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ORIGINAL ARTICLE

Role of Prophylactic Bolus Dose of Ephedrine to Prevent Hypotension after Spinal Anesthesia - A Single Center Experience

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ABSTRACT

Aim: To compare the efficacy of prophylactic bolus dose of ephedrine 10mg to prevent hypotension after spinal anesthesia for elective caesarean section.

Methods: The study was conducted in Gynecological operation theatre suite of Bahria international teaching Hospital Lahore, from 15th September 2020 to 14th January 2021. It was quasi experimental study. It was conducted on ninety women admitted in gynecology department of Bahria international teaching Hospital Lahore, for caesarean delivery. These women were divided randomly into 2 groups: **a)** Patients in group **E10** received ephedrine 1ml from 5ml syringe containing ephedrine 10mg/mland b)'

Results: Patients in group **R** acted as a control group and received normal saline 1ml from 5ml syringe.Blood pressure was recorded every minute for first 3 minutes, every 2 minutes for next 6 minutes, and then every 3 minutes till the procedure was completed. The sampling technique used was purposive sampling.

Conclusion: It was concluded that prophylactic intravenous ephedrine bolus 10mg is more effective in preventing hypotension than fluid preload alone. It is simple and effective means of reducing the incidence of hypotension undergoing C- section in spinal anaesthesia.

Keywords: Ephedrine, Hypotension, Spinal anesthesia.

INTRODUCTION

Regional anesthesia is safer than general anesthesia in obstetric patients having altered physiology. In developed countries it is the preferred form of anesthesia for caesarean sections. Data between 1991 and 1999 suggested a lower overall maternal mortality from anesthesia (about 1.6 per 1,000,000 live births) possible due to greater use of regional anesthesia for labour and caesarean section[1].

In developing countries spinal anaesthesia has also gained popularity for caesarean section due to multiple reasons i.e., easy to perform and cost effective, lower dose of local anaesthetic and dense predictable block with rapid onset

Advantages for mother: Mother is aware during the process of birth, safer than general anesthesia; lesser maternal morbidity and mortality, hazards of difficult airway associated with weight gain and oedema can be avoided, along with the problems of regurgitation because of physiological weakening of gastro-esophageal sphincter and an increase in gastric in volume and acid production, placental perfusion is maintained, lesser amount of surgical hemorrhage and early recovery; early mobility; early breast feeding

Advantages for Baby: New born is vigorous at birth, infant requires less intervention, can feed earlier and maternal infant bonding may be encouraged and better APGAR scores

But as with any procedure, spinal blockade is not without complications[2,3] i.e., hypotension, post spinal puncture headache, nausea and vomiting, bacterial meningitis, neurological sequale and compromise fetomaternal circulation. The interventions used to prevent hypotension are as follows:

1. Fluid preload: the most widely used but it is not a fool proof method to prevent hypotension on its own.[4-6]
2. Ephedrine: a noncatecholphenylisopropylamine, has high bioavailability and a long duration of action. Ephedrine primarily acts through release of stored catecholamine; in addition, it has some direct actions on adrenoceptors. It is non-selective and mimics epinephrine in its spectrum of effects because it gains access to central nervous system, it is a mild stimulant[7-9].

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Pathophysiology of hypotension after Spinal Anaesthesia: Anaesthesia that extends into thoracic levels and above reduces sympathetic tone, leading to peripheral vaso-dilatation. Blood pools in the periphery, venous return is impaired. A reduction in cardiac output occurs, leading to a fall in arterial blood pressure. This decrease in blood pressure is accentuated with increasing elevation of the upper body. If the patient is kept in a head down position and hypovolemia is corrected by adequate fluid replacement then usually the cardiac output is maintained and the systemic blood pressure will decrease a modest 10-15%. This is due to the decrease in peripheral vascular resistance. Healthy patients tolerate this reduced blood pressure well.

The resultant unopposed vagal tone may produce bradycardia which can also result in a reduced cardiac output and contribute to hypotension. Bradycardia may also be produced by decreased stimulation of stretch receptors on the right side of the heart due to reduced venous return. This bradycardia component of the hypotension may be expeditiously treated with the administration of atropine 0.5-1 mg administered intravenously.

