BMH MEDICAL JOURNAL

BMH Med. J. 2019;6(1):13-20. **Research Article**

A Prospective Randomised Double Blind Study To Compare The Effects Of Intrathecal Isobaric Ropivacaine And Levobupivacaine For Spinal Anaesthesia In Transurethral Resection Of Prostate

Vineesh Joseph, Shoba Philip

Department Of Anaesthesiology, Lourdes Hospital Kochi

Address for Correspondence: Dr. Vineesh Joseph, MBBS, DNB, Puliyilakattu House, Thiruvambady PO, Kozhikode, Kerala, India. PIN 673603. E-mail: vineeshjoseph1987@gmail.com

Abstract

Introduction: Subarachnoid block (SAB) is the most popular as well as effective technique for infraumbilical surgeries. It provides fast onset and effective sensory and motor blockade. In this study we tried to compare the clinical effects of 0.75% isobaric ropivacaine and 0.5% isobaric levobupivacaine in spinal anaesthesia for transurethral resection of prostate.

Material And Methods: A prospective randomised double blind controlled study was conducted on 70 patients aged 45-75 of ASA physical status I-II, posted for transurethral resection of prostate. The patients were divided into 2 groups A and B. Group A received 3 ml of 0.75% isobaric ropivacaine and group B received 3 ml of 0.5% isobaric levobupivacaine. The patients were assessed for the onset and duration of motor and sensory block, time for 2 segment regression of sensory block, time of request of analgesic, hemodynamic parameters and side effects. The results were compared using Students t test and Chi-square test. P value of <0.05 was considered significant.

Results: The onset of sensory and motor blockade was similar in both the groups. Ropivacaine has shorter duration of motor and sensory blockade compared to levobupivacaine. Time for 2 segment regression was also shorter in ropivacaine. Time of first request of analgesic was comparable in both the groups. There was no statistically significant difference in hemodynamic parameters and incidence of side effects.

Concusion: Isobaric Ropivacaine has shorter duration of sensory and motor block compared to isobaric Levobupivacaine. However, equivalent doses of Ropivacaine and Levobupivacaine has similar onset of sensory and motor block with comparable hemodynamic parameters and no significant side effects.

Key Words: isobaric, ropivacaine, levobupivacaine, trans urethral resection of prostate, spinal anaesthesia

Introduction

Spinal anaesthesia has been considered as the anaesthesia of choice for lower abdominal, lower limb and urological surgeries. Bupivacaine was most commonly used for spinal anaesthesia. However it has undesirable side effects like hypotension, bradycardia, prolonged duration of motor paralysis, cardiotoxicity and central nervous system toxicity. This led to identification of pure S enantiomers like levobupivacaine [1,2] and ropivacaine [3] having a better safety profile.

Levobupivacaine is a pure S (-) enantiomer of racemic bupivacaine. It is used in similar doses to bupivacaine and has a similar onset and duration of action [4-6]. Ropivacaine is a highly protein bound amide local anaesthetic having the same PKa (8.1) as bupivacaine. Compared to bupivacaine the proposed advantages of ropivacaine are less cardiotoxicity and greater motor - sensory differentiation. Many studies comparing intrathecal ropivacaine and bupivacaine for lower limb and gynaecological surgeries are available but limited data have been published on the intrathecal use of ropivacaine for urological surgeries. Hence we decided to compare the efficacy and safety of ropivacaine with levobupivacaine for urologic surgeries. We decided to select TURP as it is one of the most common urological procedures.

Materials and methods

A prospective randomised double blind controlled study was conducted after obtaining ethical committee approval and written informed consent.

Sample size was calculated based on duration of motor block in a previous study [7]. Assuming an α error of 1% and power of study 90%, the minimum sample size calculated was 29 per group. We assigned 35 patients in each group considering the drop outs.

The study was designed to compare 3 ml of 0.75% isobaric Ropivacaine with 3 ml of 0.5% isobaric Levobupivacaine for subarachnoid block with respect to onset and duration of motor block, onset and duration of sensory block, time for 2 segment regression of sensory block, intra operative hemodynamic parameters at various time intervals, time for first request of analgesic and side effects if any. Patients who were unwilling, patients with ischaemic heart diseases, valvular heart diseases and neurological deficits, patients having contraindications for spinal anaesthesia (eg: bleeding disorders, local sepsis, anticoagulant and antiplatelet drugs, allergic to local anaesthetics and patients with spinal deformities) and patients with hemodynamic instability were excluded from the study. Patients were randomised into two groups by a computer generated software, group A to receive 3 ml of 0.75% isobaric Ropivacaine and group B to receive 3 ml of 0.5% isobaric Levobupivacaine.

