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Comparative Evaluation of Two Different Bolus Doses of Nor-Epinephrine to Prevent Post Spinal Hypotension in Patients Undergoing PCNL: A Prospective Randomized Study

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ABSTRACT

Spinal anaesthesia is a recently accepted technique for PCNL. Vasopressors for prophylaxis and treatment of spinal hypotension have grown in popularity in recent years. The aim of our study was to evaluate the effectiveness of two different bolus doses of nor-epinephrine given pre-emptively for prevention of hypotension during spinal anaesthesia in patients undergoing PCNL and also to evaluate any associated adverse effects. A total 60 patients undergoing PCNL under spinal anaesthesia were enrolled in the study to receive either prophylactic nor-epinephrine bolus 10 µg (group A) or 15 µg (group B) immediately after spinal anaesthesia. Only one patient in group A developed hypotension requiring a rescue dose of vasopressor. 4 patients in group B developed systolic hypertension which settled without requiring intervention. Fall in blood pressure (systolic, diastolic and mean) were comparable between two groups. Maximum hypotension was encountered after the patient was put in prone position from supine position. From the above study we concluded that both 10 and 15 µg of Norepinephrine were effective in preventing hypotension. The dose of 15µg did not have any added benefit; rather it led to a statistically significant incidence of hypertension; which could prove hazardous in patients with pre-existing hypertension. Thus a bolus dose of 10 µg of Norepinephrine proved to be a good preventive measure against hypotension with reduced incidence of adverse effects.

Key Words: *Norepinephrine, spinal anaesthesia, percutaneous nephrolithotomy (PCNL).*

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INTRODUCTION:

Percutaneous Nephrolithotomy (PCNL) is a popular method for removal of kidney and ureteral calculi. Fernstorm and Johansson reported the removal of renal calculus through a nephrostomy tract for the first time [1]. Since then Percutaneous Nephrolithotomy (PCNL) has largely replaced open surgery in the management of renal stones [2]. Definitive indications include renal stones of ≥ 20 mm, multiple calculi, staghorn stones or stones not amenable to extracorporeal shock wave lithotripsy (ESWL) [3]. General anaesthesia has been postulated to confer many advantages over regional anaesthesia (RA) [4]; However it is associated with complications like endotracheal tube displacements, hemodynamic changes, neurologic and shoulder dislocation events especially at the time of shifting position from lithotomy to prone positions and vice versa [5]**.** Moreover, studies show that patients who underwent PCNL under regional anaesthesia had shorter mean operative time (ORT), less pain on first postoperative day, less consumption of medication and overall low cost in view of early discharges [6] making it a safe alternative to general anaesthesia.

Various strategies have been used to manage spinal blockade induced hypotension but have proved far from being satisfactory or reliable. This has shifted the focus to various vasopressin agents for prevention as well as treatment of spinal block induced hypotension which directly counter the sympathetic block derangements. Prophylactic administration of vasopressors including mephentermine, ephedrine, phenylephrine, infusion of angiotensin-2, and atrial natriuretic peptide has proved to be beneficial [7]. The ideal vasopressor would be one which has rapid onset, short duration of action, easily titrable and easy to use prophylactically with lack of any significant adverse effects.

Norepinephrine with the advantage of an overall neutral effect on heart rate [8]; has been used as both intravenous bolus as well as continuous infusion for prevention and treatment of post spinal hypotension [9,10,11]. However intermittent intravenous bolus doses may be a simpler, feasible, more acceptable method for routine practice in the low resource set up where either infusion pumps are not available or there is limited availability. Studies had investigated the best bolus dose of norepinephrine for management of a maternal hypotensive episode [12], with less tendency to decrease heart rate and cardiac output compared with phenylephrine [13]. The use of crystalloids before the spinal block is practically ineffective because of their rapid redistribution and extravasations to the 3rd space [14]. Thus we decided to co-load patients along with a pre-emptive bolus of norepinephrine; which has mainly been used as continuous infusion, with very few studies using it as intermittent bolus dose, to control spinal-induced hypotension. Primary aim was to compare the efficacy of two different doses 10µg & 15µg of nor-epinephrine on hemodynamic for prevention of spinal hypotension in patients undergoing PCNL and secondary aim was to look for any associated adverse effects.

Material Methods:

This study entitled "Comparative Evaluation of two different bolus doses of Nor-epinephrine to prevent Post Spinal Hypotension in patients undergoing PCNL:A Prospective Randomized study" was conducted in Department of Anaesthesiology and intensive care at Super Speciality Hospital Govt Medical College, Jammu.

