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Efficacy of Intramuscular Ephedrine in Reducing the Incidence of Hypotension After Spinal Anaesthesia

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Abstract

Context: Spinal anaesthesia remains one of the basic and important technique in the modern period, but associated with adverse effects like hypotension, bradycardia, post-spinal headache. Several options have been tried to prevent spinal induced hypotension but the problem continues. Therefore this study was conducted to see the efficacy of prophylactic intramuscular ephedrine in reducing the incidence of spinal induced hypotension. *Aims:* To observe the outcome of prophylactic IM ephedrine on intraoperative hemodynamic changes after spinal anaesthesia and also to see the incidence of hypotension after spinal anaesthesia *Settings and Design:* Prospective Randomised Controlled study *Methods and Material:* Study was conducted on 108 patients posted for elective lower abdominal and lower limb surgeries under spinal anaesthesia. Group A received intramuscular ephedrine 30mg (1ml), group B received intramuscular normal saline (1ml) as placebo 10 minutes before spinal anesthesia. Patients were monitored for intraoperative hemodynamics, to see the incidence of hypotension and also to see any adverse side effects during intraoperative period. *Statistical analysis used:* To find the significance on continuous scale between two groups, Student t test was used. Leven`s test used to find the homogeneity of variance. Chi-square/Fisher Exact test: used for significance of categorical scale study parameters between the groups, Fisher exact test is applied when samples are very small. *Results:* Incidence of hypotension was more in group B and proven to be statistically significant when compared to ephedrine group from 2 – 20 minutes. The numbers of patients receiving the rescue vasopressor therapy was higher among in group B. There was no side effects observed in both the groups. *Conclusions:* Intramuscular ephedrine when given prophylactically 30mg, 10 minutes before spinal anaesthesia provides better haemodynamic stability during intraoperative period without any side effects.

Keywords: Ephedrine,Hypotension, Intramuscular, Spinal Anaesthesia

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Introduction

Spinal anaesthesia is one of the basic and important technique since it came into the daily practice. It is widely practiced regional anaesthesia technique for many lower abdominal and lower limb surgeries [1]. But also associated with significant adverse effects like hypotension, bradycardia, post-spinal headache. Despite of its fast revival, prevention of post spinal hypotension still continues to be a

Major problem faced by Anaesthesiologists. Fall in Systolic Blood pressure by 30% from the baseline record is considered as hypotension.

Many methods came into existence to counter the spinal induced hypotension like preloading

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with colloid/crystalloids, leg elevation with compression bandages, stockings or inflatable boots, premedication with IV Atropine 0.6mg, IM Glycopyrolate, Ondansetron, Vasopressors[2,3,4,5,67].

For treating the hypotension after spinal anaesthesia, vasopressors are the choice. Effect of vasopressor should reduce the rise in level of sympathetic blockade, which is difficult to obtain because the alpha and beta adrenergic activities may act independently during blockade.

The Vasopressors used commonly (phenylephrine, ephedrine) have systemic effects and may have effects on organs, vascular system or fetus. One of the vasopressor is Ephedrine, which is commonly used drug in the treatment of hypotension following spinal anaesthesia. Its mechanism involves stimulating both alpha and beta adrenergic receptors and releases norepinephrine from sympathetic neurons.

It has slow onset and long duration of action than phenylephrine. It does not cause uterine vasoconstriction further preserving utero-placental blood flow while maintaining maternal blood pressure.

By increasing cardiac output and heart rate due to its action on beta-1 adreno receptor, it maintains arterial pressures and having less chance of utero-placental insufficiency even if we plan to go for general anaesthesia in case failure of spinal blockade.

Reactive increase in HR, BP in underweight patients and inadequate control of hypotension in overweight patients are some observation. IM dose less than 25 mg is ineffective to prevent decrease in BP and 50 mg is associated with increased incidence of reactive rise in BP and fetal acidosis are some of the observations made by several studies[8].

When compared mephentermine, ephedrine and phenylephrine are equally effective in preventing hypotension from SAB. Requirement of less maintenance dose with ephedrine is observed[9].

In comparison, the use of phenylephrine was associated with better fetal acid-base status, but the risk of maternal bradycardia (responsive to atropine) was larger than in those women given ephedrine[10].