All patients received oral premedication with Ranitidine 150 mg the night before surgery and on the morning of surgery along with Ondansetron 4mg.

All necessary equipments and drugs necessary for resuscitation were kept ready in the operation theatre. On arrival at the operation theatre, electrocardiogram (ECG), pulse oximeter, and non invasive blood pressure monitors were attached. The baseline blood pressure and heart rate were recorded. Intravenous line was secured and patients were preloaded with normal saline solution 10ml/Kg before the initiation of procedure.

Before the commencement of anaesthesia patients were instructed on the methods of sensory and motor assessment. The respective drug was loaded by another anaesthetist under strict aseptic precautions based on group allocation and handed the syringe to the anaesthetist performing the block so that he/she is blinded to the drug. Spinal anaesthesia was performed under aseptic precautions in sitting position with 25G Quincke's needle at L3-L4 interspace by the attending anaesthesiologist who was not involved in the study. Once free flow of clear cerebrospinal fluid was obtained, study drug was given over 15-20 seconds and the time noted at which the drug was given.

The patients were then placed in supine position. Then the observations and patient assessments were done by the chief investigator who was blinded to the drugs given. When complete motor blockade and sensory block up to T10 dermatome was achieved, patient was placed in the lithotomy position and the surgeon was allowed to proceed.

Onset of sensory blockade was defined as the time interval between intrathecal administration of the drug and time of attaining sensory block at T10. The sensory block was assessed by pinprick using a sterile 26 G needle at the midclavicular line anteriorly every minute till T10 dermatome was reached. Time for 2 segment regression was defined as the time interval between intrathecal administration of the study drug and time to regression of sensory block by 2 segments from the maximum block height. It was evaluated by pin prick at midclavicular line anteriorly every 15 minutes after the first 20 minutes in the intra operative period. Duration of sensory block was defined as the time interval from intrathecal administration of the study drug to the point of complete resolution of sensory block (time of appearance of pain sensation at S1 dermatome). The duration of sensory block was assessed by pin prick using a hypodermic needle at the lateral side of foot every 30 minutes in the post operative period till appearance of pain sensation at that site.

The degree of motor blockade was assessed by Modified Bromage Scale [8].

Onset of motor block was defined as the time interval between intrathecal administration of the study drug and complete motor block (Bromage 3) of the lower limbs. The onset of motor block was assessed every minute till complete motor block was attained. Duration of motor block was defined as the time interval from intrathecal administration of the study drug till complete motor recovery (the point in which Bromage score is back to zero). It was evaluated every 30 minutes in the post operative period till complete recovery of motor block. Duration of surgery was taken from the time of introduction of resectoscope till the end of surgery (time of removal of resectoscope).

Mean arterial pressure and heart rate were recorded before commencement of spinal anaesthesia, 3 minutes after spinal anaesthesia then at 5 minutes, 10 minutes, 15 minutes, 20 minutes, 30 minutes, then every 15 minutes till 90 minutes and then every 30 minutes till complete recovery of sensory and motor blockade. Time for patient's first request of analgesic was noted in the post operative period. It was managed with intravenous injection of Tramadol 2mg/kg. Patients were closely observed post operatively for 24 hours for complications like bradycardia (HR<50/min), hypotension (MAP <20% from baseline), post spinal headache, and transient neurological symptoms. They were subsequently managed as per standard institution protocols.

Statistical Analysis was carried out using statistical package, SPSS (version 22.0.0.0). Student's t test was used for comparison of demographic variables, time of onset and duration of sensory and motor block and hemodynamic parameters and Chi square test for testing the independence of attributes under study. In all the analysis significance level was taken to be 0.05.

Results

Comparison of demographic variables

Demographic data analysis of the study population on the basis of age, weight and height did not reveal any statistically significant difference between the two groups (**Table 1**). The two groups were also comparable in relation to mean baseline heart rate, mean base line Mean Arterial Pressure and mean duration of surgery.

