ORIGINAL ARTICLE

Optimal dose of prophylactic intravenous ephedrine for spinal-induced hypotension during cesarean section

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ABSTRACT

Objectives: The objective of this study was to compare the efficacy of 10, 15, and 20mg bolus doses of prophylactic IV ephedrine for prevention of maternal hypotension associated with spinal anesthesia for cesarean section.

Study Design: A prospective, quasi experimental study.

Place & Duration: The study was conducted at Department of Anesthesiology & Intensive Care, Shalamar Hospital Lahore (Pakistan), and was completed in six months period from January to June 2008.

Methodology: Ninety parturients of ASA grade I and II, receiving spinal anesthesia for elective C-section were included in this study. They were randomly divided into three groups. Group-I received 10mg, Group-II 15mg, and Group-III 20mg prophylactic IV ephedrine immediately after administration of spinal anesthesia. Intra operative hemodynamic changes were recorded and the data were analyzed.

Results: Incidence of hypotension was significantly higher in Group-I parturients receiving a 10mg prophylactic dose of ephedrine than in Group-II and Group-III parturients receiving 15mg or 20mg of ephedrine respectively (53.3% versus 13.3% and 3.3% respectively). There was however, a significantly higher incidence of reactive hypertension in Group-II parturients (46.7%).

Conclusions: 15mg bolus dose of prophylactic IV ephedrine can effectively prevent spinal induced maternal hypotension during cesarean section without adverse effects like reactive hypertension.

Key Words: Anesthesia; Parturients; Spinal analgesia; Ephedrine; Hypotension.

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INTRODUCTION

Spinal anesthesia is frequently used for lower abdominal and lower extremity surgeries. It is induced by injecting small amounts of local anaesthetic into the cerebrospinal fluid (CSF) at either L2-3, L3-4 or L4-5 interspinal levels. It is simple to perform and is economical requiring comparatively less time to produce more rapid onset of good quality sensory as well as motor block.[1] It has been shown to block the stress response to surgery, decreases intra-operative blood loss, lower the incidence of post operative thromboembolism , and decrease morbidity and mortality in high risk patients.[2]

Maternal hypotension is a recognized complication of spinal anesthesia with an incidence of as high as 80%, that may compromise the welfare of both mother and the baby.[3] It is associated with distressing symptoms of dizziness, nausea and vomiting, and may also interfere with surgical procedure. If uncorrected, the decreased uterine blood flow, may result in an acidotic neonate requiring

active resuscitation.

Lateral uterine displacement and preloading with crystalloids or colloids have been commonly used to prevent spinal-induced hypotension, but these alone may offer only a partial protection. A combination of preloading and vasopressor drugs has maximum efficacy in preventing spinal-induced hypotension.[4] Ephedrine is proven to be more effective for increasing arterial blood pressure with better preservation of uteroplacental blood flow as compared to other vasopressors.[5] It has a predominant ß-effect, that causes increase in arterial blood pressure by increasing cardiac output rather than by vasoconstriction.[6]

In this study, we compared hemodynamic changes with 10mg, 15mg, and 20mg bolus doses of prophylactic ephedrine. The aim of study was to find an optimal dose of prophylactic ephedrine in South Asian maternal population to prevent spinal-induced maternal hypotension effectively but without causing side effects like reactive hypertension.

METHODOLOGY

A double blind, randomized, interventional study was conducted at Department of Anesthesiology & Intensive Care, Shalamar Hospital, Lahore from January 2008 to June 2008. The subjects were selected by convenient sapling, keeping the inclusion and exclusion criteria in view. After obtaining hospital ethical committee approval and informed consent from patients, 90 parturients of ASA grade I and II, scheduled to receive spinal anesthesia for elective C-section were randomly allocated to one of three groups using a random number table. Group-I received 10mg, Group-II 15mg and Group-III 20mg bolus dose of prophylactic ephedrine IV. Parturients with gestational age <37weeks, known hypertension, preexisting cardiac or pulmonary disease or any other contraindication of spinal anesthesia were excluded from the study.

