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RESEARCH ARTICLE
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COMPARATIVE EFFECTS OF BUPRENORPHINE AND DEXMEDETOMIDINE AS ADJUVANTS TO BUPIVACAINE SPINAL ANAESTHESIA IN ELDERLY MALE PATIENTS UNDERGOING TRANSURETHRAL RESECTION OF PROSTRATE (TURP) AND TRANSURETHRAL RESECTION OF BLADDER TUMOR (TURBT): A RANDOMIZED PROSPECTIVE STUDY

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Abstract

Background: Transurethral resection of the prostate (TURP) or transurethral resection of bladder tumor (TURBT) is a commonly performed urological procedure in elderly men with spinal anaesthesia being the technique of choice. Use of low-dose spinal anesthetic drug with adjuvants is desirable. The present study was undertaken to evaluate and compare the characteristics of subarachnoid blockade, hemodynamic stability, time of first analgesia request and adverse effects of intrathecal buprenorphine and dexmedetomidine as an adjuvant to 0.5% hyperbaric bupivacaine for lower abdominal surgeries.

Methods: A total 60 elderly male patients of ASA status I/II, aged 60 years and above, scheduled for elective TURP and TURBT were enrolled and divided into two groups namely Group B and Group D of 30 each. Patients in Group B received 60µg of buprenorphine with 0.5% bupivacaine 14 mg intrathecally whereas patients in Group D received 5µg of dexmedetomidine with 0.5% bupivacaine 14 mg intrathecally. The onset time to peak sensory level, motor block, haemodynamic variables, duration of motor block, analgesia and any adverse effects were noted.

Results: There was no significant difference between groups regarding demographic characteristics and type of surgery. The motor, sensory blockade and time of rescue analgesia were significantly prolonged in Group D compared to Group B. There was no significant difference in haemodynamic variables although Group D had lower Heart Rate (HR) than Group B.

Conclusion: Dexmedetomidine as an intrathecal adjuvant with 0.5% hyperbaric bupivacaine prolonged anaesthesia, analgesia with better degree of sedation and reduced need of rescue analgesics with fewer side effects when compared to intrathecal buprenorphine.
Keywords: Spinal anaesthesia; Buprenorphine; Dexmedetomidine; Bupivacaine; Lower abdominal surgery; Analgesia

Introduction

Transurethral resection of the prostate (TURP) is a commonly performed procedure in elderly male patients [1]. Postoperatively these patients also suffer from bladder spasm associated with the use of a transurethral balloon to prevent bleeding from the prostatic bed or capsule [2, 3]. Therefore, there is a need to develop anesthetic techniques that extend postoperative analgesia without compromising patient safety.

Bladder cancer occurs at an average patient age of 65 years with a 3:1 male to female ratio. Transitional cell carcinoma of the bladder is second to prostate adenocarcinoma as the most common malignancy of the male genitourinary tract. Transurethral resection of bladder tumour (TURBT) remains to be the cornerstone for diagnosis and treatment of bladder cancer. Various guidelines emphasize the key role of TURBT, in particular complete resection of all visible tumours when technically safe and feasible [4].

Spinal anesthesia is the commonly used technique for these procedures as this is the quickest, most predictable, and reliable form of regional anaesthesia. Besides, the patients remain awake during the surgical procedure enabling early identification of complications of TURP such as transurethral resection syndrome involving osmolar disturbances, fluid overload or water intoxication [5]. TURBT, unlike TURP, is rarely associated with absorption of significant amounts of irrigating solution. A sensory level block of not more than T10 is desirable to detect the complications such as bladder perforation. Unfortunately, this level of the block with only intrathecal local anesthetics may not achieve an extended duration of postoperative analgesia. Use of higher doses of local anesthetics to achieve this may result in circulatory disturbances that can be difficult to manage as these patients are usually elderly and hence may have varying degrees of organ damage or associated systemic illness. However, a combination of low-dose local anesthetics along with other adjuvants can prolong the postoperative analgesia [5, 6]. Hence, this has become an attractive option. This study evaluates the sensorimotor effects of addition of buprenorphine or dexmedetomidine to low-dose intrathecal bupivacaine in patients undergoing TURP and TURBT.