Table 1: Comparison of demographic variables

Parameter	Group A	Group B	P value
Age in years	63.114±5.567	62.771±6.278	0.810
Height in centimeters	161.829±6.771	163.829±4.817	0.159
Weight in kilograms	60.943±9.601	60.200±9.022	0.740
Baseline HR	78.114±11.021	83.257±13.338	0.083
Baseline mean arterial pressure	96.286±11.184	96.914±11.033	0.814
Duration of surgery in minutes	26.000±6.730	27.286±6.224	0.410

Comparison of block characteristics

The block characteristics were compared using Students t test. There was no significant difference in the onset of sensory block and motor block between equivalent doses of isobaric Ropivacaine and isobaric Levobupivacaine (**Table 2**). The duration of sensory block, duration of motor block and time for 2 segment regression was less in Ropivacaine group compared to Bupivacaine group. There was no significant difference in the time of first request of analgesic.

Table 2: Comparison of block characteristics

Parameter	Group A	Group B	P value
Onset of sensory block in minutes	6.26±2.20	5.49±2.89	0.214
2 segment regression in minutes	101.57±16.71	111.00±16.35	0.020
Duration of sensory block in minutes	271.71±19.17	283.71±18.33	0.009
Onset of motor block in minutes	12.71±3.90	12.46±4.81	0.807
Duration of motor block in minutes	225.43±26.61	238.29±21.76	0.030
Time of first request of analgesic in minutes	234.86±29.54	245.14±25.71	0.125.

Hemodynamic variables

Repeated measures ANOVA is used to test the null hypothesis that there is no significant difference in mean value of HR and MAP among different time points. There was significant difference in mean values of HR and MAP among different time points (**Table 3**).

Table 3: Hemodynamic variables

	Source	Type III Sum of Squares	df	Mean Square	F	Sig.
HR	HR	9953.407	17	585.495	17.341	.000
	HR * Group	2037.299	17	119.841	3.549	.000
	Error(HR)	39030.794	1156	33.764		
MAP	MAP	19416.661	17	1142.157	21.295	.000
	MAP * Group	709.042	17	41.708	.778	.721
	Error(MAP)	62002.019	1156	53.635		

Hemodynamic variables at different time intervals were compared using Students t test. There was no significant difference in mean value of heart rate and mean arterial pressure between the two groups (**Figures 1** and **2**).

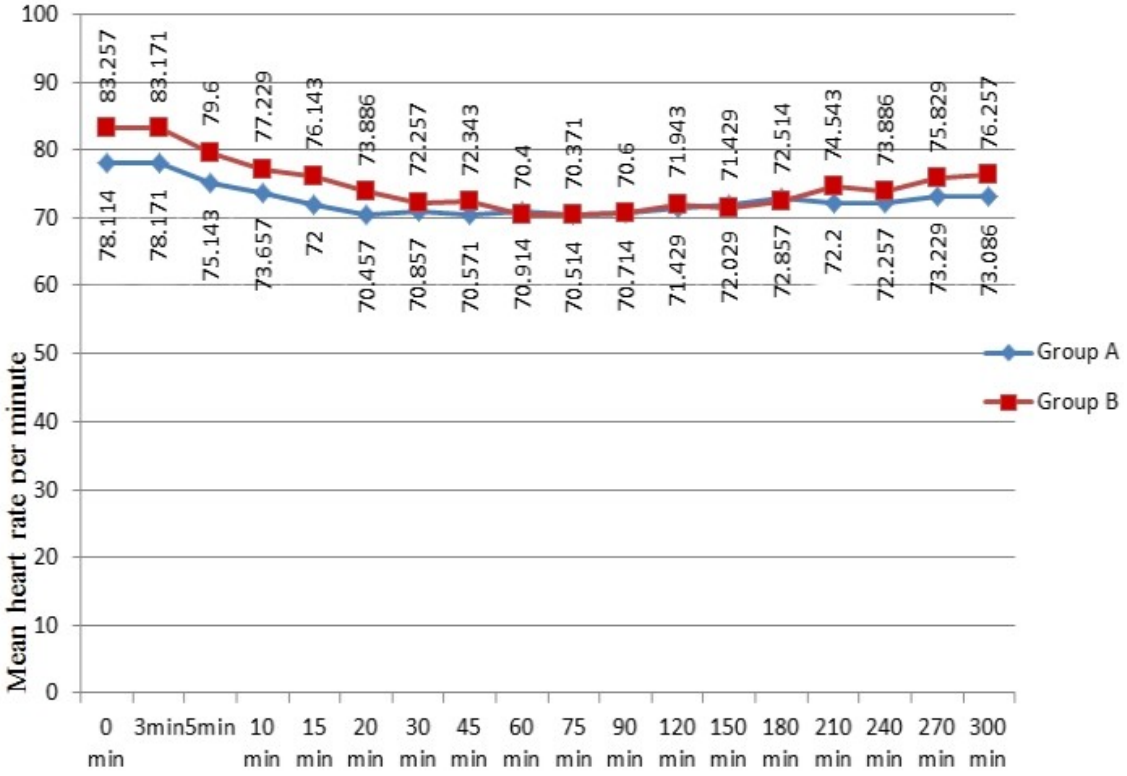

Figure 1: Comparison of mean heart rate (per minute) between group A and group B at various time intervals

