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Transurethral Resection of Prostate (Turp) in Geriatric Patients: Which Drug to Prefer: Ropivacaine or Bupivacaine?

Dr. JayashreeVenkatesan, Dr. Humane Josna D, Dr. Patkar Geeta

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ABSTRACT : Background and aims: The standard available drug Bupivacaine (hyperbaric) 0.5% is used for spinal anesthesia in Transurethral Resection of Prostate. Isobaric Ropivacaine 0.75% is claimed to be more cardiostable for spinal anesthesia in geriatric patients. We compared the solutions of the two drugs (0.5% hyperbaric bupivacaine and 0.75% isobaric ropivacaine).

Material and methods: A randomized, prospective, double-blinded study was carried out in 60 patients of ASA I/II undergoing TURP. Patients were randomised into Group R (30) receiving 2.5 ml (18.75mg) of 0.75% isobaric ropivacaine and Group B (30) 2.5ml (12.5mg) of 0.5% hyperbaric bupivacaine. Onset of sensory block was measured by pin prick method and duration of block was calculated with two dermatome regression. Onset and duration of motor blockade was assessed with the help of Bromage scale. Hemodynamic Parameters (Heart rate, Blood pressure:- systolic, diastolic, mean, oxygen saturation) were noted. Difference in demographic data between the two groups was sought by Chi square test and Student 't' test. The hemodynamic variables were analysed using paired 't' test for within the
group comparisons and unpaired 't' test for between the group comparisons. For all statistical comparisons $P < 0.05$ was taken as significant.

Results: Mean onset of sensory blockade (level of T10) was significantly faster with group B (4.53 + 1.41) minutes as compared group R (8.10 + 2.01) minutes. Mean onset of motor blockade was significantly earlier in group B (7.85 + 2.99) minutes than in group R (12.63 + 2.19) minutes. Mean duration of sensory blockade was (102.50 +19.82) minutes in group B which was significantly more as compared to (92.33 + 16.75) minutes in group R. Mean duration of motor blockade was (142.33 + 33.08) minutes in group B which was significantly more than (111.00 + 20.06) minutes in group R.

Heart rate was significantly higher in Group B as compared to Group R till 15 minutes of the surgery. Mean systolic blood pressure in Group B was lesser than Group R. Mean arterial pressure in group B was less than group R.

The incidence of complications like hypotension (B-9, R-4), bradycardia (B-2), nausea and vomiting (B-10, R-3), Shivering (B-8,R-3) were higher in group B than group R. **Conclusion:** 0.5% hyperbaric bupivacaine has a faster onset of sensory and motor blockade than 0.75% isobaric ropivacaine. However, the duration of the intrathecal blockade is prolonged with bupivacaine. There is faster regression of sensory and motor blockade with ropivacaine which may help early ambulation. 0.75% isobaric ropivacaine provides stable
intra-operative hemodynamics as compared to 0.5% hyperbaric bupivacaine and can be a better choice of drug in geriatric patients for TURP.

KEYWORDS: TURP, Geriatric patients, bupivacaine, ropivacaine.

I. BACKGROUND AND AIMS

Transurethral resection of prostate is an endoscopic procedure performed to resect the prostate. Geriatric age group is a high-risk group as it is associated with many comorbidities like hypertension, diabetes, cardiac and respiratory diseases that adds to the risk of anaesthesia. Spinal anesthesia is the common choice of anesthesia in the patients undergoing TURP.[1]In our institute, bupivacaine (hyperbaric) 0.5% is used for spinal anesthesia. Ropivacaine 0.75% is claimed to be more cardiostable in the literature. The objective of perioperative care of geriatric population is to speed recovery and avoid functional decline.[2]

We wanted to test the efficacy of ropivacaine and bupivacaine in geriatric patients as the literature had limited studies. We also wanted to establish a standard of care for patients undergoing TURP in our institute. Though many studies have been done on ropivacaine, it is still not the preferred choice of drug for intrathecal use.

II. MATERIALS AND METHODS

After institutional ethics committee approval, this randomized, prospective, double-blinded study was carried out in 60 patients of ASA

I/II undergoing TURP. A computer-generated randomization table (Microsoft® Excel 2007 software, Microsoft Corp.,

Redmond, WA) was used to assign each patient into either Group "R" (patients receiving ropivacaine) or Group "B" (patients receiving bupivacaine).