Materials and Methods

After obtaining approval from the institutional ethical committee and written informed consent from all the patients, this double blinded randomised prospective study was conducted in 60 ASA grade 1 or 2 elderly male patients aged, 65 years undergoing elective TURP) and TURBT procedure under spinal anaesthesia. Patients with history of previous spinal surgery, infection at the injection site, hypersensitivity to amide local anaesthetics, buprenorphine or dexmedetomidine, neurological disorders, coagulopathy and patients with betablockers & alpha antagonists were excluded from the study.

A thorough pre-anaesthetic evaluation was done including history, clinical examination and relevant investigations like complete hemogram for hemoglobin, leukocytes and platelets counts, blood grouping, RBS, kidney and liver function test, serum electrolytes, urineanalysis, chest X-ray, electrocardiogram, 2D echo if indicated and coagulation profile. Patients were trained for 10cm VAS score for pain and informed about feeling of tingling, warmth or heaviness that may be felt after the intrathecal injection during Pre-anaesthetic evaluation. Patient was kept nil per month for minimum

6 hours before the surgery and tab diazepam 10mg orally was given at night before surgery. They were randomly allocated into two groups, group D and group B based upon the drug they received intrathecally. Predetermined computer-generated random allocation plan was used for randomisation. In the preoperative room, pulse rate, blood pressure, SpO2 were noted in the pre-anaesthetic room. In the operation theatre, resuscitation and general anaesthesia equipment and drugs were kept ready. NBM status was confirmed on OT table. Intravenous cannula of 18/20 G was secured and patient was preloaded with 10ml/kg of Ringer lactate solution over 10-30 minutes. Standard multipara monitor containing electrocardiogram, noninvasive blood pressure (NIBP) and pulse oximeter was applied to the patient and baseline parameters e.g., pulse rate, blood pressure, Spo2 were recorded. Premedication with injection Pantoprazole 40 mg iv and injection Ondansetron 4 mg intravascular was given according to dose per kg body weight of the patient. None of the patients received sedatives as premedication. Patients were given left lateral position and table was kept horizontal.

The person who was loading the drugs in syringes and giving the drug intrathecally was different from the person recording the parameters. Thus, the person observing the parameters and also the patient was not aware of the drug used intrathecally. Under all aseptic precautions, a person who was having adequate exposure of spinal anaesthesia technique e.g. Senior resident/ Junior resident lll performed lumbar puncture via a midline approach with quinke type 25-gauge spinal needle at L2-L3 or L3-L4 interspace. After obtaining free flow of clear cerebrospinal fluid, spinal anaesthesia was given with drug as per group allotted:

Group D (dexmedetomidine group)- received 2.8mL 0.5% hyperbaric bupivacaine with 0.2 mL dexmedetomidine (5mcg) intrathecally. (Which is equivalent to 2 units on insulin syringe). **Group B (**Buprenorphine group)- received 2.8 ml 0.5% hyperbaric bupivacaine with 0.2ml buprenorphine (60mcg).

The time of injection of drug noted as '0' hour. Patients were immediately turned supine keeping the position of the table horizontal. All the observations in the study were recorded by the third person who was not aware of the drug which the patient had received. Oxygen was supplied using simple face mask at the rate of 4 lit/min. After injection patient was turned supine slowly, following sensory, motor, and hemodynamic parameters were noted and monitored. Time of injection of subarachnoid block, time of onset of sensory and motor block, duration of sensory and motor block, degree of sedation, time for sensory regression to S1 dermatome, duration of surgical procedure and time to first analgesia request were noted. Systolic and diastolic blood pressure, mean arterial blood pressure, pulse rate and oxygen saturation were recorded at 0, then every 5 minutes up to 30 minutes and thereafter 15 minutes up to 60 minutes of the procedure. Any discomfort like nausea, vomiting, shivering, pruritus and adverse events such as hypotension, bradycardia respiratory depression and ECG changes were noted. Pain assessment postoperatively was made with the help of **VAS** score.

