

Comparison of Efficacy and Safety of 0.5% Bupivacaine and 0.5% Ropivacaine for Combined Femoral Nerve Block and Sciatic Nerve Block (Anterior Approach): A randomized controlled trial

G. Dilish^{1,*}, P. Aravind Kumar², J. Radhika³

^{1,2,3}Assistant Professor, Dept. of Anaesthesiology, GMKMC, Salem, Tamil Nadu

*Corresponding Author:

Email: drdilish@yahoo.co.in

Abstract

Introduction: Regional blocks are increasingly the preferred for a wide range of lower limb surgical procedures over spinal and epidural anesthesia. Various local anesthetic agents in different concentrations have been used for combined femoral and sciatic nerve block. But the existing evidence is inconclusive on the ideal anesthetic agent and its concentration. The available evidence on relative merits of different anesthetic agents in Indian Population is even limited.

Objectives: To compare the safety, efficacy and hemodynamic parameters of 0.5% Bupivacaine and 0.5% Ropivacaine during combined femoral and sciatic nerve block.

Materials and Method: The study was a randomized double-blind controlled trial of 36 subjects, randomly assigned to 0.5% Bupivacaine and 0.5% Ropivacaine groups. Subjects between 18 to 60 years belonging to ASA grade I and II, posted for various below knee lower limb procedure were included. Time is taken for onset of sensory and motor block, duration of sensory and motor block was compared across the study groups using independent sample t-test. The occurrence of complications and hemodynamic parameters also were compared.

Results: In the current study, no statistically significant difference was observed in the time taken for onset of sensory block in either femoral nerve (13.39 and 13.69 minutes in Bupivacaine and Ropivacaine groups respectively, p value 0.39) or sciatic nerve (17.19 and 17.14 minutes, p value 0.89) The motor blockade took 21.28 and 21.64 minutes respectively in both the study groups (P value 0.53). In the current study, the duration of sensory block was slightly longer in Bupivacaine group, as compared to Ropivacaine group (933.67Vs 924.22, p value 0.19), but this difference was statistically not significant. The duration of motor block was significantly longer in Bupivacaine group (243.78 Vs 189.11, p value 0.001), as compared to Ropivacaine group. None of the study subjects in both the groups have reported any complications. There were no significant differences in hemodynamic parameters across the groups.

Conclusions

1. Both sensory and Motor block onset time were similar with 0.5% Bupivacaine and Ropivacaine in combined femoral and sciatic nerve block. The duration of sensory block also was comparable across the two groups
2. Bupivacaine had comparatively longer duration of motor block, as compared to Ropivacaine group
3. There were no clinically or statistically significant differences in hemodynamic parameters

Keywords: Combined femoral and sciatic nerve block, Bupivacaine, Ropivacaine

Introduction

Regional blocks are increasingly the preferred for a wide range of lower limb surgical procedures over spinal and epidural anesthesia.^(1,2) Combined Femoral and Sciatic nerve block is one of the blocks most commonly used method regionally for lower limb surgeries involving knee and below knee. The efficacy and safety of this method had been well established.⁽³⁻⁵⁾

Various local anesthetic agents in different concentrations have been used for combined femoral and sciatic nerve block.⁽⁶⁻¹⁰⁾ Considering the large volumes of local anesthetic medication required, high potential for development of various complications resulting from systemic absorption of the drug is a major concern.^(3,5) Hence, local anesthetic compounds or dilutions with lesser potential for development of these systemic complications and achieve comparative levels of sensory and motor blockade are preferred over their counterparts.⁽⁵⁾

Bupivacaine has been one of the most commonly used compounds in regional blocks and is reported to

provide long lasting analgesia.^(6,11) But, the reported potential for development of cardiac and neurological complications, due to accidental intravenous injection is also very high with Bupivacaine.⁽¹²⁻¹⁵⁾ Newer amide group of local anesthetic agents, more notably Ropivacaine is documented to have comparable levels and duration of analgesia, with more favorable sensory motor blockade profile, as compared to Bupivacaine.⁽¹⁶⁻²⁰⁾ The reported incidence of systemic complications is also lesser with Ropivacaine.⁽²¹⁻²³⁾ The available evidence on relative merits of these anesthetic agents in Indian Population is limited.⁽²⁴⁾

