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COMPARISON OF PROPHYLACTIC INTRAMUSCULAR EPHEDRINE WITH PRELOADING VERSUS PRELOADING ALONE IN PREVENTION OF HYPOTENSION DURING ELECTIVE CAESAREAN SECTION UNDER SUBARACHNOID BLOCK

Dr. S .Varathan[1]*, Dr. S. U. Ekanayake[2], Dr. U. Amarasinghe[3]

[1] *Senior Lecturer, Department of Anaesthesiology, Faculty of Medicine, University of Peradeniya, Sri Lanka,* [2] *Temporary Lecturer, Department of Anaesthesiology, Faculty of Medicine, University of Peradeniya, Sri Lanka,* [3] *Temporary Lecturer, Department of Anaesthesiology, Faculty of Medicine, University of Peradeniya, Sri Lanka.*

**Corresponding author: varathansr@yahoo.co.uk*

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Background:
There is a considerable dispute over the use of different techniques for the prevention of hypotension during caesarean section under subarachnoid block. We hypothesize that crystalloid preloading together with prophylactic intramuscular (i.m.) ephedrine injection prevents occurrence of hypotension during caesarean section under subarachnoid block. The best protective dose of i.m ephedrine in relation to the appropriate time intervals, in order to prevent hypotension during caesarean section was assessed in this study.

Method:
Forty six healthy pregnant mothers were randomly allocated to five groups. Group A (control group) was given crystalloid preloading within 20 minutes (min) prior to subarachnoid block. Groups B and C received im ephedrine 15 mg 10 and 20 min prior to subarachnoid block whereas Groups D and E received im ephedrine 30 mg 10 and 20 min prior to subarachnoid block. All subjects in test groups were given crystalloid preloading within 20 min prior to subarachnoid block.

Results:
In the control group A, a significant mean arterial blood pressure(MAP) drop was observed at 5 min , 8min, 10min and 20 min time intervals($P<0.01$). A significant reduction in the mean arterial blood pressure was observed in Groups C and E and a significantly higher blood pressure was recorded in Group D. Group B steadily maintained the blood pressure at all time intervals without showing any significant changes.

Conclusion:
We conclude that preloading with crystalloid along with prophylactic im ephedrine 15mg given 10min prior to subarachnoid block will effectively prevent hypotension during cesarean section under subarachnoid block.

Spinal Anaesthesia is a commonly practiced mode of regional anaesthesia for patients undergoing caesarean section (LSCS). However it is estimated that around 80% of patients who undergo LSCS under spinal anaesthesia will develop hypotension during the procedure.[1] Development of hypotension has various clinical manifestations such as nausea, vomiting and dizziness which often interferes with the surgery.[2] Techniques currently in use for the prevention of hypotension include preloading, administration of vasopressors, physical methods such as left uterine displacement and the use of leg bindings and compression stockings.[3]

The use of vasopressors for the prevention of hypotension during LSCS is well established. ephedrine and phenylephrine are the most widely used vasopressors in current practice. ephedrine is an indirectly acting sympathomimetic amine augments the α and β adrenoceptor activities[3]. Its predominant action which is on the β_1 adrenoceptors of the heart increases the cardiac output and heart rate, and thereby stabilizes the blood pressure.[3] Due to diminished action on the α adrenergic receptors, administration of ephedrine preserves sufficient uteroplacental blood flow while maintaining maternal blood pressure.

Although crystalloid preloading is widely practiced during spinal anaesthesia, hypotension associated with spinal anesthesia for LSCS cannot be eliminated by volume preloading in the supine wedged patient alone.[4] We hypothesized that crystalloid preloading along with prophylactic i.m. ephedrine prevents the occurrence of hypotension during *LSCS* under subarachnoid block. Though there were many studies in the past which assessed the effects of prophylactic administration of i.m ephedrine in the prevention of hypotension, none of those analyzed the proper dosage regime of i.m ephedrine in relation to the time interval of administration. Hence, we designed this study in order to identify the best protective dose of i.m ephedrine in relation to the appropriate time interval of administration to prevent hypotension in parturients undergoing LSCS under spinal anaesthesia. .