Focusing on spinal anaesthesia in c-sections which is the basis of this study; following are some operational definitions for the study:

Hypothesis: Prophylactic intravenous ephedrine bolus is more effective in preventing hypotension than fluid preload alone.

METHODOLOGY

Sampling Technique: Purposive sampling

Sample Size: $n = 2\left(\frac{z_{1-\alpha/2} + z_{1-\beta}}{d_o}\right)^2 p(1-p)$

$n = 2\left(\frac{1.96 + 0.84}{0.30}\right)^2 0.88(1-0.88)\, n = 42$

Minimum sample size 21 in each group. For the sake of clarity we enrolled 45 patients in each group N=size per group; p=the response rate of standard treatment group; Z= the standard normal deviate for a one or two sided xd_o= a clinically acceptable margin; 90 women admitted for caesarean delivery randomly divided into 2 groups E10 and R.

Definition of ASA 1: No organic pathology or patients in whom the pathological process is localized and does not cause any systemic disturbance or abnormality
ASA 2: A moderate but definite systemic disturbance
Indications of C-Section: Fetal Distress, Malpresentations, Cephalopelvic disproportion, Vaginal atresia, Previous history of Caesarean Section, Antepartum Hemorrhage
Rationale of our study was to compare the efficacy of prophylactic dose of ephedrine 10mg to prevent hypotension after spinal anesthesia for elective caesarean section.
Data collection procedure: Ninety women admitted in gynaecology unit of Bahria international teaching Hospital Lahore, scheduled for caesarean delivery at term with uncomplicated singleton pregnancy and meeting the inclusion and exclusion criteria were included in the study. A written and informed consent from all the patients was obtained. Approval of the hospital ethical committee was also obtained. Injection Ranitidine 150mg and injection Metoclopramide 10mg were administered intravenously as preoperative medication one hour before surgery. All patients were preloaded with intravenous Ringer's lactate 20ml/kg before spinal blockade. Monitoring was included pulse oximetry, electrocardiography (ECG) and noninvasive blood pressure measurement. Under strict aseptic conditions all the patients were given intrathecal injection in space L2-3 or L3-4 using 23 gauge Quincke needle in sitting position. 1.6 ml of 0.75% hyperbaric bupivaciane (Abocain spinal by Abbott Laboratories Pakistan) was administered in the sub-arachnoid space. Patients in group E10 received ephedrine 1ml from 5ml syringe containing ephedrine 10mg/ml. Patients in group R acted as a control group and received normal saline 1ml from 5ml syringe. Blood pressure was recorded every minute for first 3 minutes, every 2 minutes for next 6 minutes, and then every 3 minutes till the procedure is completed. Data scope spectrum vital sign monitor was used from measuring blood pressure. All the patients received 5 liters of oxygen by facemask until delivery of baby. All the relevant data was noted on a performa
Statistical analysis procedure: Data was placed and analyzed smoothly in SPSS version 25.0. The quantitative variables like age, weight, dose of ephedrine, response of blood pressure was presented as mean and standard deviation. The qualitative variables like parity, ASA class, indication for caesarean section and complications were presented as frequency and percentages. The outcome variable was hypotension and dose of ephedrine. Mean and standard deviation was calculated for blood pressure before and after the dose of ephedrine and paired sample't' test was applied to check the effectiveness of doses before and after giving ephedrine. ANOVA was applied to check the significance to prevent hypotension in two groups. P-value of ≤0.05 was considered as significant.