Daily for treating spinal induced hypotension in our hospital many treatment options have been tried, but problem still continues. This study was conducted and proven to be effective against spinal induced hypotension earlier, but found to be controversial in pregnant patients (due to its inconclusive effect on fetal outcome, this study is avoided in pregnant patients).

Therefore this study, conducted in our hospital in patients undergoing elective lower abdomen and lower limb surgeries under spinal anaesthesia to observe the outcome of prophylactic intramuscular ephedrine and to reduce the further incidence of spinal induced hypotension.

The aim of our study was to observe the outcome of prophylactic intramuscular ephedrine on the hemodynamic changes after spinal anaesthesia and also to mark the incidence of spinal induced hypotension.

Materials and Methods

Study was conducted on 108 patients undergoing lower abdominal and lower limb surgeries at tertiary care hospital during the academic year from January 2018 to May 2019.

The selection of patients were carried out randomly. Patients were briefed in the understandable language the anaesthesia procedure they are going to undergo. Pre-anaesthetic checkup was done one day before the surgery which included general physical examination, systemic examination and examination of spine.

Basic investigations like haemoglobin percentage, total blood count, differential blood count, serum electrolytes, renal function tests, urine routine, bleeding and clotting time, blood Sugars (if urine sugar positive) were advised.

On the day of surgery, drugs and resuscitation equipment checked and kept ready. The baseline Heart rates (HR) Systolic blood pressure (SBP), Diastolic blood pressure (DBP) were recorded.

Patients then were randomly allocated into two groups. 18 gauge intravenous line was secured. Group A received IM ephedrine 30 mg (1ml) 10 minutes before spinal anaesthesia. Group B received injection normal saline (1ml) (placebo) 10 minutes before spinal anaesthesia along with preloading of 15ml/kg of ringer lactate in each group.

Patients then shifted to the operation theatre. The pre subarachnoid block heart rate, systolic blood pressure, diastolic blood pressure were recorded for all patients and continuous monitoring done.

Under strict aseptic precaution lumbar puncture was done using 25-gauge disposable quincke type of spinal needle at L3-L4 spinal intervertebral space by midline approach. After the continuous

free back flow of cerebrospinal fluid, 3.2ml (0.5% 5mg/ml) heavy bupivacaine hydrochloride plus 0.3ml (90mcg) of buprenorphine was injected intrathecally irrespective of weight and height of the patients and the time noted.

Heart rate, systolic blood pressure, diastolic blood pressure were recorded in all patients at every 2 minutes interval for 10 minutes, then at every 10 minutes interval up to 45 minutes and then at every 15 minutes till the end of surgery or up to 90 minutes.

Level of sensory blockade was checked using a 23G hypodermic needle, Success of the block was defined as pinprick analgesia extending cranially to the desired dermatome. Ringer lactate was infused at the rate of 15 ml/min upto 1 hour after starting the operation in both groups then reduced to 10 ml/min if operation continued beyond 1 hour.

Following subarachnoid block, patient are monitored for any decrease in BP, nausea, vomiting, desaturation (SpO2 < 90%) or any other side effects. Hypotension was defined as a decrease in systolic blood pressure (SBP) more than 30% from the base line. If hypotension occurred, then they were treated first with 200 ml rapid infusion of ringer lactate was done. If hypotension continued they were treated with rescue vasopressor (mephentermine) administered intravenously in 6mg boluses.

Injection Atropine 0.6mg was administered intravenously if the heart rate goes below 50 per minute. Tachycardia was defined as HR more than 100 beats per min, and hypertension was defined as rise of MAP more than 20 mmHg over the baseline.

Statistics: To find the significance on continuous scale between two groups, Student t test was used. Leven`s test used to find the homogeneity of variance. Chi-square/Fisher Exact test: used for significance of categorical scale study parameters between the groups, Fisher exact test is applied when samples are very small.

Results

All patients were monitored clinically in the intraoperative period. It was noticed that none of the patients in both the groups had changes in oxygen saturation ($p = 0.372$, Not Significant, Fisher Exact Test) as shown in Table 1.

The occurrence of hypotension was more in placebo group when compared to ephedrine group and proven to be significant [Strongly significant (P value: $p \leq 0.01$)]. It was observed that hypotension occurred more in the first 20 minutes (from 2 minute) after subarachnoid block in placebo group (Table 2).

