

A Comparative Study of Dexmedetomidine and Fentanyl as Adjuvants with Bupivacaine in Adductor Canal Block Regional Anesthesia in Total Knee Replacement Surgery

Sarika S Naik¹, Channabasava Patil², Chaitra Venkategowda³, Narasimha Reddy⁴

ABSTRACT

Background/objectives: Total knee replacement surgeries being the ultimate operative modality are commonly performed for severe osteoarthritis. The challenges for the anesthesiologists are to provide optimal postoperative analgesia with minimum motor blockade, so that the patients can be ambulated early, thereby minimizing the complications of delayed ambulation.

Materials and methods: We compared the efficacy of fentanyl and dexmedetomidine in improving the analgesic efficacy of bupivacaine-driven regional anesthesia adductor canal block (ACB) in 60 patients who underwent total knee replacement surgeries. We conducted a randomized study of two different drug formulations for the same procedure with random allocation using a computerized table.

Results: The visual analog scale (VAS) score of the patients was less in group D. The number of steps walked and the time taken to stand from supine position was better in group D. The amount of local anesthetic requirement was less in group D. Nonsteroidal anti-inflammatory drug (NSAID) requirement was comparable in both the groups.

Conclusion: In our study, we observed that VAS score is less in group D, thereby promoting early ambulation and better patient satisfaction. Hence, dexmedetomidine is a better adjuvant than fentanyl for regional anesthesia.

Keywords: Adductor canal block, Bupivacaine, Dexmedetomidine, Fentanyl.

Journal on Recent Advances in Pain (2020): 10.5005/jp-journals-10046-0156

INTRODUCTION

Total knee replacement surgeries being the ultimate operative modality are performed for severe osteoarthritis.¹ The challenges for the anesthesiologists are to provide optimal postoperative analgesia with minimum motor blockade, so that the patients can be ambulated early, thereby minimizing the complications of delayed ambulation.¹ Many anesthetic techniques are used to provide postoperative analgesia for the total knee replacement surgeries and all have their own goods and odds.² Epidural analgesia was the most commonly used technique in the past, but its disadvantage is motor blockade delaying ambulation, and the need of systemic opioids or NSAIDs for postoperative analgesia has once again made the search for regional anesthesia a viable option.²

Currently using real-time assessment sonography gadgets, peripheral nerve blocks are performed for the postoperative pain management with ease and accuracy.^{3,4} Femoral nerve block was performed for many years following knee replacement surgeries.⁵ The disadvantage being blockade of motor nerve leading to quadriceps muscle weakness and delaying the ambulation.^{6,7} In recent years, adductor canal block (ACB) is being used as analgesia for total knee replacement surgeries.^{6,7} In the ACB, saphenous nerve, which is purely sensory and part of obturator nerve, is blocked.^{6,7} The adductor canal consists of the two large sensory saphenous nerves, the nerve to the vastus medialis and the articular branch of the obturator nerve. Since the ACB is distal to most of the efferent branches of the quadriceps muscle, it preserves the strength of this muscle.^{8,9} There are many studies supporting the efficacy of ACB with femoral nerve block in providing equivalent postoperative analgesia.^{10,11} In addition to excellent analgesia, ACB preserves

^{1,3,4}Department of Anesthesia and Critical Care, The Oxford Medical College Hospital and Research Center, Bengaluru, Karnataka, India

²Department of Orthopedics, The Oxford Medical College and Research Hospital, Bengaluru, Karnataka, India

Corresponding Author: Sarika S Naik, Department of Anesthesia and Critical Care, The Oxford Medical College Hospital and Research Center, Bengaluru, Karnataka, India, Phone: +91 8088000800, e-mail: bitta301@gmail.com

How to cite this article: Naik SS, Patil C, Venkategowda C, *et al.* A Comparative Study of Dexmedetomidine and Fentanyl as Adjuvants with Bupivacaine in Adductor Canal Block Regional Anesthesia in Total Knee Replacement Surgery. *J Recent Adv Pain* 2020;6(1):4–9.

Source of support: Nil

Conflict of interest: None

the quadriceps' strength, which helps in early mobilization and reducing the postoperative complications.^{10,11}

Adductor canal block is performed by the technique proposed by Kirkpatrick *et al.*, wherein the probe is placed transversely at the mid-thigh between the medial condyle of the femur and inguinal.¹² The needle is inserted anterolateral to the femoral artery which traverses beneath the sartorius muscle.¹² Rare complications like nerve injury, vascular injury, systemic toxicity, and anaphylactic reactions are seen with the drug injected under sonographic guidance.¹²

We compared the efficacy of fentanyl and dexmedetomidine adjuvants to 0.125% bupivacaine in the postoperative pain management under a double-blinded randomized study. We have made a novel approach of comparing efficacy of most commonly

used opioid, i.e., fentanyl, and an α -2 agonist, dexmedetomidine, which is most commonly used for ACB with continuous infusion using 20 g sonographic-guided catheter, enhancing postoperative analgesia. The parameters compared are time taken to stand up from supine position, number of steps walked, the amount of paracetamol used in 48 hours, hemodynamic parameters, and visual analog scale (VAS) score for 48 hours and also any other postoperative complications such as local anesthetic toxicity, nausea, vomiting, and catheter site infection.

