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INTRATHECAL HYPERBARIC BUPIVACAINE 0.5% VERSUS INTRATHECAL HYPERBARIC ROPIVACAINE 0.75% IN LOWER LIMB ORTHOPEDIC SURGERY IN ELDERLY POPULATION – A COMPARATIVE RANDOMIZED SINGLE CENTRE DOUBLE BLINDED STUDY

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ABSTRACT

Background and Aims

Ropivacaine, has been introduced into clinical practice because of its fewer toxic effects and better hemodynamic stability. 0.75% hyperbaric ropivacaine is nearly identical to bupivacaine in terms of onset of action, quality, and duration of sensory block; produces greater duration of sensory block and has better safety level. This study was aimed to compare clinical efficacy of spinal 0.75% ropivacaine fentanyl with 0.5% bupivacaine fentanyl for lower limb orthopedic surgery in geriatrics population.

Methods

This study included eighty elderly patients of either sex with American society of Anaesthesiologist (ASA) grade I, II, III scheduled for elective

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lower limb surgery. The patients were randomized to receive either 15 mg of 0.5% bupivacaine with 25 microgram injection fentanyl (BF group) or 22.5 mg of 0.75% hyperbaric ropivacaine with 25 microgram injection fentanyl (RF group) intrathecally. Intra-operative characteristics of sensory and motor nerve block and adverse effects were noted.

Results

Baseline characteristics were similar between two groups. The onset of sensory block was more rapid in group BF (6.50± 0.430 minutes) in comparison to RF (7.64± 0.573 minutes). The mean time to achieve motor block was faster in bupivacaine group then RF group. The mean duration of motor block was longer for BF group (254.08±17.574 minutes) than RF group (232.35±9.434 minutes) and mean duration of sensory block was higher in RF group (286.48±9.218 minutes) than BF group (273.58± 21.330 minutes).

Conclusion

0.75% hyperbaric ropivacaine provided near similar block characteristic and more hemodynamic stability and less complication.

Keywords

Ropivacaine, Bupivacaine, Elderly, Anaesthesia, Spinal, Hemodynamics

Main Text:

INTRODUCTION

The number of older patients in the field of orthopedics is steadily increasing. There are nearly 138 million (6.78%) elderly persons in India in 2021, including 67 million men and 71 million women [1]. The anaesthesiologist must take all measures to permit an elderly and efficient rehabilitation, a concept which is now widely recognized for improving the success of orthopedic surgical procedures.

Age is the predictor of anaesthetic stress on cardiorespiratory functions and increase the mortality in patients undergoing major surgery. These patients show a relatively higher (30-60%) prevalence of co-existing cardiovascular and pulmonary disorders [2].

Administration of general anaesthesia or central neuraxial anaesthesia is challenging in the elderly patients due to the numerous pathophysiological alteration and functional changes [3]. Neuraxial anaesthetic blockade has a definite advantage in elderly patients over General Anaesthesia, due to less surgical stress, blood loss and improved respiratory and bowel function with fewer occurrence of deep vein thrombosis. But the hemodynamic fluctuations in elderly patients are exaggerated even with conventional doses of local anaesthetics and manifested as hypotension and bradycardia [4].

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Ropivacaine is a relatively newer long-acting local anaesthetic drug, which has a wide margin of safety like less cardiotoxicity and neurotoxicity and block characteristics comparable to bupivacaine [5,6].

Hence, this study was planned to investigate efficacy of Ropivacaine and its effect on hemodynamics in elderly patients undergoing lower limb orthopedic surgery.

METHODS

This prospective blind randomized clinical study was registered in clinical trial registry, India (Registration No. CTRI/2022/07/044026) and was conducted on 80 patients of ASA I, II, III of either sex in early elderly (65-75 years) and late elderly (>75 years) population with weight range of 60-90 kg, height range of 150-170 cm, scheduled for lower limb orthopedic surgery from 15th July to 15th October 2022 in a tertiary care hospital. After approval by the Institutional Ethical Committee and written informed consent, all patients were subjected to pre anesthetic assessment. Patient with previous neurovascular deficit, bleeding disorder or local infection, history of drug and alcohol abuse, visible spinal deformities, patient with medical complications like severe anemia, heart diseases, severe hypovolemia, sepsis, patients with perioperative blood loss more than 1 liter were excluded from study. All patients were kept fasting for 8 hours and premedicated with oral Ranitidine 150 mg and Alprazolam 0.25 mg on the night before surgery.