Materials and Methods

After obtaining the Ethical Committee approval, 46 healthy pregnant mothers who were scheduled for elective LSCS under spinal anaesthesia at term were recruited to our study. Selection of subjects were made after excluding patients who were having maternal complications such as Pregnancy Induced Hypotension (PIH), pre existing hypertension, obesity resulting in impalpable lumbar spine, known cardiovascular or renal disease and diabetes mellitus. Mothers who were diagnosed to be having foetal anomalies, who were having contraindications for spinal anaesthesia and those who developed labour pains during surgery were excluded. Informed written consent of each patient was obtained prior to the procedure.

In all selected patients, baseline blood pressure and the pulse rate was recorded initially. For the assessment of blood pressure, four blood pressure measurements were taken at 5, 8, 10 and 15 minutes time intervals using an automated non invasive Blood Pressure Monitoring apparatus. The first measurement was discarded and the mean of the consecutive three measurements were taken as the baseline blood pressure value. The baseline heart rate was taken from the electrocardiogram (ECG). The patients were randomly allocated to five groups using the sealed envelope method. Group A (the control group) was given crystalloid preloading only. Group B was given 15mg of i.m ephedrine 10 minutes prior to the subarachnoid block and, 15 mg of i.m ephedrine 20 min. prior to the subarachnoid block was given to group C. Group D and E received 30mg i.m ephedrine 10 min. and 20 min. respectively prior to the subarachnoid block.

Prior to the subarachnoid block, all subjects in test groups were preloaded with a calculated amount of 0.9% normal saline (15ml/kg) over 20 minutes. The patients in the control group were also subjected to the same fluid regimen. Patients belonging to the test groups received im ephedrine injections to the left vastus lateralis muscle by an anaesthetist who was not involved in the subsequent management of the patient or in the collection of data. Spinal anaesthesia was administered in the seated position at the L_2-L_3 or the L_3-L_4 inter-space using a 25G spinal needle. A single dose of 2.5ml 0.5% hyperbaric bupivacaine with 15-25μg fentanyl was administered into the subarachnoid space. Once the procedure was over, the patients were placed in the left tilted position until the surgery began.

Maternal blood pressure and heart rate were measured at 5 min, 8 min, 10min, 15min and 20 min time intervals after the subarachnoid block by an independent observer who was blind to the procedure. The foetal outcome was assessed by the APGAR score at first and fifth minutes after the delivery. In addition the umbilical cord venous blood pH of the neonate at delivery was recorded. The incidence of maternal adverse effects to ephedrine manifesting as nausea, vomiting, sweating and palpitations were also recorded in each patient by the same independent observer. If maternal hypotension occurred, it was promptly

corrected by rapid administration of intravenous (iv) fluid and by 5 mg ephedrine iv bolus every minute until systolic pressure returned back to the initial value. Hypotension was defined as a decrease in systolic pressure to <100 mmHg or <70% of the baseline value.

Results

Study 1:

The blood pressure was recorded in all five groups at 5, 8, 10, 15 and 20 min. time intervals. The mean arterial blood pressure was best maintained by group B throughout the surgery without demonstrating any significant changes (*fig I*). In group E, the blood pressure was maintained without showing any significant changes in the initial period, a significant drop was observed at the latter part at 20 min. time interval *(P<0.01), (fig I)*. Group C failed to maintain a satisfactory blood pressure up to the 10 min. time interval *(P<0.01)*, but maintained it successfully until the end of the surgery without showing any significant changes (*fig I*). Group D showed a significantly higher blood pressure value at the onset *(P<0.01)*, however, it rapidly declined and maintained at 15 and 20 min. time intervals without showing any significant differences (*fig I*). The mean arterial blood pressure in group A demonstrated a marked drop at 5, 8, 10 and 20 min. time intervals *(P<0.01), (fig I)*.

Study 2:

The heart rate was recorded in all five groups at 5, 8, 10, 15 and 20 min. time intervals *(fig2)*. The heart rate was best maintained by the control group (Group A) throughout the surgery without showing any significant changes. All the test groups showed a significant increase in heart rates at 5, 8, 10 and 20 min. time intervals. In addition, group D demonstrated the highest heart rate at 20min time interval *(P>0.01)*. Except group D, all the other groups did not show a significantly higher heart rate at 15 min. time interval.