Inclusion criteria was ASA I/ II, age 50-80 years, BMI < 30. Patients unwilling for consent, ASA ≥ 3, Obesity with BMI > 30, contraindications for spinal anesthesia, coagulopathy, history of allergy to local anesthetics were excluded from the study.

All the patients underwent a thorough pre-anesthetic check-up. All relevant investigations were done. Inclusion and exclusion criteria were assessed and if inclusion criteria were fulfilled then patients were explained about the study and written informed consent was taken. Nil per oral status was confirmed.

Patients were taken in the operation theatre; vital parameters were checked and monitors like pulse oximeter, ECG monitor and NIBP were connected. An intravenous access was secured using 20G indwelling cannula.

Coloading with 5ml/kg Normal Saline was started. Sitting position was given for spinal anesthesia. Under all aseptic precautions, Spinal anesthesia was given in L3-L4 space by midline approach with 25G Quincke's spinal needle (Spinocan®, B. Braun Medical Ltd, Sheffield, UK) after confirmation of subarachnoid space by free flow of CSF and with negative aspiration of blood. The drug given was on the basis of the group the patient

belonged. Group R received 2.5ml of 0.75% isobaric ropivacaine (18.75mg). Group B received 2.5ml of 0.5% hyperbaric bupivacaine (12.5mg).

The anesthesiologist giving spinal anesthesia was blinded to the drug used. Anesthesiologist noting the parameters was also blinded to the drug given. Thus double blinding was achieved. Patients were given oxygen by means of nasal prongs at 2 l/min. Patient was given a lithotomy position for the procedure after the patient achieved a sensory level of T10. Patient did not receive any analgesics during the procedure.

Following parameters were assessed: Onset of sensory blockade was defined as time taken from injection of drug to achieving a level of T10. Sensory blockade was checked by pin prick method at the mid-axillary line. Duration of sensory block was calculated with two dermatome regression from peak block height for each patient.

Motor blockade was assessed using Bromage scale. Onset of motor block was calculated as time taken from injection of drug to achieving Bromage scale 3. Duration of motor block was calculated as time taken as regression from Bromage scale 3 to 2.

Hemodynamic Parameters (Heart rate, Blood pressure:- systolic, diastolic, mean, oxygen saturation) were measured every 5 minutes till 30 minutes and thereafter every 10 minutes till the end of procedure.

Adverse effects, if any were dealt as follows. Hypotension was diagnosed if there was >30% fall in systolic blood pressure and was corrected by IV fluid bolus of 50ml and Injection ephedrine 6mg bolus. Bradycardia was diagnosed with heart rate < 50/minute and was treated with Injection Atropine 0.01mg/kg. Hypothermia & shivering were avoided with forced air warmer, covering the patient, using IV fluids at body temperature and treated with Inj. Tramadol 0.5-1mg/kg IV. Nausea & Vomiting were treated with Inj. Ondansetron 0.08mg/kg. Patients were monitored post operatively every 1 hour for 6 hours for vital parameters like heart rate, blood pressure and oxygen saturation.

III. STATISTICAL ANALYSIS

To evaluate the block characteristics with intrathecal isobaric ropivacaine and hyperbaric bupivacaine, duration of sensory block was observed during a pilot study that was considered to select the sample size. In simple interactive statistical analysis, sample size of minimum 28 was derived using the formula for sample size calculation for multiple comparison (two tailed) based on the assumption of α (type 1 error) = 5%, β (type 2 error) = 0.2 and power of the study = 80%. Data were analysed using InStat computer software. The data thus obtained was expressed as mean and standard deviation.

Difference in demographic data between the two groups was sought with Chi square test and Student't' test. The hemodynamic variables were analyzed using paired't' test for within the group comparisons and unpaired't' test for between the group comparisons. For all statistical comparisons P 0.05 was taken as significant. Cases where the spinal anesthesia failed or required conversion to general anesthesia due to surgical complications were excluded from the study. No form of sedative or analgesia was given except spinal anesthesia.