Hypotension was said to have occurred if the MAP fell less than 60 mmHg and treated with 100% O2, increasing the infusion rate of IV fluids and I.V. Injection mephentermine 6mg then blood pressure was monitored every 1 minute till it was stabilised. Vasopressor treatment was repeated as & when required.

Bradycardia was defined as heart rate less than 50/min and was planned to be managed with intravenous atropine in incremental doses.

Statistical Analysis

For statistical analysis data were entered into a Microsoft excel spreadsheet and then analyzed by SPSS (version 27.0; SPSS Inc., Chicago, IL, USA) and GraphPad Prism version 5. Data had been

summarized as mean and standard deviation for numerical variables and count and percentages for categorical variables. Two-sample t-tests for a difference in mean involved independent samples or unpaired samples. Paired t-tests were a form of blocking and had greater power than unpaired tests. A chi-squared test ($\chi 2$ test) was any statistical hypothesis test wherein the sampling distribution of the test statistic is a chi-squared distribution when the null hypothesis is true. Without other qualification, 'chi-squared test' often is used as short for Pearson's chi-squared test. Unpaired proportions were compared by Chi-square test or Fischer's exact test, as appropriate. P-value ≤ 0.05 was considered for statistically significant.

Observations & Results

A total of 60 male patients were enrolled in the study and divided into two groups of 30 patients in each group i.e., Group B (Buprenorphine group) and Group D (dexmedetomidine group). Both the groups were comparable and found no significant difference with respect to demographic profile of the patients and duration of surgery as shown in table 1.

Table 1: Demographic profile of the patients and duration of surgery

Demographic data		Group B	Group D	P value
Age groups (in years)	≤60	00 (0.0%)	00 (0.0%)	0.466
	61 to 70	25 (83.3%)	23 (76.66%)	
	71 to 80	05 (16.7%)	07 (23.3%)	
	Mean	67.46±4.01	67.20±4.59	0.811
ASA	I	17 (56.66%)	17 (56.66%)	1.000
	II	13 (43.33%)	13 (43.3%)	
Surgery Done	TURBT	09 (30.0%)	06 (20.0%)	0.371
	TURP	21 (70.0%)	24 (80.0%)	
Duration of Surgery (Min)		74.20±8.33	71.56±7.78	0.211

There was no statistically significant difference between two groups regarding choice of intervertebral space with p value of 0.273 whereas statistically significant difference found in highest dermatomal level (p=0.0227) as shown in table 2.

Table 2: Choice of intervertebral space and highest dermatomal level

Variables		Group B	Group D	P value
Choice of intervertebral space	L2/L3	12 (40.0%)	08 (26.7%)	0.273
	L3/L4	18 (60.0%)	22 (73.3%)	
Highest dermatomal level	T10	19 (63.3%)	14 (14 (46.7%)	0.022
	T12	04 (13.3%)	00 (0.0%)	
	T6	00 (0.0%)	03 (10.0%)	
	T8	07 (23.3%)	13 (43.3%)	

The onsets of sensory and motor blockades were fast, and duration of sensory blockade was prolonged in dexmedetomidine group compared to buprenorphine group. The motor blockade, sensory regression to S1 and time to first analgesia request were also prolonged in dexmedetomidine group, providing better postoperative analgesia than buprenorphine, (Table 3).