Objectives

1. To compare the efficacy and safety of 0.5% Bupivacaine and 0.5% Ropivacaine for combined femoral and sciatic nerve block (anterior approach) in patients undergoing lower limb knee and below knee orthopedic procedures.
2. To compare the hemodynamic changes and complications of 0.5% Bupivacaine and 0.5%

Ropivacaine for combined femoral and sciatic nerve block (anterior approach) in patients undergoing lower limb knee and below knee orthopedic procedures.

Materials and Method

The current study a double-blinded randomized controlled trial carried out in Government hospital, Mohan Kumaramangalam Medical College, Salem, which has a tertiary level orthopedic center. The study was conducted between May 2015 to April 2016. The study population included all the subjects posted for lower limb knee and below knee orthopedic procedures during the study period, who required combined femoral and sciatic nerve block through an anterior approach. The subjects were randomized to one of the two intervention groups. Group A was administered with 0.5% Bupivacaine and group B were administered with 0.5% Ropivacaine.

Inclusion criteria:

- Assessed patients of ASA physical status I & II
- Normal biochemical and hematological parameters
- Age group between 18-60 years
- No known neurological deficit
- No local sepsis
- Informed written consent
- The weight of the patient more than 70 kg (because 35 ml of local anesthetic solution was used for blocking the nerves).

Exclusion criteria:

- Technical failure
- Patient not willing
- Neurological disorders/deformity of spine
- History of allergy to local anesthetics
- Bleeding diathesis

Sample size: Assuming the mean duration of sensory block as 17 and 13 hours respectively in 0.5% bupivacaine and Ropivacaine group respectively, with a common standard deviation of 3, as per study by Greengrass, R. A., et al. 90% power of study and 5% alpha error, the required sample size calculated was 13 subjects. To account for an attrition rate of 10%, it was decided to include not less than 15 subjects in each of the study groups. (As per the formula by Kirkwood 1988). (Reference)

Randomization method: Initially randomization sequence was decided upon as 0.5% bupivacaine for even numbers and 0.5% Ropivacaine for base numbers. The randomization sequence was generated by random number table from a standard statistical textbook.⁽²⁵⁾

Allocation Concealment: Sequentially Numbered, Opaque Sealed Envelopes (SNOSE) method as described by Doig, G.S et al have been used for allocation concealment in the study.⁽²⁶⁾ The allocated intervention sequence was kept in individual, serially numbered sealed opaque covers and was kept under the custody of a senior faculty of the department but not

involved in the study or patient care. The cardboard with the intervention sequence was covered with a silver foil to prevent the visibility. Each time when the participant was recruited the opaque cover was opened and the intervention was communicated to the investigator.

Blinding: Considering the nature of the intervention, researcher blinding could not be achieved. Participant and the statistician analyzing the data were blinded to the intervention.

Study procedure: The procedure was explained to patients and informed written consent was obtained. All the patients were pre medicated orally with Tab. Diazepam 10mg 2hrs before surgery and Inj. Midazolam 2mg iv before the procedure. Following this, Femoral nerve block was given using 15ml of local anesthetic solution. For femoral nerve block, three essential landmarks anterior superior iliac spine, pubic tubercle and femoral artery were identified. A 2 inch 22 Gauge short bevelled Teflon coated nerve stimulator needle with stimulator attached is inserted to elicit the response to nerve stimulation. The site of puncture for entry is approximately 1.5cm below the inguinal ligament and 1.5cm lateral to femoral entry. The needle is advanced slowly at an angle of 45 degrees to skin, parallel to the femoral artery in a craniodorsal direction. Visible or palpable movement of patella given at 0.2 to 0.4 mA was looked for. Precaution to avoid arterial and venous puncture were taken.

