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Hemodynamic Changes During Spinal Anesthesia with Different Bupivacaine Concentrations in Elderly Cardiac Patients Undergoing Transurethral Resection of Prostate

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: Spinal anesthesia produces hypotension more often in elderly patients than in younger patients due to decrease systemic vascular resistance mainly. Limiting the dose (and thus, extent of anesthetic spread) to the necessary dermatomes reduces the likelihood of side effects. The aim of the study was to compare hemodynamic effects of spinal anesthesia by using different bupivacaine concentrations in elderly cardiac patients undergoing TURP.
Methods: This prospective randomized controlled double-blinded study was carried out on 60 male patients aged 65 years and above, American Society of Anesthesiologists (ASA) III, with IHD (history of MI, a history of a positive treadmill test result (ECG stress test), use of nitroglycerin, chronic stable angina for more than two months, or an ECG with abnormal Q waves), with ejection

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fraction (EF) 35%-50%, undergoing TURP with prostate from 100-150 gm by using bipolar resection technique and normal saline wash during surgical procedure. Patients were randomly allocated into two equal groups: Group I (Control group): received 2.5 ml bupivacaine 0.5% + 0.5 ml fentanyl (25 mcg). Group II: received 1.75ml bupivacaine 0.5% + 0.75 ml distilled water + 0.5 ml fentanyl (25 mcg).

Results: Mean arterial blood pressure was significantly decreased in group I than group II at 6, 9, 12, 15 and 30 minutes. Heart rate and peripheral oxygen saturation were insignificantly different between both groups. Ischemia occurred in 3 (10%) patients in group I and no patients in group II & the difference between both groups was insignificant. Hypotension was found significantly higher in group I than group II (P = 0.021) while PONV, bradycardia, headache, backache and shivering were insignificantly different between both groups. TURP syndrome didn't occur in any case of our study.

Conclusions: Hyperbaric bupivacaine 8.75 mg injected at L4-L5 is sufficient to provide adequate sensory and motor block, while maintaining hemodynamic stability during TURP procedures.

Keywords: Hemodynamic changes; spinal anesthesia with different bupivacaine concentrations; elderly; cardiac; transurethral resection of prostate.

1. INTRODUCTION

Transurethral resection of the prostate (TURP) is the most common surgical intervention for patients with benign prostatic hyperplasia. Spinal anesthesia is the technique of choice in TURP [1].

There is a chance of circulatory overload due to excessive absorption of irrigation solution through open prostatic venous sinuses during the surgical procedure [2].

TURP patients are particularly vulnerable to volume overload as most of them belong to elderly age group and suffer from cardiopulmonary disorder [3]. Spinal anesthesia helps in peripheral pooling of blood, reducing the chance of circulatory overload and early detection of complications like TURP syndrome, bladder perforation. Spinal technique provides post-operative analgesia, reduces blood loss during surgery and prevents the need for tracheal intubation that may irritate the airway leading to coughing and straining and may exacerbate postoperative hemorrhage [4].

Spinal anesthesia produces hypotension more often in elderly patients than in younger patients. In spinal anesthesia due to sympathetic blockade, there is vasodilatation leading to diminished venous return which is the main contributory factor for hypotension. The chemical sympathectomy due to spinal anesthesia extends for 2-6 dermatomes above the sensory level and at the same level with epidural anesthesia. In elderly patients with cardiac disease hypotension is due to decrease systemic vascular resistance mainly [5]. Limiting the dose (and thus, extent of anesthetic spread) to the necessary dermatomes reduces the likelihood of side effects [6].

The aim of the study was to compare hemodynamic effects of spinal anesthesia by using different bupivacaine concentrations in elderly cardiac patients undergoing TURP.

2. PATIENTS AND METHODS

This prospective randomized controlled double-blinded study was carried out in Tanta university hospital in Urology Department for one year (December 2019- December 2020) after approval from institutional ethics committee and an informed consent was taken from all patients. Both patients and postoperative assessors were blind to group assignment. The research end point is 72 h. after the discharge from the recovery room.

