Comparative Evaluation of two different bolus doses of Ephedrine to prevent Post Spinal Hypotension in patients undergoing PCNL: A Prospective Randomized study.

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Submitted: 15-07-2022
Accepted: 27-07-2022

ABSTRACT: Spinal anaesthesia is a recently accepted technique for PCNL. Hypotension following spinal blockade is primarily due to preganglionic sympathetic blockades resulting in vasoconstriction and pooling of blood in the lower limbs. 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 ephedrine for prevention of hypotension during spinal anaesthesia in patients undergoing PCNL and also to evaluate any associated adverse effects. A total of 60 patients undergoing PCNL under spinal anaesthesia were enrolled in the study to receive either prophylactic ephedrine bolus 10 mg (group A) or 15 mg (group B) immediately after spinal anaesthesia. Eight patients in group A developed hypotension requiring a rescue dose of vasopressor, while two patients in group B developed hypotension requiring a rescue dose of vasopressor. We noticed that maximum hypotension was encountered after the patient was put in prone position from supine position. Fall in blood pressure (systolic and diastolic) were comparable between the groups. From the above study we concluded that 15 mg IV bolus significantly decreases the incidence of maternal hypotension without serious side effects like reactive hypertension.

Keywords: Ephedrine, spinal anaesthesia, percutaneous nephrolithotomy (PCNL).

I. INTRODUCTION:

Percutaneous Nephrolithotomy (PCNL) is a popular method for removal of kidney and ureteral calculi. PCNL has largely replaced open surgery in the management of renal stones (1). Definitive indications include renal stones of ≥ 20 mm, multiple calculi, staghorn stones or stones not amenable to extracorporeal shock wave lithotripsy (ESWL) (2). PCNL can be done under local, general or regional anaesthesia. General anaesthesia has been postulated to confer many advantages over regional anaesthesia (RA) in term of better hemodynamic and airway control, better patient and surgeon satisfaction (3). The other advantages of GA for PCNL procedure include better control of tidal volume, airway control especially in prone position, and extensibility of anaesthesia time (4). However, it is associated with complications like endotracheal tube displacement, hemodynamic changes, neurologic and shoulder dislocation events especially when patient is shifted from lithotomy to prone position and vice versa (5). Moreover, studies have suggested that patients who underwent PCNL under regional anaesthesia had shorter mean operative time (ORT), discharge of patients was earlier, and less pain on first postoperative day (6), less consumption of medication and overall low cost in view of early discharge (7).

The simplicity of the technique, reliable effect and lack of all those complications that are associated with general anaesthesia has made it a safe alternative to general anaesthesia. Various strategies have been used to manage spinal blockade induced hypotension which includes patient leg elevation on the operation table, head-down tilt and use of pressure stockings to augment venous return and increase cardiac output and may be sufficient to restore blood pressure to an acceptable level. Volume expansion can be done with crystalloid or colloid infusion. Most of the strategies for decreasing the incidence of hypotension during spinal anaesthesia have proved far from being satisfactory or reliable. This has shifted the focus to various vasopressor agents for prevention as well as treatment of spinal block induced hypotension. Vasopressors directly counter the sympathomimetic blockade derangements. This is because the neuraxial blockade is associated with cardiovascular effects similar to a phal and beta-blocker, the decrease in systemic vascular resistance and cardiac output can lead to complications especially in geriatric
Ephedrine was the first agent to be used successfully to treat hypotension induced by spinal anaesthesia (10). Ephedrine is a non-catecholamine sympathomimetic drug that stimulates alpha and beta adrenergic receptors directly and predominantly indirectly, producing its effects by releasing norepinephrine from nerve endings in the autonomous nervous system, which leads to an increase in blood pressure, heart rate, cardiac output and systemic vascular resistance. Ephedrine is deaminated in the liver and conjugation occurs. Ephedrine is a sympathetic drug that produces central nervous system stimulation produces alertness, anxiety, tremor, and insomnia. It has been used for prophyaxis and treatment against hypotension associated with spinal anaesthesia for several years; but recently there is some concern about its use due to certain complications such as supraventricular tachycardia and tachyphylaxis (11). However, intermittent intravenous bolus doses may be a simpler, feasible, more acceptable method for routine practice in the low resource setup where either infusion pumps are not available or there is limited availability. The use of crystalloids before spinal anaesthesia is practically ineffective because of their rapid redistribution and extravasations to the 3rd space (12). Thus we decided to conduct patients along with preemptive bolus of ephedrine. Primary aim was to compare the efficacy of two different doses 10mg & 15mg of ephedrine for prevention of spinal hypotension in patients undergoing PCNL and secondary aim was to look for any associated adverse effects.