The sample size was calculated on the basis of formula for differences between two means. P value was taken as 0.05 (95% confidence interval) and power of study being 80%. Based on previous study by Basant Singh Latwalet al[7]. where duration of analgesia in the bupivacaine group was 220.58 minutes (SD=11.16 minutes) and in the other group 217.18 minutes (SD=8.03minutes); minimum sample size in the present study was calculated as 39 in each group.

96 patients were assessed for eligibility who were posted for lower limb orthopedic surgery,13 patients were excluded among them. Eight (8) patients did not meet inclusion criteria and 5 patients refused to participate. Finally, 83 patients were enrolled. Forty-one (41) patients were allotted to the RF group and 42 patients were allotted in BF group.

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Flow Chart of Cases:

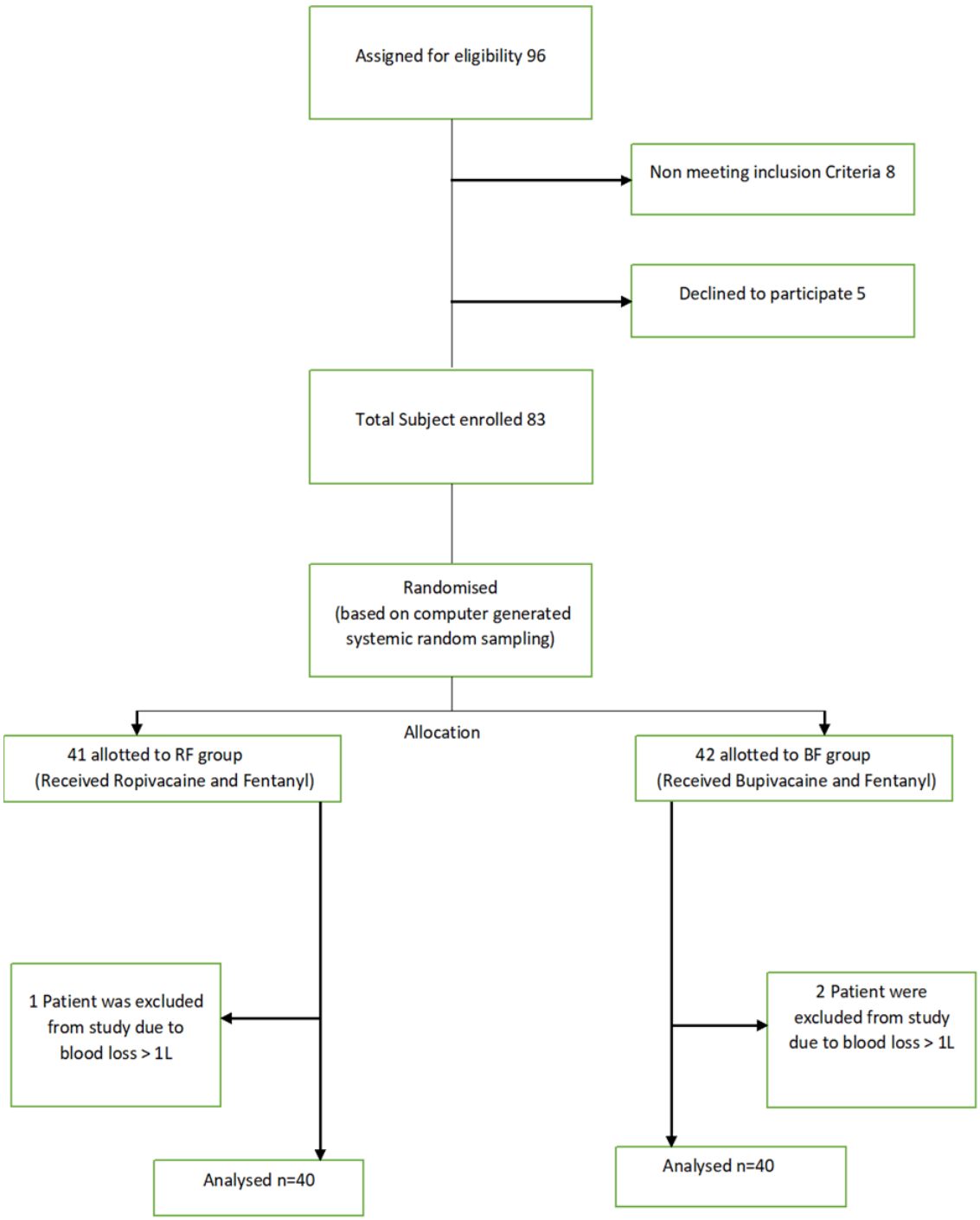

Figure 1: Flow chart

Participant were randomized using computer generated randomization scheduled in 1:1 allocation ratio to receive either intrathecal injection Ropivacaine or Bupivacaine with Fentanyl vide Fig 1. Allocation concealment was done by sequentially numbered opaque sealed envelope technique. The anaesthesiologist who administered the medication was blinded to its constituents. The observers and the patients were blinded to the group the patients belonged to. One patient from the BF group and 2

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patients from RF group were excluded from study due to intraoperative blood loss being more than 1 liter.