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IV. RESULTS

The two groups were comparable for age, ASA status and mean duration of surgery.(Table 1)

DEMOGRAPHIC DATA

TABLE (1)

PARAMETER	GROUP B	GROUP R	SIGNIFICANCE
AGE (Years)	68.17 +/- 11.81	67.57 +/- 10.18	NS
ASA I ASA II	12 (40%) 18 (60%)	17(56.7%) 13 (43.3%)	NS
DURATION OF SURGERY (Minutes)	84 + 22.68	77.33 + 25.86	NS

TABLE (2)

BLOCK CHARACTERISCS	GROUP B (Mins)	GROUP R (Mins)	p Value
Onset – Sensory blockade	4.5 + 1.4	8.1 + 2.0	*0.0000
Onset – Motor blockade	7.8 + 3	12.6 + 2	*0.0000
Duration – Sensory blockade	102.5 + 19.8	92.3 + 16.7	*0.0360
Duration – Motor blockade	142.3 + 33	111.0 + 20.0	*0.0000

Mean onset of sensory blockade (level of T10) was significantly faster with group B as compared group R. However, 10 patients (33.33%) had a level of T8 in group B as against 6 patients (20%) in group R. 7 patients (23.33%) in group B had a level of T6 compared to none in group R. Only 13 (43.3%) achieved level of T10 in group B as compared to 24 in R.

Hemodynamics showed the following variation. Heart rate was significantly higher in Group B as compared to Group R till 15 minutes of the surgery. From Induction till 40 minutes of the surgery, mean systolic blood pressure in Group B was lesser than Group R and was statistically significant. Mean diastolic blood pressure was statistically significant and lower in group B as compared to group R and the trend continued till the end of 60 minutes of surgery. After 20 min till the end of study, mean arterial pressure in group B was less and statistically significant as compared to group R.

TABLE (3)

Duration	Mean Heart rate (beats/min) ($\bar{X}$ ± SD)				p value
		Group B		Group R	

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	N		N		
Before Induction	30	76.27 + 12.87	30	71.77 + 11.04	0.1515 (NS)
After Induction 0 min	30	78.13 + 12.63	30	71.23 + 11.80	*0.0160
5 min	30	82.70 + 12.76	30	70.80 + 10.65	*0.0011
10 min	30	83.80 + 13.38	30	70.93 + 13.61	*0.0058
15 min	30	82.97 + 13.27	30	72.63 + 13.84	*0.0456
20 min	30	81.10 + 12.27	30	72.20 + 13.20	0.0778 (NS)
25 min	30	79.77 + 11.26	30	70.60 + 12.24	0.0806 (NS)
30 min	30	77.30 + 11.73	30	69.60 + 11.39	0.2720 (NS)
40 min	30	74.40 + 12.61	29	69.83 + 12.43	0.9804 (NS)
50 min	29	74.38 + 12.41	27	69.04 + 11.63	0.7952 (NS)
60 min	26	72.15 + 11.71	23	67.35 + 11.68	0.9284 (NS)
70 min	24	69.63 + 13.39	19	67.68 + 10.64	0.4732 (NS)

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80 min	19	71.63 + 14.70	15	66.67 + 10.89	0.9155 (NS)
90 min	14	70.57 + 13.18	12	66.50 + 10.96	0.9324 (NS)
100 min	11	67.55 + 11.24	10	64.90 + 11.61	0.3486 (NS)
110 min	06	63.83 + 10.80	04	62.00 + 10.52	0.4119 (NS)
120 min	03	62.67 + 11.93	03	61.33 + 10.60	0.6578 (NS

TABLE (4)

Duration	**Mean SBP (mmHg) ($\bar{X}$ ± SD)**				**p value**
	N	**Group B**	**N**	**Group R**	
Before Induction	30	133.80 + 14.84	30	135.40 + 11.31	0.6404 (NS)
After Induction 0 min	30	128.60 + 12.75	30	133.27 + 10.75	*0.0236
5 min	30	121.20 + 16.22	30	128.57 + 12.62	*0.0283
10 min	30	115.67 + 16.66	30	125.53 + 18.05	*0.0194
15 min	30	114.47 + 14.98	30	124.70 + 16.32	*0.0087
20 min	30	112.50 + 11.64	30	126.97 + 15.94	*0.0003
25 min	30	115.23 + 12.34	30	126.37 + 14.97	*0.0027
30 min	30	116.10 + 14.19	30	128.30 + 13.15	*0.0036
40 min	30	118.37 + 15.19	29	128.41 + 12.46	*0.0343
50 min	29	119.93 + 16.03	27	128.74 + 13.14	0.0928 (NS)
60 min	26	122.35 + 16.73	23	129.04 + 13.66	0.2676 (NS)
70 min	24	125.54 + 17.16	19	129.89 + 15.36	0.5667 (NS)