II. MATERIAL & METHODS:

This study entitled "Comparative Evaluation of Two Different Doses of Ephedrine to Prevent Post Spinal Hypotension in Patients Undergoing PCNL: A Prospective Randomized Study” was conducted in Department of Anaesthesiology and Intensive Care, Super Speciality Hospital Govt Medical College, Jammu.

After obtaining approval from the Institutional Ethic Committee in accordance with the Helsinki Declaration, informed written consent was obtained. 60 patients of American Society of Anaesthesiologists (ASA) grade I and II, Patients height from 140 cm 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 anaesthetics, patients with no need for supracostal punctures for stone clearance and patients with a history of hypertension. Patients were monitored for blood pressure, electrocardiogram, and pulse oximetry prior to the procedure and during the procedure. All patients were preloaded with ringer lactate 70 to 100 ml/kg before spinal anaesthesia. Ephedrine was prepared as two different 5 ml syringes containing Ephedrine 10 mg per cc and 15 mg per cc, one ml was randomly injected IV as per randomization table. After obtaining informed written consent from all the patients enrolled in the study, they were subjected to a detailed physical examination as well as systemic examination. Basic demographic characteristics like age, height, weight, sex were noted. Baseline values of heart rate, systolic and diastolic blood pressure were recorded. Routine investigations deemed necessary for the patients were undertaken. The patients were divided into two groups, Group A patients in this group received an intravenous (IV) bolus dose of 10 mg of ephedrine. Group B patients in this group received an intravenous (IV) bolus dose of ephedrine 15 mg after spinal anaesthesia. Patients were fasted over night and were given routine antacid prophylaxis on the morning of surgery. Intravesical pressure was monitored. A 6 French double pigtail catheter was inserted retrograde ureteric access after 16G cannula was secured. On arrival in the operating room, monitors like ECG, NIBP (non-invasive blood pressure), and pulse oximetry were attached. All baseline parameters like heart rate, SBP (systolic blood pressure), DBP (diastolic blood pressure) and SPO2 (oxygen saturation) were recorded. Under all septic precautions spinal anaesthesia was performed with a 25-gauge Quincke needle through L2-L3 or L3-L4 interspaces and 1.75 mg of hyperbaric 0.5% bupivacaine was injected in sitting position. Simultaneously, loading was started with RL through medical 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 T5 confirmed by pinprick method. After stabilization of anaesthesia, cystoscopy was performed.
and urethral catheter placement were done in lithotomy position. Then the patients were turned prone carefully and 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 at 4-6 L/min and verbal contact maintained with them throughout the procedure. Immediately after induction of spinal anesthesia, blood pressure (systolic and diastolic), 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 fall in systolic blood pressure > 20% of baseline) and hypertension (SBP > 120% of baseline), bradycardia (defined as heart rate < 60 beats/min) and tachycardia (> 100 beats/min) were recorded. Hypotension (fall in systolic blood pressure > 20% from the baseline value or a value less than 90 mmHg) were treated with 10 mg ephedrine intravenously. Any other adverse event like nausea, vomiting etc. noted. Any episode of bradycardia was managed with atropine 0.6 mg. Occurrence of nausea and vomiting were treated with ondansetron 4 mg intravenously. The data was collected intra-operatively and in the perioperative period.