After obtaining approval from the Institutional Ethical Committee an informed written consent was obtained. 60 patients of American society of Anaesthesiologist (ASA) grade I and II, Patients height from 140cm to 180 cm, aged 20-60 years, of either sex scheduled for elective Percutaneous Nephrolithotomy (PCNL) under spinal anaesthesia were included in this prospective randomized study. Exclusion criteria included patient refusal, contraindications to spinal anaesthesia, patients with history of allergy to local anesthetics and nor-adrenaline, patients who needed supracostal punctures for stone clearance and patients with staghorn stones. Patients were monitored for blood pressure, electrocardiogram, and pulse oximetry prior to the procedure and during the procedure. All the patients enrolled in the study were subjected to detailed general physical examination as well as systemic examination. Basic demographic characteristics like age, height, weight, sex were noted. Routine investigations including complete hemogram, LFT, RFT, and electrolytes of the patients were undertaken. The patients were divided into two groups. **Group A** patients received intravenous (IV) bolus dose of Nor-epinephrine 10µg diluted in 0.9% normal saline to a concentration of 1µg/ml to a total volume of 10 ml and **Group B** Patients received intravenous bolus dose of Nor-epinephrine 15µg diluted in 0.9 % normal saline to a concentration of 1.5µ/ml to a total volume of 10 ml after spinal anaesthesia. Patients were fasted overnight and were given routine antacid prophylaxis. On the morning of surgery in the preoperative room intravenous access with 16 or 18 Gauge cannula was secured. On arrival in the operating room, monitor was attached and all baseline parameters including heart rate, SBP (systolic blood pressure), DBP (diastolic blood pressure), MAP (Mean arterial pressure) and SPO2 (oxygen saturation) were recorded Under all aseptic precaution spinal anaesthesia was performed with a 25-gauge Quincke needle through L2-L3 or L3-L4 interspaces and 17.5mg of hyperbaric 0.5% bupivacaine was injected in sitting position. Simultaneously co-loading was started with RL through administration set with clamp fully open. The patients were located in the supine position with slight head down tilt, till level of sensory block reached T8 confirmed by pin prick method. After stabilization of anaesthesia, cystoscopy and RGC placement were done in the lithotomy position. Then the patients were turned prone carefully with the cooperation of the patients. Soft pillows of adequate thickness were placed under the patients flexed shoulders with both arms flexed forward over them in a natural comfortable position. The patients were allowed to keep their heads in neutral, left or right positions according to their choice and comfort. All patients received oxygen by bi-nasal prongs @4-6 L/min and verbal contact maintained with them throughout the procedure. Immediately after induction of spinal anaesthesia; systolic blood pressure, diastolic blood pressure and mean arterial blood pressure, heart rate and oxygen saturation were measured and recorded every 3 minutes in the first 15 minutes, then every 5 minutes until 50 minutes and thereafter every 10 minutes till the end of surgery. The incidences of hypotension (defined as systolic blood pressure <80% of baseline) and hypertension (SBP>120% of baseline), bradycardia (defined as heart rate <60 beats/m in) and tachycardia (>100 beats/min) were recorded. Any other adverse event like nausea, vomiting noted. Any episode of bradycardia was managed with atropine and hypotension with a bolus of 3mg mephentermine.

Statistical analysis:

The quantitative data was analysed using IBM SPSS-ver.20 software and expressed as mean±standard deviation(SD) and difference compared using one factor analysis of variance. The qualitative data was compared with chi-square analysis. $P<0.05$ was considered significant.

Results:

60 patients were randomly distributed into two groups: Group A received 10µg noradrenaline and Group B received 15µg of epinephrine. This prospective randomized study was conducted after obtaining clearance from the Institutional

Ethical committee and written informed consent from all patients. Patients of American society of Anesthesiologists physical status 1 and 2 scheduled for PCNL were included in this study.