All mothers received oral pre-medication of ranitidine 150mg on the morning of surgery and 0.3M sodium citrate 30ml on arrival to operating room. Standard monitoring in the operating room included heart rate, noninvasive BP measurements, pulse oximetry, and electrocardiography.

Every patient was preloaded with 500 ml ringer's solution over 15-20min. Baseline readings of blood pressure and heart rates were taken. Spinal anesthesia was administered in the sitting position at level of L3-4 or L4-5 interspaces, with 15mg hyperbaric bupivacaine 0.75%, using 25 gauge spinal needles.

Patients were then turned supine with 15 degrees left lateral tilt of operating table to prevent aortocaval compression. Bolus dose of prophylactic study medication was given IV immediately on turning the patient to supine position from a prefilled syringe. All the mothers received 3-4 L/min of oxygen by facemask. A systolic blood pressure less than 20% of baseline was considered as hypotension, and systolic blood pressure more than 20% of baseline after administration of the bolus dose of prophylactic ephedrine was considered as reactive hypertension.

Patients who developed hypotension after bolus dose of prophylactic ephedrine were given additional rescue boluses of 10mg ephedrine and IV crystalloid solutions were rushed to treat hypotension.

Hemodynamic changes were assessed by another observer who was unaware of study medication. Frequency of hypotension, reactive hypertension, nausea, vomiting, and decrease in Apgar scores at 1 and 5min were noted.

All the relevant data was recorded on a specially designed proforma and were analyzed by SPSS version 11. Mean and standard deviation of age, weight, duration of pregnancy, sensory block height, baseline heart rate and blood pressure as well as rescue bolus doses of ephedrine were calculated. These variables were compared in three groups, ANOVA test was test of significance with p0.05 as level of significance. Frequency of hypotension, reactive hypertension, nausea, vomiting, and decrease in Apgar scores at 1 and 5min were also compared in three groups,

Table-1: Patient demographics.

	Group-I (n = 30)	Group-II (n = 30)	Group-III (n = 30)	P value
Age (yrs)	27.2 ± 4.36	28.4 ± 4.06	26.7 ± 4.03	0.285
Weight (kg)	73.2 ± 10.62	70.8 ± 10.16	70.5 ± 9.65	0.543
Gestation (weeks)	38.1 ± 1.06	38.3 ± 1.18	38.2 ± 1.15	0.732
SA-delivery time (min)	20.5 ± 2.78	21.0 ± 3.57	20.0 ± 3.71	0.519
SA-end of surgery time (min)	59.3 ± 9.13	58.0 ± 8.16	58.5 ± 8.42	0.789

Results are mean ± SD.SA=Spinal anaesthesia
p-value <0.05 is significant

Table-2: Sensory height of block

Sensory block height	Group-I N (%)	Group-II N (%)	Group-III N (%)	P value
T4	18 (60%)	14 (46.7%)	18 (60%)	.776
T5	8 (26.7%)	11 (36.7%)	7 (23.3%)	
T6	4 (13.3%)	5 (16.7%)	5 (16.7%)	
Total	30 (100%)	30 (100%)	30 (100%)	

p-value <0.05 is significant

Table-3: Hemodynamic data.

Parameter	Group-I (n = 30)	Group-II (n = 30)	Group-III (n = 30)	P value
Baseline heart rate (beats/min) mean±SD	91.1 ± 5.32	91.7 ± 4.84	89.9 ± 4.69	.364
Baseline systolic BP(mmHg) mean±SD	117.3 ± 5.83	119.8 ± 7.13	117.5 ± 6.53	.257
Hypotension N (%)	16 (53.3%)	4 (13.3%)	1 (3.3%)	<0.001*
Reactive hypertension N (%)	0 (0%)	4 (13.3%)	14 (46.7%)	<0.001*
Rescue IV ephedrine N (%)	16 (53.3%)	4 (13.3%)	1 (3.3%)	<0.001*

* p-value <0.05 is significant

Table-4: Rescue ephedrine given to treat hypotension.

