Original Research Article

Effectiveness of prophylactic phenylephrine against placebo in prevention of post-sub arachnoid block hypotensive response in elective urological surgeries: A randomized double-blind controlled study

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Abstract

Background: The most common complication of this anaesthetic technique is hypotension, with a particularly frequent incidence in the elderly. Various techniques are being used to control the hypotension. The main mechanical method is lower limb compression by elastic or pneumatic stocking or wrappings. Because of the poor efficacy of non-pharmacological technique in effectively managing hypotension – a vasopressor is almost always required. **Aims and objectives:** To study was the efficacy of IM phenylephrine against spinal anaesthesia-induced hypotension in normotensive patients scheduled for Elective Urological Surgeries. **Materials and method:** The present randomized controlled, double blind study was conducted in the department of anaesthesia of tertiary care institute to study complications after prophylactic phenylephrine and Placebo used for prevention of post Sub Arachnoid Block hypotensive response in patients undergoing elective urological surgeries under Sub Arachnoid Block". Total 60 patients were enrolled in the present study and were divided in to two groups containing 30 patients each. A computer generated randomized plan was made, which placed patients randomly in the two groups. Group P (Phenylephrine group) and Group C (Control group). The collected data was recorded in excel sheet and was analysed with appropriate tests. A value of $P<0.05$ was considered statistically significant. **Results:** Both the groups were similar in age, ASA status, sex distribution and baseline hemodynamic variables. There was no significant difference in baseline SBP of both the groups. Fall in systolic blood pressure during 4-8min after sub- arachnoid block was observed. The fall in SBP observed in group C as compared to group P was significant which corresponds with the time taken to achieve required sensory dermatomal level. In 3.33% patient in group P while in 43.33% patients in group C and the difference observed statistically significant. **Conclusion:** In conclusion, we demonstrated that prophylactic injection of 2 mg of phenylephrine IM is a effective means for reducing the incidence of hypotension associated with hyperbaric bupivacaine spinal anaesthesia during elective urological surgeries in normotensive patients, including both young and elderly.

Key Word: subarachnoid anaesthesia, Intramuscular phenylephrine, hypotension,

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Spinal, epidural, and caudal neuraxial blocks result in sympathetic blockade, sensory analgesia, or anesthesia and motor blockade, depending on the dose, concentration, or volume of local anesthetic, after insertion of a needle in the plane of the neuraxis.1 Spinal anesthesia is commonly practiced neuraxial anesthesia for various surgeries including gynecological, obstetrics, urological, orthopedics, etc. The most common impediments to the effective use of neuraxial blocks are the predictable decreases in arterial blood pressure and heart rate through the accompanying sympathectomy with

