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COMPARISON BETWEEN EPHEDRINE AND PHENYLEPHRINE IN THE PREVENTION OF POST SPINAL HYPOTENSION DURING ELECTIVE CESAREAN SECTION

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ABSTRACT

Objective: To compare the effectiveness and safety of ephedrine compared with phenylephrine given prophylacticaly in the prevention of maternal hypotension during spinal anaesthesia for elective cesarean delivery.

Material and Methods: This study was conducted in the Department of Anesthesia at Khyber Teaching Hospital, Peshawar during a period of one year. The study design was randomized controlled trail. 134 patients under going elective cesarean section by spinal anaesthesia were randomly divided into two groups. Group E (n = 67) received prophylactic dose of ephedrine 10mg IV and group PE (n = 67) received prophylactic Phenylephrine 80 μgm IV. Hypotension (blood pressure < 80% of baseline value) was treated with bolus administration of vasoconstrictor at 50% of initial dose. Incidence of hypotension, reactive hypertension, bradycardia, nausea vomiting and apgar score (in 1st and 5th minute) were evaluated.

Results: Demographic parameters such as age, weight and American Society of Anestheslogist (ASA) class, had similar distribution in both the groups. Hypotension was found higher in phenylephrine group which was 34.3% while 28.4% in ephedrine group although statistically it was found insignificant with p-value=0.288 with chi square test. The incidence of nausea, vomiting and bradycardia were found higher in phenylephrine group. The apgar score was equal in both groups after 1st and 5th minute.

Conclusion: Ephedrine was found to be more effective than phenylephrine in the prevention of maternal hypotension and with fewer side effects.

Key Words: Obstetric anaesthesia, hypotension, ephedrine, phenylephrine, cesarean section.

INTRODUCTION

Spinal anaesthesia is nowadays considered the standard anesthetic technique for elective cesarean section[1] due to its cost effectiveness making it relatively inexpensive and with less amount of surgical hemorrhage[2]. However, hypotension being a major limitation to this technique, the incidence of which is more than 80% without any prophylactic measures[3]. Hypotension, with or without bradycardia, has detrimental effects on both mother and fetus[4]. Maternal symptoms include reduced cardiac output, nausea vomiting and altered level of consciousness.

The incidence of hypotension can be lowered by several ways; however over the last few years there is a trend to rely more on vasopressors than either crystalloid or colloid alone. Simple methods of preventing hypotension, such as IV preload and left uterine displacement, have generally not been effective alone, thus prophylactic ephedrine/ phenylephrine has been considered.

Ephedrine remains one of the extensively studied vasopressors used to treat hypotension in obstetric population. It has both direct and indirect mechanism of action, stimulating mainly beta receptors (b_1 and b_2), causing increased cardiac output, heart rate and systolic and diastolic blood pressure. Thus it returns uterine blood flow towards normal[5]. It may be used prophylactically or therapeutically as intravenous boluses of 5-10 mg or an infusion (0.01%), which can be titrated to maintain blood pressure in the appropriate range.

Phenylephrine, a selective α_1 adrenergic agonist, has been suggested to be as effective as ephedrine in the treatment of spinal hypotension. If tachycardia is undesirable phenylephrine may be better than ephedrine. It may be given IV in 20-100 μgm increments. It has the advantage of not being inotropic or chronotropic and so it strictly elevates the blood pressure with out increasing the heart rate or contractility. This is especially useful if the heart is already tachycardiac and/or has a cardiomyopathy.

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The hypothesis of this study being, if ephedrine is found to be effective than phenylephrine so we will suggest it to be routinely used in the prevention of maternal hypotension during spinal anesthesia for elective cesarean section.

MATERIAL AND METHODS

This study was conducted in the Department of Anesthsia at Khyber Teaching Hospital, Peshawar during a period of one year from October 2010 to October 2011. After approval by the hospital ethical committee informed written consent was obtained from the patients included in the study. All patients had pre anesthetic examination and assessment done. Patients with history of pregnancy induced hypertension (PIH), chronic hypertension, cerebrovascular disease, fetal abnormality, history of allergy to drugs used, severely anaemic (<10mg/dl) and other contraindications to spinal anesthesia (bleeding tendencies, valvular heart disease, low backache, sepsis) were excluded from the study to control confounders and bias in the study results.