Following observations were made during the course of the study:

Table1: Patients demographics, duration of surgery. Values are mean ± standard deviation and percentage.			
	Group A	Group B	P value
Age (yrs)	41±10.8	42.13±9.5	0.59
M/F	73%/27%	68%/32%	
Operation time (in min)	74.1±7.18	72.8±7.29	0.424
BMI kg/m2	29.5±2.5	27.9±4.1	0.69

Table 2: Baseline comparison of two groups of patients (Means ± SE)

Attribute	Group A	Group B	p-value	Significance
Heart rate (bpm)	89.28±5.25	90.93±5.01	0.155	NS
Systolic blood pressure (mmHg)	129.48±6.57	128.93±4.69	0.785	NS
Diastolic blood pressure (mmHg)	84.35±8.41	83.33±6.78	0.550	NS
Oxygen Saturation(%)	99.00±93	98.80±1.01	0.793	NS

NS: Statistically non-significant

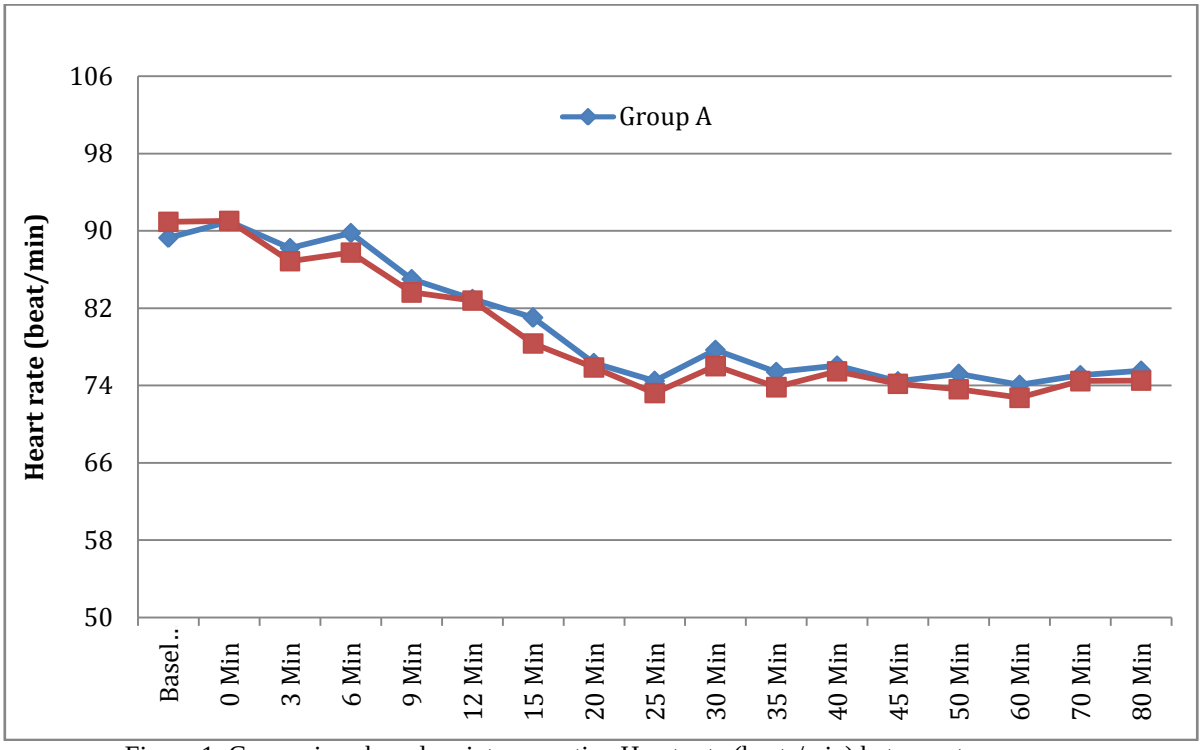

Figure 1: Comparison based on intraoperative Heart rate (beats/min) between two groups