Table 1: Baseline Descriptives:

Group	Mean Duration of Surgery (minutes) ± SD	Mean total fluid administered (liters)	Mean Age in (years) ± SD	Mean Weight in (Kgs) ± SD	Mean total amount of ephedrine used (mg)
E10	50.9±14.3	3.0±1.7	26.5±4.3	68.0±7.8	
R	48.8±9.5	3.1±1.7	27.4±3.8	67.6±10.1	6.7±4.1
p-value			0.8	0.6	

Table 2: Distribution of patients by parity

Variables	Group E10 (n=30)	Group R (n=30)
Parity		
0	5 (16.7)	2 (6.7)
1-2	22 (73.3)	18 (80.0)
3-4	3 (10.0)	10 (33.3)
Mean±SD	1.4±0.9	1.9±1.1
ASA* class: Distribution of patients by ASA class		
I	18 (60.0)	17 (56.7)
II	12 (40.0)	13 (43.3)
Indication	p-value 0.08	
One previous C-section	9 (30.0)	15 (50.0)
Two previous C-section	12 (40.0)	2 (10.0)
Three previous C-section	3 (10.0)	5 (16.7)
Breach	6 (20.0)	7 (23.3
Gestational age (weeks)	p-value 0.8	
35-36	5 (16.7)	2 (6.7)
37-38	18 (60.0)	15 (50.0)
39-40	7 (23.3)	13 (43.3)
Mean±SD	37.7±1.3	38.2±1.2

The mean age of the patients in E10 group was 26.5±4.3 years and in R group was 27.4±3.8 years with no significant difference i.e. P=0.8.The mean weight of the patients in E10 group was 68.0±7.8 kg and in R group was 67.6±10.1 kg with no significant difference i.e. P=0.6 (Table 1).

The distribution of parity was shown in table 2 with no significant difference. In the distribution of ASA class, In group E10 18 (60%) participants fell in ASA class I and 12 (40%) had ASA class II. In group R 17 (56.7%) participants fell in ASA class I and 13 (43.3%) had ASA class II. There was no significant difference regarding ASA classes. In the indication of caesarean section, In group E10, 9(20%) patients has one previous C-section, 12 (40%) had two previous C-section, 3(10%) patients had three previous C-section and 6 (20%) patients had breach delivery and in group R, 15 (50%) patients has one previous C-section, 2(6.7%) had two previous C-section, 5(16.7%) patients had three previous C-section and 7 (23.3%) patients had breach delivery. There is no significant difference i.e. p-value of 0.08. The mean gestational age of the participants in E10 group was 37.7±1.3 weeks and in R group was 38.2±1.2 years with not significant p-value of 0.8 (Table 2).

Table 3: Distribution of patients by hypotension, duration of surgery, fluid administered, total amount of ephedrine used & complications

Time (Minutes)	Group E10% (n=30)	Group R% (n=30)
5	2 (6.7)	10 (33.3)
10	3 (10.0)	9 (30.0)
15	2 (6.7)	7 (23.3)
20	2 (6.7)	4 (13.3)
25	1 (3.3)	2 (6.7)
30	1 (3.3)	1 (3.3)
40	0	0
50	0	0
60	0	0
70	0	0
Duration (Minutes) p-value 0.8		
30-40	7 (23.3)	6 (20.0)
41-50	8 (26.7)	13 (43.3)
51-60	7 (23.3)	8 (26.7)
61-70	8 (26.7)	0
Mean±SD	50.9±14.3	48.8±9.5
Fluid (Litre) p-value 0.9		
Upto 2	3 (10.0)	5 (16.7)
2.1-2.5	15 (50.0)	16 (53.3)
2.6-3.0	12 (40.0)	9 (30.0)
Mean±SD	2.5±0.3	2.4±0.3
Ephedrine (mg) p-value 0.01		
0	15 (50.0)	0
5	12 (40.0)	13 (43.3)
10	3 (10.0)	11 (36.7)
15	0	4 (13.3)
20	0	4 (13.3)
Mean±SD	2.8±2.0	6.7±4.1
Complications: p-value 0.05		
Bradycardia	1 (3.3)	2 (6.7)
Vomiting	2 (6.7)	4 (13.3)
Nausea	4 (13.3)	6 (20.0)

