

Study on Efficacy of Bolus Dose of Ephedrine, Mephentramine and Phenylephrine in Management of Hypotension During Spinal Anaesthesia for Inguinal Hernia Repair

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Abstract: ***Background:** Hypotension following spinal anesthesia is the most common complication faced during hernia surgery. Vasopressors like ephedrine, mephentermine, phenylephrine, metaraminol and methoxamine are used for treating hypotension. **Objectives of the study:** Compare the efficacy of ephedrine, mephentermine and phenylephrine in treating the hypotension following spinal anesthesia for inguinal hernia repair. **Methodology:** Ninety patients were recruited and divided into three groups and group I received Inj. Ephedrine 6mg IV bolus on developing hypotension, Group II received Inj. Mephentermine 6mg IV on developing hypotension, Group III received Inj. Phenylephrine 100mg IV bolus on developing hypotension. Systolic blood pressure, diastolic blood pressure, mean arterial pressure and heart rate were recorded at various points through surgery. **Results:** All the three vasopressors namely Ephedrine, Mephentermine and Phenylephrine are effective in IV bolus form in maintenance of arterial pressure within 20% limit of baseline values, though Phenylephrine has quicker peak effect, in comparison to Ephedrine and Mephentermine and it causes reduction in heart rate, which may be advantageous in patients in whom tachycardia is undesirable*

Keywords: Ephedrine, Phenylephrine, Mephentramine, spinal anesthesia, Hypotension

1. Introduction

Inguinal hernia is a problem of all ages with a predilection to middle aged men. The lifetime risk for men to develop hernia is 27%. It is the most common surgical problem in middle aged men. The morbidity is based on the nature of the content, jeopardy to vascular supply of the content, obstruction of the lumen and duration of herniation. Since the roots of nerve supply of herniated organs lies higher than that of groin, adequate blockade levels should be achieved. Hypotension during spinal anaesthesia may be dangerous to middle aged men with masked coronary insufficiency. Careful positioning, and volume preloading with crystalloids & colloids has been used to prevent it, but these are not complete measures, and vasopressor is required to correct hypotension quickly. Vasopressors like ephedrine, mephentermine, phenylephrine, metaraminol and methoxamine are used for treating hypotension. In this study we compare the efficacy of ephedrine, mephentermine and phenylephrine in treating the hypotension

2. Aims

Compare the efficacy of ephedrine, mephentermine and phenylephrine in the management of hypotension during spinal anesthesia for inguinal hernia repair surgeries

3. Materials and Methods

Study was conducted in the institute of Anesthesia, Madras Medical College, Chennai, between July 2010 to September 2010, on 90 patients undergoing elective inguinal hernia repair (Herniorrhaphy / Hernioplasty) surgeries. The study

was done after getting institutional approval. Written informed consent was obtained from all the patients included in the study. This study was a prospective randomized, single blinded, case control study. The patients were divided into 3 groups of each 30, patients meeting the inclusion criteria were incorporated into the study. Group I: Inj. Ephedrine 6mg IV bolus on developing hypotension. Group II Inj. Mephentermine 6mg IV on developing hypotension. Group III: Inj. Phenylephrine 100mg IV bolus on developing hypotension. Adult males of age group 18-40 years were included for the study, patients undergoing elective Inguinal hernia repair surgery and those who gave valid informed consent were included and Patients on whom no sedation has been used were included. Those who not satisfying inclusion criteria, Diabetics patients, Hypertensives, Patients with coronary artery disease, Patients with COPD & Asthma. Patients with known allergy to drugs used in the study, Very short patients <145cm, Very obese patients >75 kg, Anxious patients, Patients showing drastic haemodynamic changes, Shivering patients, Patients in whom adequate levels of blockade (T₆-T₈) have not been achieved were excluded. Systolic blood pressures, diastolic blood pressure, mean arterial pressure and heart rate at various points through surgery