Study 3:

Fetal outcome represented by APGAR score at 1 min and 5 min was assessed and the scores were in the normal range in all groups. The umbilical cord venous blood pH of the neonate at delivery was recorded and the recordings were found to be in the normal range with the umbilical venous blood pH between 7.2 and 7.4 (normal range for umbilical venous blood pH 7.10 – 7.42)

Study 4:

Approximately 10% of pregnant mothers received fluid preloading alone(Group A) and 15% of preloaded mothers who received 15mg i.m ephedrine 10 min. prior (Group B) had experienced nausea, but none of the other groups had a similar experience.

Only 10% of preloaded pregnant mothers who were given 30mg i.m ephedrine 10 min. prior (Group D) had experienced sweating *(fig3).*

Discussion

The prevention and treatment of maternal hypotension associated with spinal anesthesia for Lower Segment Cesarian Section still remains as a challenge to all Anesthetists. Though the ideal prophylactic sympathomimetic drug has not yet been identified, ephedrine is still in use, mostly in Asian countries due to its cost effectiveness. Phenylephrine is preferred over ephedrine in the prevention of hypotension after spinal anesthesia due to its fewer side effects on mothers and minimal foetal adverse effects.[5]However, iv ephedrine is commonly used in many centers to prevent hypotension in LSCS following subarachnoid block. Intramuscular prophylactic vasopressors have also been advocated for preventing hypotension associated with spinal anaesthesia for LSCS.[6] Though many studies have been performed in order to identify a suitable prophylactic dose of i.m ephedrine, a proper dosage regime is yet to be finalized. Here, we administered i.m ephedrine in different doses at various time intervals and identified a suitable regime that has more effective and less unwarranted effects.

Reactive hypertension is one of the unwarranted effects frequently identified after administration of prophylactic i.m ephedrine, especially with doses exceeding 40 mg. It has been demonstrated that a single dose of iv ephedrine (5 mg) decreased the occurrence of the severity of hypotension in preloaded pregnant mothers who underwent LSCS under subarachnoid block.[7]Another similar study using prophylactic iv ephedrine identified that the least effective dose of ephedrine that could reduce the incidence of hypotension was 30 mg.

However, this dose did not completely eliminate hypotension and on the other hand caused reactive hypertension in addition to nausea, vomiting, and fetal acidosis[8]. Several studies have been undertaken using i.m ephedrine and A. A. Webb et al, concluded that a large dose (37.5mg) of i.m ephedrine prevented hypotension without causing reactive hypertension or tachycardia. However i.m ephedrine provided more sustained cardiovascular support than iv ephedrine.[8]

In the present study we demonstrated that the 15 mg i.m ephedrine given 10 min. prior to the subarachnoid block (Group B) prevented hypotension without causing any fluctuation in the blood pressure. However, there was a significant increase in heart rate at 5min and 10min time intervals in this group. Though the mean arterial blood pressure was maintained reasonably well in the group which received 30mg i.m ephedrine 10 mins prior to the subarachnoid block (group D), severe tachycardia was noted at the onset (5min) and towards the latter part of the surgery (20min). In addition though there was mild to moderate hypotension observed at 5min and 8min time intervals in the group which was given 15 mg i.m ephedrine 20mins prior to surgery (group C) the blood pressure was maintained satisfactorily thereafter. However severe tachycardia was noted in this group at 5min, 8min and 10min time intervals. Moreover the mean arterial blood pressure was not adequately maintained in the control group which received fluid preloading alone (group A). Here marked hypotension was observed at the onset of surgery and continued until the end.

Heart rate difference of the control group and the test groups were calculated during the period of surgery. Both the control group and the test groups showed an increase in the heart rate change at 5min and 8min respectively, but none of the mothers complained of palpitations. The incidence of maternal adverse effects to ephedrine manifesting as nausea, vomiting, sweating and palpitations were also recorded. Neonatal APGAR scores at 1min and 5min were also recorded which was found to be in the normal range in all groups. There was no association observed between the use of i.m ephedrine and fetal acidosis in our review

Conclusion:

According to our findings we believe that combination of preloading with prophylactic i.m ephedrine is more effective in preventing hypotension during spinal anesthesia for elective cesarean delivery than preloading alone. Furthermore our study clearly demonstrated that 15 mg of prophylactic i.m ephedrine given 10 min prior to the subarachnoid block with preloading, reduced hypotension and provided greater haemodynamic stability. In addition this regime did not cause any maternal and fetal side effects.

