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RESEARCH ARTICLE

COMPARATIVE STUDY OF EPIDURAL ROPIVACAINE 0.5% AND 0.75% WITH CLONIDINE FOR LOWER LIMB SURGERIES

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ABSTRACT

Central neuraxial blockade in the form of epidural is very popular for lower abdominal and lower limb surgeries as these techniques avoids the disadvantage associated with general anaesthesia. We have conducted such study to find out and compare appropriate concentration of ropivacaine with clonidine for lower limb surgeries in epidural anaesthesia. We have compared the efficacy of 0.5% ropivacaine+clonidine combination against 0.75% ropivacaine+clonidine combination during epidural anaesthesia in 60 healthy patient of ASA grade one or two scheduled for elective lower limb surgeries. Result shows that onset of action and duration of analgesia is longer with Ropivacaine 0.75% but haemodynamic stability is more with 0.5% Ropivacaine. So it was concluded that Ropivacaine 0.5% concentration provides better haemodynamic stability with shorter duration of motor block for day care surgeries but for longer procedures, 0.75% ropivacaine will be preferred because of intense motor blockade, higher level of analgesia and prolonged sensory block.

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INTRODUCTION

Epidural anesthesia can be used as sole anesthetic for procedures involving the lowerlimbs, pelvis, perineum and lower abdomen. It has the ability to maintain continuous anesthesia after placement of an epidural catheter, thus making it suitable for procedures of long duration as compared to spinal anesthesia (Touhy, 1944). This feature also enables the use of this procedure for intra and post – operative analgesia by blunting autonomic, somatic and endocrine responses. Adjuncts; such as clonidine, opioids, epinephrine, ketamine etc, have been added to improve quality of blocks; reduce local anesthetic dose thus reducing its side effects (Kaur, 2014; Schnaider, 2005 and Huang, 2007). Ropivacaine, the recently introduced long acting amide local anesthetic is pure S(-) enantiomer of Propivacaine, claimed to have lesser cardiovascular side effects. Resuscitation is also better after Ropivacaine than bupivacaine if toxicity develops (Santos, 1991). The addition of adjuvants like α-2 agonists as clonidine is to be used to decrease the dose requirement, prolongation of duration and permits use of more dilute solutions, thus reducing side effects (Bajwa, 2010; Bajwa, 2011). Clonidine is centrally acting selective partial alpha-2 adrenergic agonist with selectivity ratio 200:1 (Bischoff, 1993). It inhibits voltage gated Na channels and suppresses the generation of action potential in tonic firing dorsal horn neurons-causing analgesia. (Yaksh, 1981) Clonidine provides pain relief by an opioid independent mechanism. It produces anti nociception by stimulating post synaptic alpha-2 adrenergic receptors in the dorsal horn of spinal cord.

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MATERIAL AND METHODS

This study is randomized, prospective, double blind carried out on admitted patients of Gandhi Memorial & Associated Hospitals, KG medical university, Lucknow, (former CSSMU) undergoing elective lower limb surgeries under epidural anaesthesia after getting approval from Ethical Committee, King George's Medical University, UP, Lucknow and obtaining a written consent from the patient relative. For this purpose a total of 60 patients of either sex of age group between 18-60 yrs, body weight between 40-85 kg and ASA grade I&II were chosen. Patients of renal, pulmonary, cardiovascular, neurological, neuromuscular diseases and deranged liver function test were excluded from our study.