Table 1: Comparision of oxygen saturation

SpO_2%	Total	Group I	Group II
97	3(2.8%)	2(3.7%)	1(1.9%)
98	14(13%)	8(14.8%)	6(11.1%)
99	54(50%)	27(50%)	27(50%)
100	37(34.3%)	17(31.5%)	20(37%)
Total	108(100%)	54(100%)	54(100%)

Table 2: Mean arterial pressures among two groups

MAP (mm Hg)	Total	Group I	Group II	P value
Basal	96.89 ± 10.07	97.3 ± 9.81	96.48 ± 10.41	0.676
Imme-diately after sab	94.9 9 ± 10.23	96.2 ± 9.89	93.78 ± 10.5	0.219
2 mins	90.99 ± 10.25	93.2 ± 9.22	88.78 ± 10.82	0.024*
4 mins	88.06 ± 11.99	91.43 ± 11.15	84.69 ± 11.94	0.003**
6 mins	85.48 ± 11.55	88.65 ± 11.45	82.31 ± 10.85	0.004**
8 mins	83.80 ± 01.59	87.8.110.91	79.80 ± 10.94	<0.001**
10 mins	83.20 ± 10.63	86.44 ± 10.53	79.96 ± 9.79	0.001**
20 mins	83.03 ± 9.94	86.39 ± 9.62	79.67 ± 9.17	<0.001**
30 mins	83.35 ± 9.49	85.07 ± 10.00	81.63-8.71	0.059+
40 mins	84.67 ± 8.79	84.56+9.65	84.78 ± 7.94	0.896
60 mins	84.70 ± 8.24	85.00+8.79	84.41 ± 7.73	0.711
80 mins	85.72 ± 7.51	84.98+8.37	86.46 ± 6.53	0.308
90 mins	87.22 ± 8.19	86.81+9.28	87.63 ± 7.00	0.608

Table 3: Rescue agents used among two groups

Drugs Used	Total (n = 108)	Group I (n = 54)	Group II (n = 54)
Nil	69 (63.9%)	48 (88.9%)	21 (38.9%)
Yes	39 (36.1%)	6 (11.1%)	33 (61.1%)
Mephentermine 6 mg	6 (5.6%)	28 (51.9%)	34 (63%)
Atropine .6 mg	0 (0%)	4 (7.4%)	4 (7.4%)
Mephentermine at 30 mm, atropine .6 mg at 80. Min	0 (0%)	1 (1.9%)	1 (1.9%)

Table 4: Heart rate among two groups

Heart Rate (beats/min)	Total	Group I	Group II	P value
Basal	83.31 ± 12.32	85.74 ± 14.23	80.91 ± 9.58	0.041*
Immediately after sab	84.03 ± 13.83	87.07 ± 16.26	80.98 ± 10.14	0.021*
2 mins	82.96 ± 14.48	87.04 ± 17.12	78.89 ± 9.82	0.003**
4 mins	82.26 ± 14.16	86.74 ± 16.37	77.78 ± 9.81	0.001**
6 mins	80.2 ± 12.81	84.22 ± 14.3	76.19 ± 9.7	0.001**
8 mins	78.99 ± 12.65	82.7 ± 14.02	75.28 ± 9.91	0.002**
10 mins	78.56 ± 14.54	83.21 ± 16.68	73.91 ± 10.23	0.001**
20 mins	78.55 ± 13.4	82.94 ± 4.55	74.15 ± 10.56	<0.001**
30 mins	78.64 ± 12.71	82.98 ± 11.7	74.3 ± 12.28	<0.001**
40 mins	78.21 ± 11.85	81.04 ± 11.93	75.39 ± 11.18	0.013*
60 mins	78.16 ± 12.38	81.17 ± 13.71	75.15 ± 10.16	0.011*
80 mins	77.85 ± 10.9	79.87 ± 11.29	75.79 ± 10.19	0.053+
90 mins	78.1 ± 11.31	80.19 ± 11.76	76.02 ± 10.54	0.055+

The requirement of rescue agent is seen in 39 patients, in which 6 patients were from ephedrine group and 33 patients were from placebo group. Our study is similar to the below studies done with prophylactic ephedrine.

It is observed that heart rate when compared to two groups, placebo group shows drop in heart rate between (2 to 30) minutes and proven to be statistically significant using student t test [Strongly significant (p value ≤ 0.01)] as shown in Table 3.

There was no incidence of nausea, vomiting and any other side effects in both the groups.