In the operation theatre, appropriate equipment for airway management and emergency drugs were kept ready. Patients were shifted to the operation theatre. The horizontal position of the operating table was checked. The patients were made to lie supine with a pillow under the head. The patients were connected to non-invasive sphygmomanometer, ECG & pulse oximetry monitor. Intra venous access was obtained with 18 G IV cannula. All patients were preloaded with Ringerlactate 15ml/kg rapidly. The baseline systolic BP,

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diastolic BP, mean arterial pressure were all recorded and noted. Patients were placed in right lateral position. A pillow as kept. Skin over the back was prepared with antiseptic solution and draped with sterile towel. The L3-L4 interspace was identified and 23G quinckeabcock needle was introduced in this space through a midline approach. Once the needle pierced the dura and was in the subarachnoid space, stylet was removed and free flow of CSF was verified and 3,5 of 0.5% Bupivacaine was administered intra thecally. The patients were turned supine and oxygen was administered at a rate of 6 lit/mt by a face mask.IVF were administered at a rate of 1000ml/hr throughout the surgery. Systolic BP, Diastolic BP, MAP, SPO₂ were noted every minute till the onset of hypotension and then recorded every 2 minutes for 10 minutes thereafter every 5 minutes after study drug usage, till the end of surgery. The highest level of sensory block was assessed by pinprick method 5 minutes after SAB. The incidence of tachycardia (HR>120/mt) and its time of onset was noted. The occurrence of hypertension (>20% increase in systolic BP from baseline values) was noted. Total intravenous fluids given and urine output was also noted.

The descriptive statistics of the variables studied were represented as two-way tables. The categorical factors were represented by the number and frequency (%) of cases. The continuous variables were represented by measures of central frequency and deviation. The differences in the proportions of are tested for statistical significance using non-parametric Chi-square test for variables measured on nominal scale. When testing for two factors, the Mann-Whitney "U" test or Wilcoxon two sample test was used. Fisher's exact probability test was used wherever indicated. For variables measured on a continuous scale, one-way analysis of variance (ANOVA) was employed to elicit the statistical significance of variation when three variables were taken together. When testing for two groups (pair wise), Student "t" test is used to test for statistical significance in the differences of the two means.

4. Results

The variation in the mean distribution of cases by age between Group I, Group II and Group III was not statistically significant (p=0.52). The variation in the mean values by height between Group I, Group II and Group III was not statistically significant. The variation in the mean values by weight between Group I, Group II and Group III was not statistically significant. The distribution of time to develop hypotension values between Group I, Group II and Group III did not reveal any statistically significant differences. The results were similar when the groups were compared in pairs. The distribution of SAB-Delivery values between Group I, Group II and Group III did not reveal any statistically significant differences. The results were similar when the groups were compared in pairs. The comparison of mean lowest systolic BP values between the three groups was not statistically significant. The results were the same for pair wise comparisons of groups. The mean distribution of anthropometric values of the heart rate, systolic BP and MAP at baseline between the three groups was not statistically significant. The results were the same for pair wise comparisons of groups.

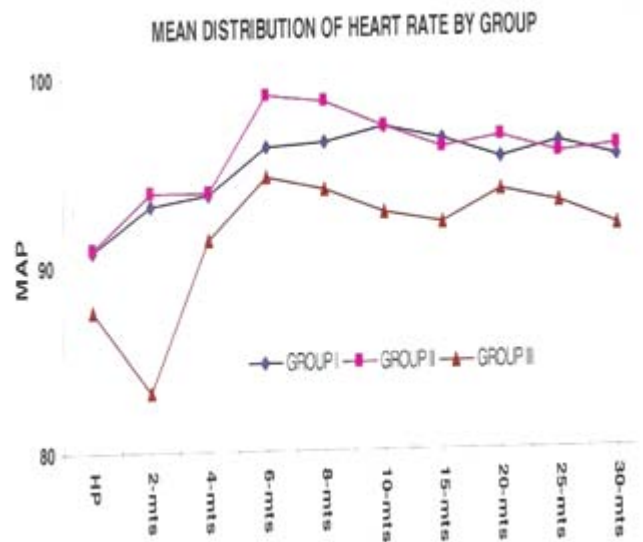


Figure 1: Mean Distribution of Heart Rate

The mean value of heart rate was generally the highest in Group II followed by Group I and Group III. The mean variation of heart rate values between the three groups was statistically significant at 2mts. Pair wise comparison of groups showed that the differences in mean values were statistically significant between Group II and III and between Group I and III at 2-minutes