Any contraindication to epidural anaesthesia (local site infection, Coagulopathy, Vertebral anomalies, Sepsis, Raised Intracranial pressure), allergy to local anaesthetic drugs and clonidine, peripheral neuropathy, patient's refusal and physical dependence on narcotics were also excluded from the study. A general physical and detailed clinical examination supported by routine blood, urine and biochemical test as per need was carried out. Patients were also explained about the epidural technique with catheter in situ, its advantages and disadvantages. The cases were randomally allocated into two groups the group I and group II. The Group I received 0.5% Ropivacaine15 ml with Clonidine 60 µg and Group II received 0.75% Ropivacaine15 ml with Clonidine 60 µg. On the day of surgery in the pre-operative room, an intravenous line was secured and the patient was preloaded with 15 ml/kg Ringer's lactate, 10 minutes prior to epidural anesthesia. All standard monitor ECG, pulse oximetry, noninvasive blood pressure temperature probe were attached and base line vitals were recorded. Procedure was started in patient's sitting position and all aseptic precautions were taken into account for painting and draping. The subject was given 3 ml of 2% lignocaine as local anesthesia of skin and subcutaneous tissues in L3-4 and then epidural block was performed with 18 gauge Touhy needle after localising and confirming the epidural space by loss of resistance technique. An epidural catheter was introduced and secured into the epidural space in a cephalic direction 5 cm into the epidural space after negative aspiration of cerebrospinal fluid or blood. The catheter was secured to skin surface and subjects were repositioned to supine with a pillow placed below the head. Thereafter, 3 mL of 2% lignocaine HCl with 1 in 2 lakh adrenaline solution was administered as a test dose and any untoward effect was observed for 5 minutes. Now epidural drugs were given randomally by third party who was not the part of study by applying a computer derived random number sequence and sealed opaque envelops. Surgical procedure was initiated after establishment of adequate surgical analgesia effect with level upto T_{10} dermatome. Bilateral pinprick method was used to evaluate and check sensory level while the Modified Bromage Scale was used to measure motor blockade.

Modified Bromage Scale (Bromage, 1965)

Grade 0: Full flexion of knees and feet,
Grade 1: Inability to raise extended leg, just able to flex knees, full flexion of feet,
Grade 2: Unable to flex knees, but some flexion of feet possible.
Grade 3: Unable to move legs or feet.

Standard monitoring was carried out in the form of pulse oximetry, heart rate, respiratory rate, ECG and non-invasive arterial blood pressure (both systolic and diastolic). Recordings were made every 5 minutes for 30 minutes and at 10-minutes intervals thereafter up to 60 minutes and then at 15-minutes intervals for the next hour and finally at 30 minutes till the end of surgery. Patients were given supplementary O_2 with the help of venturi mask. Patients were observed for comparison of variables like block characterstics (onset of analgesia, level of maximum sensory and grade of motor blockage, complete recovery of motor blockage and duration of analgesia), hemodynamic stability, any side effect and need of rescue analgesia. For rescue analgesia i.v. Fentanyl was given in the dose of 0.5 µg/kg body weight, if the patient developed pain after initiation of surgery and before any dose for top up was given. Post operative pain was assessed by Visual Analogue Scale (VAS). Duration of analgesia was assessed by VAS scores, more than 4 is considered for requirement of top up dose of ropivacaine through epidural catheter. Patients were topped with 10 mL 0.5% Ropivacaine with Clonidine 40 µg in group I and 10 mL 0.75%Ropivacaine with Clonidine 40 µg in group II at the time of pain during surgery. Time to first epidural top up requirement during surgery was recorded. The data were analyzed statisticaly. The statistical analysis was done using SPSS (Statistical Package for Social Sciences) Version 15.0 statistical Analysis Software. The values were represented in Number (%) and Mean±SD.

RESULTS

A total of 60 patients requiring epidural analgesia fulfilling inclusion criteria and giving their written informed consent for inclusion were randomly divided into two groups of equal number of cases, 30 patients were given 0.5% Ropivicaine (15ml) with Clonidine (60µg) and rest 30 patients were given 0.75% Ropivacaine (15 ml) with Clonidine (60µg). Out of 60 patients, in 4 cases general anesthesia was required. In which 3 cases was in group 1 and 1case in group 2. These 4 cases were excluded from study. Group wise distribution of study population is given in Table 1 and Figure 1 that shows equal numbers of patients are in group I and II that statistically not signifaicant

Table 1. Distribution of Study Population

Group	Dose of Anesthetic agent	No. of patients	Percentage
Group I	0.5% Ropivacaine with Clonidine	30	50.00
Group II	0.75% Ropivacaine with Clonidine	30	50.00
	Total	60	100.00

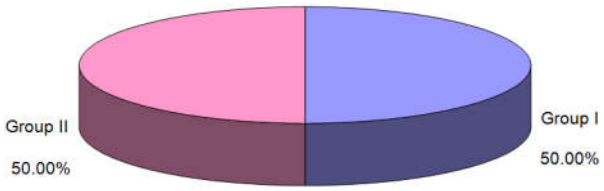

Figure 1. Pie chart showing Distribution of Study Population

Table 2 shows that there is no statistically significant difference in demographic variables like age and gender distribution between the two groups (p=0.543 and p=1.00).

