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HYPOTENSION AFTER SPINAL ANAESTHESIA;

EFFICACY OF EPHEDRINE AND PHENYLEPHRINE FOR TREATMENT DURING ELECTIVE CAESAREAN SECTION

Dr. Aijaz Ali, Dr.Shmyla Hamid, Dr.Raja Mushtaq Hussain, Dr. M.Rashid Iqbal, Dr.Raza Ali Abidi

ABSTRACT... Objective: Aim of the study is to compare the efficacy of Ephedrine and Phenylephrine for treatment of hypotension after spinal anaesthesia for elective caesarean section. **Study design:** Randomized Clinical Trial. **Setting:** Operation theatre Department of Anaesthesiology, Combined Military Hospital Quetta. **Duration of study:** Six month from 16th Sep 2011 to 15th March 2012. **Material and Method:** Seventy women undergoing LSCS for singleton pregnancy under spinal anesthesia were randomly assigned in group A and B (35 in each group). All patients preloaded with Lactated Ringer's solution 15ml/kg body weight 10 minutes before administration of spinal anaesthesia. Mean Arterial Pressure (MAP) was recorded before administration of spinal anaesthesia considered as Base-line MAP and then at 1 Minute, 3 minutes & at 5 minutes after administration of spinal anaesthesia. When hypotension developed (MAP falls >20% from base line), intravenous single dose of ephedrine administered in group A patients, while in group B, Phenylephrine was given. Blood pressure was recorded after 1 minute following drug administration and up to 3 minutes at 1 minute interval. Patient handed over for procedure after 10 minutes of spinal block. The SPSS version 13 was applied to the data. Mean and standard deviation were computed for numerical variables like age, weight, height, systolic blood pressure, Diastolic blood pressure, and Mean Arterial pressure; whereas frequency and percentages were employed to assess the categorical variable like efficacy. Chi-square test was used to compare the efficacy of intravenous bolus of ephedrine and phenylephrine. Statistical significance was taken at $p<0.05$. **Results:** There was significant difference in the efficacy of both the drugs, in the treatment of maternal hypotension. 74.29% were successfully treated in group "A" with a single dose of Ephedrine, as compared to group B where 51.43% were successfully treated with a single dose of Phenylephrine. (p-value = 0.048). **Conclusions:** Intravenous ephedrine has more efficacy than phenylephrine in the treatment of maternal hypotension after spinal anesthesia for elective cesarean section.

Key words: Ephedrine, Phenylephrine, Spinal Anesthesia, LSCS, MAP, Maternal Hypotension

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INTRODUCTION

The number of caesarean delivery is steadily increasing in recent times and most common indications for caesarean delivery include prior caesarean delivery (35%), dystocia (14%), breech presentation (12%), non-reassuring fetal heart rate pattern (9%) and others (30%)[1]. There are five practical methods of providing anaesthesia for elective caesarean section each with its pros and cons[2]. When choosing regional or general anaesthesia for caesarean delivery, one must consider outcome for both the mother and neonate. The speed and reliability of general anaesthesia is sometimes forgotten in the detailed consideration of its disadvantages. Spinal Anaesthesia is a commonly practiced mode of regional anaesthesia for patients undergoing lower segment caesarean section (LSCS). The common complication of spinal anaesthesia is hypotension which may explain the decreased umbilical artery pH and decreased APGAR score as compared with both epidural and general anaesthesia[3]. Hypotension after spinal anaesthesia for caesarean section has an incidence of up to 80% without prophylactic management[4]. It can have detrimental effects on both mother and neonate; these effects include decreased uteroplacental blood flow, impaired fetal oxygenation and fetal acidosis, and maternal symptoms of low cardiac output, such as nausea, vomiting, dizziness, and decreased consciousness[5]. Hypotension due to spinal anaesthesia is usually prevented by fluid preload, lateral tilt, use of leg binders, Thromboembolic stockings[6]. Epidural Volume Extension (EVE)[7-9] and use of vasopressors. Ephedrine and Phenylephrine are the most widely used