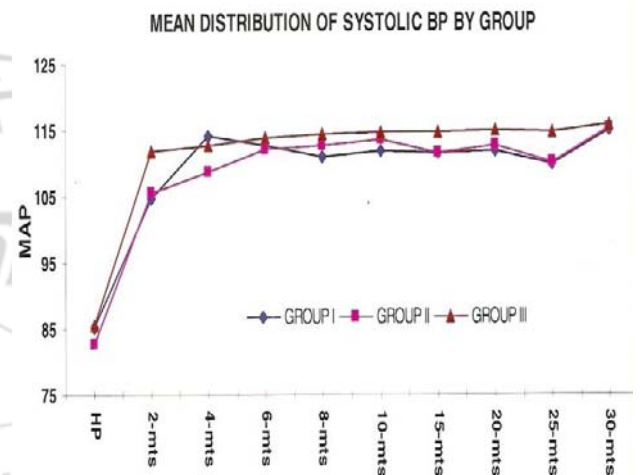


Figure 2: Mean Distribution of Systolic B.P

The distribution of mean values of systolic BP was generally the highest in Group III especially after 6 minutes. The variation in mean systolic values between the three groups was not statistically significant at any time point studied. The mean value of diastolic BP was greater in Group III than Group I or Group II values at 2nd and 4th minutes. The variation in the mean values of diastolic BP between the three groups was statistically significant at 2-minutes (p=0.01) and between 20 and 30 minutes. Pair wise comparison of groups revealed that the mean differences were statistically significant between Group I and Group II at 8-minutes (p=0.02).

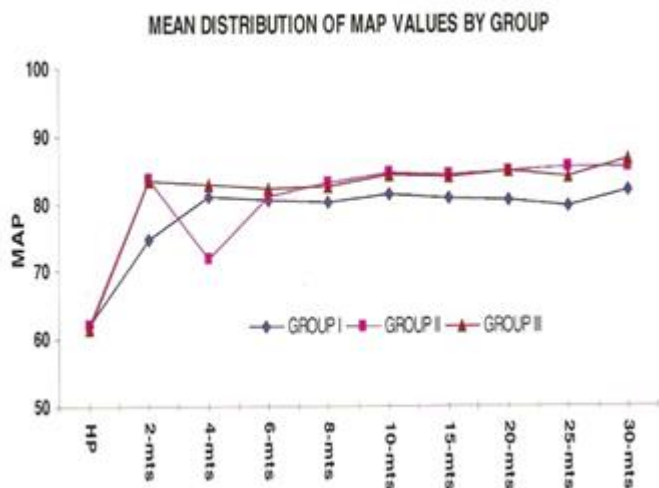


Figure 3: Mean Distribution of Mean Arterial Pressure

The mean differences in MAP values between the three groups were statistically significant at 2-minutes ($p=0.003$), 4 minutes ($p<0.001$) and 25-mts ($p=0.04$). The pair wise comparisons between Group I and Group II was statistically significant at 25-minutes ($p=0.02$) and between Group I and Group III at 30-mts ($p=0.03$).

Table 1: Distribution of cases by groups and MAP

MAP	Group I (n=30) Mean \pm S.D	Group II (n=30) Mean \pm S.D	Group III (n=30) Mean \pm S.D	p-value
Base line	89.2 \pm 5.57	92.3 \pm 7.11	90.3 \pm 6.93	0.19
HP (VP given)	62.2 \pm 7.69	62.1 \pm 7.47	61.4 \pm 7.33	0.89
2mts after VP	74.6 \pm 13.38	83.7 \pm 7.60	83.3 \pm 11.7	0.003*
4 mts	81.0 \pm 13.28	71.8 \pm 5.95	82.8 \pm 13.31	<0.001*
6 mts	80.6 \pm 10.11	80.9 \pm 8.47	82.1 \pm 10.74	0.83
8 mts	80.2 \pm 8.11	83.1 \pm 6.79	84.2 \pm 12.50	0.35
10 mts	81.2 \pm 8.43	84.4 \pm 9.46	84.2 \pm 10.11	0.35
15 mts	80.8 \pm 8.42	84.2 \pm 9.09	83.9 \pm 9.00	0.26
20 mts	80.5 \pm 6.82	84.8 \pm 8.13	84.9 \pm 9.07	0.054
25 mts	N=29 79.6 \pm 7.68	N=30 85.3 \pm 9.65	N=30 83.9 \pm 8.66	0.04*
30 mts	N=28 82.0 \pm 7.03	N=30 85.4 \pm 9.16	N=29 86.6 \pm 8.40	0.10