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its attendant vasodilation and blockade of cardioaccelerator fibers. Maintaining arterial blood pressure and heart rate at normal values during these blocks often requires the administration of vasoactive drugs and intravenous fluids.1 The most common complication of this anaesthetic technique is hypotension2,3, with a particularly frequent incidence in the elderly.4-6 This problem is a particularly important issue in elderly patients with cardiovascular disease such as hypertension, because their risk of ischemia secondary to hypotension is thus increased.7The cardiovascular effects of neuraxial blocks are similar in some ways to the combined use of intravenous α1- and β- adrenergic blockers: decreased heart rate and arterial blood pressure. The sympathectomy that accompanies the techniques depends on the height of the block, with the sympathectomy typically described as extending for two to six dermatomes above the sensory level with spinal anesthesia and at the same level with epidural anesthesia.8 This sympathectomy causes venous and arterial vasodilation, but because of the large amount of blood in the venous system (approximately 75% of the total volume of blood), the venodilation effect predominates as a result of the limited amount of smooth muscle in venules; in contrast, the vascular smooth muscle on the arterial side of the circulation retains a considerable degree of autonomous tone. Various techniques are being used to control the hypotension. The main mechanical method is lower limb compression by elastic or pneumatic stocking or wrappings. This augments circulating volume and has been shown to reduce the incidence of hypotension. However, this technique has not gained popularity, probably because it has limited efficacy and is not viewed as convenient. Intravenous hydration is common practice to give IV fluids before and during spinal anesthesia to prevent hypotension. In elderly patients, however, fluid preloading is not always effective.4,9 Because of the poor efficacy of non-pharmacological technique in effectively managing hypotension – a vasopressor is almost always required. However, there is controversy regarding both the choice of vasopressor and the optimal method of administration. Usually an IV bolus dose of a vasopressor is commonly used. An alternative approach suggested by a number of recent authors is the use of an IM depot injection of a vasopressor. However, the best vasopressor to avoid the heart rate (HR) and blood pressure sequelae of spinal anesthesia remains a controversial topic among anesthesiologists. Ephedrine is a long established and readily available drug that is familiar to most anaesthetist. Ephedrine is a non-specific adrenergic agonist, and increase blood pressure mainly by increasing cardiac output with a smaller contribution from vasoconstriction. Ephedrine's action is mainly indirect, via stimulating release of norepinephrine from sympathetic nerve terminals. Clinical studies now show that alpha- agonists such as phenylephrine and metaraminol seem to be safe and effective agents for use in regional anesthesia. The use of IM ephedrine, a mixed α- and β-adrenergic agonist, prophylactically given with moderate preloading to prevent bradycardia caused by spinal anaesthesia-induced sympathetic block, has been reported for elderly patients.9-11 However, the prophylactic use of ephedrine has been criticized because of the associated frequent incidence of severe hypertension and tachycardia.12-14Phenylephrine, a pure α-adrenergic agonist whose action is expected to counteract the decrease in systemic vascular resistance induced by spinal anesthesia without increasing the HR, has been found to be effective when given IM. However, there has been little study on the use of α-agonists for the prevention of hypotension in elderly patients undergoing spinal anesthesia. The aim of this study was to determine the efficacy of IM phenylephrine against spinal anaesthesia induced hypotension in normotensive patients scheduled for Elective Urological Surgeries.

AIMS AND OBJECTIVES

To study was the efficacy of IM phenylephrine against spinal anaesthesia-induced hypotension in normotensive patients scheduled for Elective Urological Surgeries.

MATERIALS AND METHOD

The present randomized controlled, double blind study was conducted in the department of anesthesia of tertiary care institute to evaluate the effectiveness of prophylactic IM 2mg dose of Phenylephrine against placebo in prevention of post Sub Arachnoid Block hypotensive response in patients undergoing elective urological surgeries under Sub Arachnoid Block".

Following criteria was used to select the study subjects.

- Patients between the ages of 15 to 65 years undergoing elective urological surgeries.
- With ASA grade I/II.
- No history of bleeding disorders, infection at the site of lumber puncture, neurological disease and chronic backache.
- No history of hypertension, myocardial infarction, anemia and other systemic disorders.

With reference to above mentioned selection criteria total 60 patients were enrolled in the present study and were divided in to two groups containing 30 patients each.

A computer generated randomized plan was made, which placed patients randomly in the two groups.

- Group P (Phenylephrine group): Patients who received phenylephrine(2mg i.m.)

- Group C (Control group): Patients who did not receive phenylephrine.

A thorough pre-anesthetic checkup of all the patients was carried out and necessary investigations were performed preoperatively. Details of the procedure were explained to all the patients and written consent was obtained. This computer generated randomization sheet was handed over to the pharmacist so as to make and supply syringes of the drug and placebo according to the patient number in the sheet. Observations were made by the anesthesiologist conducting the case. After the data collection of 60th patient, proforma case sheets were segregated in two groups – group P and group C- according to the randomization sheet.

Anesthesia Technique: A vein was cannulated with a wide bore intravenous cannula; Ringer lactate solution 500ml was infused as preload. The patient was monitored with non-invasive BP, ECG monitor and pulse oximeter. After pre loading patient was given an IM dose of 2mg phenylephrine, 15 min prior to administration of subarachnoid block. After careful antiseptic preparation and draping, subarachnoid block was given in sitting position. A Quincke spinal needle 26gauge was passed into the subarachnoid space at L2-3 or L3-4. After observing free flow of cerebrospinal fluid, inj bupivacaine 0.5% hyperbaric 2.5 ml plus 20mcg of inj Fentanyl was given through the spinal needle. The patient was made supine.