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80 min	19	125.89 + 17.77	15	133.07 + 14.78	0.3612 (NS)
90 min	14	127.14 + 18.00	12	130.33 + 13.47	0.8024 (NS)
100 min	11	125.64 + 17.17	10	134.00 + 13.21	0.2964 (NS)
110 min	06	128.00 + 13.45	04	130.25 + 15.24	0.9241 (NS)
120 min	03	131.00 + 18.52	03	128.67 + 24.54	0.8161 (NS)

TABLE (5)

Duration	**Mean DBP (mmHg) ($\bar{X}$ ± SD)**				**p value**
	N	**Group B**	**N**	**Group R**	
Before Induction	30	83.20 + 8.52	30	80.13 + 8.60	0.1701 (NS)
After Induction 0 min	30	80.37 + 8.41	30	79.03 + 7.33	*0.0086
5 min	30	77.20 + 9.22	30	77.40 + 7.78	*0.0238
10 min	30	73.47 + 9.40	30	75.90 + 9.86	*0.0013
15 min	30	73.27 + 9.49	30	75.73 + 9.03	*0.0005
20 min	30	71.70 + 7.52	30	76.63 + 7.78	*0.0000
25 min	30	72.23 + 6.58	30	77.03 + 7.26	*0.0000
30 min	30	72.33 + 5.92	30	77.93 + 6.74	*0.0000
40 min	30	72.37 + 6.65	29	77.17 + 6.06	*0.0003

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50 min	29	74.17 + 7.45	27	78.04 + 6.98	*0.0038
60 min	26	75.27 + 7.96	23	78.65 + 6.45	*0.0168
70 min	24	76.50 + 8.73	19	78.00 + 6.28	0.1051 (NS)
80 min	19	77.53 + 8.55	15	78.07 + 6.61	0.2940 (NS)
90 min	14	78.36 + 9.04	12	79.58 + 7.32	0.2583 (NS)
100 min	11	78.36 + 8.96	10	81.20 + 7.79	0.1827 (NS)
110 min	06	78.33 + 8.64	04	80.25 + 10.56	0.4099 (NS)
120 min	03	82.33 + 10.02	03	79.00 + 11.36	0.9805 (NS

TABLE (6)

Duration	**Mean Arterial pressure (mmHg) ($\bar{X}$ ± SD)**				**p value**
	N	**Group B**	**N**	**Group R**	
Before Induction	06	107.67 + 12.69	30	98.40 + 9.13	0.0976 (NS)
After Induction 0 min	06	103.83 + 11.09	30	96.67 + 7.90	0.0867 (NS)
5 min	06	101.67 + 7.81	30	94.10 + 9.05	0.4834 (NS)
10 min	06	96.50 + 8.48	30	92.03 + 12.07	0.0709 (NS)

15 min	06	96.67 + 9.40	30	91.70 + 10.98	0.0914 (NS)
20 min	06	90.50 + 6.72	30	93.13 + 10.00	*0.0026
25 min	06	88.67 + 8.94	30	93.13 + 9.10	*0.0002
30 min	06	88.17 + 7.83	30	94.43 + 8.28	*0.0001
40 min	06	85.50 + 7.99	29	93.79 + 7.33	*0.0000
50 min	06	87.00 + 10.60	27	94.67 + 7.99	*0.0017
60 min	06	87.50 + 10.99	23	95.04 + 7.80	*0.0047
70 min	05	87.40 + 12.60	19	94.95 + 8.28	*0.0090
80 min	05	89.60 + 12.95	14	96.64 + 8.16	*0.0216
90 min	05	93.60 + 11.01	11	96.73 + 8.81	*0.0309
100 min	04	89.25 + 9.91	10	98.40 + 9.36	*0.0001
110 min	02	87.50 + 9.19	04	96.50 + 11.56	*0.0273
120 min	01	84.00 + 0.00	03	95.00 + 14.93	*0.0290

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TABLE (7)

