Intrathecal Dexmedetomidine as an Adjuvant to Low Dose Hyperbaric 0.5% Bupivacaine on Haemodynamic Parameters in Patients Undergoing Transurethral Resection of Prostate

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ABSTRACT

Objective: To determine the role of dexmedetomidine in potentiating the local anaesthetic efficacy of a low dose of bupivacaine when used as an adjuvant.

Study Design: A prospective, double-blind, randomised study.

Place and Duration of the Study: Department of Anaesthesia, Sindh Institute of Urology and Transplantation, Karachi, Pakistan, from July 2021 to February 2022.

Methodology: One hundred and eight patients of ASA physical class I-III undergoing transurethral resection of the prostate (TURP) under sub-arachnoid block (SAB) were enroled and distributed into two equal groups. Group BUPIPURE (BP) was given 7.5 mg of pure 0.5% hyperbaric bupivacain whereas group BUPIDEX (BD) was given 6 mg of 0.5% hyperbaric bupivacain with 3 µg dexmedetomidine intrathecally. The effects in Both groups were compared using chi-square and unpaired t-tests. A significance level of $p < 0.05$ was used to evaluate the statistical significance.

Results: Both groups demonstrated a steady decrease in mean heart rate (mean HR 98.9-62.7 per minute as compared to 79.1-59.4 per minute in groups BP and BD, respectively), however, no patient reached to HR <50/min. Group BP had a higher HR variability than group BD. The two groups' median peak sensory levels were similar. However, a statistically significant difference was revealed in the time taken for 2-segment regression (87.5 ± 11.3 min *vs.* 115.5 ± 6.2 min $p < 0.001$ in BP and BD), as well as the time to reach T10 sensory level (13.56 ± 2.5 min *vs.* 10.9 ± 3.0 min $p < 0.001$).

Conclusion: In patients having TURP, intrathecal dexmedetomidine combined with low-dose bupivacaine results in a quicker start, extended sensory and motor block, and a decreased need for rescue analgesics.

Key Words: *Adjuvants, Dexmedetomidine, Spinal anaesthesia, Transurethral Resection of Prostate*.

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INTRODUCTION

Transurethral prostate resection is commonly required among elderly males.[1] These patients usually have chronic cardiovascular, respiratory, and endocrine diseases and are vulnerable to adverse outcomes.[2] These patients usually receive a subarachnoid block with a local anaesthetic, hyperbaric bupivacaine.[3]

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For bladder distension and other procedural analgesia, a sensory block upto the T10 dermatome is desirable.[4,5] Normally, 10-15 mg of bupivacaine is required to attain this sensory level. However, this dose may cause haemodynamic instability due to the blockade of the thoracic sympathetic ganglia. Adjuvants such as intrathecal opioids and α2 agonists, along with a reduced dose of local anaesthetic, have been studied to achieve the necessary sensory level along with haemodynamic stability in this vulnerable elderly population.[6-8]

Dexmedetomidine has been used by many researchers to potentiate bupivacaine's effect. It is an alpha-agonist that inhibits unmyelinated C-fibre transmitter release, hyperpolarises post-synaptic dorsal horn neurons, and reduces substance P release, making it an anti-nociceptive.[4,8,9] Dexmedetomidine was launched in Pakistan a few years ago. However, the local institutes have published only a limited amount of research on dexmedetomidine, particularly in TURP cases.[10-13]

To strengthen the local data, this study was conducted to determine the haemodynamic effects of dexmedetomidine as an adjuvant with a low dose of hyperbaric 0.5% bupivacaine during transurethral resection of the prostate (TURP).

METHODOLOGY

This study was conducted at the Sindh Institute of Urology and Transplantation, Karachi, as a double-blind, randomised trial from July 2021 to February 2022. It was registered on clinicaltrials.gov (NCT05993975) after obtaining the Institutional Ethical Review Committee's approval.

Patients with ASA physical status I, II, or III, aged 50-75 years, scheduled for TURP under subarachnoid block (SAB) were included in the study. It excluded patients with absolute SAB contraindications, such as their refusal or bleeding diatheses. Patients with ASA physical status IV, a history of spine surgery, an infectious focus on the lower back, drug abuse, unstable neurological status such as Alzheimer's disease, movement disorders such as Parkinsonism, paralysis with difficulty in sitting for subarachnoid block, or hypersensitivity to bupivacaine or dexmedetomidine were also excluded.

