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ORIGINAL ARTICLE

LOW VS HIGH DOSE SPINAL HYPERBARIC BUPIVACAINE ON HEMODYNAMIC VARIABLES IN PATIENTS UNDERGOING TRANSURETHRAL RESECTION OF THE PROSTATE: A PROSPECTIVE TWO ARM OPEN LABEL RANDOMISED COMPARATIVE STUDY

R. Prabhavathi[1], G. Chaitanya Kumar[2], P. Narasimha Reddy[3], P. Pradeep[4], K. Krishna Chaitanya[5], Sujith T. R[6], Surya Prakash[7], Varaprasad[8]

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ABSTRACT: BACKGROUND: Spinal anesthesia for transurethral resection of the prostate (TURP) leads to high incidence of arterial hypotension. We hypothesized that the reduction of this dose from 15 mg to 7.5 mg without much change in baricity would minimize hypotension without altering anesthetic benefits. **METHODS:** 60 ASA-1 & ASA-2 patients scheduled for TURP were randomized into two groups A and B receiving 7.5 and 15 mg of hyperbaric bupivacaine both with 90 µg of buprenorphine respectively in spinal anesthesia. Intravenous ephedrine was administered for each episode of hypotension. We recorded sensory and motor block, intra operative vitals, pain, nausea and vomiting. **RESULTS:** Duration of analgesia found statistically significantly high in group B as compared to group A (421.6±35.6 vs. 133.8±27.4 min respectively, p=<0.0001) Also, use of ephedrine as a vasopressor was more in group B patients (36.6%) as compared to group A patients(10%) and was statistically significant(p=0.03). **CONCLUSION:** A dose of 7.5 mg of hyperbaric bupivacaine reduced incidence of hypotension without altering pain relief.

KEYWORDS: Hyperbaric bupivacaine, Buprenorphine, Spinal anesthesia, TURP, Hypotension.

INTRODUCTION: TURP is one of the most common procedures performed in elderly men with spinal anesthesia as the technique of choice[1] as it is the fastest, most predictable and reliable form of regional anesthesia. Addition of intrathecal narcotics to local anesthetic solution enhances the sensory blockade of local anesthetics without affecting the sympathetic activity and hence prolongs the duration of anesthesia and analgesia.[2, 3]

Buprenorphine a mu receptor opioid agonist with low intrinsic activity can also be administered safely in the subarachnoid space.[4] It has a high molecular weight and lipophilicity which may prevent its rostral spread. When used intrathecally in combination with bupivacaine it has improved the quality and duration of postoperative analgesia compared to bupivacaine alone.[5]

Sub-arachnoid analgesia rarely lasts more than 3-4 hours with the drugs currently available and is therefore of limited use for postoperative analgesia. The administration of local anesthetics, opioids or a combination neuroaxially (sub-arachnoid or epidural) is an excellent technique for managing postoperative pain following abdominal, pelvic or orthopedic procedures on the lower extremities. Patients often have better presentation of pulmonary function, are able to ambulate early and benefit from physical therapy with lower risk for postoperative venous thrombosis.

Spinal anesthesia with a T10 (10th Thoracic vertebra) sensory level provides excellent anesthesia and good operating condition for cysto-endoscopic surgery. The low dose hyperbaric

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spinal anesthetic provides a block that is dense in lower thoracic, lumbar and sacral areas and is ideally suited to perineal, urologic and lower extremity surgery.

Because the block does not extend into the upper thoracic level, it results in a partial sympathetic block with minimum hemodynamic changes. A large intravenous preload is rarely necessary or advisable as it may increase the risk of TURP syndrome. The aim of this study was to compare and evaluate the onset of action, duration of analgesia, quality of block, effects on hemodynamic status and other complications by decreasing the concentration of bupivacaine to 0.25% and adding small dose of buprenorphine intrathecally.

MATERIALS AND METHODS: This two arm open label randomized parallel group prospective study was carried out in the Department of Anesthesia in Narayana medical college & specialty hospital, Nellore during period from September 2011 to November 2012. The Institutional Ethical Committee approved the study protocol. Informed consent was also taken from each study subject. Total 60 male patients of grades ASA I and ASA II (American Society of Anesthesiologist Classification) were randomly selected and studied for routine endourological procedures under sub-arachnoid block (SAB).

Those patients were allocated by computer generated randomization table into two groups each having thirty patients. One group received 1.5 ml of 0.5% hyperbaric bupivacaine(0.25%/ 7.5 mg), 1.5 ml 5% Dextrose and 90 microgram of buprenorphine (Group - A) and the other group received 3 ml of 0.5% hyperbaric bupivacaine (0.5%/ 15 mg) and 90 microgram of buprenorphine (Group- B). Preexisting fluid deficit was corrected prior to anesthesia by giving fluid at the rate of 1.5 ml/kg for every hour of fasting.