Sixty male patients aged 65 years and above, American Society of Anesthesiologists (ASA) III, with IHD (history of MI, a history of a positive treadmill test result (ECG stress test), use of nitroglycerin, chronic stable angina for more than two months, or an ECG with abnormal Q waves), with ejection fraction (EF) 35%-50%, undergoing TURP with prostate from 100-150 gm by using bipolar resection technique and normal saline wash during surgical procedure were included in this study.

Exclusion criteria were patients under 65 years, patients with any diseases that increase intra-abdominal pressure (e.g. any intra-abdominal

mass), general contraindications of spinal anesthesia as patient refusal, coagulation disorders, local infection at site of the block, psychiatric illness, patients with anomalies of the spinal column like kyphosis or scoliosis or any other contraindications for spinal anesthesia and recent decompensated heart failure, unstable angina, ventricular arrhythmias, severe AS, severe MS and EF below 35% or above 50%.

2.1 Group Allocation

Patients were randomly allocated into two equal groups by computer generated sequence through sealed opaque envelopes. Each group included 30 patients:

2.1.1 Group I (Control group)

Received 2.5ml bupivacaine (heavy Marcaine ®) 0.5% (12.5mg) + 0.5ml fentanyl (25mcg), so the total volume is 3 ml.

2.1.2 Group II

Received 1.75ml bupivacaine (heavy Marcaine ®) 0.5% (8.75mg) + 0.75ml distilled water [7] + 0.5ml fentanyl (25mcg), so the total volume is 3 ml.

A chief nurse who did not participate in patient care or data collection opened the envelopes and determine group assignment at the morning of operation, another blind assistant doctor did the preparation of the anaesthetic agents with different doses and the same volume as discussed before, none of them participated in the procedure.

2.2 Pre-operative Preparation

- History taking as IHD is defined as history of MI, a history of a positive treadmill test result (ECG stress test), use of nitroglycerin, chronic stable angina(attacks of chest pain on exercise, relieved by rest, for more than two months), or an ECG with abnormal Q waves [8].
- Clinical examination
- Routine laboratory investigations including CBC, Prothrombin time and prothrombin activity, bleeding time, clotting time, liver function tests and kidney function tests also ECG and echocardiography in addition to the regular physical examination, measurements of patient's height, weight.

2.3 Anesthetic Technique

All patients were connected to standard monitoring, hemodynamic variables such as heart rate (HR) by ECG and mean arterial pressure (MAP), systolic blood pressure and diastolic blood pressure by non-invasive blood pressure and O_2 saturation by pulse oximetry were recorded as baseline measurements. IV access was established. 100 mL of IV fluid normal saline was given before starting the procedure over 20 minutes.

Proper positioning of the patient in sitting position, then spinal anesthesia was performed at the L3-4 or L4-5 interspaces through 25-gauge pencil-point needle by midline or paramedian approaches, the side-port of the needle pointing laterally, this is done under complete aseptic precautions using pre-packed sterile spinal kit.

2.4 Group I (Control group)

Received 2.5ml bupivacaine (heavy Marcaine ®, Astrazeneca, Egypt) 0.5% (12.5 mg) + 0.5ml fentanyl (25 mcg) (Sunny pharmaceutical under license of Hamlen pharmaceutical, Egypt), so the total volume is 3 ml.

2.5 Group II

Received 1.75 ml bupivacaine (heavy Marcaine ®) 0.5% (8.75mg) + 0.75 ml distilled water [7] + 0.5ml fentanyl (25 mcg), so the total volume is 3 ml.

Immediately after injection, the patient was positioned supine, then after 10 minutes patient was positioned in lithotomy position with O_2 mask 4-6 L/min.

If the systolic blood pressure dropped below 25% of the baseline recorded pre-spinal blood pressure or MAP < 65mmHg, incremental doses of intravenous ephedrine (5 mg with a maximum dose 30 mg [9]) were given. A heart rate less than 50 per minute was treated with incremental doses of intravenous atropine (0.01 mg/kg [10]).