Discussion

In view of lesser efficacy of mechanical and volume expansion methods to correct spinal induced hypotension, pharmacological methods have come into practice to reduce the occurrence of spinal induced hypotension. Several studies have done and proven that administration of vasopressors prophylactically in correcting hypotension are effective.

Among the Vasopressors Ephedrine, has better results in correcting the non-cardiac circulatory complications of spinal anaesthesia than a single alpha or beta-adrenergic agonist.

But intramuscular use of vasopressor is in borderline particularly when given before spinal anaesthesia because of rise in blood pressure risk and placental perfusion inadequacy, if subarachnoid block fails. But spinal anaesthesia procedure is easy to perform and <1% is its failure rate [11] and thus we excluded those patients who have spine anomalies to perform subarachnoid block in turn limiting the chances of block failure.

Ephedrine maintains arterial pressure by increasing cardiac output and heart rate. Due to its action on beta1 adreno receptor there is small chance of utero-placental insufficiency even if we have to go for general anaesthesia due to spinal anaesthesia failure.

We have used prophylactic intramuscular ephedrine 30 mg, in lesser dose when compared to other studies which have shown positive effect and also to see the potency of the drug in reducing the spinal induced hypotension and to look after any adverse side effects associated with it.

All patients were monitored clinically in the intraoperative period in our study. It was noticed that none of the patients in both the groups had changes in oxygen saturation (p = 0.372, Not Significant, Fisher Exact Test).

We defined hypotension as 30% decrease in mean arterial pressures from baseline. We observed that

occurrence of hypotension was more in placebo group when compared to ephedrine group and proven to be significant. It was observed that hypotension occurred more in the first 20 minutes (from 2 minute) after subarachnoid block in placebo group.

Even in our study, ephedrine has proven to be effective but the difference is other studies have compared between the dosages and timing of giving ephedrine along with preloading. Results showed that giving ephedrine 10 minutes before SAB is more effective [7,12].

In our study, the rescue agent used is mephentermine 6mg IV boluses when the MAP is less than 30% from the baseline. Whenever the baseline MAP is between 20-30%, initially resuscitated with crystalloids. But when the MAP is below 30% of the baseline, rescue agent was given in IV bolus and observed for the pressures to improve. But even if pressures fail to improve, patient was given the repeated IV bolus of mephentermine 6mg.

We noticed that the requirement of rescue agent is seen in 39 patients, in which 6 patients were from ephedrine group and 33 patients were from placebo group. Our study is similar to the below studies done with prophylactic ephedrine.

Bhar D in 2011, noted that ephedrine requirement was significantly less ($p<0.05$) in group E10 compared to other groups. Total dose of rescue IV ephedrine and delayed hypotension was less in both group E10 and E20 compared to group C but no difference was seen in E10 and E20 group. Time of first requirement of ephedrine was more in both group E10 and E20 compared to group C [7].

Ahmed H O, Hossam M, Adel A in 2016, made observations that hypotension was significantly more in fluid group when compared to ephedrine group. P value was 0.03. Ephedrine bolus dose required to correct hypotension was significantly lower in ephedrine group (0.3 ± 0.54) when compared to fluid group (0.6 ± 0.8) p value 0.046* [13].

In our study, it is observed that heart rate when compared to two groups, placebo group shows drop in heart rate between (2 to 30) minutes and proven to be statistically significant using student t test.

Bhar D in the year 2011, noticed that HR intraoperatively was more in ephedrine group E10 and E20 significantly compared to group C ($p < 0.05$). No difference was seen among group E10 and E20 [7].

Heart rate was higher in Ephedrine group when compared to Fluid group. But it was not statistically significant, P value more than 0.05 was the observations made by Ahmed HO, Hossam M, Adel A in 2016.[13]

Nausea and Vomiting side effects may because of the decrease in flow of blood to the trigger zone, and Ephedrine is the drug which increases mean arterial pressure and tries to improve the medullary blood flow. Due to the preganglionic sympathetic denervation, increase in peristalsis may also stimulate during spinal anesthesia, but whether Ephedrine could prevent or reduce thisaction is unknown.

Double blinded randomized prospective study done by Iqbal M S, Ishaq M, Masood A, Khan M Z in 2010 drawn a conclusion that the occurrence of nausea and vomiting wasmore in group-I (ephedrine 10 mg IV) and was related to hypotension (53%) whencompared to other groups with 15 mg and 20 mg IV prophylactically[14].