Interventions and Observations: After preloading pulse rate, systolic and diastolic blood pressure were recorded. The same parameters were recorded at following intervals:

1. just prior to administration of inj phenylephrine (baseline),
2. after subarachnoid block,
3. every 2 min for 15 min and
4. there after every 5 min till the end of the surgery.

Whenever hypotension i.e. a fall in systolic blood pressure of 20% from the base line value occurred, intermittent IV bolus of 3mg ephedrine was given as rescue drug. The bradycardia i.e. a pulse rate of 50/min or less was treated by inj Atropine 0.3 mg IV. Hypertension i.e. rise in systolic B.P. of 20% from the baseline value was treated with s/l depin administration. The maximum level of sensory block was assessed by pinprick method 5 min after the SAB. The collected data was recorded in excel sheet and was analysed with appropriate tests. A value of $P<0.05$ was considered statistically significant.

RESULT

Table 1: Distribution of patients according to baseline data

Characteristic	Group P	Group C
Age (mean±SD)	51.26±11.01 years	50.70±10.99 years
Sex (M:F)	30:0	30:0
ASA Status (I:II)	1:1	1:1
Baseline HR (mean±SD)	76.06±9.13 bpm	85±9.50 bpm
Baseline SBP (mean±SD)	120.6±11.32 mm Hg	120.73±12.23 mm Hg
Sensory dermatomal level	T9(t8-t10)	T9(8-10)

In the present study total 30 patients were enrolled in each group. The mean age of patients in group P and group C was 51.26±11.01 years and 50.70±10.99 years respectively. All the patients were of ASA grade I and II with 15 cases each in both the groups. The baseline heart rate in group P and group C was 76.06±9.13 bpm and 85±9.50 bpm respectively. The mean systolic blood pressure was 120.6±11.32 mm Hg and 120.73±12.23 mm Hg in group P and group C respectively. The average Sensory dermatomal level among both the groups was T9 with range from T8 to T10. Thus both the groups were similar in age, ASA status, sex distribution and baseline hemodynamic variables.

Table 2: Comparison of Mean Systolic Blood at various Time Intervals in Group P and Group C

Time	Group P	Group C	't' value	Significance
Baseline	120.60±11.33	120.73±12.23	0.04	Not significant
0 minutes	122.00±14.17	123.13±12.35	0.32	Not significant
2 minutes	118.00±13.78	116.53±11.34	-0.44	Not significant
4 minutes	115.00±14.52	107.00±13.53	-2.17	Significant
6 minutes	109.53±14.90	99.47±12.10	-2.82	Highly significant
8 minutes	108.47±14.80	101.53±10.57	-2.05	Significant
10 minutes	109.00±14.03	103.40±9.38	-1.78	Not significant
12 minutes	109.27±14.30	105.27±9.53	-1.25	Not significant
15 minutes	109.67±13.78	106.80±9.43	-0.92	Not significant

It was seen that there was no significnat diiference in baseline SBP of both the groups.Fall in systolic blood pressure during 4-8min after sub- arachnoid block was observed. The fall in SBP obserfed in group C as compred to group P was significant which corresponds with the time taken to achieve required sensory dermatomal level.

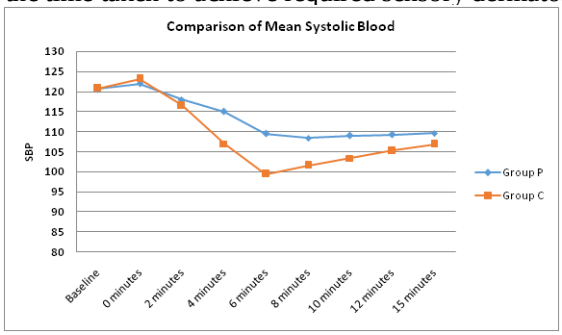

Table 3: Effect of IM phenylephrine against spinal anesthesia-induced hypotension

Parameter	Group P		Group C	
	No.	%	No.	%
Hypotension seen	1	3.33	13	43.33
Hypotension not seen	29	96.67	17	56.67
Total	30	100.00	30	100.00

X2 = 13.14, df=2,p<0.01 (highly significant) Hypotension was observed in 3.33% pateinst in group P while in 43.33% patients in group C and the difference observed statistically significant.