2.6 Postoperative

After the end of the surgery, patients were discharge to PACU (Postanesthesia care unit). The patients were discharged from the recovery room after complete regression of the block.

Patients were followed up for the next 24 hours and checked for the manifestations of any of the complications of spinal anesthesia like headache, backache, nerve deficits, shivering, nausea and vomiting.

ECG was done every 24 hours for 3 days and if the patient complained symptoms of ischemia (thoracic pain and dyspnea).

Troponin test (Cardiac troponin T concentration was measured with the use of high-sensitivity electrochemiluminescence assays) and Echocardiography were done if the patient complained of symptoms of ischemia (thoracic pain and dyspnea), or ECG showed new ST-segment changes, new left bundle branch block or pathologic Q waves.

2.7 Measurements

1) Heart rate, mean arterial blood pressure and arterial oxygen saturation were recorded before the start of spinal anesthesia, immediately after injection of the drug, every 3 minutes for the first 15 minutes and every 5 minutes for the end of the operation.
   If the systolic blood pressure dropped below 25% of the baseline recorded pre-spinal blood pressure or MAP < 65 mmHg, incremental doses of ephedrine 5 mg [9] (Chemical Industries Development "CID", Giza, Egypt) were given, with calculation of number of patients need ephedrine and total dose for each patient.
   A heart rate less than 50 per minute was treated with incremental doses of IV atropine 0.01mg/kg [10] (Chemical Industries Development "CID", Giza, Egypt), with calculation of number of patients need atropine and total dose for each patient.
2) The onset and duration of sensory block were measured and recorded using ice in a finger of a surgical glove in mid-clavicular line. The onset of sensory block was taken as the time of achievement of block to T12 from the time of injection of the drug, this is repeated every 1 minute until recording time of the onset. The duration of sensory block was taken as the time from onset of block until regression of the block three segments below the highest level of block, this is repeated every 10 minutes after the onset time. Surgical intervention was allowed after sensory block above T10. The onset and duration of motor block was assessed using the Bromage scale Table 1 [11]. The onset of motor block was taken as the time of achieving 33% block from the time of injection. The duration of motor block was taken as the time from the onset of 33% block until the reappearance of 33% of the motor block.
3) Manifestations of any of the complications of spinal anesthesia like headache, backache, nerve deficits, shivering, nausea and vomiting. Vomiting was treated by IV 4 mg ondansetron (Zofran®, GlaxoSmithKline, Egypt).
4) ECG was done every 24 hours for 3 days and if the patient complained symptoms of ischemia (thoracic pain and dyspnea).
5) Troponin level and echocardiography were done if the patient complained of symptoms of ischemia (thoracic pain and dyspnea), or ECG showed new ST-segment changes, new left bundle branch block or pathologic Q waves.

The primary outcome was mean arterial blood pressure and the secondary outcomes were changes in heart rate, oxygen saturation, onset and duration of sensory block, onset and duration of motor block, incidence of post-operative coronary artery diseases (Clinical symptoms of acute coronary syndrome and ECG changes of ischemia)

Table 1. Bromage scale [11]

Grade	Criteria	Degree of block
I	Free movement of legs and feet	Nil (0%)
II	Just able to flex knees with free movement of feet	Partial (33%)
III	Unable to flex knees, but with free movement of feet	Almost complete (66%)
IV	Unable to move legs or feet	Complete (100%)

2.8 Justification of Sample Size

The sample size calculation is performed using EpI-Info 2002 software statistical package designed by World Health Organization (WHO) and by Centers for Disease Control and Prevention (CDC), Atlanta, Georgia, USA version 2002. The calculation was based on the following considerations (α error: 0.05, β error: 0.2, group ratio 1:1, expected 25% decrease in MAP in group I compared to group II and three cases were added to each group to overcome dropout). Therefore, we recruited 30 patients in each group.