vasopressors[10]. Recent studies have not shown intravenous crystalloid prehydration to be very effective. Colloids are more effective but are expensive and have potential adverse effects[11]. Rapid infusion of intravenous crystalloid after induction (cohydration) appears more effective than prehydration. Traditionally, ephedrine is the drug of choice in obstetric anesthesia, "which has a strong α-adrenergic and a weaker α-adrenergic effects" its low propensity to reduce uteroplacental blood flow but its position has been challenged because of potential complication that supra- ventricular tachycardia, tachyphylaxis, and most importantly fetal acidosis[12], recent studies support use of α-agonists such as Phenylephrine, can be used for prevention and treatment of maternal hypotension, it reduces the incidence of nausea and vomiting as well as fetal acidosis, but it may cause maternal bradycardia[13]. However some authors still suggested that ephedrine is a more potent vasopressor than phenylephrine but some current evidence suggests that Phenylephrine is more suitable than ephedrine in obstetrics[14]. Still there is no final consensus about the appropriate choice of vasopressor in prevention and treatment of post spinal hypotension as well as no local literature available to support this fact.

The aim of this study was to compare the efficacy of intravenous bolus of ephedrine and phenylephrine in the treatment of maternal hypotension after spinal anesthesia for elective cesarean so that appropriate vasopressor drug will be opted in the future to overcome this morbidity.

MATERIAL AND METHOD

Study design

Randomized Clinical Trial

Setting

Operation theatre. Department of Anaesthesiology, Combined Military Hospital Quetta.

Duration of study

Six month from 16th Sep 2011 to 15th March 2012.

Sample size

- The sample size was calculated by using WHO sample size calculator.
- Level of significance 5%.
- Power of the test 80%.
- Anticipated population proportion1 (P1) is 70% and population proportion 2 (P2) is 93%.
- Sample size is 35 in each group.

Sampling technique

Consecutive sampling.

Inclusion Criteria

- Patients having American Society of Anaesthesiology (ASA) status -1.
- Patients age between 20 – 35 years.
- Patients undergoing planned elective caesarean section and developing hypotension.

Exclusion Criteria

- Patients who are unwilling for the study.
- Patients with cardiovascular, pulmonary, renal or liver disease.
- Emergency caesarean section.
- Twin pregnancy.
- Patients having history of drug allergy.
- Failed spinal block

DATA COLLECTION PROCEDURE

After approval from Ethical review committee of Combined Military Hospital Quetta, informed consent taken. A total of seventy women undergoing elective caesarean section; fulfilled the inclusion criteria, were included in the study.

Patients developed hypotension divided randomly into two equal groups, A and B (35 patients in each group based on table of random numbers to minimize sampling bias.

After routine check of anesthesia equipments and resuscitation trolley, non-invasive blood pressure monitor (NIBP) on Dynamap, pulse oximeter and ECG monitor were applied for measuring blood pressure, pulse rate, oxygen saturation and ECG respectively. Base line vitals were obtained followed by maintenance of intravenous access with two 18 gauge cannulae. All patients preloaded with Lactated Ringer's solution 15ml/kg body weight 10 minutes before administration of spinal anaesthesia. Mean Arterial Pressure (MAP) will be recorded before administration of spinal anaesthesia considered as Base-line MAP and at 1 Minute, 3 minutes and at 5 minutes interval after administration of spinal anaesthesia by trainee anaesthesia or Anaesthetist incharge of case. When hypotension develops, intravenous single dose of ephedrine 0.25mg/kg/B.Wt was administered in patients of group A, while Phenylephrine 1ug/kg/B.Wt as a single IV bolus was given to women of group B ,and MAP recorded after 1 minute following drug administration and up to 3 minutes at 1 minute interval. The Anaesthetist would be blind regarding the drug. All these readings will be entered in a proforma by trainee Anaesthesia. The spinal block will be achieved by 2ml of 0.75% Abocain spinal (15 mg Hyperbaric Bupivacain) at L3-L4 interspace level with 25G Quincke spinal needle. Patient will be handed over for procedure after 10 minutes of spinal block.

Confounding variables were controlled by excluding those who were hypertensive, pre-eclamptic or eclamptic, and hyperthyroid; those who had contraindication to spinal anesthesia; and those who had history of hypersensitivity to local anesthesia. Stratification was also performed to control confounders. To minimized bias, all procedures were performed by senior residents (postgraduate trainee 3rd - 4th years) under supervision of consultant anesthetist and all data were filled by independent observer who monitored the patient.