Duration	**Mean SPO2 (%) ($\bar{X}$ ± SD)**				**p value**
	N	**Group B**	**N**	**Group R**	
Before Induction	30	98.50 + 1.07	30	98.87 + 0.43	0.0841 (NS)
After Induction 0 min	30	98.47 + 1.17	30	98.80 + 0.81	0.8321 (NS)
5 min	30	98.90 + 0.80	30	99.23 + 0.63	0.8243 (NS)
10 min	30	98.93 + 0.87	30	99.10 + 0.66	0.3490 (NS)
15 min	30	98.80 + 0.71	30	99.20 + 0.61	0.8882 (NS)
20 min	30	99.07 + 0.83	30	99.40 + 0.67	0.8546 (NS)
25 min	30	99.10 + 0.76	30	99.23 + 0.68	0.3217 (NS)
30 min	30	99.20 + 0.61	30	99.13 + 0.57	0.0664 (NS)
40 min	30	99.07 + 0.69	29	99.10 + 0.56	0.1748 (NS)
50 min	29	99.00 + 0.53	27	99.04 + 0.44	0.1463 (NS)
60 min	2	99.00 +	2	99.04 +	0.1714

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	6	0.69	3	0.71	(NS)
70 min	24	99.13 + 0.85	19	99.26 + 0.45	0.4601 (NS)
80 min	19	99.05 + 0.62	15	98.87 + 0.52	0.0688 (NS)
90 min	14	99.07 + 0.47	12	99.25 + 0.45	0.6716 (NS)
100 min	11	99.18 + 0.60	10	99.00 + 0.82	0.2452 (NS)
110 min	06	99.33 + 0.82	04	99.25 + 0.50	0.4398 (NS)
120 min	03	99.67 + 0.58	03	99.33 + 0.58	0.2082 (NS)

COMPLICATIONS

TABLE (8)

N=30	Group B	Group R
Hypotension	9	4
Bradycardia	2	0
Nausea/Vomiting	10	3
Shivering	8	3

V. DISCUSSION

The standard protocol in our institute is to give a low dose of 2.5ml of 0.5% hyperbaric bupivacaine (12.5mg) to achieve a level of T10, which is appropriate for TURP. This low dose of the drug restricts the spread of block which is especially required in geriatric patients. 0.75% isobaric ropivacaine was chosen as the study drug as it was more cardiostable according to the literature and was not used in our institute for intrathecal use.

Scott et al, in their human volunteer study, had found that ropivacaine was less toxic to the CNS as 25 % more drug was tolerated, and depression of cardiac conduction occurred at lower concentration with bupivacaine than ropivacaine. Therefore, ropivacaine is thought to have a greater margin of safety.[3]

Gautier et al., concluded in their study that 12mg of ropivacaine was approximately equivalent to 8mg of bupivacaine intrathecally (3:2)[4]. So, 2.5ml (18.75mg) of 0.75% isobaric ropivacaine was used for spinal anesthesia in group R and our standard dose of 2.5ml (12.5mg) of 0.5% hyperbaric bupivacaine was used in group B (3:2).

McClure[5] did a study on ropivacaine to prove its clinical efficiency and effect on sensory and motor blockade. He concluded that ropivacaine provided a sensory block similar to that of bupivacaine though it produced a motor block,

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which was slower in onset, shorter in duration and lesser in intensity than the equivalent dose of bupivacaine. Similar results were found in our study in spite of the dose of ropivacaine being higher (18.75mg ropivacaine as against 12.5mg bupivacaine)

Shreideh et al[6] proved that bupivacaine has adequate sensory blockade with good post-operative analgesia at the expense of longer duration of blockade with sensory block sometimes extending beyond the required segmental level T10 to T5-6. We had a similar finding, wherein bupivacaine had a longer duration of sensory and motor blockade with a propensity to spread to higher dermatomal levels.

Mantouvalou et al[7] performed a study in 120 ASA I-III patients comparing 3 drugs bupivacaine, levobupivacaine and ropivacaine. They noted that the onset of motor block(time to achieve Bromage score 3) was significantly faster in the bupivacaine group (8 ± 5 min) compared with that in the ropivacaine group (12 ± 5 min) and almost the same of that in the levobupivacaine group (11 ± 7 min). Ropivacaine presented a shorter duration of both motor and sensory block than bupivacaine and levobupivacaine (269 ±20 min; 278 ± 70 min and 273 ± 80 min) respectively. They also noticed that there was a fall in mean arterial pressure in all groups after immediate subarachnoid block but was significant in bupivacaine only. Intraoperative hypotension requiring IV Ephedrine was more in the bupivacaine group (42.5%) as against ropivacaine (25%). Bradycardia was also more common in the bupivacaine group (5 patients) than in the ropivacaine group (2 patients), respectively (P= 0.04). We got similar results for bupivacaine and ropivacaine.