Sciatic nerve block was given by the anterior approach of Beck using 20ml of local anaesthetic solution. A standard 15 cm 20 G Short bevel insulated nerve stimulating needle is advanced in the direction of the shaft of the femur. After bony contact, the needle was withdrawn and redirected medially and advanced beyond the shaft of the femur to elicit dorsiflexion or plantar flexion of the foot. After the initial stimulation of the sciatic nerve is obtained, the stimulating current is gradually decreased until twitches are seen at 0.2 to 0.4 mA. The assessment was done every minute for first 20 minutes and then every 5 minutes thereafter for sensory and motor blockade. The onset of sensory blockade was noted by testing for pinprick sensation. The degree of motor blockade was assessed by Bromage scale. The degree of pain during surgery was assessed with a 3-point Verbal rating scale score (VRS). Vital signs were monitored. Postoperatively, all the patients were followed up until complete recovery of sensory and motor function of the limb was regained.

Ethical issues: The study was approved by the Institutional Human Ethics Committee. Informed written consent was obtained from all the study participants. Confidentiality of the study participants was maintained throughout the study.

Statistical methods: Time taken for onset of sensory and motor blockade was considered as primary outcome measures. Duration of sensory and motor blockade was considered as secondary outcome

parameters. Hemodynamic parameters like heart rate, mean arterial pressure etc. were considered as other outcome parameters. Type of drug used for anesthesia was the primary explanatory variable. Both the study groups were compared with respect to all the baseline parameters. The quantitative outcome parameters were compared using mean and standard deviations,

categorical parameters were compared by cross tabulation and comparison of proportions. Independent sample t-test and chi-square test were used to test the statistical significance of the associations respectively. P value < 0.05 was considered as statistically significant. IBM SPSS version 21 was used for statistical analysis.

Results

Table 1: Comparison of baseline parameters across both study groups

Parameter	Bupivacaine (Mean ±SD)	Ropivacaine (Mean ±SD)	P value
Age in Years	41.72 ± 8.288	40.44 ± 9.269	0.67
Weight in Kg	74.94 ± 3.24	74.78 ± 3.50	0.89
Baseline heart rate	79.61 ± 4.258	79.22 ± 5.242	0.80
Mean arterial Pressure	96.17 ± 4.706	95.39 ± 3.987	0.59
Duration of surgery	70.00 ± 11.412	69.39 ± 11.521	0.87

A total of 36 subjects were randomly allocated 18 subjects each to 0.5% Bupivacaine and 0.5% Ropivacaine groups. The mean age of the study participants was 41.72 ± 8.288 and 40.44 ± 9.269 in Bupivacaine and Ropivacaine groups respectively. The mean weight, baseline heart rate, baseline mean arterial pressure were comparable across the study groups. The mean duration of surgery was 70.00 ± 11.412 minutes and 69.39 ± 11.521 in Bupivacaine and Ropivacaine groups respectively (P value 0.87). (Table 1)

Table 2: Comparison of onset of anesthesia across the study groups

Parameter	Bupivacaine (Mean ±SD)	Ropivacaine (Mean ±SD)	P value
Onset of sensory block in Femoral nerve	13.39 ± 1.33	13.69 ± 0.62	0.39
Onset of sensory block in Sciatic nerve	17.19 ± 1.29	17.14 ± 1.23	0.89
Onset of motor blockade	21.28 ± 1.574	21.64 ± 1.805	0.53

The mean time taken for onset of sensory block in femoral nerve was 13.39 seconds in Bupivacaine group and 13.69 seconds in Ropivacaine group. The difference in the sensory block onset time in femoral nerve was statistically not significant (P value 0.39). In the Sciatic nerve, the sensory block onset time was 17.19 and 17.14 minutes in the two study groups respectively, with no statistically significant difference. The motor blockade took 21.28 and 21.64 minutes respectively in both the study groups (P value 0.53). (Table 2)