III. RESULTS:

| Table 1: Patients demographics, duration of surgery. Values are mean ± standard deviation and percentage. |
|---------------------------------|-------------------|-------------------|-----------------|
| Age (yrs)                       | Group A           | Group B           | P value         |
|                                 | 36.8±13.07        | 38.2±12.56        | 0.639           |
| M/F                             | 50%/50%           | 60%/40%           |                 |
| 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            |

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 DBP (mmHg) in two groups.

Figure 4: Comparison of patients receiving repetition of vasopressor.
### Table 2: The number of people receiving the repetition of vasopressor

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group A</th>
<th>Group B</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Repetition of vasopressor</td>
<td>No. 8</td>
<td>No. 2</td>
<td>% 26.6% SS</td>
</tr>
</tbody>
</table>

### Table 3: Adverse effects

<table>
<thead>
<tr>
<th>Adverse Effects</th>
<th>Group A</th>
<th>Group B</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shivering</td>
<td>5</td>
<td>7</td>
<td>NS</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>1</td>
<td>1</td>
<td>NS</td>
</tr>
<tr>
<td>Nausea/Vomiting</td>
<td>1</td>
<td>1</td>
<td>NS</td>
</tr>
<tr>
<td>Pleuralpuncture</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Shoulder dislocation</td>
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Spinal anaesthesia has proved to be an excellent alternative to general anaesthesia for variety of surgical procedures. There are many advantages for spinal anaesthesia over general anaesthesia. Various methods are employed for the management of hypotension. Nowadays vasopressors are becoming one of them against the management of spinal hypotension. Vasopressors infusions, however, have been associated with a large amount of drug being used, increasing possibilities of side effects and toxicity. Different studies have compared ephedrine different doses in prevention of spinal hypotension. We compared two different doses (10 mg and 15 mg) of ephedrine intravenously in this study. The demographic profile including age, sex, BMI (body mass index) of the patients in the both groups were comparable and statistically nonsignificant. Duration of surgery in both groups were comparable and statistically nonsignificant. The difference in baseline mean heart rates and baseline blood pressure (systolic, diastolic) among the two groups was comparable and statistically nonsignificant. Mean heart rate did not vary significantly at any interval and difference in intraoperative heart rates among the two groups was statistically nonsignificant.

In our study the decrease in the blood pressure (systolic and diastolic) was more at 3, 6, 15, 20, 25 and 30 minutes post spinal anaesthesia, but this difference was statistically significant (P<0.05). When patients were in lithotomy position, there was a decrease in the blood pressure from the lower extremities to the heart when patient is put in lithotomy position. Increase in the venous return was greater in the lithotomy position (13). In prone position there is significant decrease in the the cardiac index (14). We noticed maximum hypotension when patient is put in prone position from supine.

Our study on local perioperative pain is shown in Table 1. Patients receiving a 10 mg prophylactic dose of ephedrine had significantly higher incidence compared to 15 mg and 20 mg ephedrine. There was however, a significantly higher incidence of reactive hypertension in patients receiving 20 mg ephedrine.

Our study is not in accordance with Ngan Kee WD et al. (17) they found that systolic arterial pressure (SAP) in the first 12 min after the spinal injection was greater in the 30 mg group compared with other groups (P<0.05). They concluded that smallest effective dose was 30 mg. King SW and Rosen MA 1998 (18) they determined whether intravenous ephedrine prophylaxis would benefit prehydrated obstetrical patients presenting for elective cesarean section. They found that hypotension occurred in 6/10 control patients, 5/10 bolus patients and 5/10 infusion patients. Tseng LC et al. (19) they found that 10 mg IV ephedrine given at the time of spinal anaesthesia, and after a 10 mL/kg RL fluid bolus, does not diminish the incidence or severity of hypotension in parturients undergoing cesarean delivery. Overall incidence of hypotension was 70% in both groups. Various studies have compared the effect of ephedrine and phenylephrine on blood pressure and found no difference in the effectiveness to prevent spinal anaesthesia associated hypotension. Al-Day Munoz E et al. (20) they found that the ability of ephedrine and phenylephrine to prevent hypotension was not different with other groups (P<0.05). They concluded that patients receiving 15 mg and 20 mg ephedrine. There was however, a significantly higher incidence of reactive hypertension in patients receiving 20 mg ephedrine.