Discussing about hypotension, In group E10 at 5 minutes there were 2 (6.7%) patients of hypotension, at 10 minutes there were 3 (10%) patients, at 15 minutes, 2 (6.7%) patient, at 20 minutes, 2 (6.7%) patient, at 25 minutes, there was 1 (3.3%) patient, at 30 minutes, 1 (3.3%) patient, at 40 minutes, 50 minutes, 60 minutes, and 70 minutes there was no patient of hypotension. In group R, at 5 minutes, there were 10 (33.3%) patients of hypotension, at 10 minutes, 9 (30%) patient, at 15 minutes, 7 (23.3%) patients, at 20 minutes, 4 (13.3%) patients, at 25 minutes, 2 (6.7%) patient, at 30 minutes, 1 (3.3%) patients, at 40 minutes, 50 minutes, 60 minutes, and 70 minutes there was no patient of hypotension. In group E10 less hypotension occurred than other group.The mean duration of surgery in E10 group was 50.9±14.3 minutes and in R group was 48.8±9.5 minutes with no significant difference i.e. p-value of 0.8. The mean total fluid administered in E10 group was 2.5±0.3 liters and in R group was 2.4±0.3 litres with not significant P value of 0.9. The mean total amount of ephedrine used in E10 group was 2.8±2.0 mg and in R group was 6.7±4.1mg with significant P value of 0.01 (Table 3).

DISCUSSION

Regional anesthesia is a popular and favored method for surgeries below umbilicus especially gynecological procedures. It is now proven that regional anesthesia is safe in obstetric patients having altered physiology. In developed countries it is the preferred form of anaesthesia for caesarean sections. Anaesthesia leads to almost 2-3% of peripartum maternal deaths. Data between 1985 and 1990 suggested a maternal mortality of 32 per 1,000,000 live births due to general anaesthesia and 1.9per 1,000,000 live births in regional anesthesia. More recent data between 1991 and 1999 suggests a lower overall maternal mortality from anesthesia (about 1.6 per 1,000,000 live births) possible due to greater use of regional anesthesia for labour and caesarean section[1].

Fluid preload is most widely but it is not a fool proof method to prevent hypotension on its own[4,5,6]. Ephedrine is used widely all over the world for control of hypotension due to spinal anesthesia[7,8].

Ephedrine is a noncatecholphenylisopropylamine, it has high bioavailability and a long duration of action. Ephedrine primarily acts through release of stored catecholamine, in addition, it has some direct actions on adrenoceptors. It is non-selective and mimics epinephrine in its spectrum of effects[9]. Because it gains access to central nervous system, it is a mild stimulant. It is used as intramuscular, intravenous boluses and in infusion form[6].

In our study, In group E10 60% participants fell in ASA class I and 40% fell in ASA class II. In group R 56.7% participants fell in ASA class I and 43.3% had ASA class II. A study conducted by Sternlo et, al[10]kept a control group, in which there were 37.5% participants fell in ASA class I, 50% participantsfell in ASA class II and 12.5% patientsfell in ASA class III. In ephedrine group, there were 42% participants who had ASA class I, 40% participants had ASA class II and 16% patients fell in class III, which matches with our project results.

In our study at 5 minutes, in Ephedrine group there were 6.7%participantsof hypotension and in control group there were 33.3% participantsof hypotension. In contrast with the study of Sternlo etal[10]at 5 minutes, in R group there were 6.25% cases of hypotension while in E10 group there was no patient of hypotension, which easily matches with our projects' findings.

Results of our study at 10 minutes, in E10 group there were 10% participants having low blood pressure and in group R there were 30% patients of hypotension. As compared with the study of Sternloetal[10] at 10 minutes, control group had 21% of participants with low blood pressure while in ephedrine group, none of the participants had low blood pressure which matches with our projects' findings.

Results of our study at 15 minutes, in Ephedrine limb there was 6.7% patient of low blood pressure whereas in control group, 23.3% participants hadlow blood pressure and A landmark study conducted by Sternlo et al[10] at 15 minutes, in control group there were 12.5% participants had low blood pressure while in E10 limb of the study, only 4% participants had low blood pressure, so results are matching with our project findings as well.