* significant ($p < 0.05$)

5. Discussion

After subarachnoid block for inguinal hernia repair surgeries, hypotension can be minimized by the use of IV fluid preload, appropriate levels of blockade, and judicious use of vasopressor agent. For the purpose of this study, hypotension was defined as a decrease in arterial pressure greater than 20% from baseline systolic pressure.

In our study the mean value of heart rate was generally highest in Mephentermine Group followed by Ephedrine and Phenylephrine Groups. Also the mean variation of heart rate between the three groups was statistically significant at 2 minutes. Pair wise comparison between the three groups were also statistically significant between the three groups at 2 minutes after administration of the vasopressor. In spinal anaesthesia, since there is decreased venous return, decreased venous pressure and a decreased right heart pressure thus slowing of the heart rate is expected on the

basis of the Bain bridge reflex. Bradycardia is also expected in high spinal, probably due to some paralysis of the cardio-accelerator nerves. We found that the maternal heart rate was slower with Phenylephrine than with Ephedrine and Mephentermine. This is consistent with the mechanism of action of these drugs that the decrease in heart rate found in Phenylephrine group was due to pure α receptor activity compared with Ephedrine and Mephentermine as they had got a mixed action directly as well as indirectly on α and β receptors. Similar results were seen in many studies which was consistent with our study.

In the study done by Dinesh Sahu et al found Phenylephrine to cause significant reduction in heart rate after the bolus dose [1]. Systematic review by NganKee et al concluded that Phenylephrine may decrease maternal heart rate and cardiac output [2]. In David Cooper et al's study on comparing the effects of Ephedrine and Phenylephrine when administered alone and in combinations they found that mean heart rate was higher in Ephedrine group than in the Phenylephrine group [3]. NganKee WD et al's showed on comparing the effects of prophylactic infusion and bolus Phenylephrine they found that heart rate was significantly slower over time in the infusion group compared with the control group [4].

The systolic, diastolic and mean arterial pressure were decreased statistically significant at the onset of hypotension and increased after the bolus dose of drug in all the three groups. The pressures generally remained high in Mephentermine and Phenylephrine groups when compared with Ephedrine group. Systolic blood pressure was generally highest in Phenylephrine group immediately after the administration. The diastolic blood pressure was also greater in Phenylephrine group when compared with ephedrine and Mephentermine groups, especially after 2 minutes and 4th minute, after administration of the drug. In Ephedrine group the diastolic blood pressure was generally less throughout the study period, when compared with other two drugs. MAP was also less in Ephedrine group when compared with Mephentermine and Phenylephrine groups. The mean differences in MAP between the three groups were statistically significant at 2nd 4th and 25th minute after the administration of vasopressor. This finding is consistent with the onset of action and efficacy of the drug that Phenylephrine has quicker onset of action and better maintenance of arterial pressures when compared with the other two drugs.

Dinesh Sahu et al studied the effects of bolus Ephedrine, Mephentermine, Phenylephrine for the maintenance of arterial pressure during spinal anaesthesia for LSCS [5]. In their study all the three vasopressor effectively maintained arterial pressure within 20% of baseline value though Phenylephrine maintained better in first 6 minutes of bolus dose as compared with Ephedrine and Mephentermine and Phenylephrine has a quicker peak effect. This finding is consistent with our study.