2.9 Statistical Analysis

Organization, tabulation, presentation and analysis of data were performed by SPSS v25 (IBM©, Chicago, IL, USA). Normality of data (parametric or not) was checked with Shapiro-Wilks test and histograms. Quantitative parametric variables were presented as mean and standard deviation (SD) and were compared between the two groups by unpaired student's t-test and within the same group by paired T test. Quantitative non-parametric variables were presented as median and range and compared between the two groups by Mann Whitney (U) test and within the same group by Wilcoxon test. Qualitative variables were presented as frequency and percent and were analysed utilizing the Chi-square test or Fisher's exact test when appropriate. A two tailed P value < 0.05 was considered significant.

3. RESULTS

In this study, 178 patients were assessed for eligibility, 111 patients did not meet the criteria and 7 patients refused to participate in the study. The remaining 60 patients were randomly allocated into two groups (30 patients in each one). All 60 patients were followed-up and analyzed statistically Fig. 1.

Patients' characteristics (age, weight, height, BMI and duration of surgery) were insignificantly different between both groups Table 2.

Mean arterial blood pressure was significantly decreased in group I than group II at 6, 9, 12, 15 and 30 minutes (P <0.001, 0.034, 0.013, <0.001 and 0.014 respectively) and was insignificantly different between both groups at preoperative value, after induction, 3, 45, 60, 75 and 90 minutes Table 3.

Heart rate was insignificantly different at all time measurements between both groups Fig. 2

Peripheral oxygen saturation was insignificantly different at all time measurements between both groups Fig. 3.

Total dose of ephedrine was significantly increased in group I than group II (P <0.001). The number of patients who received ephedrine was significantly higher in group I than group II (P = 0.021). Total dose of atropine was insignificantly different between both groups. The number of patients who received atropine was insignificantly different between both groups Table 4.

The onset of sensory block was insignificantly different between both groups. The onset of motor block was significantly decreased in group I than group II (P <0.001). Duration of sensory block was insignificantly different between both groups. Duration of motor block was significantly increased in group I than group II (P = 0.019) Table 5.

In our study, ischemia occurred in 3(10%) patients in group I and no patients in group II & the difference between both groups was insignificant.

Hypotension was found significantly higher in group I than group II (P = 0.021) while PONV, bradycardia, headache, backache and shivering were insignificantly different between both groups. TURP syndrome didn't occur in any case of our study Table 6.

4. DISCUSSION

Elderly patients undergoing TURP may have preexisting cardiac or cerebral dysfunction. Maintaining hemodynamic stability is essential [12]. Spinal anesthesia, in comparison to general anesthesia, is usually preferred for elderly patients for TURP due to its relatively limited effect on myocardial performance, blood pressure, and cardiac output. To ensure adequate sensory and motor block for TURP, spinal anesthesia should extend to at least the 10th thoracic dermatome. In order to reduce the side effects of the standard dose of hyperbaric bupivacaine, many authors suggest the addition of opioids to reduce the total mg dose [13].