The patients fasted as required for general anesthesia. No pre-medication was given; but all patients were reassured and the anesthetic procedure was explained on the day before the operation. Intravenous access was established in all patients in the operating room. Base line heart rate and blood pressure (non-invasive) were obtained. Each patient received an intravenous fluid load of 300 ml of Ringer lactate solution over 15 minutes and they also received 40% oxygen by face mask throughout the anesthetic period. Every patient received a subarachnoid block in the sitting position at the L2-3 or L3-4 level via 25G Quincke Babcock needle.

The anesthetic agents were injected intrathecally over 20 seconds after confirming the free flow of cerebrospinal fluid coming through the needle with the bevels facing laterally. The patients were then turned to the supine position leaving a sterile dressing over the lumber puncture site.

During the first 90 minutes after spinal anesthesia, the patients were assessed as follows: non-invasive blood pressure, heart rate (continuous lead II ECG), SpO2 recorded at just after block, after 5 minutes, after 10 minutes and thereafter every 5 minutes interval up to 30 minutes then after every 15 minutes upto 90 minutes. Level of sensory block was assessed using cold sensation (ether swabs) every minutes. Motor block was assessed by the modified Bromage scale every 5 minutes. The definitions of the modified Bromage scale are:

Score 0: Able to move hip, knee and ankle;
Score1: Unable to lift straight legs but able to flex knee and ankle;
Score 2: Unable to flex knee but able to move ankle;
Score 3: Unable to move hip, knee and ankle.

Intraoperative pain was graded on a visual analog pain score (VAS) from 0 to 100. Each patient was assessed and recorded regarding shivering, nausea, vomiting, hypotension, bradycardia

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at intervals till the surgical procedure was completed and on arrival at recovery room. Any reduction of systolic arterial blood pressure of more than 30% of the base line was promptly treated with 5 mg IV boluses of ephedrine. Amount of ephedrine and total fluid infused till the end of surgery were also recorded.

After reassessing and stabilizing the vital parameters in the recovery area the patients were sent to the postoperative ward, where they were assessed for sensory & motor regression in every half an hour interval. The time taken to request for first analgesia as well as the degree of sedation, respiratory depression, pruritus, nausea, vomiting were recorded on a preformed data sheet during the first 24 hours post-operatively.

STATISTICAL ANALYSIS: The statistical analysis will be carried out with SPSS version 20 & Graph pad prism software Version-5, USA. Categorical data will be presented as actual numbers and percentages. For normally distributed data will be presented as Mean±SD, analyzed using unpaired "t" test and one-way repeated-measures analysis of variance (ANOVA). Non-normally distributed data will be analyzed by using non-parametric “Mann-Whitney U test”. Categorical variables will be analyzed with “Fischer’s exact test”. For statistical significance, a two tailed probability value of less than 0.05 will be considered.

RESULTS: In the present comparative study, there was no statistically significant difference in the demographic parameters like age (64±10.21 vs. 62.3±9.92 yrs., p=0.43), height (162.8±20.12 vs. 166.9±5.21 cm, p=0.28), weight (71.6±19.06 vs. 67.2±5.92 kg, p=0.23) between A and B group respectively. On classifying patients based on ASA, 24 patients were in grade II and 6 patients were in grade III in group A whereas, 22 patients were in grade II and remaining 8 in grade III in group B (p=0.72)**.** On evaluation of the baseline hemodynamic parameters, there was no significant difference in heart rate (HR 75.2±7.94 vs. 75.6±7.47 beats/min, p=0.84) systolic blood pressure (SBP 129.5±14.5 vs. 124.3±11.6 mmHg, p=0.13) and diastolic blood pressure (DBP 77.9±11.7 vs. 76.4±10.9 mmHg, p= 0.61) in A and B group respectively.