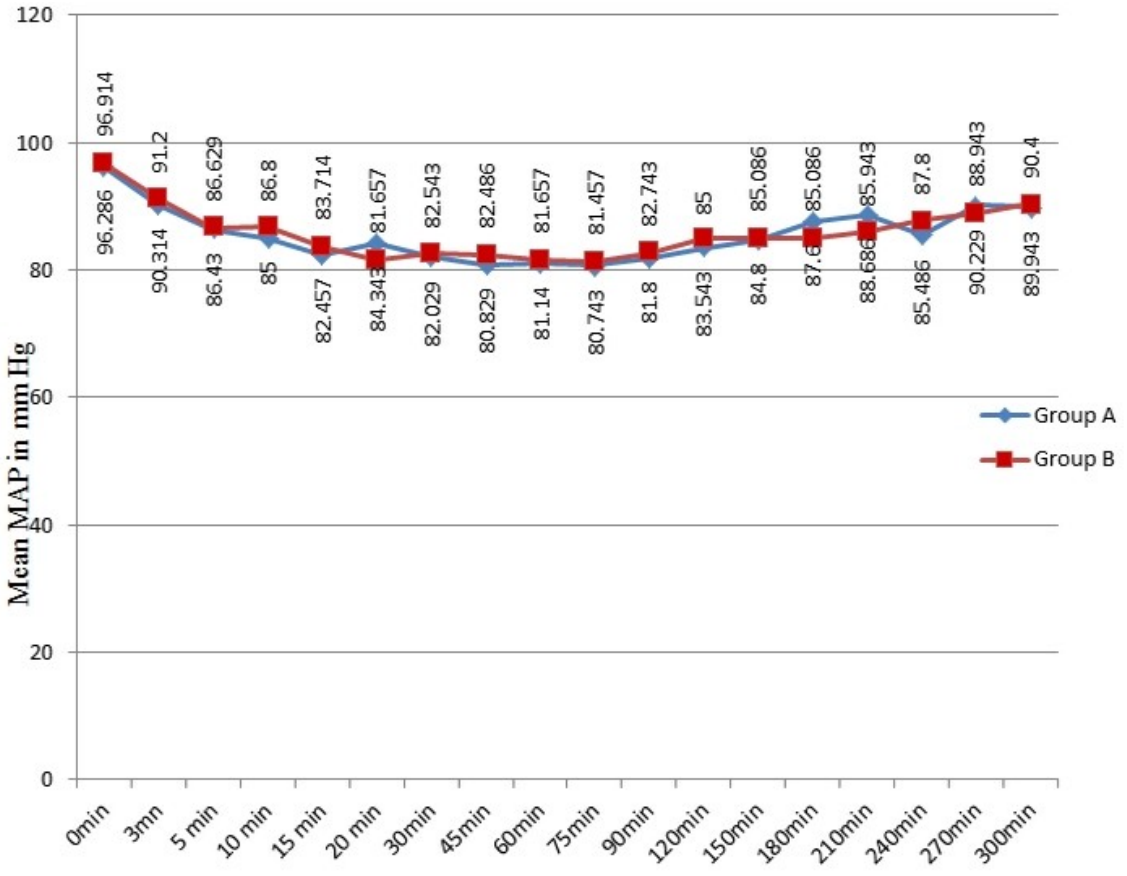

Figure 2: Comparison of mean value of mean arterial pressure at various time intervals

Side effects and complications

The incidence of complications were compared using chi square test which showed no statistically significant difference between the two groups (**Table 4**).

Table 4: Side effects and complications

Side effects and complications	Group A	Group B	P value
Bradycardia requiring atropine	1	None	0.314
Hypotension requiring ephedrine	3	4	0.690
Post spinal headache	1	2	0.555
Transient neurological symptoms	None	None	

Discussion

Subarachnoid block (SAB) is the most popular as well as effective technique for infraumbilical surgeries. It provides fast onset and effective sensory and motor blockade.