MATERIALS AND METHODS

We compared the efficacy of fentanyl and dexmedetomidine in improving the analgesic efficacy of bupivacaine-driven regional anesthesia ACB in 60 patients who underwent total knee replacement surgeries. We conducted a randomized study of two different drug formulations for the same procedure with random allocation using a computerized table. All the patients were explained about the type of drug and postoperative pain management, and the advantages and disadvantages of the procedures. Also the safety approval of both the drugs were explained with printed handouts. Written informed consents were taken from the patients in their preferred language.

On the day of the surgery, once the patients were shifted to the operation theater, all monitors were connected and 18 g cannula was inserted, Ringer's lactate was started. Subarachnoid block was given with 2.5 to 3 mL of 0.5% bupivacaine in all patients. After spinal anesthesia, the patients were positioned supine and under aseptic precaution 20 g catheter was inserted in the adductor canal with sonographic guidance and the catheter was placed posterior to the sartorius muscle. No infusion was started through this catheter intraoperatively. After the procedure, the patient was shifted to the postoperative recovery room and going by the rules of randomization, an allotted nurse (S1) took care of the concentration, dosage, and prepared the drug as allocated and handed over the drug to the anesthesiologist (AI 1 assistant investigator).

The syringe is loaded by S1 with either with 2 μ g/mL dexmedetomidine with 0.125% bupivacaine to a group or fentanyl 2 μ g/mL with 0.125% bupivacaine. The dilutions of the drug in syringes are made identical to 50 mL to avoid observer bias. The S1 noted down the formulation given to 60 patients. All the patients were given the loading dose of 10 mL of the drug and an infusion started at 8–10 mL/hour.

The infusion was adjusted depending on the VAS score and the rescue analgesia of 1 g paracetamol was given by A1 if the VAS score is more than 4. Hemodynamic parameters are monitored for 48 hours, time taken by the patients to stand up from the sitting position are noted down, and the number of steps walked after 6 hours are counted in both the groups. Paracetamol consumption was calculated for 48 hours and the VAS score was recorded for 48 hours every sixth hourly. All the data were recorded and entered by another sister (S2) involved in the study. The principal investigator who is unaware of the formulations given to either groups finally analyzes the data and compares the significance of the data between the two groups (group D is the dexmedetomidine group and group F is the fentanyl group).

RESULTS

The demographic profile of the patients in both the groups was comparable with regard to age, weight, and height. The American

Society of Anesthesiologists (ASA) grading was comparable in both the groups (Table 1). The average mean blood pressure in group D ranged from 71.2 to 85.33 mm Hg and the average mean blood pressure in group F ranged from 73.77 to 85.9 mm Hg. Hypotension was reported in five patients in group D in the first hour and three patients in group F. Only in three patients of group D, mephentermine was given to treat hypotension. Hypotension responded to mephentermine and intravenous fluid (Table 2).

The average heart rate in group D ranged from 67.13 to 82.23 per minutes; and in group F, it ranged from 74.30 to 85.23 per minutes. A significant difference in heart rate was observed in the two groups in the initial 50 minutes. After 50 minutes, there was significant difference in the two groups. In group D, six patients and in group F two patients had bradycardia, which responded to one dose of atropine.

The average duration of the surgery in group D was 140.17 minutes, with a standard deviation of 19.45 minutes and the average duration of the surgery in group F was 145.33, with a standard deviation of 13.51. The *p* value was 0.237, which was statistically not significant. Hence, there was no significant difference in the duration of the surgery in both the groups.

In group D, the mean time taken to raise up from the bed at 6 hours was 108.63 seconds, and in group F, it was 183.90 seconds, with a standard deviation of 35.88 seconds and a *p* value of 0.0001, which is highly significant. Hence, the need to stand up from supine position was higher in group F.

The VAS score at 4, 8, and 12 hours and every 4 hours for 48 hours is better in dexmedetomidine group and the *p* value is shown in the Table 3. Hence, the postoperative pain control is better in group D.

In group F, the mean number of steps walked after 6 hours was 131.63, with a standard deviation of 11.61 steps; in group D, the mean number of steps walked was 150.43, with a standard deviation of 15.73 steps. The *p* value is 0.0001, which is statistically significant. Hence, the number of steps walked in group D was more than that in group F.