The duration of surgery did not significantly varied between A and B group (73.6±19.6 vs. 75.6±18.4 min, p=0.68) respectively. However, Duration of analgesia found statistically significantly high in group B as compared to group A (421.6±35.6 vs. 133.8±27.4 min respectively, p=<0.0001) (Table-1)

Parameters	Group A 0.25% (n=30)	Group B 0.5% (n=30)	P value
Age (yrs.)	64±10.21	62.3±9.92	0.43
Wt. (kg)	71.6±19.06	67.2±5.92	0.23
Ht (cm)	162.8±20.12	166.9±5.21	0.28
ASA grade (II/III)	24/6	22/8	0.72
Baseline Heart Rate (BPM)	75.2±7.94	75.6±7.47	0.84
Baseline Systolic BP (mmHg)	124.3±11.6	129.5±14.5	0.13
Baseline Diastolic BP (mmHg)	77.9±11.7	76.4±10.9	0.61
Length of surgery (MIN)	73.6±19.6	75.6±18.4	0.68
Duration of analgesia (MIN)	133.8±27.4	421.6±35.6	< 0.0001

Table 1: Baseline parameters between group A and group B

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As shown in Table 2, there was no significant difference between group A and B in occurrence of adverse effect. Interestingly, use of ephedrine as a vasopressor was more in group B patients (36.6%) as compared to group A patients(10%) and was statistically significant(p=0.03). We found statistically significant higher bromage score in group B as compared to Group A. (Table-3). Intra-operative hemodynamic variations are shown in Figure 1-3.

Parameters	Group A 0.25% (n=30)	Group B 0.5% (n=30)	P value
Nausea & Vomiting	0	2(6.6%)	0.47
Pain	2(6.6%)	0	0.47
Bradycardia	0	0	-
Ephedrine (Vasopressor)	3(10%)	11(36.6%)	0.03

Table 2: Adverse effects and use of vasopressor

Parameters	Group A 0.25% (n=30)	Group B 0.5% (n=30)	P value
(L3-L4)/(L4-L5)	29/1	28/2	1.00
T10/T8/T6/T4/T2	30/0/0/0/0	25/1/2/1/1	0.34
Bromage score 2/ 3	26/4	1/29	< 0.0001

Table 3: Sensory and Motor block

Figure1: Intra-operative variation in Heart Rate between Group A (0.25%) vs. Group B (0.5%).

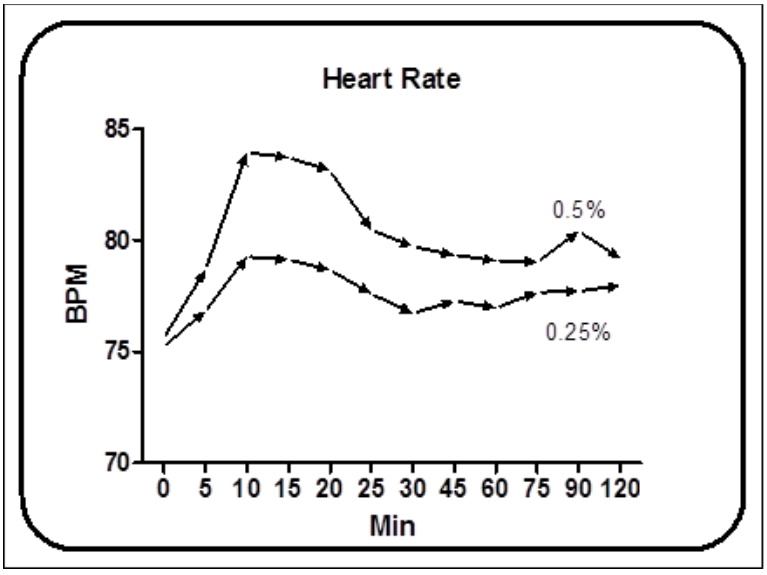

Figure 1

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Figure 2: Intra-operative variation in systolic blood pressure between Group A (0.25%) vs. Group B (0.5%)

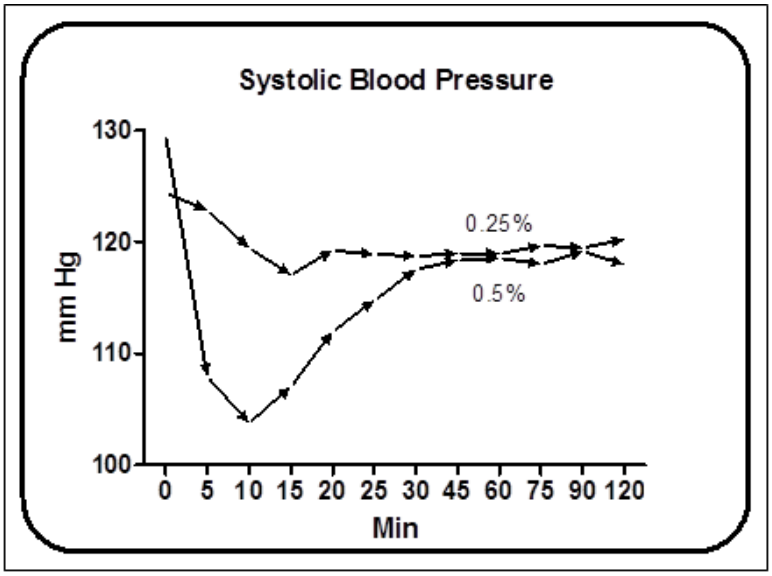

Figure 2

Figure 3: Intra-operative variation in diastolic blood pressure between Group A (0.25%) vs. Group B (0.5%)