In operation theatre, routine hemodynamic monitoring of blood pressure, heart rate, electrocardiography, pulse oximetry was performed. Preloading with intravenous infusion of ringer lactate was started @ of 8-10 ml /kg of body weight before initiation of intrathecal administration of drugs at L4-L5 OR L3-L4 level in sitting posture using a 25-gauge Quincke Babcock spinal needle. It has been administered over 20-30 seconds and patients were placed in supine position immediately. Multichannel monitor was connected to the patients for monitoring of electrocardiogram (ECG), non-invasive blood pressure, heart rate and oxygen saturation (SpO2).

Success of sensory block was assessed by loss of pin-prick sensation in mid-clavicular line after administration of study drug monitored every 30 seconds. Parameter noted were onset of sensory block (time from deposition of study drug into the subarachnoid space till the patient did not feel pin prick at T10 level), time of achieving peak sensory block (time from deposition of the study drug to maximum sensory block was attained).

The degree of motor blockade was assessed by loss of antigravity movements of the leg by Bromage scale every 30 seconds. Parameter noted were onset of motor blockade (time took in minute from deposition of study drug into the subarachnoid space to the Bromage grade-2/3 block). Duration of motor block (time in minute from deposition of study drug to the regression of motor block to Bromage 0) was noted. No patient required analgesia intra-operatively. Assessment of analgesia was done by VAS score. Duration of analgesia was defined as the time from the deposition of the study till the injection first rescue analgesia when VAS score was $\geq$ 4. Side effects hypotension, bradycardia and cardiac arrythmias was noted. Hypotension was described as 20% decreased in blood pressure from base line values, was treated with fluid therapy and intravenous mephentermine /phenylephrine/ ephedrine. Bradycardia was defined as pulse rate <50 beats/minutes and treated with injection Atropine.

For statistical analysis data were entered into a Microsoft excel spreadsheet and then were analyzed by SPSS 25.0. Categorical variables were tabulated with help of frequency and percentages. Continuous variables were expressed as mean and standard deviation in both the groups and differences of their mean were calculated with the help of unpaired t test. P value $\leq$0.05 was considered for statistically significant.

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RESULTS

A total 80 patients were enrolled in the study among whom 40 received ropivacaine and another 40, bupivacaine.

Table 1 : Demographic profile of patients

Parameters		Gr RF (n=40)	Gr BF (n=40)
Age (yrs.)	65-75	31 (77.5%)	34 (85%)
	>75	9 (22.5%)	6 (15%)
Sex	Male	21 (52.5%)	19 (47.5%)
	Female	19 (47.5%)	21 (52.5%)
Weight (kg) [mean ± SD]		68.92 ± 4.599	70.30 ± 4.713
Height (cm) [mean ± SD]		157.12 ± 5.110	148.52 ± 5.822
ASA Grade I/II/III	I	12 (30%)	14 (35%)
	II	24 (60%)	22 (55%)
	III	4 (10%)	4 (10%)
Duration of surgery in minutes		116.15 ± 24.225	108.95 ± 33.573

Baseline parameters such as age, gender, weight, height, ASA status, duration of surgery was comparable between the groups (table 1). Nine (22.5%) patients belonged to late elderly age group among RF Group compared to 6 (15%) patients in BF group. Mean duration of surgery in minutes was 112.55 (SD 29.31).