Table 2. Between Group Comparison of Demographic Variables

	Total (N=60)	Group I (n=30)		Group II (n=30)	
		No.	%	No.	%
Age Group (years)					
Upto 20	1	0	0.00	1	3.33
21-30	26	11	36.67	15	50.00
31-40	14	7	23.33	7	23.33
41-50	12	8	26.67	4	13.33
51-60	7	4	13.33	3	10.00
		χ^2=3.092(df=4); p=0.543			
Mean±SD	35.77±11.09	37.17±11.47		34.37±10.70	
(Range)	(18-60)	(21-60)		(18-60)	
Gender					
Female	8	4	13.33	4	13.33
Male	52	26	86.67	26	86.67
		χ^2=0.000(df=1); p=1.000			

Table 3 shows distribution of subjects according to their weight, height and BMI and on comparing data statistically no significant intergroup difference was observed (p=0.747, 0.149& 0.444 respectively).

Between Group Comparison of Block Characteristics

Table 4 shows comparison of block charactersticks that shows there was statistically significance difference in onset of analgesia, time of 2 segment regression and complete sensory recovery between group I and II(p<0.001) but no significant difference in time of complete recovery(p=0.054). Table 5 and figure 2 shows that there is statistically significant difference in level of sensory block (p=0.010) and grade of motor block (p<0.001) between the two group. Table shows that in group I maximum level of sensory level is upto T_6 level while in group II it was upto T_4whereas minimum is T_8 and T_{10} respectively. Motor blockade was minimum 1 and maximum 3 in both group. Table 6 and figure 3 shows proportion of patients who required rescue analgesia was higher in Group I (18.52%) as compared to that in Group II (3.45%) but this difference was not found to be statistically significant (p=0.068).

Table 7 shows comparison of time of epidural top-up in groups. Out of 56 patients in the study, epidural top up was required by only 15 patients. Of these 15 patients, 8 were from Group I and 7 from Group II. Time of Top-up requirement was earlier in Group I (131.25±25.04 minutes) as compared to Group II (182.14±53.53 minutes) and difference in time of top-up requirement was found to be statistically significant (p=0.031). Table 8 and Figure 4 shows; hypotension was found in 8 patients (1 patient in group I compared to 7 patients in group II) and all patients required mephentermine. Bradycardia was observed in 8 patients (all belongs to group II) but none of them required Atropine, while shivering was reported by 17 patients.

Table 3. Between Group Comparison of Anthropometric Variables

	Group I (n=30)		Group II (n=30)		Statistical significance (Student 't' test)	
	Mean	SD	Mean	SD	't'	'p'
Weight (kg)	64.13	7.19	63.50	7.91	0.325	0.747
Height (cm)	168.53	5.54	166.40	5.75	1.464	0.149
BMI (kg/m^2)	22.52	1.58	22.86	1.86	-0.771	0.444

Table 4. Between group comparison of Time of Onset of Analgesia at T10 level, Time of two segment regression time of complete motor and sensory recovery

	Group I (n=27)		Group II (n=29)		Statistical significance (Student 't' test)	
	Mean	SD	Mean	SD	't'	'p'
Onset of analgesia at T10 level (min.)	16.22	3.49	12.28	3.49	4.226	<0.001
Time of two segment regression (min.)	101.30	8.94	110.52	6.03	-4.553	<0.001
Time of complete motor recovery (hrs)	4.03	0.65	4.47	0.98	-1.974	0.054
Time of complete sensory recovery (hrs)	5.28	0.53	6.63	0.75	-7.732	<0.001

Table 5. Between Group Comparison of Maximum Level of Sensory

	Level of Sensory Block – Thoracic dermatome level		Motor Block Grade	
	Group I	Group II	Group I	Group II
No. of subjects	27	29	27	29
Minimum	8	10	1	1
Maximum	6	4	3	3
Median	8.00	6.00	1.00	3.00
Mean	7.11	6.41	1.41	2.66
S.D.	1.01	1.12	0.57	0.55
Statistical significance (Mann-Whitney U test)	Z=2.589; p=0.010		Z=5.556; p<0.001	