A total of 134 patients (which were calculated at WHO software for sample size determination with hypotension 70% vs 93% in ephedrine vs. phenylephrine respectively[9], with 95% power of test and 95% confidence level) scheduled for elective cesarean section by spinal anesthesia were divided into Group E (n = 67) received prophylactic dose of ephedrine 10mg IV and group PE (n = 67) received prophylactic dose of phenylephrine 80 μgm IV. First patient was randomly assigned through lottery method and each next patient was allotted alternatively to one of the two groups, keeping double blinding through out the study. Patients belonging to ASA I & II scheduled for elective cesarean section with single fetus, within age group 18 to 40 years were included in the study.

On arrival to the operating room, all patients had received 1000ml bolus of lactated ringer solution through an 18 gauge IV cannula prior to the neural block. Baseline blood pressure and heart rate were recorded. The patients were than positioned in sitting posture, cleaned, draped and received spinal anaesthesia with 23-25G spinal needle between L3-4 or L4-5 interspaces. 2ml of hyperbaric bupivacaine (15mg of 0.75%) was given after identification of cerebrospinal fluid. Immediately after sub-arachnoid block all patients were placed supine with left uterine displacement to avoid aorto-caval compression. The block was maintained at T_5-T_6 level in all patients and the surgery allowed to start. At the time of intrathecal injection, group E patients had received a prophylactic IV dose of 10mg ephedrine and group PE had received a prophylactic IV dose of 80 μmg of phenylephrine. Maternal blood pressure (BP), peripheral oxygen saturation (S_PO_2), pulse rate, nausea vomiting and fetal Apgar score were recorded. BP was monitored every 2 min for the 1st 10 min, every 5 min from 10-30 min and every 15 min from 30-60 min. Neonatal monitoring was performed by the attending neonatologist at 1st and 5th min using apgar scoring ratio. Maternal hypotension was taken as a blood pressure < 80% of the baseline value and when occurred, was treated with bolus 50% of the initial dose of vasopressors. Reactive hypertension was considered as blood pressure 20% higher than the baseline level after use of vasopressors. Heart rate below 50 beats per minute (bpm) was characterized as bradycardia when accompanied by hypotension and was treated with atropine 0.01mg/Kg IV bolus.

Neonatal outcome (as acid-base status, hypoxaemia) could not be monitored due to technical deficiencies. Data was collected by anesthetist through pre designed performa and the analysis was done through statistical package for social sciences (SPSS Version 11).

RESULTS

Majority of the patients had age 26-30 years in both the groups. The average age was 25.8±5.03SD in ephedrine and 25.6±4.93SD in phenylephrine group and was insignificant with p-value=0.897. Similary, majority of the patients have weight 75-80kg in both groups with average weight of 80Kg ± 5.29SD in ephedrine and 78±4.82SD in phenylephrine group. While ASA class I and II were also insignificantly distributed in both the groups with p-value of 0.302. Table 1.

Hypotension was compared and found higher in phenylephrine group which was 34.3% while 28.4% in ephedrine group although statistically it was found insignificant with p-value=0.288 with chi square test. Graph 1.

When side effects were observed, it was shown that nausea was significantly higher in phenylephrine as compared to ephedrine with p-value=0.003.

Table 1: Age weight and ASA classes

	Group		
	Ephedrine (E)	Phenylephrine (PE)	
	Mean±SD	Mean±SD	p-value
Age	25.8±5.03SD	25.6±4.93SD	0.897
Weight	74.5±3.89SD	78.09±3.99SD	0.456
ASA			
Class I	34(50.7%)	38(56.7%)	0.302
Class II	33(49.3%)	29(43.3%)	

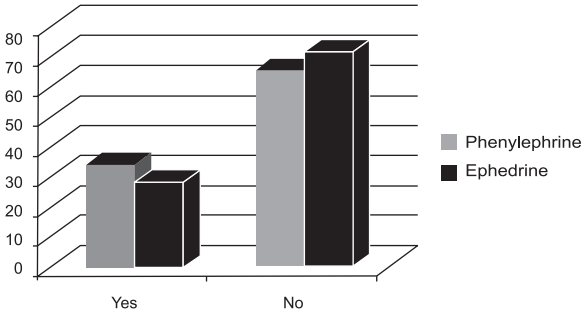

Fig. 1

Similarly, vomiting and reactive hypertension was also higher in phenylephrine group, although it was insignificant statistically in both the groups.

