influence of hypotension on neonatal outcome. *Anesthesia* 1982; 37:658-62.
 12. Jackson R, Ried JA, Thorburn J. Volume preloading is not essential to prevent spinal induced hypotension at caesarean section. *Br. J Anesthesia* 1995;75:262-5.
 13. Tanaka M, Balki M, Parkes RK. ED95 of Phenylephrine to prevent spinal- induced hypotension and /Or nausea at elective ceasarean delivery. *Int J Obset Anesth* 2009; 18:125-8.
 14. Ngan Kee WD, Khaw KS. Vasopressors in obstetrics: what should we be using? *Curr Opin Anesthesiol* 2006; 19:238-83.
 15. Macarthur A, Riley ET. Obstetric anesthesia controversies: vasopressor choice for posspinal hypotension during cesarean delivery . *Int Anesthesiol Clin* 2007; 45:115-32.
 16. Langesaeter E, Rosseland LA, Stubhaug A. Continuous invasive blood pressure and cardiac output monitoring during cesarean delivery: a randomized, double-blind comparison of low-dose versus highdose spinal anesthesia with intravenous phenylephrine or plavebo infusion. *Anesthesiology* 2008; 856-63.
 17. Dyer RA, Reed AR, van Dyk D. Hemodynamic effects of ephedrine, Phenylephrine, and the coadministration of Phenylephrine with oxytocin during spinal anesthesia for elective cesarean delivery. *Anesthesiology* 2009; 111:753-65.
 18. Thomas DG, Robson SC, Redfern N, Hughes D, Boys RJ. Randomized trial of bolus Phenylephrine or Ephedrine for maintenance of arterial pressure during spinal section. *Br J Anesth*1996:76:61-5
 19. Moran DH, Dutta S, Perillo M, Laporta RF, Bader A. Phenylephrine in the prevention of hypotension following spinal anesthesia for Caesarean delivery. *J Clin Anesth* 1991; 3:301-5
 20. Ramanathan S, Grant GJ. Vasopressor therapy for hypertension due to epidural anesthesia for caesarean section. *Acta Anesthesiol Scand* 1988; 32:559-65.
 21. Hall PA, Bennet A, Wilkes M.P. Lewis M. Spinal anesthesia for Caesarean section: comparison of infusions of Phenylephrine and Ephedrine. *Br J Anesth* 1994; 73:471-4.
 22. Crocke BC, Datta S, Ostheinar GW. Spinal anesthesia for caesarean section. The influence of hypotension on neonatal outcome. *Anesthesia* 1982; 37:658-62.