Table 3: Characteristics of spinal block

Block characteristics (min)	Group B	Group D	P value
Onset of sensory block	3.60±0.49	3.16±0.64	0.0052
Onset of motor block	4.46±0.62	3.90±0.80	0.0035
Duration of Sensory Block	367.53±111.02	502.80±12.83	<0.0001
Duration of Motor Block	288.10±22.38	431.30±12.48	<0.0001
Time of Sensory regression to S1	274.86±13.67	398.0±6.46	<0.0001

Time to the first analgesic request	399.70±12.41	529.0±29.06	<0.0001

Both the groups had stable and comparable hemodynamics during the study period as depicted in figure 1 to figure 4.

Figure 1: Comparison of mean heart rate at different time interval between two groups

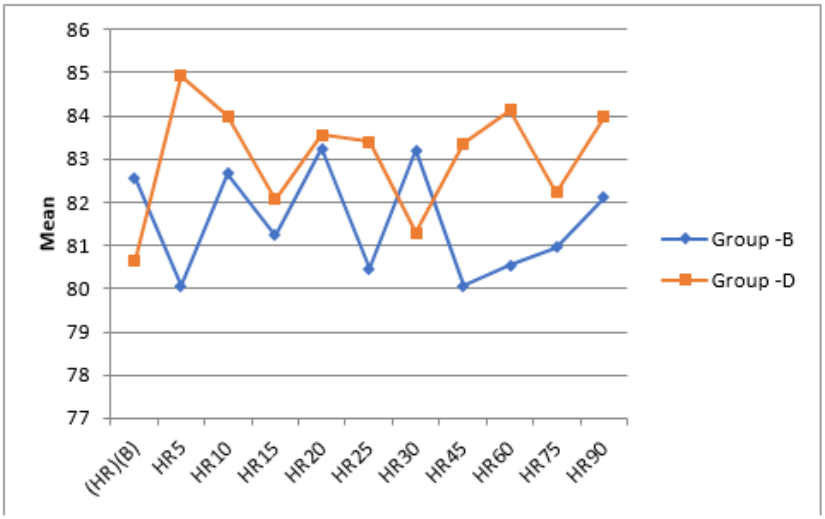


Figure 2: Comparison of mean SBP at different time interval between two groups

Figure 3: Comparison of mean DBP at different time interval between two groups

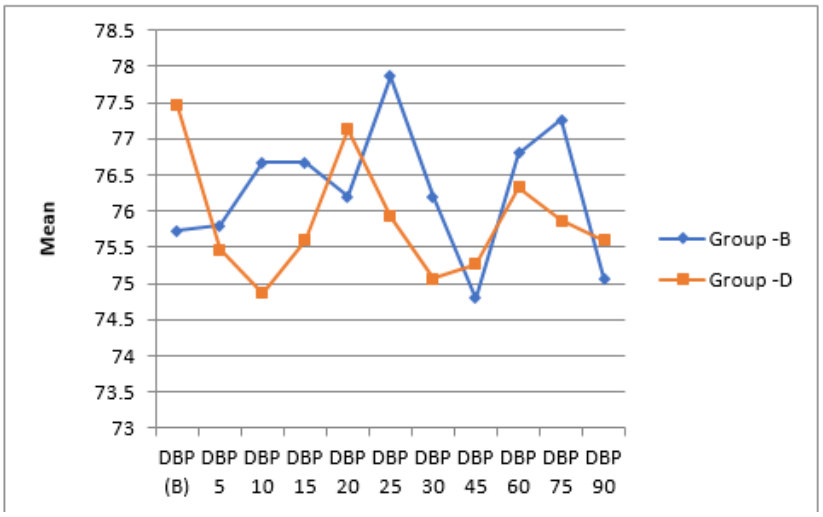
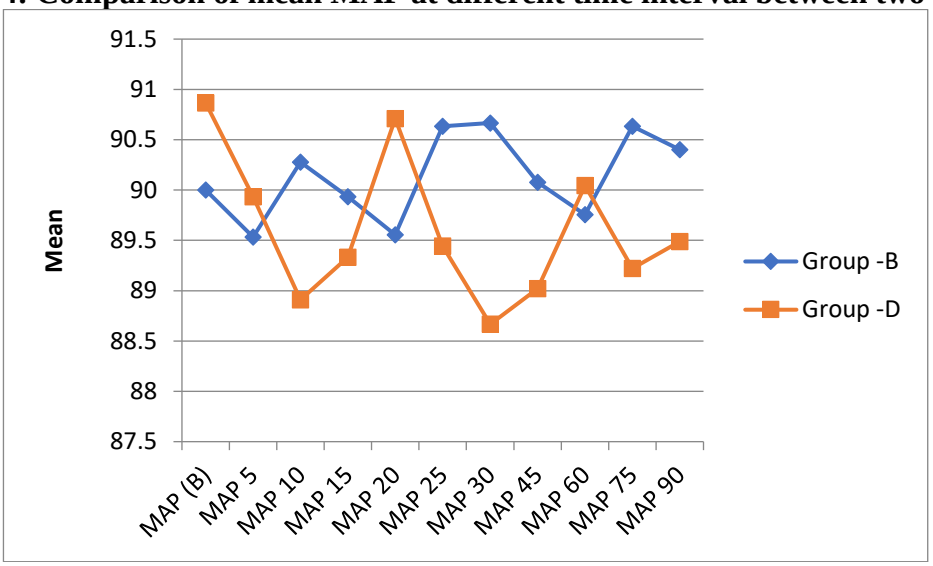
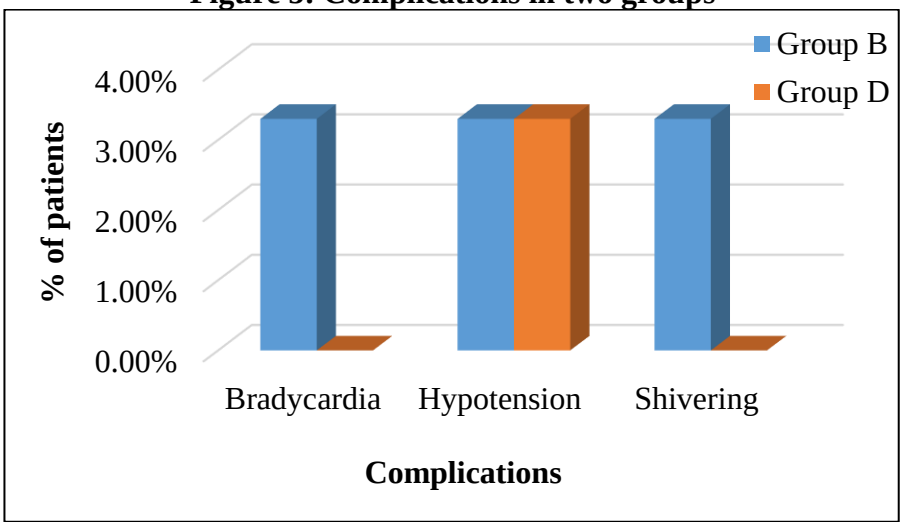


Figure 4: Comparison of mean MAP at different time interval between two groups



Compared to buprenorphine, intrathecal administration of dexmedetomidine as additive to hyperbaric bupivacaine was associated with fewer side effects. Complication with group was not statistically significant (p=0.5577) as shown in figure 5.

Figure 5: Complications in two groups



Discussion

Even though there are lot of adjuvants, in present study we chose 5µg dexmedetomidine and 60µg of buprenorphine as an additive to hyperbaric bupivacaine because there were only very few studies in the literature comparing the benefits and side effects of these two adjuvants to bupivacaine for TURP and TURBT. Also, they are pharmacologically different drugs, but their effects are similar in terms of hemodynamic stability, onset of sensory and motor block and adverse effects. But these two drugs differ in the clinical effects especially in the duration of sensory and motor block, sensory regression, and degree of sedation [7].