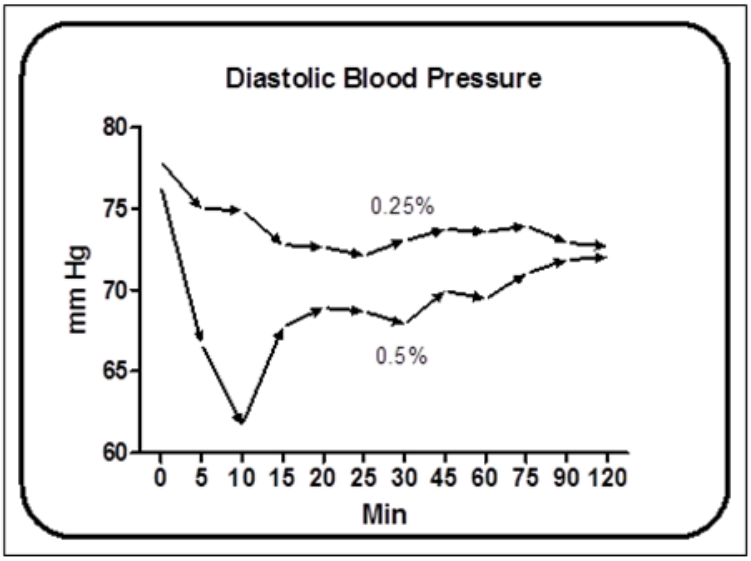

Figure 3

DISCUSSION: Perioperative complications impeding the effective and safe use of spinal anesthesia are hemodynamic instability in extremes of age. Most of such patients undergoing endoscopic urological procedures are elderly, and a majority of them have coexisting cardiac, pulmonary and other co-morbid conditions. Different techniques to lower the incidence of the above hemodynamic

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complications include unilateral spinal anesthesia, use of low-dose local anesthetics and addition of narcotics or other adjuvants to local anesthetics.

Although low-dose bupivacaine reduced the cardiovascular effects, it was not enough to provide an adequate level of sensory blockade.[6] Intrathecal opioids are synergistic with local anesthetics and intensify the sensory block without increasing the sympathetic block.[7]

Combination of drugs allows the use of a lower dose of the local anesthetic agent with adjuvants, which offers hemodynamic stability. Opioids in conjunction with local anesthetics improve the quality of intraoperative analgesia and prolong the duration of postoperative analgesia.[8]

Local anesthetics such as bupivacaine act mainly by blockade of voltage-gated Na+ channels in the axonal membrane and presynaptic inhibition of calcium channels.[9] The μ-agonists sufentanil butorphanol and buprenorphine exert their action by opening the K+ channels and reducing the Ca++ influx, resulting in inhibition of transmitter release.[10, 11] A combination of these effects may explain the observed synergism between bupivacaine and buprenorphine. The synergism is characterized by increased somatic analgesia without an effect on the degree or level of local anesthetic-induced sympathetic or motor blockade.[11]

The lumbar interspace chosen for injection of hyperbaric bupivacaine may influence the level of the block.[12] All patients in our study, had the anesthetic solution injected in the L3-L4 interspace with the same velocity and the orifice of the spinal needle turned cephalad.

Our study suggests that intrathecal injection of the low dose (Group A) 7.5 mg of bupivacaine with 90 μg of buprenorphine induced less profound short-acting motor block but provides the same adequate level of analgesia for endoscopic urologic surgery than the combination of bupivacaine 15 mg and 90 μg of buprenorphine (Group B). With the use of opioids in combination with low dose of local anesthetic, the quality of block has improved along with minimizing the complications of sympathetic blockade.[13]

Several studies have shown that the volume and concentration variations without modification of the total dose of local anesthetic solutions, did not modify the highest level of motor or sensory block.[14,15] To avoid a possible modification in the baricity of the solutions we added 5% dextrose 1.5 ml to bring the baricity of the solutions to near normal.

Extension and duration of the block were classically dependent on dose of the local anesthetic injected.[16] The number of segments blocked depended on the dose used.[14] In fact, there is no linear relation between the number of segments blocked and the dose of local anesthetic. Reducing by half the quantity of the drug injected does not reduce by half the number of segments blocked.[16, 17] This hypothesis is confirmed by Burgess et al[12] about continuous spinal anesthesia and the efficiency of 3.75 mg and 5 mg hyperbaric bupivacaine, in peripheral vascular surgery.