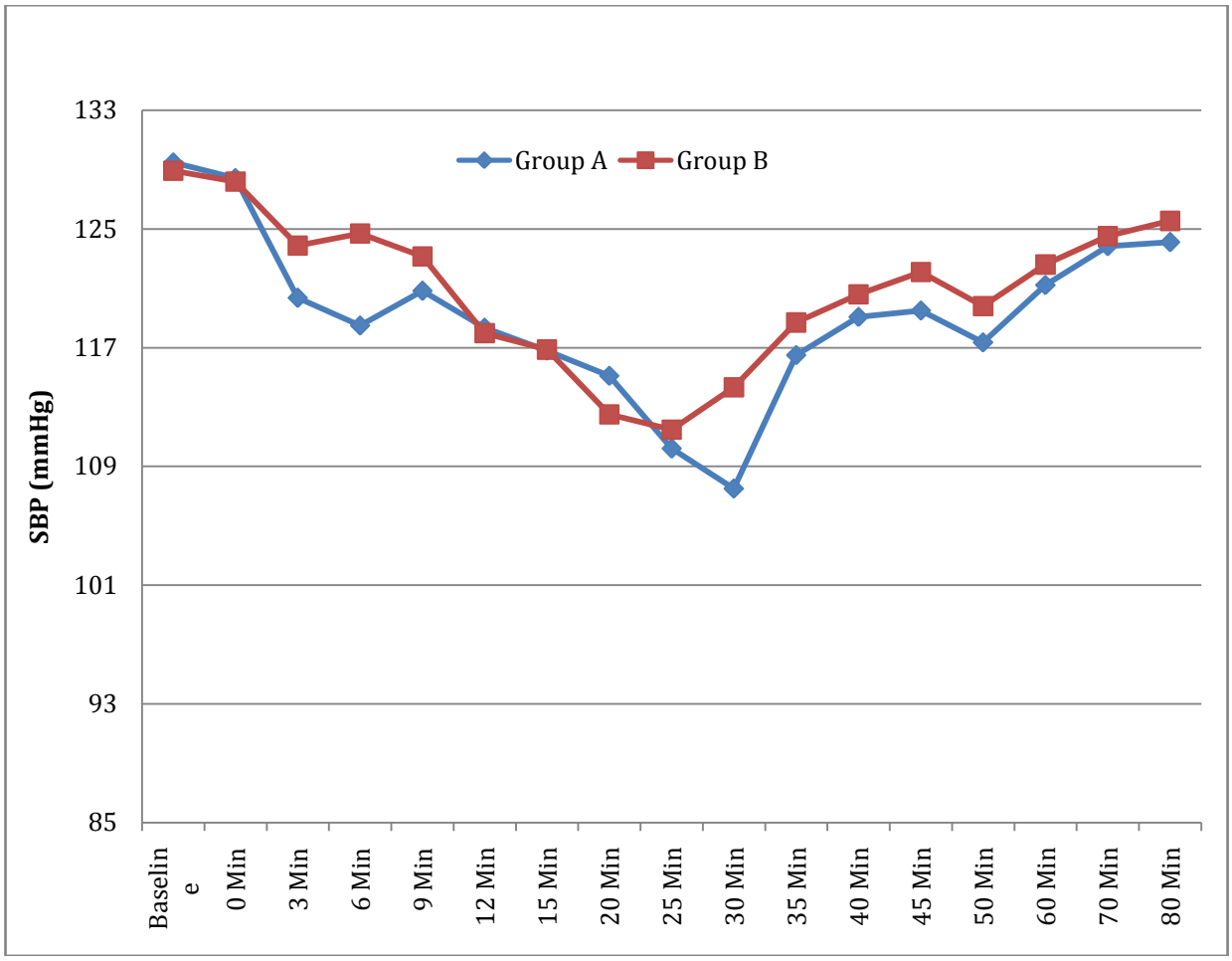

Figure 2: Comparison based on intraoperative SBP (mmHg) between two groups