In the present study, the mean onset of sensory block in buprenorphine group was 3.60 minutes whereas in dexmedetomidine group it was 3.16 minutes. The mean onset of motor block in buprenorphine group was 4.46 minutes whereas in dexmedetomidine group, 3.90 minutes. Thus, early onset of sensory and motor block found in dexmedetomidine group with statistically significant difference. These findings are correlated with the study done by Kaur N et al [5] and Al-Mustafa et al [8].

Duration of analgesia was taken from the time of intrathecal injection of drugs to the first supplementation of rescue analgesic when patient complained of pain. In current study, the mean duration of analgesia was 399.70 minutes in buprenorphine group and 529.00 minutes in dexmedetomidine group. In this study, Dexmedetomidine group had prolonged duration of analgesia compared to Buprenorphine group which was 32% higher than the later. Similar findings are reported in previous studies [5, 7, 9, 10]. The prolonged analgesic action of intrathecal α2 agonist is by decreasing the release of C-fibres neurotransmitters and by causing hyperpolarisation of neurons in the post synaptic dorsal horn [11].

The duration of motor block was taken from time of intrathecal drug administration to the time taken to attain modified bromage 3. The mean duration of motor block in Buprenorpine group was 288.1 minutes and in dexmedetomidine group was 431.303 minutes (p value 0.00). This was similar with the study conducted by Kaur N et al [5], Gupta M et al [7] and Gupta R et al [10]. In present study itself, motor blockade in dexmedetomidine group was about 49% prolonged than Buprenorpine group. Such a prolongation of motor blockade may not be liked by many patients who have undergone surgeries that would end by one hour. In this perspective, Buprenorphine would be a better adjuvant. Still, Dexmedetomidine is a better drug as it would spare the rescue analgesic requirements.

The mean duration for sensory regression to S1 in buprenorphine group was 274.86 minutes and in dexmedetomidine group, 398.00 minutes which is comparable with the study done by Kaur et al [5]. However, in Gupta M et al study [7] the mean duration for sensory regression to S1 in buprenorphine group was 225.9 min which was lower than our study. But in dexmedetomidine group it was 451.4 min that was higher than the same group in our study. Gupta R et al [10] have shown that the mean time for sensory regression to S1 was 476 min in dexmedetomidine group which is higher than our study. This may be because either the usage of higher concentration(0.75%) of isobaric ropivacaine or due to the potentiation of intrathecal ropivacaine by intrathecal dexmedetomidine [12]. S1 dermatome is used as the sensory regression point in most of the studies. S1dermatome is well below the dermatomes those are involved in the surgery (T8 – L1) in our study. But patients in both groups never complaint of pain at the time of sensory regression to S1. More than that, analgesia was extended to the time for first analgesic requirement. This is the classical effect of adding an adjuvant to the local anesthetics i.e., improving patients' comfortness and reducing both the postoperative analgesic requirement and side effects.

Addition of buprenorphine or dexmedetomidine resulted in comparative hemodynamic stability in our study. One patient in each group had transient hypotension following the injection of spinal anaesthesia needing a single bolus of IV mephentermine 6 mg to maintain blood pressure within 30% of the baseline. One patient in dexmedetomidine group developed bradycardia. They were managed successfully with the use of atropine 0.6 mg I. V. None of the patients had an SpO2 <90%. Al-Ghanem et al in their study noted that the use of intrathecal dexmedetomidine to be associated with decrease in blood pressure and heart rate [13].

In present study no incidence of nausea and vomiting were more seen in buprenorphine and dexmedetomidine group. Intraoperative shivering was seen one patient in buprenorphine group. SPO2 was in the range of 97–100 % without oxygen supplementation. No incidence of respiratory depression, pruritus and ECG changes were found in both the groups. These findings are correlated with the other studies [7, 14, 15].

Conclusion

Dexmedetomidine as an intrathecal adjuvant with 0.5% hyperbaric bupivacaine prolonged anaesthesia, analgesia with better degree of sedation and reduced need of rescue analgesics with fewer side effects when compared to intrathecal buprenorphine.

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