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Figure 1: Mean change in the mean arterial blood pressure with the duration of time courses. (*p<0.01*).

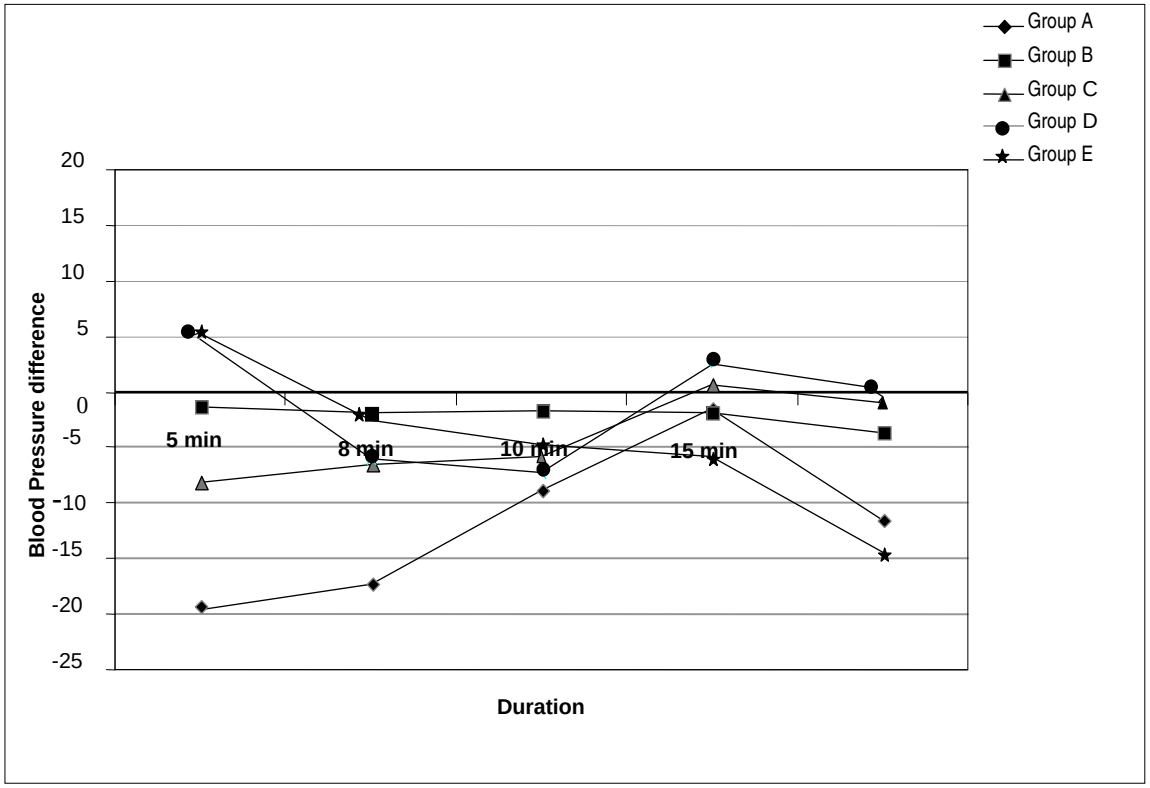


Figure 2: Mean change in the heart rate from basal value with the time courses. (*p<0.01*).