Total ephedrine used (mg)	Group-I N (%)	Group-II N (%)	Group-III N (%)	P value
No	14 (46.7)	26 (86.7)	29 (96.7)	<0.001*
10	2 (6.7)	4 (13.3)	1 (3.3)	
20	11 (36.7)	-	-	
30	3 (10.0)	-	-	
Total	30 (100)	30 (100)	30 (100)	

* p-value <0.05 is significant

Table-5: Side effects and neonatal outcome.

Parameter	Group-I N (%)	Group-II N (%)	Group-III N (%)	P value
Nausea	12 (40.0%)	2(6.7%)	-	<0.001*
Vomiting	3 (10.0%)	-	-	.045*
Apgar score 1 min (<7)	2 (6.7%)	2 (6.7%)	1(3.3%)	.809
Apgar score 5 min (<8)	1 (3.3%)	-	-	.364

* p-value <0.05 is significant

Chi-square test was test of significance with p 0.05 as level of significance.

RESULTS

A total of 90 parturients were included in the study, 30 each in three groups. All parturients completed the study. The groups were comparable in age, weight, duration of pregnancy, interval of spinal anesthesia to delivery, interval of spinal anesthesia to end of surgery (Table-1). There were no significant differences in baseline heart rate, systolic BP and sensory block height (Table-2, 3).

The incidence of hypotension was 53.3%, 13.3% and 3.3% in Group-I, II and III respectively. The incidence of hypotension was significantly lower in Group II and III receiving 15mg and 20mg bolus doses of ephedrine respectively (Table-3). These two groups also required lower doses of rescue IV ephedrine to treat hypotension (Table-4).

The incidence of reacative hypertension was 0, 13.3% and 46.6% in Group-I, II and III respectively. So Group III had significantly higher incidence of reactive hypertension.

The incidence of nausea and vomiting was higher in group-I and was related to hypotension. There was no statistically significant difference between the groups in 1min and 5min Apgar scores (Table-5).

DISCUSSION

The prevention and treatment of maternal hypotension associated with spinal anesthesia for C-section remains a problem. Protocols that aim to prevent hypotension during spinal anesthesia for cesarean delivery may result in better outcomes than those designed to treat hypotension after it has occurred. Prehydration with crystalloid solutions is an important method to prevent hypotension dung regional anesthesia . . Rout et al.[3] demonstrated that the incidence of hypotension decreased significantly from 71% to 55% for un-preloaded versus preloaded subjects, respectively. Increasing the crystalloid preload from 10 to 30 ml/kg may further reduce the incidence of hypotension.[7] However, two studies demonstrated that 1000ml of crystalloids alone did not appear to be more effective than preloading with 200ml or no prehydration at all.[8,9] It is time consuming to administer and potentially dangerous in susceptible mothers by risking circulatory overload after delivery and also by causing significant hemodilution. Fluid loading has been shown to cause rapid increase in CVP not only when administered before onset of sympathetic block[10], but also when infused rapidly during the onset of extradural block.[11] In women with normal cardiovascular system this is probably not harmful; circulatory overload rarely occur in routine clinical practice despite the fact that during normal pregnancy lung capillaries are more permeable to water with increased susceptibility to pulmonary edema.[12] The effect of large volume fluid preload may be exacerbated by placental auto-transfusion which occurs after delivery. However the risk of circulatory overload resulting in pulmonary edema in women suffering from myocardial insufficiency or pre-eclampsia is increased after large volume preloads.

Colloid solutions have also been studied and shown to produce a lower incidence of hypotension. Albumin 5% is probably the most effective solution, but is expensive and not universally available.[13,14] Other colloids have been shown to be less effective than albumin, but they carry a risk of significant anaphylactic reactions.[15]

For ethical reasons in our study all the parturients were preloaded with 500ml of crystalloid solution.