DATA ANALYSIS

Data was analyzed by using SPSS version 13.0 on computer. Mean and standard deviation were computed for numerical variables like systolic blood pressure, Diastolic blood pressure, and Mean Arterial pressure, age, weight, and height; whereas frequency and percentages were employed to assess the categorical variable like efficacy of vasopressor. Chi-square test was used to compare the efficacy of intravenous bolus of ephedrine and phenylephrine and final outcome. Statistical significance was taken at $p<0.05$. Stratification was done with regard to age, weight, height and to observe effectiveness on outcome.

RESULTS

In our study, a total of seventy patients undergoing elective cesarean section in spinal anesthesia, were identified who fulfilled the inclusion criteria. They were randomly allocated in group A and B. Each group comprised of 35 women. Intravenous ephedrine was administered in group "A" women; however, intravenous phenylephrine was given in women of group "B". Efficacy of intravenous bolus of ephedrine and phenylephrine in the treatment of maternal hypotension after spinal anesthesia for elective cesarean section was then determined. The mean age, height and weight were similar in both the groups (Table-I) In group A mean (+SD) SBP, DBP, and baseline MAP were, 129.05 (±12.99) mmHg, 81.1429 ± 10.96 mmHg, and 98.37 (±11.59) mmHg respectively; while in group B, mean (+SD) SBP, DBP, and baseline MAP recorded were 135.28 ± +11.67 mmHg, 83.91 ± 11.48mmHg, and 103.62 (±11.74) mmHg respectively. In group A mean (+SD) MAP recorded as baseline, @1, @3 and 5min were 98.37 (+11.59), 74.08 (+18.66) mmHg, 67.80 (+18.08) mmHg, and 71.94 (+14.48) mmHg, while in group B mean (+SD) MAP baseline, @1, @3 and 5min were 103.62 (+11.74), 78.91 (+15.00), 68.65 (+16.09) mmHg, and 73.40 (+16.16) mmHg respectively(Table-II). This study showed that

Intravenous single bolus of ephedrine was effective in correcting hypotension in twenty six, 74.29% women, while phenylephrine corrected hypotension only in eighteen, 51.43% women. Hypotension in nine, 25.71% women of group A had not been corrected by single intravenous bolus of vasopressor, whereas hypotension in Seventeen, 48.57% patients of the group B had not been corrected after vasopressor. More patients in group B were developed hypotension than group A (p-value = 0.048) as shown in (Table-III)

	Group A	Group B
	Mean (SD)	Mean (SD)
Age (yrs)	27.8±4.02	28.3±4.12
Height (cm)	155.85±6.2	156.92±4.8
Weight (kg)	72.68±7.65	67.91±7.93

Table-I. Demographic distribution

MAP (mm of Hg)	Group A (Ephedrine group) (n=35)	Group B (Phenylephrine group) (n=35)
Systolic	129.05±12.99	135.28±11.67
Diastolic	81.1429±10.96	83.91±11.48
Baseline MAP	98.37(±11.59)	103.62(±11.74)
MAP @ 1 min	74.08(±18.66)	78.91(±15.00)
MAP @ 3 min	67.80 (±18.08)	68.65 (±16.09)
MAP @ 5 min	71.94 (±14.48)	73.40 (±16.16)

Table-II. Baseline patient vitals distributions in both groups (n=70)

Effective against hypotension	Group A (Ephedrine group) (n=35)	Group B (Phenylephrine group) (n=35)	*p-value
Yes	26 (74.29%)	18 (51.43%)	0.048
No	9 (25.71%)	17 (48.57%)	

Table III: Effective against Hypotension (n=70)

DISCUSSION

The result of current study showed a significant effectiveness of ephedrine, it was 74.29% effective in the treatment of hypotension after spinal anesthesia in women undergoing LSCS, while phenylephrine was 51.43% effective against hypotension. Hence, parenteral ephedrine bolus was more effective in preventing maternal hypotension during caesarian section than phenylephrine parenteral bolus.

Half a million women die each year because of pregnancy related complications, 95% of these belongs to the developing world[15,16]. High maternal and neonatal mortality and morbidity rate in Pakistan, due to birth related complications, approximately thirty thousand women die every year[17]. Epidural and spinal anesthesia are blessing in this regard. Failed intubation in general anesthesia is one of the cause of maternal deaths world wide as well as in Pakistan[18]. It is recommended that each and every cesarean section should be performed under spinal anesthesia, until and unless there is any contraindication for this techniques.