Table 2 : Sensory & motor block profile of RF & BF

	RF (n = 40)	BF (n = 40)	p-value

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Onset of Sensory block [mean ± SD]		7.64 ± 0.573	6.50 ± 0.430	0.056
Time taken to achieve maximal sensory block (min) [mean ± SD]		12.88 ± 0.729	11.39 ± 0.746	0.382
2 segmental regressions from maximal level of sensory block (min) [mean ± SD]		114.22 ± 4.588	119.92 ± 4.763	0.409
Duration of Analgesia [mean ± SD]		286.48 ± 9.218	273.58 ± 21.330	0.003
Complete recovery of motor block (min) [mean ± SD]		232.35 ± 9.434	254.08 ± 17.574	0.092
Degree of motor block – Bromage II/III	II	2 (5%)	3 (7.5%)	
	III	38 (95%)	37 (92.5%)	

The sensory and motor block characteristics of both groups are shown in table-2. The mean onset time of adequate sensory analgesia of T10 dermatome was faster in BF group (6.50± 0.430 min.) than RF group (7.64±0. 573 min.). Mean duration of Motor block was longer for BF group than that in RF group. Duration of sensory block was longer in RF group (286.48± 9.218 min) than BF group (273.58± 21.330 min) which is statistically significant (p = 0.003). Degree of grade III motor block was higher in RF gr (95%) than in BF group (92.5%). Time taken for complete recovery of motor block was higher in BF group (254.08± 17.574 min) than RF group (232.35 ± 9.434 min). Time taken for 2 segmental regressions from maximal level of sensory block in minute was higher in BF group (119.92 ± 4.763) than RF group (114.22 ± 4.588).

Table 3: Hemodynamic parameters of patients

	Parameter group								
	Heart rate (BPM) [mean ± SD]			SBP (mmHg) [mean ± SD]			DBP (mmHg) [mean ± SD]		
Timing	RF	BF	**P value**	RF	BF	**P value**	RF	BF	**P value**

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Preoperative [mean ± SD]	80.75 ± 9.912	81.78 ± 8.444	0.212	127.60 ± 9.695	128.00 ± 7.961	0.216	78.58 ± 6.151	78.85 ± 6.546	0.475
5 min after SA [mean ± SD]	75.32 ± 9.968	76.62 ± 8.883	0.461	120.10 ± 10.280	119.55 ± 12.814	0.844	73.00 ± 6.401	73.82 ± 6.492	0.695
10 min after SA [mean ± SD]	72.70 ± 10.437	72.85 ± 9.963	0.86	117.30 ± 10.771	114.80 ± 12.769	0.885	71.22 ± 7.062	70.42 ± 7.411	0.879
15 min after SA [mean ± SD]	72.82 ± 10.551	71.85 ± 9.048	0.378	118.12 ± 9.174	112.32 ± 13.244	0.578	72.00 ± 6.626	67.40 ± 7.689	0.656
20 min after SA [mean ± SD]	73.82 ± 9.663	70.32 ± 8.885	0.517	118.62 ± 9.353	111.25 ± 13.410	0.706	71.52 ± 7.082	66.85 ± 6.371	0.317
25 min after SA [mean ± SD]	74.25 ± 9.901	69.90 ± 8.427	0.464	118.45 ± 9.004	111.08 ± 13.067	0.62	71.72 ± 6.706	66.3 ± 6.215	0.437
ss30 min after SA [mean ± SD]	75.02 ± 10.108	70.80 ± 7.387	0.126	118.90 ± 8.428	111.82 ± 12.449	0.588	72.80 ± 6.153	66.90 ± 6.242	0.542
60 min after SA [mean ± SD]	76.08 ± s10.890	70.58 ± 7.071	**0.043**	119.30 ± 8.428	112.05 ± 12.241	0.505	72.85 ± 6.083	67.40 ± 5.247	0.239
75 min after SA [mean ± SD]	76.45 ± 9.5(46	70.82 ± 7.452	0.202	120.02 ± 8.229	112.52 ± 12.075	0.614	73.48 ± 6.312	67.98 ± 4.335	**0.018**

SBP: Systolic blood pressure; DBP: Diastolic blood pressure; SA: Spinal anaesthesia

The hemodynamic parameters i.e. heart rate and systolic and diastolic blood pressure at different time interval are shown in Table 3. Both intrathecal RF and BF produced an initial fall in systolic and diastolic blood pressure at 10 to 15 minutes in keeping with the expected sympathetic blockade produced by spinal anaesthesia. Hypotension requiring treatment with ephedrine occurred in 1 (2.5%) patient in group RF compared to 6 (15%) patients in group BF. Among total seven patient who received ephedrine, five belonged to late elderly age group.

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Heart rate and systolic blood pressure are shown in Diagram 1 and 2 which indicates that bupivacaine caused more fall in heart rate, systolic and diastolic blood pressure in comparison to ropivacaine. It is seen that there was no significant difference in baseline systolic and diastolic mean blood pressure in pre operative period (T0) but at T75 minutes difference between the 2 groups in terms of diastolic blood pressure was statistically significant (0.018). Comparison of 2 groups in terms of heart rate with time shows more reduction in heart rate in BF Group than RF Group and the value is statistically significant at 60 minutes (0.043).