Table 3: Comparison of duration of anesthesia across the study groups

Parameter	Bupivacaine (Mean ±SD)	Ropivacaine (Mean ±SD)	P value
Duration of sensory block	933.67 ± 21.774	924.22 ± 0.587	0.19
Duration of motor block	243.78 ± 9.564	189.11 ± 9.887	0.001

The duration of sensory block was longer in Bupivacaine group (933.67 ± 21.774), as compared to Ropivacaine group (924.22 ± 0.587), but this difference was statistically not significant (P value 0.19). The duration of motor block was significantly longer in Bupivacaine group (243.78 ± 9.564), as compared to Ropivacaine (189.11 ± 9.88) group (P value 0.001). (Table 3)

None of the participants in both the study groups have reported any complications.

Table 4: Trend diagram comparing heart rate across the two study groups

Heart Rate	Bupivacaine (Mean ±SD)	Ropivacaine (Mean ±SD)
0 minutes	86.28 ± 6.04	84.11 ± 6.42
5 minutes	85.44 ± 5.56	83.61 ± 6.15
10 minutes	84.72 ± 7.13	82.78 ± 6.27
15 minutes	84.67 ± 5.89	83.17 ± 5.63
30 minutes	85.50 ± 5.87	84.22 ± 7.18
45 minutes	86.33 ± 6.23	83.61 ± 5.74
60 minutes	85.11 ± 6.30	84.44 ± 6.19
75 minutes	85.44 ± 5.80	83.17 ± 6.71
90 minutes	85.17 ± 4.66	85.11 ± 6.32
105 minutes	85.17 ± 4.06	84.61 ± 6.55
120 minutes	85.56 ± 4.94	84.44 ± 5.41

150 minutes	85.89 ± 5.26	84.78 ± 6.43
180 minutes	84.56 ± 7.23	83.22 ± 5.99

The heart rate was constantly higher in Bupivacaine group, as compared to Ropivacaine group. But the difference in heart rate was very minimal (ranging from 0 to 4 beats per minute) and can be considered clinically non-significant. (Table 4)

Table 5: Trend diagram comparing Mean Arterial pressure across the two study groups

MAP	Bupivacaine (Mean ± SD)	Ropivacaine (Mean ± SD)
0 minutes	98.67 ± 5.83	97.89 ± 6.12
5 minutes	96.39 ± 7.44	95.94 ± 6.59
10 minutes	95.89 ± 4.81	94.44 ± 7.07
15 minutes	95.89 ± 5.96	94.33 ± 6.52
30 minutes	98.00 ± 5.52	96.61 ± 6.25
45 minutes	98.22 ± 5.31	97.44 ± 5.87
60 minutes	98.94 ± 4.22	98.83 ± 5.74
75 minutes	99.78 ± 5.00	98.61 ± 5.95
90 minutes	97.72 ± 4.99	98.28 ± 5.57
105 minutes	98.67 ± 4.95	98.44 ± 5.52
120 minutes	99.11 ± 4.52	99.44 ± 5.49
150 minutes	97.89 ± 6.43	97.94 ± 5.08
180 minutes	96.06 ± 5.99	94.78 ± 6.80

The mean arterial pressure was comparable across the study groups at various points of time after the administration of the drug, with very minimal differences. (Table 5)

Discussion

Even though peripheral nerve blocks have gained wider popularity for a wide range of infra-umbilical surgeries in recent times, controversies still exist regarding the choice of anesthetic medication, their combination and ideal concentration.^(1,2) The balance of existing evidence does not clearly recommend any one particular compound over the others. Hence many authors have highlighted the need for more randomized controlled trials on the subject, to strengthen the existing evidence. The studies from developing countries, including India are even sparser.⁽²⁴⁾

In the current study, no statistically significant difference was observed in the time taken for onset of sensory block in either femoral nerve (13.39 and 13.69 minutes in Bupivacaine and Ropivacaine groups respectively, p value 0.39) or sciatic nerve (17.19 and 17.14 minutes, p value 0.89) The motor blockade took 21.28 and 21.64 minutes respectively in both the study groups (P value 0.53). In the current study, the duration of sensory block was slightly longer in Bupivacaine group, as compared to Ropivacaine group (933.67Vs 924.22, p value 0.19), but this difference was statistically not significant. The duration of motor block was significantly longer in Bupivacaine group (243.78 Vs

189.11, p value 0.001), as compared to Ropivacaine group.