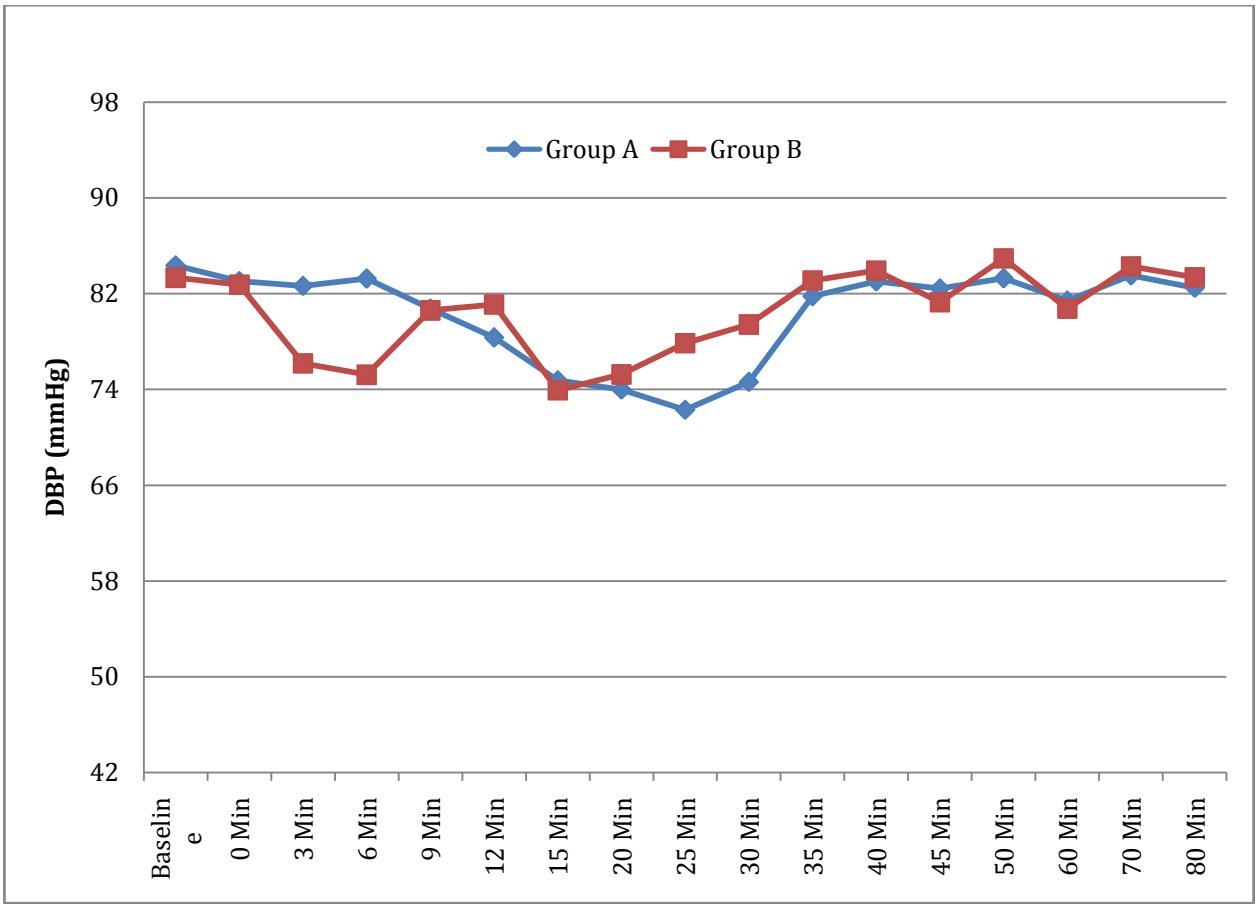

Figure 3: Comparison based on intraoperative DBP (Diastolic blood pressure) between two groups