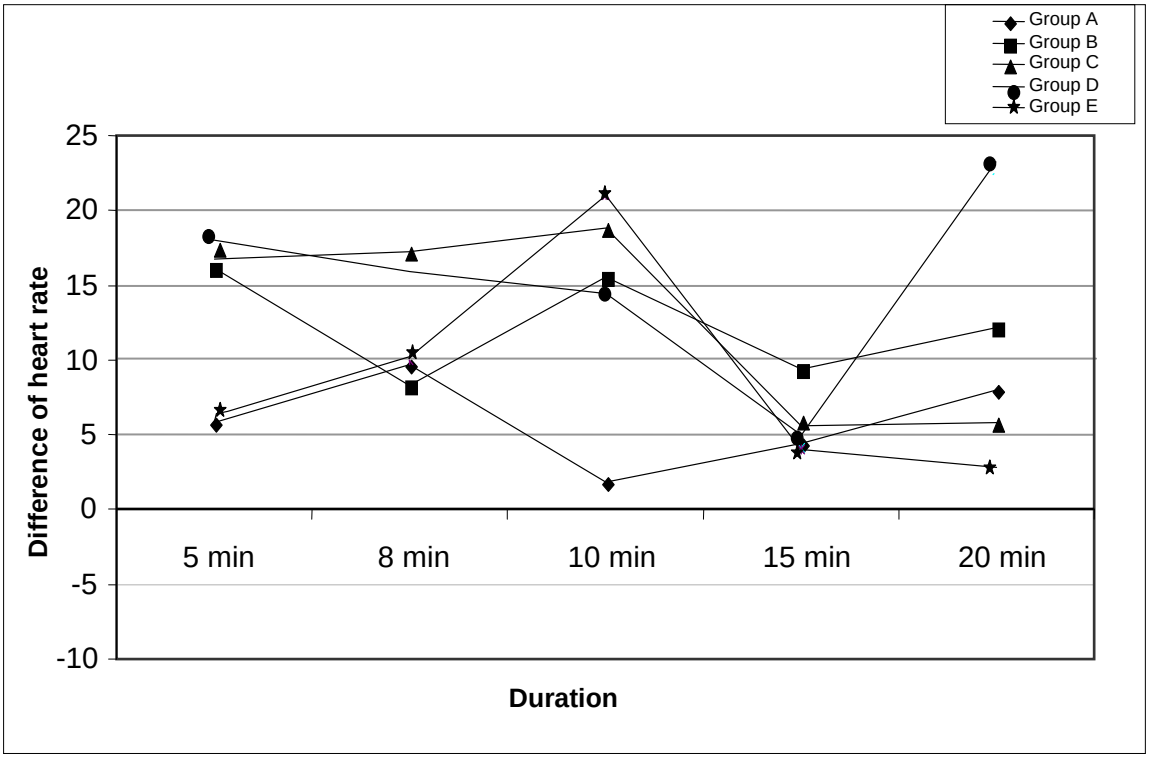
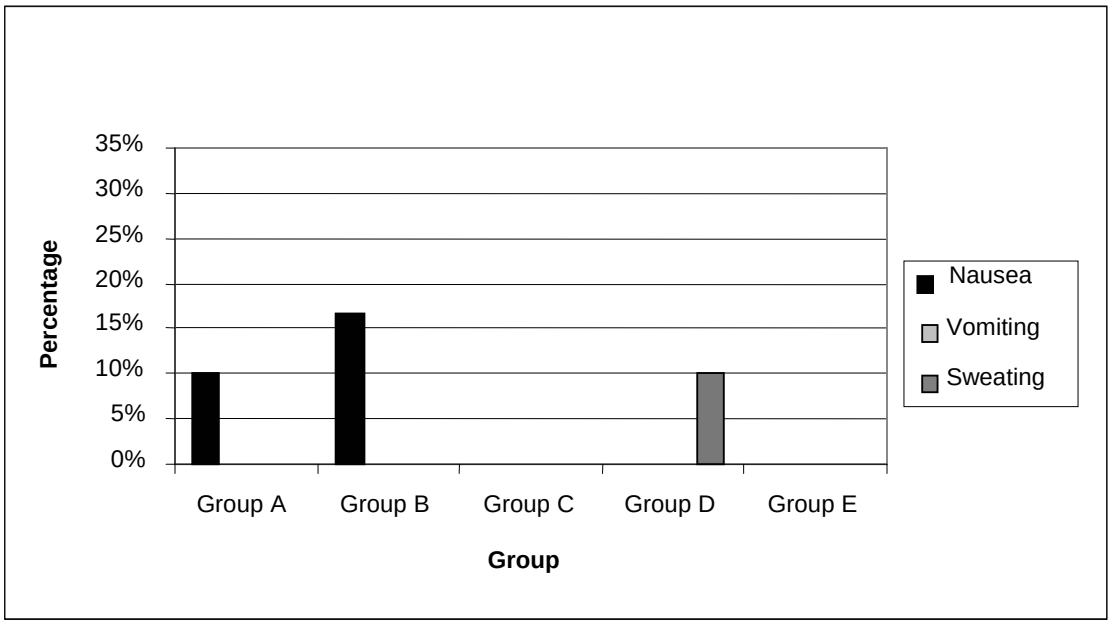


Figure 3
Incidence of maternal adverse effects (*p<0.01*).



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