Due to its long duration of action, racemic bupivacaine is one of the commonest local anaesthetics used. However, profound myocardial depression and even cardiac arrest can occur after accidental intravascular injection. This led to the introduction of newer local anaesthetics like ropivacaine and levobupivacaine with better safety profile. So in our study we tried to compare the clinical effects of ropivacaine and levobupivacaine for subarachnoid block in transurethral resection of prostate as very limited data are available of the use of the drugs in urological procedures. Demographic data analysis of age, weight, height, mean base line heart rate, mean baseline mean arterial pressure and duration of surgery were comparable in both the groups.

Mean time of onset of sensory block for ropivacaine was 6.26±2.20 minutes, where as for levobupivacaine) was 5.49±2.89 minutes (p value 0.214). There is no significant difference in the onset of sensory block at T10 level between equivalent doses of isobaric ropivacaine and isobaric levobupivacaine which is similar to the studies done by Vampugalla PS et al [9], Bozkirli F et al [10], S N Bhat et al [11] and Malinowski et al [12], Moizo et al [13].

In our study the mean time for 2 segment regression or ropivacaine was 101.57±16.71 minutes and for levobupivacaine was 111.00±16.35 minutes. The p value is 0.020 which is statistically significant. This means that regression of sensory block is faster with ropivacaine compared with levobupivacaine. Similar results were obtained by SN Bhat et al [11] and Malinowsky et al [12].

The mean duration of sensory blockade for ropivacaine was 271.71±19.17 minutes and for levobupivacaine was 283.71±18.33 minutes(p value 0.009). Patients in Ropivacaine group recovered from sensory block faster compared to Levobupivacaine similar to the observations by Athar M et al [14], Vampugalla PS et al [9], J F Luck et al [15] and S N Bhat et al [11].

The mean time of onset of motor blockade in Ropivacaine group was 12.71±3.90 minutes while that of Levobupivacaine group was 12.46±4.81 minutes(p value 0.807). There was no difference in the onset of motor blockade similar to the studies by Vampugalla PS et al [9] S N Bhat et al [11] and Malinovsky et al [12].

In our study the mean duration of motor blockade in Ropivacaine group was 225.42±26.61 minutes and in the Levobupivacaine group was 238.29±21.76 minutes (p value 0.030). When equivalent doses of isobaric Ropivacaine and Levobupivacaine are used for subarachnoid block there is early recovery of motor blockade with Ropivacaine compared to Levobupivacaine. This is comparable to

the studies done by Koltka K et a [l7], Vampugalla et al [9], SN Bhat et al [11] Athar M et al [14], Erturk et al [16] and Verma et al [17].

The mean time for first request of analgesic for Ropivacaine was 234.86±29.54 minutes and for Levobupivacaine was 245.14±25.71 minutes. The difference between them was not statistically significant similar to studies by Bozkirli F et al [10] Taspinar et al [18] and Ogun C O et al [19].

Mean values of heart rate and mean arterial pressure at 3 min, 5 min, 10 min, 15 min, 20 min, 30 min, 45 min, 60 min, 75 min, 90 min and then every 30 minutes till sensory and motor recovery were achieved was compared. There was no statistically significant difference between the two groups in the mean heart rate at various time intervals. Similar findings were reported by Vampugalla et al [9] Bhat S N et al [11], Malinowsky et al [12], Luck et al [15] and Mantouvalou et al [20]. Though there was a fall in mean arterial pressure in both the groups there was no statistically significant difference between the two groups at various time points. Similar findings were reported by Vampugalla et al [9] Bhat SN et al [11] and Athar M et al [14].

There was no statistically significant difference in the incidence of bradycardia, hypotension, headache and transient neurological symptoms in both the groups. So both the drugs are safe to be used in spinal anaesthesia.

Conclusion

We conclude that isobaric Ropivacaine has shorter duration of sensory and motor block compared to isobaric Levobupivacaine in patients given spinal anaesthesia for transurethral resection of prostate. However, equivalent doses of Ropivacaine and Levobupivacaine has similar onset of sensory and motor block with comparable hemodynamic parameters. The time for first request of analgesic was comparable between the two groups. The incidence of post operative complications also was insignificant with both the drugs.

References

1. Aberg G. Toxicological and local anaesthetic effects of optically active isomers of two local anaesthetic compounds. Basic and Clinical Pharmacology and Toxicology 1972;31:273-86.