Table 4 : Comparison of complications between two groups

Complications	RF (n=40)	BF (n=40)
Bradycardia	2 (5%)	3 (7.5%)
Tachycardia	1 (2.5%)	1 (2.5%)
Hypotension	2 (5%)	8 (20%)
Pruritus	1 (2.5%)	1 (2.5%)
Nausea, vomiting	0 (0%)	2 (5%)
Hypotension + bradycardia	2 (5%)	6 (15%)
No complication	32 (80%)	19 (47.5%)

32 (80%) patients experienced no complication in RF group whereas 19 (47.5%) patients were without complications in BF group. Major side effects were hypotension and bradycardia. The other commonly occurring adverse effect was the nausea, vomiting, tachycardia, pruritus. Mild pruritis was observed in only one patient in RF group and two patients in BF group which required no treatment. None of the cases reported any episode of lethal cardiac arrythmia, allergy and respiratory depression in the present study.

DISCUSSION

Ropivacaine is stereoselective and pure S-enantiomer, has less affinity to voltage gated Na+ channel. Its short length of the carbon side chain on the tertiary Nitrogen atom is responsible for less lipid solubility. These factors make Ropivacaine less cardio and CNS toxic than Bupivacaine. Ropivacaine penetrates less into large myelinated motor fibres (Aβ) and has selective action on the pain transmitting (Aδ) and C fibres [8].

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The present study demonstrated that in both RF and BF an adjuvant provided satisfactory anaesthetic conditions for lower limb surgeries. Most of the sub-arachnoid block characteristics were comparable between the RF and BF groups and there was early motor recovery with RF group.

Mc Namee et al. studied the efficacy and safety of two concentrations of intrathecal Ropivacaine -7.5 mg/ml (18.75mg) and 10 mg/ml (25 mg) for total hip arthroplasty. They found satisfactory anaesthetic conditions in term of sensory and motor block [9].

In the present study, 95% patient had grade 3 block in RF group and 92.5% patient had grade 3 block in BF group and sensory and motor block duration was comparable between two groups. Ninety five percent (95%) patients in BF group and 90% patient in RF group achieved maximum peak level of sensory block upto T9-T4 in our study.

Luck et al[10] studied efficacy of ropivacaine for major orthopaedic surgeries as an alternative to bupivacaine, using equi-milligram dose (15 mg) but the present study was conducted with equi-volume drug with different concentration (0.5% bupivacaine and 0.75% ropivacaine).

Malinovsky et al. compared intrathecal ropivacaine to bupivacaine in patients scheduled for transurethral resection of prostate [11]. They found that 15 mg of intrathecal ropivacaine had similar motor and hemodynamic effects but less potent anaesthesia than 10 mg bupivacaine for endoscopic urological surgery.

Lipid soluble opioid such as sufentanil and fentanyl are the most commonly used adjuvants [12,13]**.** Studies have shown that intrathecal opioid can greatly enhance analgesia of local anaesthetic agent seems to be the most frequently used combination to increase the duration of sensory analgesia without intensifying the motor blockade or prolonging recovery from spinal anaesthesia [14,15]. In the present study fentanyl was used as adjuvant. The potency of ropivacaine may be altered by co-administration with opioid. Local anaesthetic blocks propagation and generation of neuronal action potential by a selective effect on sodium channels, whereas opioid acts on opioids receptors to increase potassium conductance. Thus, combination of two may effectively inhibit multiple areas of neuronal excitability, thereby enhancing the potency of surgical anaesthesia.

For spinal anaesthesia hyperbaric bupivacaine is commercially available in concentration of 0.5%. This concentration was found adequate for providing effective sensory as well as motor block of spinal anaesthesia [16]. 0.75% Ropivacaine used in the present study is a newly introduced

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preparation, 3 ml solution of which was found to be equipotent in block profile, have better hemodynamic response and less complication in elderly age group.

CONCLUSION:

Hyperbaric 0.75% ropivacaine may be good alternative to bupivacaine for geriatric population undergoing operations under spinal anaesthesia in terms of safe hemodynamic response, block characteristics and less complication. Considering the age and poor cardiorespiratory reserve, the hyperbaric ropivacaine with fentanyl might be considered as anaesthetic technique of choice for lower limb orthopaedic surgery in high-risk elderly patients.

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