Stratification of hypotension among age show that majority of the patients 61(45.5%) have come with age 26-30 years of age followed by 20-25 years of age which were 41(30.6%) while the age above 36 years have no hypotension found and hypotension have statistically insignificant role over age with p-value=0.056. The neonatal Apgar score of both the groups showed scoring >8 at one minute and 05 minutes respectively.

DISCUSSION

The indication of regional block in obstetrics has gained acceptance due to the reduction in maternal and fetal morbidity and mortality[6]. Moving the uterus to the left and pre-loading with intravenous fluids have been used to reduce the severity of hypotension, but with limited efficacy, as recent studies have demonstrated the inefficacy of prior hydration due to fast redistribution[7]. In our study, parameters associated with post spinal hypotension were controlled in order to evaluate which drug would be more effective in the prevention of hypotension. The administration of vasopressors is frequently necessary[8].

In our study, phenylephrine showed lower efficacy (34.3%) on the prevention of hypotension than ephedrine (28.4%) demonstrated by the number of patients who developed hypotension. Magalhaes E et al also reported more episodes of hypotension in phenylephrine group than in ephedrine group[9]. This probably was secondary to the shorter duration of action of this vasopressor and the way it was administered, as a prophylactic bolus, repeating it only when blood pressure was equal or lower than 80% of baseline levels. Although phenylephrine showed less effectiveness in controlling blood pressure, deleterious repercussion on the fetus analyzed by Apgar score were not detected with the drugs. A quantitative systematic review by Lee A et al, also supported prophylactic ephedrine for prevention of maternal hypotension, but does not improve antenatal outcome[10].

Different dosing regimens have been used for both the vasopressors. In our study, a minimum effective dose of 10mg of ephedrine was chosen prophylacticaly to prevent maternal hypotension. A 2004 metaanalysis[11] concluded that doses above 14 mg of ephedrine did not reduce the incidence of maternal hypotension but caused reactive hypertension in the mother. Similarly, a dose of 80 μgm of phenylephrine was chosen, based on a prior study that demonstrated it as effective intravenous bolus dose, without severe side effects[4]. For practical purpose, it was decided to administer the medication as bolus, since several studies have demonstrated similar efficacy of ephedrine and phenylephrine for prevention of hypotension, both when used in bolus or continuous infusion[12,13].

Phenylephrine showed higher incidence of nausea (n=21, 15.7%) and vomiting (n=13, 9.7%) as compared to ephedrine (n=7, 5.2% and n=8, 6%). These adverse effects developed in those patients in whom hypotension was observed probably related to reduced cerebral blood flow due to hypotension. Anti-emetic (ondensetron 4mg IV bolus) and colloid infusion were substituted.

Historically, ephedrine has been the vasopressor of choice in obstetrics despite the uncertainty about its superiority,[14] believed to increased maternal blood pressure, thereby preserving uterine and placental blood flow due to its beta-adrenergic action, while pure alpha-agonist vasopressors were associated with reduction in this blood flow. However subsequent studies demonstrated that in the treatment of post spinal hypotension in cesarean section, ephedrine and phenylephrine have similar efficacy[15,16]. Where as phenylephrine is increasingly being used as suggested by improved fetal acid- base status in addition to prevent hypotension[17,18].

However in our study, hypotension was compared and found higher in phenylephrine group which was 34.3% while 28.4% in ephedrine group although statistically it was found insignificant with p-value=0.288. Hence the results of present study only give partial support to the hypothesis guiding this study which could be justified as technical deficiencies of the method and the small size of the study population which may lead to give the insignificance in both the drugs.

CONCLUSION

Ephedrine was found to be more effective than phenylephrine in the prevention of hypotension and with fewer side effects.

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