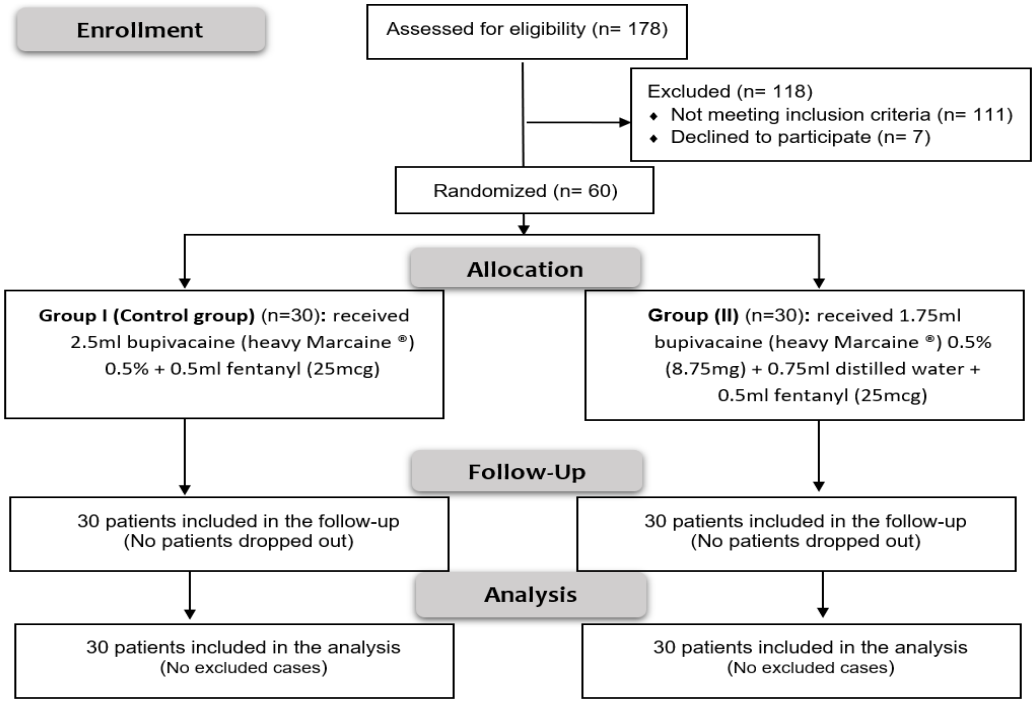

Fig. 1. CONSORT flow diagram of the participants through each stage of the trial

Table 2. Patients' characteristics in both studied groups

		Group I (n = 30)	Group II (n = 30)	P value
Age (years)	Mean ± SD	74.2 ± 4.40	72.4 ± 5.41	0.179
Weight (kg)	Mean ± SD	71.9 ± 10.16	75.6 ± 12.40	0.203
Height (m)	Mean ± SD	1.67 ± 0.07	1.69 ± 0.07	0.344
BMI (kg/m^2)	Mean ± SD	25.9 ± 4.28	26.7 ± 4.99	0.522
Duration of surgery (min)	Mean ± SD	75.2 ± 9.68	76.6 ± 9.34	0.562

BMI: body mass index

Table 3. Mean arterial blood pressure (mmHg) in both studied groups

	Group I (n = 30)	Group II (n = 30)	P value
	Mean ± SD	Mean ± SD	
Pre	94.30 ± 9.66	95.60 ± 8.64	0.585
After	92.73 ± 9.72	94.70 ± 8.73	0.413
3min	90.63 ± 9.57	93.23 ± 8.54	0.272
6min	78.80 ± 13.75	91.67 ± 8.20	**<0.001***
9min	80.40 ± 15.61	88.63 ± 13.62	**0.034***
12min	79.20 ± 13.11	88.53 ± 15.14	**0.013***
15min	80.80 ± 10.99	91.37 ± 8.60	**<0.001***
30min	87.97 ± 10.78	94.37 ± 8.68	**0.014***
45min	91.87 ± 9.34	96.10 ± 8.12	0.066
60min	94.87 ± 9.82	95.87 ± 8.90	0.681
75min	95.17 ± 9.92	96.80 ± 8.63	0.499
90min	95.10 ± 10.17	95.50 ± 9.46	0.875