The amount of bupivacaine 0.125% used through the infusion in group D was 347.10 mL with a standard deviation of 21.18 mL; and the amount of bupivacaine used in group F was 361.50 mL with a standard deviation of 20.43 mL. The *p* value was 0.0096 which is statistically significant. Hence, the bupivacaine requirement was less in dexmedetomidine group. We observed that dexmedetomidine is a better adjuvant than fentanyl for the postoperative pain management in the total knee replacement surgeries (Table 4).

The mean paracetamol consumption in 48 hours in group F was 2.17 g, with a standard deviation of 1.02 g and in group D the mean consumption was 2.04 g, with a standard deviation of 0.84 g. The *p* value was 0.596, which is statistically not significant.

Table 1: Demographic profile

Group	Group D	Group F	<i>p</i> value
Age in years	66.13	65.87	0.8858
Weight in kg	54.45	55.39	0.778
Height in cm	155.41	156.11	0.2590
ASA 1 and 2	25 males/ 5 females	23 males/ 7 females	0.768
Sex	19 males/ 11 females	20 males/ 10 females	0.866

Table 2: Mean blood pressure

	Group	Mean blood pressure	Standard deviation	Standard error of mean	p value
Basal	Group D	84.45	6.25	1.15	0.3404
	Group F	85.93	5.52	1.01	
10th minute	Group D	84.00	6.03	1.10	0.6099
	Group F	84.73	5.00	0.91	
20th minute	Group D	72.20	4.71	0.86	0.0001
	Group F	76.77	3.49	0.64	
30th minute	Group D	78.20	7.22	1.32	0.0006
	Group F	84.20	5.42	0.99	
40th minute	Group D	81.10	7.32	1.34	0.0025
	Group F	85.93	4.06	0.74	
50th minute	Group D	75.13	5.75	1.05	0.0001
	Group F	83.93	4.06	0.74	
1 hour	Group D	73.77	4.84	0.88	0.0001
	Group F	82.97	3.56	0.65	
2nd hour	Group D	71.37	4.77	0.87	0.0030
	Group F	74.70	3.47	0.63	
3rd hour	Group D	72.20	4.71	0.86	0.0001
	Group F	76.77	3.49	0.64	
4th hour	Group D	72.97	4.86	0.89	0.0001
	Group F	79.37	3.41	0.62	
5th hour	Group D	72.30	6.09	1.11	0.0016
	Group F	77.63	6.40	1.17	
6th hour	Group D	73.03	5.88	1.07	0.0007
	Group F	78.80	6.61	1.21	
10th hour	Group D	85.27	6.37	1.16	0.7735
	Group F	85.67	4.10	0.75	
14th hour	Group D	82.270	7.25	1.32	0.0567
	Group F	85.07	5.51	1.01	
18th hour	Group D	83.33	7.40	1.35	0.2379
	Group F	85.33	5.45	0.99	
24th hour	Group D	84.53	7.74	1.41	0.6511
	Group F	85.30	5.05	0.92	
30th hour	Group D	84.87	5.81	1.06	0.643
	Group F	85.50	4.68	0.85	
36th hour	Group D	84.87	5.90	1.08	0.6024
	Group F	85.60	4.90	0.89	
48th hour	Group D	82.23	15.1	2.77	0.319
	Group F	85.23	6.14	1.12	

Hence, the paracetamol consumption in both the groups was not significant. There were no postoperative complications in both the groups.

DISCUSSION

Peripheral nerve block can be considered the procedure of choice for postoperative analgesia when compared to the conventional methods like epidural analgesia, systemic opioids, NSAIDs.^{3,4} Regional anesthesia or peripheral nerve block is the postprocedural anesthetic management of choice which improves early ambulation and decreases systemic side effects.^{13,14} The amount of local anesthesia if increased may lead to systemic toxicity, hence adjuvants that increase the effect of the drug are used.^{15,16}

Other techniques like epidural analgesia, systemic opioids, and NSAIDs have their own advantages and disadvantages.^{15,16}

In the present study, we have compared the efficacy of the two most commonly used adjuvants in the regional anesthesia technique to prolong the effect of local anesthesia, namely, fentanyl, which is most commonly used opioid anesthetic agent and an α -2 agonist dexmedetomidine which prolongs the effect of local anesthetic agent. Dexmedetomidine is an α -2 adrenoreceptor agonist which has revolutionized the effect on peripheral nerve blocks by acting as an adjuvant.¹⁷ Perineural dexmedetomidine acts by blocking the hyperpolarization-activated cation current or I_h current.¹⁷ The I_h current brings a neuron back to the resting potential from the hyperpolarized state that follows an action potential.¹⁷ By blocking the I_h current, dexmedetomidine causes