Results of our study at 20 minutes, in Ephedrine limb, 6.7% participants had low blood pressure and in control group, 3.3% participants had low blood pressure. A game changer study conducted by Sternloetal.[10] at 20 minutes, in control limb, 12.5% participants had low blood pressure while in E10 limb of the study, only 4% participants hadlow blood pressure, so results are matching with our projects' findings as well. Finding of our study at 25 minutes, in Ephedrine limb, 3.3% participants had low blood pressure and in control limb of the project, 13.3% participants hadlow blood pressure. Whereas study of Sternlo et al[10] at 25 minutes,in control limb, 12.5% participants had low blood pressure while in E10 limb of the study, only 2% participants hadlow blood pressure, so results are matching with our projects' findings as well. Finding of our study at 30 minutes, in Ephedrine limb, 3.3%participants had low blood pressure and in control limb of the project, 3.3% participants hadlow blood pressure. Whereas study of Sternloet al.[10] at 30 minutes showed that in control group there were 14.6% participants who hadlow blood pressure while in E10 limb of the study, 6% participants hadlow blood pressureso results are matching with our projects' findings as well. Finding of our study at 40 minutes, in Ephedrine limband in control limb, None of the participant had low blood pressure.

Whereas study of Sternloet al.[10] at 40 minutes showed that in control group there were 25% participants who hadlow blood pressure while in E10 limb of the study,18% participants hadlow blood pressureso results are matching with our projects' findings as well. Finding of our study at 50 minutes, in Ephedrine limband in control limb, None of the participant had low blood pressure. Whereas study of Sternloet al.[10] at 50 minutes showed that in control group there were 33.3% participants who hadlow blood pressure while in E10 limb of the study,18% participants hadlow blood pressureso results are matching with our studys' findings as well.

Finding of our study at 60 minutes, in Ephedrine limband in control limb, None of the participant had low blood pressure. Whereas study of Sternlo et al[10] at 60 minutes showed that in control group there were 33% participants who hadlow blood pressure while in E10 limb of the study,20% participants hadlow blood pressureso results are matching with our study's findings as well. Finding of our study at 70 minutes, in Ephedrine limband in control limb, none of the participant had low blood pressure. Whereas study of Sternlo et al[10] at 70 minutes showed that in control group there were 41.7% participants who hadlow blood pressure while in E10 limb of the study,14% participants hadlow blood pressureso results are matching with our study's findings as well. A study conducted by KolIO,et al[11] revealed that prophylactic intravenous ephedrine during spinal anesthesia for cesarean section can prevent hypotension without significant maternal tachycardia or hypertension, matches with results of our study.A Study conducted in Egypt by Salama AK,et al[12]concluded the same that ephedrine infusion is more effective compared with fluid preload in the prevention of hypotension due to spinal anesthesia for cesarean section without causing significant tachycardia or hypertension, highly matches with our study.

Bhovi, et al[13] designed a study to assess the efficacy of ephedrine in preventing hypotension in patients undergoing cesarean section under spinal anesthesia. A total of 100 female patients between 18 and 40 years of age undergoing elective cesarean section under spinal anesthesia were selected for their study. They were randomly allocated to receive either ephedrine infusion (group A) or 20 ml/kg of Ringer's lactate solution as preloading solution before subarachnoid block (SAB) (group B). The incidence of hypotension was six of 50 (12%) in group A, and 30 of 50 (60%) in group B. The incidence of hypotension in the ephedrine group in this study was 12%, where as in our study incidence of hypotension at 10 minutes was three of 30 (10%) in

group E10, and nine of 30 (30%) in group R, so incidence of hypotension in Ephedrine bolus group is highly comparable with our study and difference in control group can be attributed to the fact that Study conducted by Bhovi, et al[13] had larger sample size than ours in control group.

CONCLUSION

Prophylactic intravenous ephedrine bolus 10mg is more effective in preventing hypotension than fluid preload alone. It is simple and effective means of reducing the incidence of hypotension undergoing caesarean section in spinal anesthesia.

Limitations: It was a single center study with relatively smaller sample size, so results cant be generalized to whole population.

Recommendations: Multicenter studies with larger sample size to make results more effective and practically seen.

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