Beaulieu, P., et al.⁽²⁷⁾ had reported findings similar to current study with no difference in block onset, but early recovery with Ropivacaine, when compared to Bupivacaine. Casati, A., et al.⁽²⁸⁾ have reported a mean sensory block onset time of 30 min (5-60 min) with levobupivacaine and 15 min (5-60 min) with ropivacaine (P = 0.63), but no differences in the block recovery time in sciatic nerve block. Cuvillon, P., et al.⁽⁶⁾ who have compared bupivacaine with ropivacaine (plus epinephrine) and their equal volume mixtures with lidocaine have reported mixtures of long-acting local anaesthetics with lidocaine induced faster onset blocks of decreased duration. But the study could not provide conclusion regarding safety benefit, but opined that “decreased concentration of long-acting local anaesthetic may be offset by the presence of a significant plasma concentration of lidocaine.” Studies by Fournier, R., et al.⁽²⁹⁾ Greengrass, R. A., et al.⁽³⁰⁾ and have reported similar findings of comparable block onset times with prolonged block duration with bupivacaine as in the current study.

In contrast to the current study, Fanelli, G., et al.⁽³¹⁾ who have compared ropivacaine, bupivacaine, and mepivacaine have reported similar sensory and motor blockade onset times in Groups ROPI and MEPI, which are significantly shorter compared to Group BUPI (P = 0.002 and P = 0.001, respectively). Resolution of motor block occurred later in Groups ROPI and BUPI than in Group MEPI (P = 0.005 and P = 0.0001, respectively). Khairnar, P., et al.⁽³²⁾ have also reported similar findings. Studies by Maheshwari, V., et al.⁽³³⁾ Nader, A., et al.⁽⁹⁾ and Pham Dang, C., et al.⁽³⁴⁾ have reported comparable for block onset, quality, and duration along with similar hemodynamic profile when given in same concentration for both the drugs.

In the current study, no significant differences were observed in the hemodynamic parameters across both the study groups. None of the subjects in both the study groups reported any systemic complications in the study. None of the previous randomized controlled trials conducted on the subject like studies by Fournier, R., et al.⁽²⁹⁾ Fanelli, G., et al.⁽³¹⁾ Beaulieu, P., et al.⁽²⁷⁾ and Khairnar, P., et al.⁽³²⁾ have reported any significant differences in the hemodynamic parameters or occurrence of complications between Bupivacaine and Ropivacaine in combined sciatic and femoral nerve block.

Conclusions

1. Both sensory and Motor block onset time were similar with 0.5% Bupivacaine and Ropivacaine in combined femoral and sciatic nerve block. The duration of sensory block also was comparable across the two groups
2. Bupivacaine had comparatively longer duration of motor block, as compared to Ropivacaine group

3. There were no clinically or statistically significant differences in haemodynamic parameters between the two groups
4. Peripheral nerve block for combined sciatic and femoral nerve either with Bupivacaine or Ropivacaine can be considered highly safe, as no major complications reported with either of the drugs.