**significant as P value <0.05*

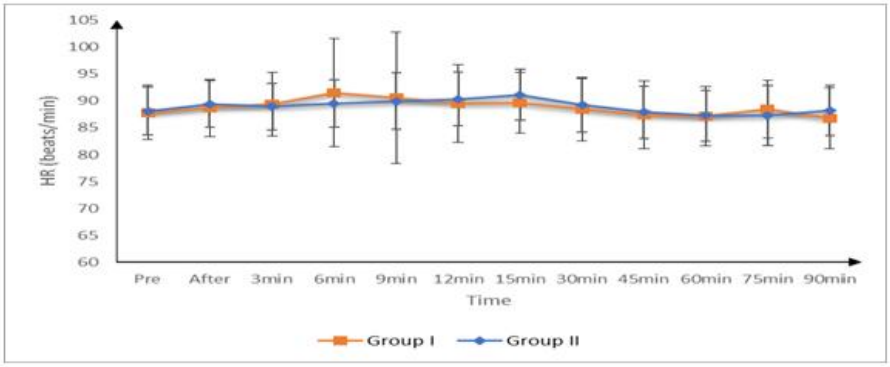

Fig. 2. Heart rate in both studied groups

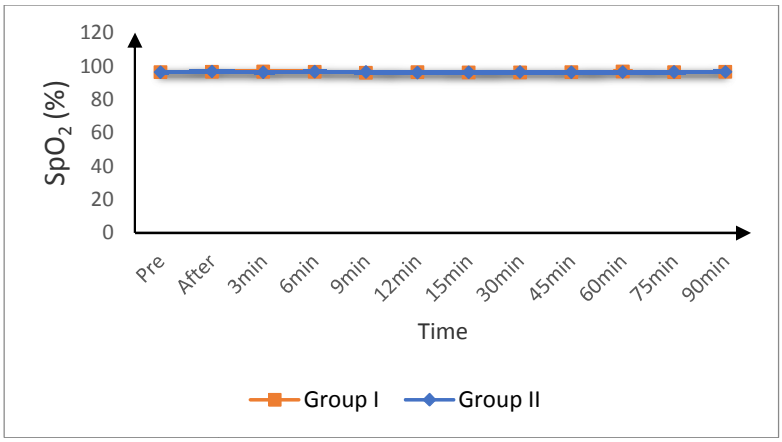

Fig. 3. Peripheral oxygen saturation in both studied groups

Table 4. Number of patients received ephedrine in both studied groups

		Group I (n = 30)	Group II (n = 30)	P value
Total dose of ephedrine (mg)	Median	7.5	0	<0.001*
	IQR	0-13.75	0-5	
Patients received ephedrine		19 (63.33%)	10 (33.33%)	0.021*
Total dose of atropine (mg)	Median	0	0	0.154
	IQR	0-0	0-0	
Patients received atropine		2 (6.67%)	0 (0%)	0.492

*IQR: Interquartile range *significant as P value <0.05*

Table 5. Onset and duration of sensory and motor block in both studied groups

		Group I (n = 30)	Group II (n = 30)	P value
Onset of sensory block (min)	Mean ± SD	4.6 ± 1.59	5.5 ± 2.01	0.060
Onset of motor block (min)	Mean ± SD	5.9 ± 2.01	8.6 ± 2.10	<0.001*
Duration of sensory block (min)	Mean ± SD	112.3 ± 14.61	105.8 ± 12.39	0.068
Duration of motor block (min)	Mean ± SD	102.5 ± 14.96	94.0 ± 12.06	0.019*

**significant as P value <0.05*

Table 6. Adverse effects in both studied groups

	Group I (n = 30)	Group II (n = 30)	P value
PONV	6 (20%)	5 (16.7%)	0.739
Hypotension	19 (63.33%)	10 (33.33%)	0.021*
Bradycardia	2 (6.7%)	0 (0%)	0.492
Headache	2 (6.7%)	1 (3.3%)	1
Backache	2 (6.7%)	3 (10%)	1
Shivering	13 (43.3%)	14 (46.7%)	0.795
TURP syndrome	0	0	---

*PONV: Postoperative nausea and vomiting, TURP: Transurethral rection of prostate *significant as P value <0.05*

Our study demonstrated no deleterious effects on hemodynamics, with the use of low dose bupivacaine injected intrathecally. It was not surprising to observe this hemodynamic stability in the low dose bupivacaine group in view of its less extensive spread. It is likely that any sympathetic blockade was more restricted and of slower onset, resulting in less hemodynamic change.

This result was in agreement with Gafar et al 2019 [14] who studied 120 patients scheduled for emergency lower limb surgeries. Patients were randomly grouped into two groups: Group 1 received 10 mg of 0.5% bupivacaine and 10 µg of fentanyl, whereas group 2 received 7.5 mg of 0.5% bupivacaine and 10 µg of fentanyl. They reported more hypotension in group 1 than group 2.