This trial included 108 patients, 54 in each of the two groups. The sample size was estimated based on a previous study using WHO software with Alpha = 5%, power of the test 1-beta = 90, and mean time to sensory blockade (10.7 ± 3.5 *vs*. 12.7 ± 3.9 min).[4] Non-probability consecutive sampling was used to induct the patients in this study. A computer-generated randomisation table divided patients into two groups. Group BUPIDEX received 6 mg of 0.5% hyperbaric bupivacaine in 1.2 mL, along with 3 µg of dexmedetomidine (0.3mL of 10µg/mL solution). The BUPIPURE group received 7.5 mg (1.5mL) of pure 0.5% hyperbaric bupivacaine. A consultant anaesthetist who was not involved in the trial prepared the study medicine in a 3 mL syringe, marked it according to the randomisation table, and handed it over to the primary investigator, who did not know the composition until decoding. Under rigorous aseptic circumstances, both experimental groups received 1.5 mL of drug solution in the subarachnoid space.

As patients shifted into the operating room, baseline HR, NIBP, SpO_2, respiration rate, and temperature were measured according to ASA guidelines. All patients received a crystalloid preload (7 mL per kg of body weight) for 15–20 minutes. Under all aseptic measures, a lumbar puncture was performed with a 25-gauge Quincke spinal needle in the L3–L4 intervertebral space while the patients were positioned sitting. After ensuring the free flow of cerebrospinal fluid, 1.5 ml of the study drug was administered in the subarachnoid space, and then the patients were laid supine. For 10 minutes, haemodynamic variables (HR, NIBP), SpO_2, and respiratory rate were monitored every 2 minutes, then every 5 minutes till the operation ended. With a 22-gauge, blunt-tipped needle, the sensory block was assessed. The duration of intrathecal injection and attainment of T10 sensory level block time were recorded. If a block height was consistent throughout the three assessments, it was considered the highest. Surgery was then allowed. If the anaesthetised sensory level was insufficient or patients complained of intraoperative discomfort, nalbuphine 2–3 mg IV boluses were given until patients were comfortable.

To treat hypotension (MAP <20% of baseline), phenylephrine 25 – 50 micrograms and atropine 0.5 mg intravenously were administered. Patients experiencing Bradycardia (HR <50 beats/min) received 0.6 mg of intravenous atropine. Patients with hypoxaemia (SpO_2 <92%) received 4-5 L/min of oxygen *via* a face mask. Postoperative pain was measured using the 10-cm Visual Analogue Scale (VAS) from 0 (no pain) to 10 (severe pain). The time from SAB to the first analgesic demand was called analgesia duration. Patients received 100 mg intravenous tramadol and 10 mg antiemetic metoclopramide for a VAS value of 4 or above, and the administration time was recorded.

The data was analysed using SPSS version 20.0. In groups BUPIPURE and BUPIDEX, researchers calculated the mean and standard deviations of age, height, weight, HR, MAP, sensory blockage, motor blockade, and analgesia. The study used the Kolmogorov-Smirnov test to report the mean ± standard deviation for normally distributed quantitative variables. However, non-normal quantitative variables had medians and IQRs. As needed, chi-square and unpaired t-tests or Mann-Whitney U tests compared both groups' effects. A significance level of $p < 0.05$ was used to assess statistical significance.

RESULTS

The present study had 108 patients, with no drop-out. Patients in both groups had similar characteristics (Table I). Eighty-one of 108 (75%) patients had one or more than one comorbidities such as cardiovascular illnesses, diabetes or asthma, while smoking history was positive in 43 (39.8%) patients.

Both groups showed similar HR changes after SAB, with a steady reduction in mean heart rate. However, no patients required anticholinergic medication for severe bradycardia (HR <50 beats/min). Group BP had more HR variability, while Group BD had a more uniform mean HR (Figure 1).

The mean arterial pressure changes in the BP and BD groups were similar and mostly within acceptable limits (Figure 2). Only 7 (6%) out of 108 patients experienced temporary hypotension (MAP <60 mmHg), which was managed with a 250-500 mL normal saline bolus. In three refractory cases, phenylephrine (25 - 50 micrograms) was given intravenously with atropine (0.5 mg) due to the lack of ephedrine.

Although there were no significant variations in peak sensory levels between the groups BP and BD, the median time to reach the T10 sensory block was 13.0 (12 - 15) min and 10.0 (8.75 - 13.0) min, respectively, indicating statistical significance. BP and BD have significantly different dermatome regression periods (Table II).