In 2011, Bhar D in his study noted that due to improved hemodynamic stability in E10 group (Ephedrine 30 mg, 10 minutes before SAB), occurrence of nausea and vomiting was significantly less compared to other groups.[7]

With above studies conducted and stating that with better stability of hemodynamic status, the occurrence of nausea and vomiting is reduced. In our study we didn't notice any occurrence of nausea and vomiting in both the groups.

Golakiya H N in 2016, in their randomized double blinded parallel study on 150 parturient with comparison between mephentermine, ephedrine, and phenylephrine. It was noted that, there is no difference between mephentermine, ephedrine and phenylephrine immediately after the SAB. It was found that, there was less requirement of maintenance dose with ephedrine. Phenylephrine have shown episodes of maternal bradycardia.[15]

Yadav A S, Shakya M L, Dwivedi S in 2016, on their comparative evaluation of prophylactic IM ephedrine and mephentermine made the observations that ephedrine and mephentermine when given IM prophylactically before SAB reduces the occurrence of hypotension. Apgar score was lower in mephentermine group 50.[16]

Kaur D, Khan A L, and Pathak A in 2018, on the comparative study between the three vasopressors, Phenylephrine, ephedrine, mephentermine concluded that phenylephrine is fast -acting

and short-lived normotensive effect added with a bradycardia effect. However, ephedrine and mephentermine had a steady progression and stable normotensive effect with no bradycardia effect. Hence, mephentermine and ephedrine were similar in performance, had a better hemodynamics control and had less recurrence when compared to phenylephrine.[17]

When topic comes to the standard vasopressor for the treatment of spinal induced hypotension, the above studies have concluded their observations of the advantages and disadvantages. In our hospital we traditionally use mephentermine intra-operatively to treat hypotension. There were lot of studies conducted on phenylephrine with its advantages being on good fetal outcome. But studies regarding ephedrine were reduced, may be because of poor fetal outcome which was still controversial. But when compared to ephedrine and phenylephrine, both have shown their efficacy on reducing the incidences on hypotension but with regard to phenylephrine, it has shown episodes of bradycardia and also the requirement of maintenance rescue agent is more. Hence we used prophylactic ephedrine IM 30 mg aiming to reduce the incidence of post spinal hypotension and also to have good hemodynamics intra-operatively. Our study have shown the expected results.

Study conducted on comparison between prophylactic ephedrine and preloading with fluids by Varathan S, Ekanayake U S, Amarasinghe U in 2009, in patients undergoing elective cesarean section under spinal anesthesia have come with conclusion that APGAR scores at 1min and 5min was found to be in the normal range in either of the groups. No association was found between the IM ephedrine and fetal acidosis.[12]

Varghese N, Gurumurthy T in 2013, studied the effect of prophylactic ephedrine infusion and compared it with crystalloid preloading on neonatal acid-base outcome in elective caesarean section following SAB and concluded that, the APGAR score at 1 min and 5 min were good in both the groups. There were no case of fetal acidosis. There was ($p > 0.05$) no difference significantly in the umbilical blood gas values between Group Iand Group II.[18]

With the above conclusions made on the efficacy of ephedrine on fetal outcome by various studies, it is still inconclusive to use ephedrine in pregnant females undergoing cesarean section under spinal anesthesia. Therefore we have carried out this study on ephedrine in patients undergoing lower abdominal and lower limb surgeries under spinal anaesthesia excluding cesarean sections.

Strengths and Limitations

We have used very low dose of ephedrine that was effective in preventing hypotension and bradycardia without causing any side effects and the drug was cost effective.

We have excluded parturients in our study, may be low dose ephedrine in this group of patients may reduce incidence of hypotension and fetal acidosis.

Conclusion

The prophylactic administration of IM Ephedrine in ASA Grade I & II patients undergoing lower abdominal and lower limb surgeries under spinal anaesthesia, is a potent measure in bringing down and arresting the incidence of hypotension without causing any predicted side effects like central nervous system stimulation, tachycardia or arrhythmias.

To conclude, this study demonstrates that prophylactic IM Ephedrine is a simple, easy, effective and reliable method in reducing the occurrence of hypotension.

Key Messages: Ephedrine has faired better in maintaining blood pressures and heart rate when given pre-emptively, thus preventing unwanted hypotension that may result because of sympathetic blockade secondary to subarchnoid block.

Conflict Of Interest: ***None***

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