Prophylactic ephedrine alone is at least as good as fluid preload alone in combating the hypotension associated with spinal anesthesia for caesarean section.[8,16] This was

also demonstrated by Datta et al.[17], who compared parturients who were given ephedrine 10–30 mg as soon as any decrease in arterial pressure was detected, with parturients in whom treatment with IV boluses of ephedrine 10 mg was withheld until hypotension occurred. They found that parturients who received early administration of ephedrine had less nausea and vomiting and better neonatal acid-base status.

Intramuscular injection of ephedrine has been recommended, but this has not been consistently effective.[18] Furthermore, absorption of IM ephedrine is unpredictable; it may be difficult to predict the peak effect, and reactive hypertension may be a problem, particularly if spinal anesthesia is unsuccessful.[19] In comparison, the advantages of IV administration include the ability to withhold drug administration until after the onset of anesthesia is confirmed and better timing of drug effect to the onset of sympathetic block.

There is no consensus about the dose of prophylactic IV ephedrine for prevention of spinal induced maternal hypotension. Previously, Ngan Kee et al.[20] suggested that ephedrine 30 mg was the most effective IV bolus dose to prevent hypotension, but at the expense of an increased incidence of reactive hypertension. Some studies showed that low doses of prophylactic IV ephedrine significantly reduced the incidence of maternal hypotension.[21,22] In these studies low dose of hyperbaric bupivacaine along with intrathecal opioids were used. These both factors lead to less cardiovascular instability which can be managed even with low doses of prophylactic IV ephedrine. In our setup usually high dose of hyperbaric bupivacain, without intrathecal opioids, is used for spinal anesthesia for C-section to get effective block height, causing greater haemodynamic changes. Therefore, in our study, low doses of prophylactic IV ephedrine were related with higher incidence of maternal hypotension compared with other studies.

Ephedrine is not a potent arterial vasoconstrictor, it maintains BP mainly by increasing cardiac output and heart rate.[23] This may be the reason that high doses of prophylactic IV ephedrine are associated with significant side effects like reactive hypertension. Considering the risk and benefit ratio, 15mg bolus dose of prophylactic IV ephedrine was found optimal as it significantly reduced the incidence of maternal hypotension without increased incidence of reactive hypertension.

Spinal induced hypotension occurs in first few minutes after establishment of subarachnoid block due to blockage of sympathetic nervous system. Therefore in our study, hypotension that occurred before delivery was considered as spinal induced hypotension. Hypotension after the delivery of fetus was ignored, as it may be related to excessive blood loss during C-section.

The primary focus of this study was on maternal hemodynamics, therefore only Apgar scores of new borns were recorded to exclude any impact of ephedrine therapy on the fetus. There was no significant difference among the groups in terms of 1min and 5min apgar scores.

CONCLUSION

We conclude that the prophylactic use of ephedrine in 15mg IV bolus significantly decreases the incidence of maternal hypotension without serious side effects like reactive hypertension. We suggest that 15mg is the optimal dose of prophylactic IV ephedrine when compared to higher doses e.g. 20 or 25mg for prevention of spinal-induced maternal hypotension during cesarean sections.

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Patients are the Experts

"Patients with long term medical conditions become the experts on living with those conditions, even if they aren't necessarily the experts on the science of their treatment. They are also repeated users of the health care system and are an incredibly under-used resource in how that system actually works for, or sometimes against, them." Forbes B.A.

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A Tribute to Grass

Grass doesn't make a fuss. It doesn't try to be beautiful or outstanding. It doesn't want to attract attention. It is so humble that it even allows people to walk all over it. Yet it possesses such strength. It glows in healthy green despite being stepped all over. When a typhoon strikes and all the flowers die and all the tall trees get uprooted, the humble grass survives. I think a virtuous person should be like grass. Humble, unnoticed, yet possessing great strength and kindness.
-- Tan Chade Meng, Budhist Contemplation.