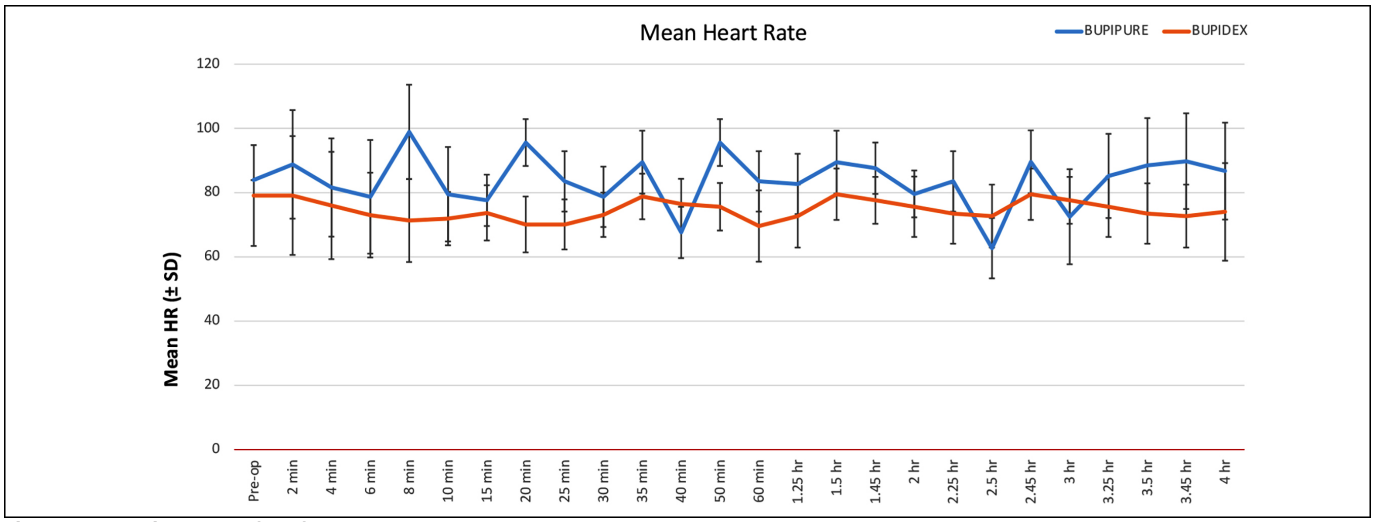

Figure 1: Mean heart rate (±SD).

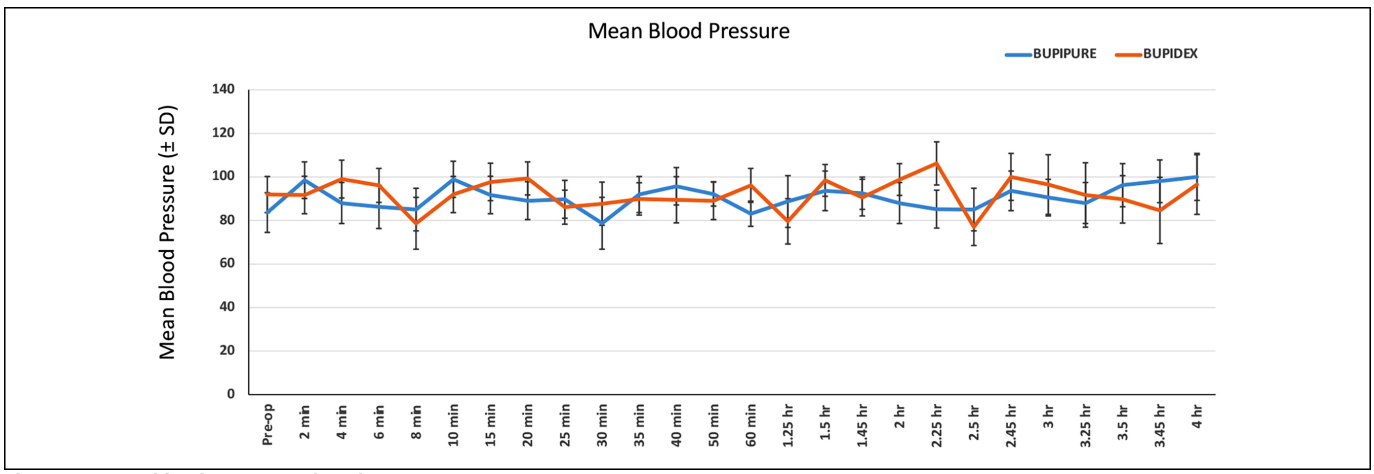

Figure 2: Mean blood pressures (±SD).

Table I: Demographics and intraoperative data.