DISCUSSION

The present study was conducted with the aim to determine the efficacy of IM phenylephrine against spinal anesthesia-induced hypotension in normotensive patients scheduled for elective urological surgeries. In the present study total 30 patients were enrolled in each group. The mean age of patients in group P and group C was 51.26±11.01 years and 50.70±10.99 years respectively. All the patients were of ASA grade I and II with 15 cases each in both the groups. The baseline heart rate in group P and group C was 76.06±9.13 bpm and 85±9.50 bpm respectively. The mean systolic blood pressure was 120.6±11.32 mm Hg and 120.73±12.23 mm Hg in group P and group C respectively. The average Sensory dermatomal level among both the groups was T9 with range from T8 to T10. Thus both the groups were similar in age, ASA status, sex distribution and baseline hemodynamic variables. Thus both the groups were comparable with each other. It was seen that there was no significant difference in baseline SBP of both the groups. Fall in systolic blood pressure during 4-8min after sub-arachnoid block was observed. The fall in SBP observed in group C as compared to group P was significant which corresponds with the time taken to achieve required sensory dermatomal level. The peak effect of IM injection of phenylephrine has been suggested by results of pharmacokinetic studies to be 10–15 minutes after administration.[15] However, in our study, we found reductions in the incidence of spinal anesthesia-induced hypotension in phenylephrine group. Additionally, only one incidence of hypertension was found after IM administration of phenylephrine, when a peak effect of phenylephrine would have been expected. This suggests that the prophylactic IM administration of phenylephrine before the induction of spinal anesthesia is not too late to achieve a beneficial effect. Hypotension was observed in 3.33% patients in group P while in 43.33% patients in group C and the difference observed statistically significant. The incidence of hypotension during spinal anesthesia appears to be directly related to the level of sensory block.[16-18] Carpenter *et al*[17] suggested that a peak block height of T5 or higher confers a threefold increase in the odds of developing hypotension. In this study, the sensory block height was T9, with a range of T8 to T10. Thus, one of the most effective methods for preventing hypotension during spinal blockade is to avoid a high level of analgesia. As for the occurrence of adverse events in the use of phenylephrine, Critchley and Conway[19] also pointed out that metaraminol was very potent and could cause hypertension because of prophylactic infusions. Thus, the administration of the minimal effective dose of phenylephrine is recommended for elderly patients. The main reason there has been no study on the use of α-adrenergic agonists for elderly patients undergoing spinal anesthesia is that spinal anesthesia-induced sympathectomy and management with α-agonists can lead to bradycardia, which can be associated with decreased MAP and sudden cardiac arrest. Bradycardia during spinal anesthesia is believed to result from at least two causes: blockade of sympathetic

cardioaccelerator fibers and decreased venous return to the heart. A high level of sensory blockade by spinal anesthesia causes both of these effects. However, decrease in preload has been reported to be the main cause of large decreases in HR.[20,21] Therefore, severe bradycardia can develop during spinal anesthesia even when the sensory blockade level is below that necessary to produce complete sympathetic blockade. Carpenter *et al*[17] observed that peak sensory block height causing the development of severe bradycardia was above T5; moreover, the use of phenylephrine for the treatment of spinal hypotension has been cautioned against because bradycardia can develop when the level of sensory block is above T7.[4] In our study, in addition to the low level of sensory block, crystalloid preloading of 500 mL of RL was performed, with preload given before intrathecal injection. The low level of block positioning and the moderate fluid preloading might have been the main factors counteracting the development of bradycardia. The total number of patients in this study, however, was too small to determine the safety against bradycardia or hypertension. Therefore, a large-scale study may be needed to confirm the safety of this approach. The timing of IM injection of phenylephrine to achieve optimal efficacy is difficult to predict.

CONCLUSION

In conclusion, we demonstrated that prophylactic injection of 2 mg of phenylephrine IM is affective means for reducing the incidence of hypotension associated with hyperbaric bupivacaine spinal anesthesia during elective urological surgeries in normotensive patients, including both young and elderly.

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