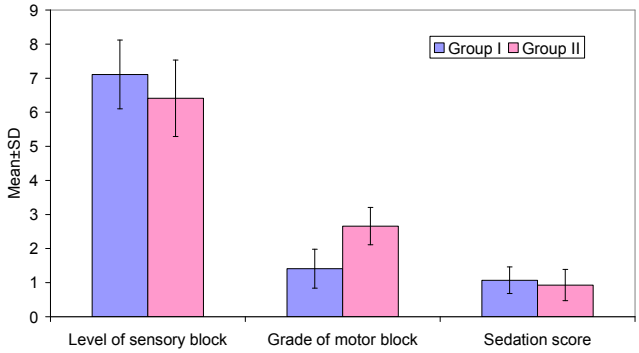

Figure 2. Between Group Comparison

Table 6. Between Group Comparison of Requirement of Rescue Analgesia

Rescue analgesia	Total (N=56)	Group I (n=27)		Group II (n=29)	
		No.	%	No.	%
Required	6	5	18.52	1	3.45
Not required	50	22	81.48	28	96.55
		χ^2=3.319(df=1); p=0.068			

Incidence of hypotension, bradycardia and shivering was found in higher proportion of patients of Group II as compared to Group I (24.14% vs. 3.7%; 27.59% vs. 0.0% and 37.93% vs. 22.22%). Between group difference in incidence of hypotension and bradycardia was found to be statistically significant (p=0.029, p=0.003 respectively) while difference in incidence of shivering was not found to be statistically significant (p=0.201). None of the patient in the present study was found to have pruritis, nausea and vomiting.

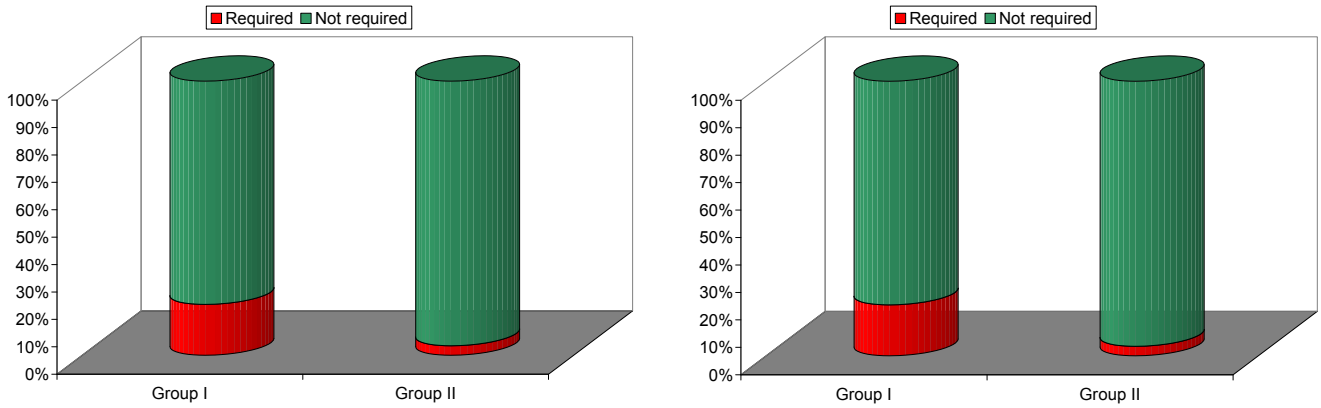

Figure 3. Between Group Comparison of Requirement of Rescue Analgesia

Table 7. Between Group Comparison of Time for Epidural Top Up (minutes)

Group	No. of subjects	Min.	Max.	Median	Mean	SD
Group I	8	90	175	130	131.25	25.04
Group II	7	115	270	175	182.14	53.53

't'=2.414; p=0.031

Table 8. Between Group Comparison of Incidence of Side Effects

	Total (N=56)	Group I (n=27)		Group II (n=29)		Statistical significance	
		No.	%	No.	%	χ^2	P
Hypotension	8	1	3.7	7	24.14	4.768	0.029
Bradycardia	8	0	0.00	8	27.59	8.690	0.003
Nausea & Vomiting	0	0	0.00	0	0.00	–	–
Pruritis	0	0	0.00	0	0.00	–	–
Shivering	17	6	22.22	11	37.93	1.632	0.201
Others	0	0	0.00	0	0.00	–	–