	BUPIPURE (BP) (n = 54)	BUPIDEX (BD) (n = 54)	p-value
Age (years) mean ± SD	64.89 ± 8.05	66.61 ± 7.53	0.231
Weight (kg) median (IQR)	67 (60 - 74.25)	65 (59 - 73)	0.509
Height (cm) median (IQR)	166 (162 - 168)	172.5 (168 - 174.25)	<0.001*
Duration of surgery (min) median (IQR)	43 (38.75 - 47.0)	44 (38.75 - 52.0)	0.377
Duration of resection (min) median (IQR)	10 (9 - 11)	9.5 (8 - 10.5)	0.123
Volume of irrigation fluid (L) median (IQR)	23 (20 - 25)	18 (17 - 24)	0.001*
Prostate volume (g) median (IQR)	40 (37 - 45)	40 (35 - 44)	0.367

Independent student two sample "t" test, Mann-Whitney U test. BUPIPURE (BP): Control group, BUPIDEX (BD): Dexmedetomidine group.

Table II: Characteristics of sensory and motor block.

Point in time	BUPIPURE (BP) n = 54	BUPIDEX (BD) n = 54	p-value
Peak sensory level T10 or above (n)	37 (68.5%)	43 (79.6%)	0.188
Time to reach T10 (minutes) *median* (*IQR*)	13 (12 - 15)	10 (8.75 - 13)	<0.001*
Two-segment regression time (minutes) *median*(*IQR*)	85.5 (78 - 96)	116 (109.78 - 120)	<0.001*
Complete motor recovery (minutes) *median* (*IQR*)	185 (180 - 192.75)	199.5 (190 - 208.25)	<0.001*
1st Postoperative analgesia demand (minutes) *median* (*IQR*)	262 (253 - 284)	298 (280 - 316)	<0.001*
Intra-operative rescue analgesia (n)	6 (11.1%)	4 (7.4%)	0.507

Mann-Whitney U test, Chi-square of independence test. BUPIPURE (BP): Control group, BUPIDEX (BD): Dexmedetomidine group.

DISCUSSION

TURP frequently requires SAB. Administering local anaesthetic in a normal dose of bupivacaine may cause mild hypotension, but in the elderly, the same amount can travel up to the mid-thoracic level and block the sympathetic ganglia, causing severe and refractory hypotension.[14]

Many studies have examined adding dexmedetomidine to intrathecal bupivacaine (10 - 15 mg), which induced haemodynamic instability.[15] Therefore a reduced dose of bupivacaine was used in this study. During the pilot phase, many patients in BP group receiving 6 mg of plain hyperbaric 0.5% bupivacaine had a low sensory level, making it difficult to make them comfortable intraoperatively. Therefore, plain bupivacaine was increased to 7.5 mg for BP group and compared it to bupivacaine 6 mg combined with dexmedetomidine 3 micrograms.

A median sympathetic block level of T10 was attained using 6 mg bupivacaine and dexmedetomidine 3 microgram, ranging from T9 to T11. Except for 7 patients in both groups, the combination did not produce perioperative hypotension or bradycardia. Although most of the patients had systemic diseases, however, the dose used in this study provided excellent surgical conditions while maintaining haemodynamic stability.

The control group reached T10 and the study group T9 level, however, it took 13.0 (12 - 15) and 10.0 (8.75 - 13.0) minutes to reach T10 which is a statistically significant difference (Table II).

BP and BD groups had a statistically significant median two-segment regression time of 85.5 (78 - 96) and 116 (109.78 - 120) minutes, respectively (Table II).

Devanad *et al.* used 0.5% hyperbaric bupivacaine 6 mg in both groups with 5 micrograms of dexmedetomidine in the study group and found that analgesia lasted 321 and 459 minutes, respectively.[16] Their notable divergence from this study's findings is likely due to perianal procedures, which need lower sensory levels.

As a few patients in both groups needed intra-operative analgesia, it is suggested to test bupivacaine 7.5 mg with a minor dosage of dexmedetomidine to solve the study's limitations.

CONCLUSION

Intrathecal use of a combination of a low dose of hyperbaric 0.5% bupivacaine and a small dose of dexmedetomidine maintained the haemodynamic stability while providing excellent surgical conditions, extended sensory and motor block, and delayed the first postoperative analgesia.

ETHICAL APPROVAL:

Ethical approval was taken from the Ethical Review Committee of the Sindh Institute of Urology and Transplantation, Karachi, prior to enrolling the study population and the research work.

PATIENTS' CONSENT:

Informed consent was obtained from all the study subjects to publish the data regarding this research.

COMPETING INTEREST:

The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:

NS: Concept, study design, conduction of study, and manuscript writing.
SMA: Acquisition, resources, analysis, data collection, processing, and manuscript writing.
MQA: Analysis and interpretation of manuscript and critical review.
MFF: Resources, materials, and literature search.
MS, SM: Analysis and interpretation of literature and final approval of the version to be published.
All authors approved the final version of the manuscript to be published.

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