Laporta et al compared maternal and neonatal catecholamine concentrations, following the use of either bolus Phenylephrine or Ephedrine to treat a drop in maternal blood pressure after spinal anaesthesia for caesarean section. They

found that Phenylephrine appears to be safe and effective as Ephedrine in treatment of drop in blood pressure in healthy non-laboring parturient undergoing LSCS[6].

Anna Lee et al in their quantitative systematic review, they found that for the management (prevention and treatment) of hypotension, there was no difference between Phenylephrine and Ephedrine and both effectively maintained the systolic BP within 20% of baseline values [7]. Thomas DG et al in their study compared the efficacy of bolus Ephedrine and Phenylephrine for maintenance of arterial pressure during spinal anaesthesia for caesarean section and found that maternal systolic BP and cardiac output changes are similar in both groups [8].

Cyna AM et al studied the randomized controlled trials comparing the interventions to prevent hypotension during spinal anaesthesia for caesarean section. they found that Ephedrine was significantly more effective than control or crystalloid in preventing hypotension. There were no significant differences between Ephedrine and Phenylephrine in treating hypotension. Similar results were obtained from our study also [9]. Ram Nathan et al assessed the maternal hemodynamic changes and neonatal acid-base status in 127 healthy patients undergoing elective caesarean under epidural anaesthesia and concluded that both Ephedrine and Phenylephrine increase cardiac preload and effectively maintained the systolic blood pressure within 20% of baseline values [10].

David Cooper et al compared Phenylephrine. Ephedrine 3mg/ml and Phenylephrine 50 jig/ml & Ephedrine 1.5mg/ml in combination given by infusion to maintain maternal systemic arterial pressure at baseline during spinal anaesthesia for LSCS and found that the mean systolic arterial pressure was similar in three groups[11]. Lauckner W et al studied the effects of IV Mephentermine in 10 late pregnant women with hypotension after SAB and found that Systolic and diastolic blood pressure increased significantly. The cause of this rise in arterial blood pressure is due to increase in stroke volume exclusively and no significant changes occurred in heart rate. They finally concluded that Mephentennine is suitable for the treatment of hypotension during pregnancy [12].

Kansai A et al compared the effects of IV infusions of Ephedrine and Mephentermine for maintenance of maternal arterial pressure receiving subarachnoid block for LSCS and found that baseline hemodynamic parameters, hemodynamic changes subsequent to the start of vasopressor infusion, were statistically similar in both groups [13]. Smith N et al investigated circulatory effects of single intravenous injections of 0.75 mg/kg Mephentermine in five healthy volunteer subjects. They found that first injection of Mephentermine increased mean arterial pressure, systemic vascular resistance, and left ventricular minute work, with no change in the other variables [14]. Brooker RF et al studied sequential infusion of Phenylephrine to manage hypotension. In their study also Phenylephrine was effective at restoring systolic blood pressure after spinal anaesthesia[15]. Yap JC et al on comparing the efficacy of fluid preloading with two fluid-vasopressor regimens IV ephedrine boluses was more effective in maintaining systolic blood pressure [16].

Alahutta S et al studied the effects of Ephedrine and Phenylephrine to maintain the systolic arterial pressure 20% above the baseline values during spinal anaesthesia for caesarean section. In this study also both the vasopressors restored maternal arterial pressure effectively [17].

All the three vasopressors maintained the arterial pressure effectively within 20% of baseline values. The mean value of heart rate was highest in Mephentermine group followed by Ephedrine and Phenylephrine groups. The mean values of Systolic BP, Diastolic BP and MAP were higher in Phenylephrine group followed by Mephentermine group and Ephedrine group throughout the study period. The heart rate generally remained low throughout the study period in Phenylephrine group and the incidence of bradycardia was more in Phenylephrine group when compared with other two. In conclusion, we found that all the three vasopressors namely Ephedrine, Mephentermine and Phenylephrine are effective in IV bolus form in maintenance of arterial pressure within 20% limit of baseline values, though Phenylephrine has quicker peak effect, in comparison to Ephedrine and Mephentermine and it causes reduction in heart rate, which may be advantageous in patients in whom tachycardia is undesirable.

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