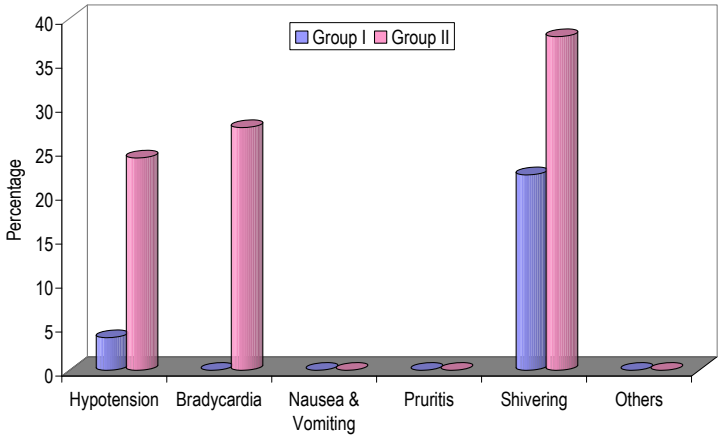

Figure 4. Between Group Comparison of Incidence of Side Effects

DISCUSSION

Lower limb surgeries can be performed under General Anesthesia, regional blocks or by central neuraxial blocks. Central neuraxial block is a better choice among these as they are easy to perform and with few side effects. It is also cost effective and reduces time of hospital stay by early recovery. Among central neuraxial block, epidural anesthesia along with catheter in situ provides space for longer duration of surgery and prevention of post operative pain and chronic pain syndrome. Local anesthetics are the mainstay of epidural anesthetic technique but are associated with major hemodynamic changes when used alone (Simon, 2002; Bosenberg, 2002).

So, many adjuvants have been studied to reduce the concentration and amount of local anesthetic being used, thereby reducing the side effects. The epidural administered drug, including hypno-sedative adjuvants, are absorbed in systemic circulation and there by manifest their systemic

effects. The present prospective, randomized, double blind study was conducted after approval by the ethical committee, in the Department of Anaesthesiology, King George's Medical University, Lucknow, UP to find out appropriate concentration of Ropivacaine with Clonidine for Epidural anesthesia in elective lower limb surgeries in patients of ASA grade I-II, age between 18-60 years. This study was conducted on 60 patients, who were randomly divided into two groups with 30 patients each. Mean Time of onset of analgesia in patients of Group I was found to be 16.22±3.49 minutes while that in Group II was 12.28±3.49 minutes and this difference was found to be statistically significant ($p<0.001$). So, onset is earlier in Ropivacaine 0.75%, shows higher concentration of drug has rapid onset of action.

McGlade DP *et al*. (McGlade, 1997), measured the onset and duration of analgesia at the T_{10} dermatome (median, interquartile range) was 10 (5-15) minutes and 3.5 (2.7-4.3) hours respectively for epidural 0.5% ropivacaine 20 ml. In a study of epidural anaesthesia, conducted by Manjunath Thimmappa* *et al*. (2014) found that patients receiving 19ml 0.75% ropivacaine with 75 microgram(mcg) clonidine had mean onset of analgesia at T_{10} level 9.17±1.21 minutes. Bajwa *et al*. (2010) also found that patients receiving 20ml 0.75% ropivacaine with 75 microgram (mcg) clonidine in epidural space for elective caesarean section had mean onset of analgesia at T_{10} level 8.64±2.56 minutes. In an another study by Bajwa *et al*. (2010) onset of analgesia at T_{10} level in a group of patients receiving 20 ml 0.75% Ropivacaine with clonidine 75µg in epidural space for lower abdomen surgery was 8.24±3.56 minutes. In my case onset was slightly delayed as group I used lower concentration of ropivacaine.