McNamee[8] did a comparative study in 66 ASA I-II in major orthopaedic surgery. They found that the median time of onset of sensory block at the T10 dermatome was 2 min (range 2-5 min) in Group R and 2 min in Group B (range 2-9 min). The median duration of sensory block at the T10 dermatome was 3hours (range 1.5-4.6 h) in Group R and 3.5 h (2.7-5.2 h) in Group B (P<0.001). The median duration of complete motor block (modified Bromage Scale

3) was significantly shorter in the ropivacaine group compared with the bupivacaine group (2.1hours vs 3.9 hours, P<0.001).

Kallio et al[9] did a study of comparison of intrathecal plain solutions containing ropivacaine 20 or 15 mg versus bupivacaine 10 mg in 90 ambulatory lower extremity surgery and the results were, ropivacaine 15 mg provided faster recovery of motor block (150 min) than did bupivacaine 10 mg (210 min; P = 0.005), but the median duration of sensory block at T10 (140 min) did not differ significantly from that with bupivacaine 10 mg (140 min). They concluded that the duration of sensory block of ropivacaine was two thirds and the duration of motor block was half when compared with bupivacaine, with calculations based on the duration-per-milligram of the local anesthetic. Our results of onset and duration of intrathecal block were similar to the above studies.

Singh et al[10] conducted a study comparing isobaric ropivacaine 0.75% (24mg) and hyperbaric bupivacaine 0.5% (12.5mg) for elective cesarean section delivery in 46 ASA I-II patients. There was no significant difference between two groups related to heart rate however there were 8 episodes of bradycardia in the bupivacaine group as compared to 2 patients in ropivacaine group (P<0.013). Also, bupivacaine group had a faster onset than ropivacaine group with higher episodes of hypotension, nausea and vomiting. 14 of 23 patients in bupivacaine experienced hypotension as against 6 of 23 in ropivacaine group (P <0.027). The

faster onset and higher block probably may have resulted in the increased incidence of hypotension and nausea in hyperbaric bupivacaine. The duration of motor block was shorter in the ropivacaine group (112.5+/-45 minutes) than in the bupivacaine group (165+/-26 minutes) with less haemodynamic changes. This is similar with our findings of less hemodynamic changes with group R than group B and also shorter duration of blockade in group R.

Serapatabekoglu et al[11] did a comparative study of the clinical effects of intrathecal ropivacaine and bupivacaine in geriatric patients undergoing transurethral resection in 60 ASA I to III patients, over 65 years. They were randomized to receive an intrathecal injection of one of two local anaesthetic solutions. Group R (n=30) received 3 mL of ropivacaine 7.5 mg/mL (22.5 mg) and Group B (n=30) received 3mL of bupivacaine 5 mg/mL (15 mg). Changes in MAP measurements were similar between the groups throughout the study. There were no statistically significant differences in ephedrine requirements between the two groups. Changes in heart rate were similar between the groups; however, bradycardia was observed in 2 patients in Group R and in 8 patients in Group B (P<0.05). They concluded that intrathecal ropivacaine and bupivacaine both were well tolerated and provided similar, effective anesthesia in geriatric patients undergoing resection of bladder or prostate in the

ratio of equivalent doses of R:B = 3:2. We used the same ratio of the dose and got similar results for complications.

VI. CONCLUSION

From our study, we hereby conclude that 0.5% hyperbaric bupivacaine and 0.75% isobaric ropivacaine were found to be safe local anaesthetics in spinal anaesthesia for TURP surgery in geriatric patients. 0.5% hyperbaric bupivacaine has a faster onset of sensory and motor blockade than 0.75% isobaric ropivacaine. However, the duration of the intrathecal blockade is prolonged with bupivacaine. There is faster regression of sensory and motor blockade with ropivacaine which may help early ambulation. 0.75% Isobaric ropivacaine provides stable intra-operative hemodynamics as compared to 0.5% hyperbaric bupivacaine and can be a better choice of drug in geriatric patients for TURP.

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