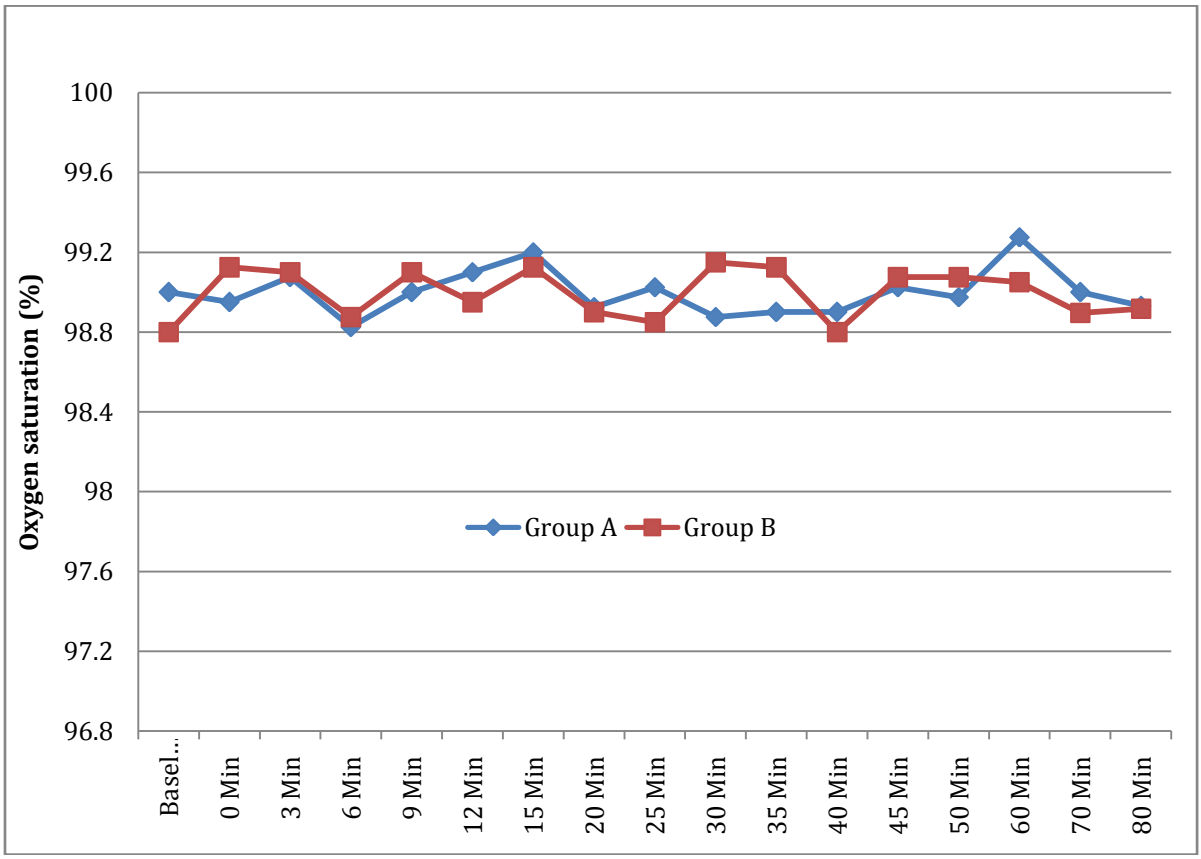

Figure 4: Comparison based on intraoperative oxygen saturation between two groups.

Table 3: Adverse Effects

	Group A	Group B
Hypertension	0	4
Bradycardia	1	1
Rescue Vasopressor (Mephenteramine/3mg)	1	0
Nausea	1	1
Vomiting	0	0

DISCUSSION:

Different studies have compared norepinephrine and phenylephrine for maintaining BP during spinal anaesthesia and concluded that norepinephrine was effective in maintaining blood pressure during spinal anaesthesia. We thus decided to compare the different doses of norepinephrine and our results showed that both were equally effective in preventing hypotension. The result of our study are in tandem with Wang Xian et al [15] who used a bolus of 8µg norepinephrine for spinal anaesthesia induced hypotension in LSCS and observed a greater cardiac output and stroke volume as compared to phenylephrine group patients. Also they found there is lower incidence of bradycardia with norepinephrine compared to phenylephrine when an intermittent bolus of each was injected which is similar to our study in group A and B both, however; the 15µg bolus receiving group showed a statistically significant increase in the BP which settled by its own.

Wei C et al [16] they concluded that ED50, ED80, and ED95 were 0.029, 0.068, and 0.105µg/kg/min respectively. Onwochei DN et al [17] they found a bolus of 6µg norepinephrine was effective at preventing hypotension in 19 of the 20 patients receiving this dose. Ngan Kee WD et al [18] they found that in patients receiving spinal anaesthesia manually titrated infusion of 5µg/ml of norepinephrine was effective for maintaining blood pressure and decreasing incidence of hypotension.

In our study the decrease in the blood pressure (systolic, diastolic and mean) initially was statistically non-significant (P>0.05). When patients were put in lithotomy position after spinal for cystoscopy and urethral catheter placement blood pressure increased but blood pressure further decreased after prone position. The reason may be due to the return of pooled blood from the lower extremities to the heart when the patient is put in lithotomy position. Increase in the venous return was greater in the lithotomy position; Miyabe M et al [19]. In a prone position there is significant decrease in the cardiac index Hatada T et al [20]. We noticed maximum hypotension when the patient is put in a prone position from supine and vice versa.

Only one patient in both groups had bradycardia which was corrected by Inj Atropine 0.3 mg i.v. stat and only one patient in Group A developed hypotension requiring a rescue dose of vasopressor, 3 mg mephentermine. 4 patients in group B developed systolic hypertension (statistically significant) which settled without requiring intervention. Only one patient in both groups had nausea which was comparable and statistically non significant. From the above study we concluded that though both 10µg & 15µg of norepinephrine were effective in preventing hypotension, the dose of 15µg did not have any added advantage; rather it lead to statistically significant incidence of hypertension, which though was not of much significance in our patients, but could prove hazardous in patients with pre-existing hypertension. Thus the 10µg Norepinephrine proved to be a good preventive measure against hypotension with reduced incidence of adverse effects.

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