References

1. Montes FR, Zarate E, Grueso R, Giraldo JC, Venegas MP, Gomez A, et al. Comparison of spinal anesthesia with combined sciatic-femoral nerve block for outpatient knee arthroscopy. *J Clin Anesth.* 2008;20(6):415-20.
2. Bansal L, Attri JP, Verma P. Lower limb surgeries under combined femoral and sciatic nerve block. *Anesth Essays Res.* 2016;10(3):432-6.
3. Casati A, Cappelleri G, Aldegheri G, Marchetti C, Messina M, De Ponti A. Total intravenous anesthesia, spinal anesthesia or combined sciatic-femoral nerve block for outpatient knee arthroscopy. *Minerva Anesthesiol.* 2004;70(6):493-502.
4. Kurnaz MM, Ersoy A, Altan A, Ervatan Z, Unlu N. [Comparison of hemodynamics, recovery profile and postoperative analgesia of unilateral spinal anaesthesia with combined sciatic-femoral nerve block in knee arthroscopy]. *Agri.* 2014;26(4):171-8.
5. Li J, Deng X, Jiang T. Combined femoral and sciatic nerve block versus femoral and local infiltration anesthesia for pain control after total knee arthroplasty: a meta-analysis of randomized controlled trials. *J Orthop Surg Res.* 2016;11(1):158.
6. Cuvillon P, Nouvellon E, Ripart J, Boyer JC, Dehour L, Mahamat A, et al. A comparison of the pharmacodynamics and pharmacokinetics of bupivacaine, ropivacaine (with epinephrine) and their equal volume mixtures with lidocaine used for femoral and sciatic nerve blocks: a double-blind randomized study. *Anesth Analg.* 2009;108(2):641-9.
7. Casati A, Fanelli G, Borghi B, Torri G. Ropivacaine or 2% mepivacaine for lower limb peripheral nerve blocks. Study Group on Orthopedic Anesthesia of the Italian Society of Anesthesia, Analgesia, and Intensive Care. *Anesthesiology.* 1999;90(4):1047-52.
8. Magistris L, Casati A, Albertin A, Deni F, Danelli G, Borghi B, et al. Combined sciatic-femoral nerve block with 0.75% ropivacaine: effects of adding a systemically inactive dose of fentanyl. *Eur J Anaesthesiol.* 2000;17(6):348-53.
9. Nader A, Kendall MC, De Oliveira GS, Jr., Puri L, Tureanu L, Brodskaja A, et al. A dose-ranging study of 0.5% bupivacaine or ropivacaine on the success and duration of the ultrasound-guided, nerve-stimulator-assisted sciatic nerve block: a double-blind, randomized clinical trial. *Reg Anesth Pain Med.* 2013;38(6):492-502.
10. Sawhney KY, Kundra S, Grewal A, Katyal S, Singh G, Kaur A. A Randomized Double Blinded Comparison of Epidural Infusion of Bupivacaine, Ropivacaine, Bupivacaine-Fentanyl, Ropivacaine-Fentanyl for Postoperative Pain Relief in Lower Limb Surgeries. *J Clin Diagn Res.* 2015;9(9):Uc19-23.
11. Kaur A, Singh RB, Tripathi RK, Choubey S. Comparison between bupivacaine and ropivacaine in patients undergoing forearm surgeries under axillary brachial plexus block: a prospective randomized study. *J Clin Diagn Res.* 2015;9(1):Uc01-6.
12. Albright GA. Cardiac arrest following regional anesthesia with etidocaine or bupivacaine. *Anesthesiology.* 1979;51(4):285-7.
13. Bacsik CJ, Swift JQ, Hargreaves KM. Toxic systemic reactions of bupivacaine and etidocaine. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 1995;79(1):18-23.
14. Guay J. Adverse events associated with intravenous regional anesthesia (Bier block): a systematic review of complications. *J Clin Anesth.* 2009;21(8):585-94.
15. Mulroy MF. Systemic toxicity and cardiotoxicity from local anesthetics: incidence and preventive measures. *Reg Anesth Pain Med.* 2002;27(6):556-61.
16. Arthur GR, Feldman HS, Covino BG. Comparative pharmacokinetics of bupivacaine and ropivacaine, a new amide local anesthetic. *Anesth Analg.* 1988;67(11):1053-8.