Median level of sensory block in Group I was T8 while that of Group II was T6. Difference in level of sensory block between Group I and Group II was found to be statistically significant ($p=0.010$). Thus, in Ropivacaine 0.75% the level of analgesia was found to be higher dermatome level, showing that higher concentration of drug had higher level of analgesia. McGlade DP *et al*. (McGlade, 1997) observed maximum block height median T_6 for epidural 0.5% ropivacaine 20 ml. In another study by ShalinaChandran *et al*. (Chandran, 2014), the mean maximum sensory level reached was T_8 with epidural 0.75% ropivacaine 20 ml. Bajwa *et al*. (2010) also found that patients receiving 20ml 0.75% ropivacaine with 75microgram(mcg) clonidine in epidural space for elective caesarean section had on average T_5-T_6 level of effect. Time of complete sensory recovery in patients of Group I (5.28±0.53 hours) was earlier than that of Group II (6.63±0.75 hours), and this difference was found to be statistically significant ($p<0.001$).

Time of Top-up requirement intraoperatively was earlier in Group I (131.25±25.04 minutes) as compared to Group II (182.14±53.53 minutes) and difference in time of top-up requirement was found to be statistically significant ($p=0.031$). So in my study I found that higher concentration of ropivacaine (0.75%) had longer duration of analgesia. Bajwa *et al*. (2010), also found that duration of anesthesia was 156.78±10.28 minute with epidural ropivacaine 0.75% with clonidine in lower abdominal and lower limb surgeries. Bajwa *et al*. (2010), in their study of epidural ropivacaine 0.75% with clonidine in cesarean section found time of 1st top up was 138.46±25.42 minutes and duration of anesthesia was 173.50±32.44 minute Time of two-segment regression of patients of Group II (110.52±6.03 minutes) was found to be higher than that of Group I (101.30±8.94 minutes), and this difference was found to be statistically significant ($p<0.001$). Bajwa *et al*. (2010) found 2 segment regression time of 96.86±6.78 minutes in their study with epidural ropivacaine 0.75% with Clonidine in lower abdomen surgery. Bajwa *et al*. (2010) in their study of epidural ropivacaine 0.75% with clonidine in cesarean section found 2 segment regression time of 102.8±18.38 minutes. Median grade of motor block in Group I was 1 and that in Group II was 3. Difference in grade of motor block between the above two groups was found to be statistically significant ($p<0.001$). So, Ropivacaine 0.75% has more powerful motor blockade characteristic as compared to Ropivacaine 0.5%, showing that higher concentration of the drug had higher motor blockade characteristic. Time of complete motor recovery of patients of Group II (4.47±0.98 hours) was found to be higher than that of Group I (4.03±0.65 hours), but this difference was not found to be statistically significant ($p=0.054$). Hypotension was found in 3.7 % patients in group I and 24.14 % in group II with requirement of mephentermine. And this was found to be statistically significant ($p=0.029$), showing that0.5% Ropivacaine had less incidence of fall in blood pressure as compared to 0.75%Ropivacaine. In my study, I found that there was no episodes of bradycardia (HR<60 bpm) with 0.5%Ropivacaine as compared to 27.59 % patients in 0.75% Ropivacine but none of them had HR<50bpm so atropine was not required in any of my patient. Ropivacaine 0.5% thus had better hemodynamic profile as compared to 0.75%.

In a study of epidural anesthesia, conducted by ManjunathThimmappa* *et al*. (2014), patients receiving 19 ml 0.75% ropivacaine with 75 microgram(mcg) clonidine had bradycardia in 13.3% of patients (HR<55 bpm).Bajwa *et al*. (2010), also observed that patients receiving 20ml 0.75% ropivacaine with 75microgram (mcg) clonidine in epidural space had 14.81% incidence of bradycardia (HR<55 bpm). Shivering was found in higher proportion of patients with ropivacaine 0.75% as compared to 0.5% (37.93% vs. 22.22%) but this difference was not found to be statistically significant ($p=0.201$). Neither respiratory depression nor any other side effects were observed during my study in any of the group. Bajwa *et al*. (2010), also observed shivering in 10% cases and no respiratory depression in a group of patients receiving 20 ml 0.75% ropivacaine with clonidine 75µg in epidural space for lower abdominal surgeries. Proportion of patients who required rescue analgesia (Intravenous Fentanyl) was higher in Group I (18.52%) as compared to that in Group II (3.45%) but this difference was not found to be statistically significant ($p=0.068$).

Conclusion

Therefore I conclude that for day care surgeries 0.5% Ropivacaine is better as it has shorter duration of motor block with lesser hemodynamic variability and for longer procedures 0.75% Ropivacaine will be preffered because of intense motor blockage, higher level of analgesia and prolong sensory block.

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