The incidence of hypotension was significantly higher in patients receiving a 10 mg prophylactic dose of ephedrine than in patients receiving 15 mg and 20 mg ephedrine. There was however, a significantly higher incidence of reactive hypertensive patients receiving 20 mg ephedrine.

In our study, we found one patient in each group have bradycardia and required atropine for treatment. In our study eight patient in group A required ephedrine 10 mg as a rescue vasopressor while two patients in group B required ephedrine, the difference was statistically significant. In our study 5 patients in group A and 7 patients in group B have shivering which was comparable and statistically nonsignificant. In our study incidence of nausea and vomiting were comparable and statistically nonsignificant. In our study 5 patients in group A and 7 patients in group B have hemoglobin transfusions. There was no incidence of complications such as intrathec al block, plus rescue boluses of levothyroxine and ephedrine for elective cesarean section. In our study 5 patients in group A received ephedrine 10 mg as a rescue vasopressor while two patients in group B received ephedrine, the difference was statistically significant. In our study 5 patients in group A and 7 patients in group B have shivering which was comparable and statistically nonsignificant. In our study incidence of nausea and vomiting were comparable and statistically nonsignificant. In our study incidence of nausea and vomiting were comparable and statistically nonsignificant.

| Local perioperative pain | 0 | 0 |

IV. DISCUSSION:

Various studies have compared the effects of ephedrine and phenylephrine on blood pressure and found no difference in the effectiveness to prevent spinal anaesthesia associated hypotension. Ngan Kee WD et al. (17) found that systolic arterial pressure (SAP) in the first 12 min after the spinal injection was greater in the 30 mg group compared with other groups (P<0.05). They concluded that smallest effective dose was 30 mg. King SW and Rosen MA 1998 (18) determined whether intravenous ephedrine prophylaxis would benefit prehydrated obstetrical patients presenting for elective cesarean section. They found that hypotension occurred in 6/10 control patients, 5/10 bolus patients and 5/10 infusion patients. Tseng LC et al. (19) found that 10 mg IV ephedrine given at the time of spinal anaesthesia, and after a 10 mL/kg RL fluid bolus, does not diminish the incidence or severity of hypotension in parturients undergoing cesarean delivery. Overall incidence of hypotension was 70% in both groups. Various studies have compared the effect of ephedrine and phenylephrine and found no difference in the effectiveness to prevent spinal anaesthesia associated hypotension. Al-Day Munoz E et al. (20) found that the ability of ephedrine and phenylephrine to prevent hypotension was not different with other groups (P<0.05). They concluded that patients receiving 15 mg and 20 mg ephedrine. There was however, a significantly higher incidence of reactive hypertension in patients receiving 20 mg ephedrine.
shoulder dislocation in our study. In our study no patients was converted to general anaesthesia. Our study are in accordance to Abraham AA and Das V (23) they found that PCNL can be done under spinal anesthesia to the satisfaction of the patient, surgeon and anesthesiologist. Mehrabi S and Karimzadeh Shirazi K (24) evaluated the impact of spinal anesthesia on intraperitoneal and postoperative outcome in patients undergoing PCNL. They found that spinal anesthesia is safer and effective for performing PCNL, and is a good alternative for general anesthesia (GA) in adult patients.

From the above study we concluded that the prophylactic use of ephedrine in 15mg IV bolus significantly decreases the incidence of maternal hypotension without serious side effects like reactive hypertension.

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[18]. King SW, Rosen MA. Prophylactic