17. Hofmann P, Metterlein T, Bollwein G, Gruber M, Plank C, Graf BM, et al. The myotoxic effect of bupivacaine and ropivacaine on myotubes in primary mouse cell culture and an immortalized cell line. *Anesth Analg.* 2013;117(3):634-40.
18. Katz JA, Sehlhorst CS, Thompson GA, Denson DD, Coyle D, Bridenbaugh PO. Pharmacokinetics of intravenous and epidural ropivacaine in the rhesus monkey. *Biopharm Drug Dispos.* 1993;14(7):579-88.
19. McClellan KJ, Faulds D. Ropivacaine: an update of its use in regional anaesthesia. *Drugs.* 2000;60(5):1065-93.
20. Markham A, Faulds D. Ropivacaine. A review of its pharmacology and therapeutic use in regional anaesthesia. *Drugs.* 1996;52(3):429-49.
21. Karmakar MK, Aun CS, Wong EL, Wong AS, Chan SK, Yeung CK. Ropivacaine undergoes slower systemic absorption from the caudal epidural space in children than bupivacaine. *Anesth Analg.* 2002;94(2):259-65, table of contents.
22. Knudsen K, Beckman Suurkula M, Blomberg S, Sjøvall J, Edvardsson N. Central nervous and cardiovascular effects of i.v. infusions of ropivacaine, bupivacaine and placebo in volunteers. *Br J Anaesth.* 1997;78(5):507-14.
23. Scott DB, Lee A, Fagan D, Bowler GM, Bloomfield P, Lundh R. Acute toxicity of ropivacaine compared with that of bupivacaine. *Anesth Analg.* 1989;69(5):563-9.
24. Bansal L, Attri JP, Verma P. Lower limb surgeries under combined femoral and sciatic nerve block. *Anesthesia, Essays and Researches.* 2016;10(3):432-6.
25. Kirkwood BR. *Essentials of medical statistics:* Blackwell Scientific Publications; 1988.
26. Doig GS, Simpson F. Randomization and allocation concealment: a practical guide for researchers. *Journal of critical care.* 2005;20(2):187-91.
27. Beaulieu P, Babin D, Hemmerling T. The pharmacodynamics of ropivacaine and bupivacaine in combined sciatic and femoral nerve blocks for total knee arthroplasty. *Anesth Analg.* 2006;103(3):768-74.
28. Casati A, Borghi B, Fanelli G, Cerchierini E, Santorsola R, Sassoli V, et al. A double-blinded, randomized comparison of either 0.5% levobupivacaine or 0.5% ropivacaine for sciatic nerve block. *Anesth Analg.* 2002;94(4):987-90.
29. Fournier R, Faust A, Chassot O, Gamulin Z. Levobupivacaine 0.5% provides longer analgesia after sciatic nerve block using the Labat approach than the same dose of ropivacaine in foot and ankle surgery. *Anesth Analg.* 2010;110(5):1486-9.
30. Greengrass RA, Klein SM, D'Ercole FJ, Gleason DG, Shimer CL, Steele SM. Lumbar plexus and sciatic nerve block for knee arthroplasty: comparison of ropivacaine and bupivacaine. *Can J Anaesth.* 1998;45(11):1094-6.

31. Fanelli G, Casati A, Beccaria P, Aldegheri G, Berti M, Tarantino F, et al. A double-blind comparison of ropivacaine, bupivacaine, and mepivacaine during sciatic and femoral nerve blockade. *Anesth Analg.* 1998;87(3):597-600.
32. Khairnar P, Agarwal M, Verma UC, Kumar R. Comparative efficacy of ropivacaine and levobupivacaine in combined femoral and lateral femoral cutaneous nerve block with adjuvant magnesium for post-operative analgesia. *Indian J Anaesth.* 2016;60(8):584-9.
33. Maheshwari V, Rasheed MA, Singh RB, Choubey S, Sarkar A. Comparison of ropivacaine with levobupivacaine under epidural anesthesia in the lower limb orthopedic surgeries: A randomized study. *Anesth Essays Res.* 2016;10(3):624-30.
34. Pham Dang C, Langlois C, Lambert C, Nguyen JM, Asehnoune K, Lejus C. 0.5% levobupivacaine versus 0.5% ropivacaine: Are they different in ultrasound-guided sciatic block? *Saudi J Anaesth.* 2015;9(1):3-8.