2. Burlacu CL, Buggy DJ. Update on local anesthetics: Focus on levobupivacaine. Ther Clin Risk Manag 2008;4:381-92.

3. McClure J H. Ropivacaine. Br J Anaesth 1996;76:300-7.

4. Alley EA, Kopacz DJ, McDonald SB, Liu SS. Hyperbaric spinal levobupivacaine: a comparison to racemic bupivacaine in volunteers. Anesth Analg 2002;94:188-93.

5. Glaser C, Marhofer P, Zimpfer G. Levobupivacaine versus racemic bupivacaine for spinal anesthesia. Anesth Analg 2002;94:194-8.

6. Fattorini F, Ricci Z, Rocco A, Romano R, Pascarella MA , Pinto G. Levobupivacaine versus racemic bupivacaine for spinal anaesthesia in orthopaedic major surgery. Minerva Anestesiologica 2006;72:637-44.

7. Koltka K, Uludag E, Senturk M, Yavru A, Karadeniz M, Sengul T, et al. Comparison of equipotent doses of ropivacaine-fentanyl and bupivacaine-fentanyl in spinal anaesthesia for lower abdominal surgery. Anaesthesia and intensive care 2009;37:923-8.

8. Bromage PR, Burfoot MF, Crowell DE, Pettigrew RT. Quality of epidural blockade.I. Influence physical factors. Br J Anesth 1964:36:342-52.

9. Vampugalla PS, Vundi VR, Perumallapalli KS, Kumar CV, Kambar C, Mahalakshmi M, et al. A comparative study of intrathecal ropivacaine with fentanyl and L-bupivacaine with fentanyl in lower abdominal and lower limb surgeries. Int J Basic Clin Pharmacol 2015;4:1147-55.

10. Bozkırlı F ,Atabekoglu S. Comparison of the clinical effects of intrathecal ropivacaine and bupivacaine in geriatric patients undergoing transurethral resection. Gazi Medical Journal 2007;18:182-5.

11. Bhat SN, Himaldev, Upadya M. Comparison of efficacy and safety of ropivacaine with bupivacaine for intrathecal anesthesia for lower abdominal and lower limb surgeries. Anesthesia, Essays and Researches 2013;7:381-5.

12 .Malinowsky JM, Charles F , Cozian A, Malige M , Kick O, Lepage J Y et al. intrathecal anaesthesia ropivacaine versus bupivacaine. Anaesthesia analg 2000;91:1457-60.

13. Moizo E, Marchetti C, Bergonzi PC. Unilateral spinal anesthesia for inguinal hernia repair: a prospective, randomized, double-blind comparison of bupivacaine, levobupivacaine and ropivacaine. Minerva Anesthesiol 2004;70:542-3.

14. Athar M, Ahmed SM, Ali S, Doley K, Varshney A, Siddiqi MM. Levobupivacaine or ropivacaine: A randomised double blind controlled trial using equipotent doses in spinal anaesthesia. Colombian Journal of Anesthesiology 2016;44:97-104.

15. Luck JF, Fettes PDW, Wildsmith JAW. Spinal anaesthesia for elective surgery: a comparison of hyperbaric solutions of racemic bupivacaine, levobupivacaine, and ropivacaine. Br J Anaesth 2008;101:705-10.

16. Erturk E, Tutuncu C, Eroglu A, Gokben M. Clinical comparison of 12mg Ropivacaine and 8mg Bupivacaine both with fentanyl 20 mcg in spinal anaesthesia for major orthopaedic surgery in geriatric patients. Med Princ Pract 2010;19:142-7.

17. Reetu Verma, Shikha Mehrotra. Comparison between intrathecal isobaric bupivacaine 0.5% with isobaric ropivacaine 0.75% for lower limb orthopaedic surgeries: a double blind randomized controlled study. International Journal of Contemporary Medical Research 2017;4:867-70.

18. Taspinar V, Sahin A, Donmez NF, Pala Y, Selcuk A, Ozcan M, et al. Low-dose ropivacaine or levobupivacaine walking spinal anesthesia in ambulatory inguinal herniorrhaphy. J Anesth 2011;25:219-24.

19. Ogun CO, Kirgiz EN, Duman A, Okesli S, Akyurek C. Comparison of intrathecal isobaric bupivacaine-morphine and ropivacaine-morphine for Caesarean delivery. B J Anaesth 2003;90:659-64.

20. Mantouvalou M. et al. Spinal anesthesia: Comparison of plain ropivacaine, bupivacaine and levobupivacaine for lower abdominal surgery. Acta Anaesth. Belg., 2008;59: 65-71.