Hypotension after spinal anesthesia has remained the major issue of concern in anesthetic practice especially in obstetric, because of its detrimental effects on mother and fetus. Different methods has been used to address this problem, including the use of vasopressor drugs particularly ephedrine and phenylephrine to combat this problem, combined therapy e.g. fluid preload and vasopressors provide the best overall preventive management strategy. Unfortunately, use of vasopressor drugs is still debatable and uncommon in Pakistan because of lack of familiarity of their use and free availability. Furthermore, in international literature, many controversies exist regarding the appropriate choice of vasopressor drug.

Historically, ephedrine has been recommended as the best vasopressor in obstetrics. Animal studies

showed it caused less reduction in uterine blood flow compared with alpha-agonists[19]. Ephedrine is associated with a dose dependent depression of fetal pH and base-excess[20-21]. There is a suggestion that in the compromised, already acidotic fetus, this ephedrine related acidosis could become clinically relevant, and some authors now recommend phenylephrine as the first line vasopressor. However, some authors still suggested that ephedrine is a more potent vasopressor than phenylephrine and neonatal outcomes appear unaffected with the use of this vasopressor drug.

Hence, considering the debate, this study was conducted at Department of Anesthesiology, Combined Military Hospital Quetta, in an endeavor to resolve this issue. In this study, parenteral bolus dose of ephedrine (0.25mg/kg body weight) and phenylephrine (1microgram/kg body weight) were administered in women, assigned in two equal groups "A" and "B", who underwent elective caesarian section. The efficacy of both vasopressors was observed in treating maternal hypotension after spinal anesthesia. This was based on the hypothesis that there is significant difference in treating the hypotension with intravenous bolus of ephedrine and phenylephrine after spinal anesthesia for caesarian section.

On evaluating the control of hypotension, several studies have demonstrated with similar efficacy of ephedrine and phenylephrine on the prevention and treatment of this complication, both when used in bolus or continuous infusion.

Ayorinde and co-workers randomly assigned one hundred and eight women into parenteral ephedrine and phenylephrine groups underwent elective cesarean section[22]. They reported that phenylephrine 4 mg administered intramuscularly was clinically similar to ephedrine 45 mg given by the same route.

In another study Moran and colleagues[23] randomly assigned sixty patients into two groups to assess maternal hypotension receiving IV bolus of ephedrine and phenylephrine. They concluded that phenylephrine if used in small incremental bolus injections is as effective as ephedrine in the treatment of maternal hypotension, and, it appears to have no adverse neonatal effects in healthy, non-laboring parturient.

On the contrary, this study showed significantly lower efficacy of phenylephrine in treating hypotension than ephedrine, demonstrated by the number of patients who developed hypotension after intravenous bolus. Intravenous single bolus of ephedrine was effective in correcting hypotension in twenty six, 74.29% women, while phenylephrine corrected hypotension only in eighteen, 51.43% women. Hypotension in nine, 25.71% women of group A had not been corrected by single intravenous bolus of vasopressor, whereas hypotension in Seventeen, 48.57% patients of the group B had not been corrected after vasopressor. More patients in group B were again developed hypotension than group A.

CONCLUSION AND RECOMMENDATIONS

In summary, intravenous ephedrine is more effective than phenylephrine in the treatment of maternal hypotension after spinal anesthesia for elective cesarean section. Therefore, it should be used routinely after spinal anesthesia for cesarean section to avoid this morbidity.

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AUTHOR(S):

1. **DR. AIJAZ ALI**
   FCPS Part-II Trainee Anaesthesia
   Combined Military Hospital
   Quetta cantt
2. **DR. SHMYLA HAMID**
   Quetta Institute of Medical Sciences
   Quetta Cantt
3. **DR. RAJA MUSHTAQ HUSSAIN, FCPS**
   Department of Anaesthesia
   Combined Military Hospital
   Quetta cantt
4. ***Dr. M. Rashid Iqbal, FCPS***
   Department of Anaesthesia
   Combined Military Hospital
   Quetta cantt
5. ***Dr. Raza Ali Abidi***
   FCPS Part-II Trainee Anaesthesia
   Combined Military Hospital
   Khariyan cantt

Correspondence Address:
Dr. M. Rashid Iqbal
Department of Anaesthesia
Combined Military Hospital
Quetta Cantt
rashid_203@yahoo.com

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