Also our results were in agreement with Özmen et al. [15] who studied 77 ASA II–III patients were preloaded with 500 ml 0.9% NaCl solution before regional anesthesia. In group E (n:27) epidural anesthesia were achieved by applying 75 mg bupivacaine heavy + 50 µg fentanyl in the L3–L4 intervertebral space. In group SP(n:28) 15 mg bupivacaine heavy + 50 µg fentanyl were used for spinal anesthesia (L3–L4 intervertebral space) while in group SA(n:30) 10 mg bupivacaine heavy + 50 µg fentanyl were used with saddle blockade. They reported that intraoperative MAP values were more stable in group with lowest dose heavy bupivacaine than other groups. Heart rate was decreased significantly in the three groups after 15 minutes of hydration.

Similar results were observed by a study by Sahran et al 2018 [16] who found that higher dose of intrathecal bupivacaine resulted in higher incidence of hypotension (40% in group A [15 mg bupivacaine], 10% in group B [12.5 mg bupivacaine] and 4% in group C [10 mg bupivacaine]).

In agreement with our results, Abdelmonem [12] reported that patients in group I exhibited a more stable blood pressure and heart rate during the study time period and less requirement for ephedrine and atropine.

Other studies explained that the hypotension after spinal anesthesia with bupivacaine is dose related. Intrathecal fentanyl (neither by itself nor in combination with bupivacaine) causes any depression of sympathetic activity [17].

Other study showed that addition of Fentanyl (25µg) to Bupivacaine (7.5 mg) [Group BF] given intrathecally provided better hemodynamic stability compared to bupivacaine 12.5 mg dose given without Fentanyl [Group B] in elderly patients as significant fall in systolic blood pressure was noted in Group B compared to group BF. Patients in group B (27%) experienced hypotension more than in group BF (10%). Lalita Gauri Mitra et al. also observed that hypotension in group B (13/31) was significantly higher compared to group BF (4/31) and the requirement of Mephantermine also was higher in group B than Group BF (7.5±4.5 versus 3.0±0 mg) [18].

Martyr and Clark recommended less than 10mg of Bupivacaine to avoid hypotension in elderly patients [19].

In our study, ischemia occurred in 3 (10%) patients in group I and no patients in group II. Occurrence of ischemia was insignificantly different between both groups.

Near to our results, Edwards et al. [20] studied the incidence and duration of perioperative myocardial ischemia using ambulatory ECG monitoring in 100 patients undergoing transurethral surgery, who were allocated randomly to receive either general or spinal anesthesia. The overall incidence of myocardial

ischemia increased from 18% to 26% between the preoperative and postoperative periods. Patients with ischemic heart disease had a significantly greater incidence of myocardial ischemia after operation than patients without known ischemic heart disease ($P < 0.05$). There was an increase in both the incidence and duration of myocardial ischemia after operation with both anaesthetic techniques, but no significant difference between the two.

In our study, hypotension was found significantly higher in group I than group II ($P = 0.026$) while PONV, bradycardia, headache, backache and shivering were insignificantly different between both groups ($P = 1$, 0.237, 1, 2 and 0.795 respectively).

In agreement to our results, Abdelmonem [12] reported that hypotension was significant higher in group II than group I.

One of the most common complications of regional anesthesia is hypotension. This is directly related to decrease in the systemic vascular resistance seen with the sympathetic blockade. It is important to note, however that cardiac output is maintained with the decrease in the SVR [21].

Further studies are needed on a larger sample size and on multi-center and to evaluate the effect of smaller dose by continuous lumbar spinal block.

5. CONCLUSIONS

Hyperbaric bupivacaine 8.75 mg injected at L4-L5 is sufficient to provide adequate sensory and motor block, while maintaining hemodynamic stability during TURP procedures.

CONSENT AND ETHICAL APPROVAL

This prospective randomized controlled double-blinded study was carried out in Tanta university hospital in Urology Department for one year (December 2019- December 2020) after approval from institutional ethics committee and an informed consent was taken from all patients.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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