Gentili, [13] using 8, 6 and 4 mg of hyperbaric bupivacaine for lower limb saphenous vein stripping, found that small doses (6-8 mg) provide adequate sensory block within about 1 hour of mean duration. The 4-mg dose failed to achieve surgical anesthesia in some cases (13%). In other studies, [18] the addition of fentanyl with the local anesthetic, enhances and increases the duration of the sensory blockade without increasing the intensity of motor block.

The synergistic interaction between spinal opioids and local anesthetics is characterized by enhanced somatic analgesia without effect on the degree or level of the local anesthetic-induced sympathetic or motor blockade.[19,20] The time to achieve the highest levels is longer with smaller doses of bupivacaine and is not modified by the use of opioid.[18]

The maximum upper level of sensory block achieved was higher in the patients of group B T2 in one patient, T4 in one patient, T6 in two patients T8 in one patient, and T10 in all other patients, but in patients of group A, T10 was achieved in all patients which is sufficient for TURP surgeries but one patient in group complained discomfort intraoperatively which was managed with iv fentanyl and midazolam.

In our study, the absence of complete motor block in Group A was not a problem for the surgical procedure. Possible reasons for the incomplete motor block in Group A could be the low dose of bupivacaine. If the motor block was less intense, the recovery and mobilization of the patient could be faster. These findings were demonstrated by the studies of Vaghadia when comparing a small-dose hypobaric lidocaine fentanyl spinal anesthesia and conventional-dose hyperbaric lidocaine.[21]

Regarding side-effects, the incidence of hypotension was high in Group B and less in Group A. Endoscopic urological surgeries are carried out in elderly patients wherein hypotension is more dangerous because they might have a decreased physiological reserve and compromised blood supply to various vital organs.[22]

Also, to avoid procedure-related complications like TURP syndrome, restricted fluid has to be administered, which is unavoidable with ongoing hypotension, which were more prevalent in group B. We used intraoperative ephedrine in 11 patients in Group B, and in three patients in Group A. Opioids delivered by the spinal route decrease the dose of bupivacaine but may produce nausea, vomiting, urinary retention and respiratory depression and pruritus as the side-effects.

In this study, the primary side-effects were nausea in two patients in Group B. No severe bradycardia occurred in our study, however it was a side effect (9-30%) described with the use of high doses of bupivacaine.[23, 24] No respiratory depression in our study. No urinary retention as these patients on catheter post operatively.

Duration of analgesia was longer in Group B. The problem of the shortness of the sensory block with the low dose of bupivacaine is resolved by adding buprenorphine. Kuusniemi showed that adding 25 μg of fentanyl to 10 mg of bupivacaine compared to 10 mg of bupivacaine only, will prolong the sensory block.[25]

CONCLUSION: The practice of low-dose local anesthetic with adjuvant is gaining popularity in day care surgeries because it is a safe, rapid, inexpensive technique with lower postoperative morbidity. Small-dose bupivacaine provides successful anesthesia and gives better cardiac output stability than a large dose. Low-dose bupivacaine use in TURP surgieres should be promoted in view of reduced incidence of hemodynamic adverse effects in the geriatric population. The sample size in our study was small but had significantly important results, and we suggest future studies to be undertaken with a larger population size.

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AUTHORS:

1. R. Prabhavathi
2. G. Chaitanya Kumar
3. P. Narasimha Reddy
4. P. Pradeep
5. K. Krishna Chaitanya
6. Sujith T. R.
7. Surya Prakash
8. Varaprasad

PARTICULARS OF CONTRIBUTORS:

1. Associate Professor, Department of Anaesthesiology, Narayana Medical College & Hospital.
2. Assistant Professor, Department of Anaesthesiology, Narayana Medical College & Hospital.
3. Professor and HOD, Department of Anaesthesiology, Narayana Medical College & Hospital.
4. Assistant Professor, Department of Anaesthesiology, Narayana Medical College & Hospital.
5. Assistant Professor, Department of Anaesthesiology, Narayana Medical College & Hospital.
6. Post Graduate, Department of Pharmacology, Narayana Medical College & Hospital.
7. Professor and HOD, Department of Urology, Narayana Medical College & Hospital.
8. Assistant Professor, Department of Surgical Gastroenterology, Narayana Medical College & Hospital.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. R. Prabhavathi,
Associate Professor,
Department of Anesthesiology,
Narayana Medical College & Hospital,
Nellore-524002.
Email: prabhavathi95gmc@gmail.com

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