Table 3: The visual analog scale scores

Time	Group	Mean	Standard deviation	Standard error of mean	p value
6th hour	Group D	2.73	1.39	0.25	0.006
	Group F	4.03	2.08	0.38	
12th hour	Group D	2.63	1.22	0.22	0.001
	Group F	4.27	1.17	0.21	
18th hour	Group D	2.53	1.14	0.21	0.008
	Group F	3.57	1.14	0.21	
24th hour	Group D	2.27	0.64	0.12	0.009
	Group F	2.90	0.76	0.14	
36th hour	Group D	2.17	0.99	0.18	0.689
	Group F	2.07	0.94	0.17	
48th hour	Group D	1.40	0.50	0.09	0.448
	Group F	1.50	0.51	0.09	

prolonged hyperpolarization of the nerve, thereby delaying the restoration of resting potential and preventing the conduction of a new action potential.¹⁷

Dexmedetomidine blockade is more effective in unmyelinated fibers, thus sparing the motor nerve and enhancing faster recovery.¹⁸ Many studies have shown that dexmedetomidine when used in a dosage of 0.2–2 µg/kg as an adjuvant to local anesthetic provides adequate analgesia.¹⁸ Keplinger et al. in their study concluded that dexmedetomidine in a dosage of 50, 100, and 150 µg increases the duration of the sensory block by 60, 72, and 57%, respectively, when given as adjuvant with ropivacaine compared to when given alone.¹⁹ However, 150 µg dexmedetomidine caused deep sedation and paresthesia in one third of the patients.¹⁹

In our study, bupivacaine dose has significantly reduced in dexmedetomidine group compared to the fentanyl group. Hence, we have observed that dexmedetomidine is a better adjuvant than fentanyl to reduce the dosage of local anesthetic.

A separate study by Abdulatif et al. reported that addition of 25 µg of dexmedetomidine hardly made any difference in the pharmacodynamics of bupivacaine in femoral nerve blocks.² A placebo-controlled trial was done by Andersen et al. on patients who underwent total knee replacement.²⁰ Here ACB was given in both the groups with ropivacaine and dexmedetomidine and ropivacaine with placebo.²⁰ They showed a statistical increase in duration of sensory block to temperature (22 vs 20 hours), pinprick (23 vs 20 hours), pain during tonic heat stimulation (22 vs 20 hours), and warmth detection threshold (23 vs 21 hours; $p < 0.05$) but not to heat pain detection threshold (21 vs 20 hours; $p = 0.068$) in the dexmedetomidine group as compared to ropivacaine group. Clinical relevance of this study with mild statistical significance has not been documented.²⁰ Mild to moderate sedation occurred in all patients in the dexmedetomidine group during the first 4 hours after the block.²⁰ One participant in the dexmedetomidine group experienced numbness in an area in the leg after receiving dexmedetomidine.²⁰

This corresponds to our study where the sensory blockade lasted longer in group D. The mean number of steps walked after 6 hours in group F is 131.63 with a standard deviation of 11.61 steps, and the mean number of steps walked in group D was 150.43 with a standard deviation of 15.73 steps. The p value was 0.0001, which is statistically significant. Hence, the number of steps walked in group D was more than that in group F.

The VAS score for 48 hours was better with dexmedetomidine in our study, supporting the study done by Andersen et al., where

the sensory block anesthesia was prolonged by addition of dexmedetomidine to the local anesthesia.

Goyal et al. in their study of 150 patients undergoing total bilateral knee replacement used two different concentrations of dexmedetomidine with ropivacaine in ACB.²¹ They found increase in duration of analgesia (18 hours) in patients administered 0.5 µg dexmedetomidine when compared to 0.25 µg (10.8 hours) along with ropivacaine.²¹ Postoperative pain scores and 24 hours tramadol consumption were less in patients receiving dexmedetomidine 0.5 µg/kg, and the number of steps taken on day 1 after surgery was better in the group given higher concentration of dexmedetomidine (0.5 µg/kg).²¹ Fentanyl is the most commonly used intermittent acting opioid for peripheral nerve block regional anesthesia. In our study, we used 2 µg/mL of fentanyl along with 0.125% bupivacaine as an infusion in the postoperative period.²¹

Rajkhowa et al. reported fentanyl as an adjuvant in brachial plexus block, where the mechanism of prolongation of the analgesia may be due to the peripheral receptors; however the mere existence of peripheral receptors is still questionable.²² It was also noted that fentanyl used as an adjuvant prolongs the duration of sensory and motor blockade, by directly binding with the receptors on the dorsal nerve roots and diffusion in the systemic circulation leading to the central action.²² Bharti et al. noted that when fentanyl was used as an adjuvant with local anesthetic for brachial plexus block, the analgesic effect prolonged by 3 hours and motor by 4 hours compared to the group where only anesthetic was used.²³ Farooq et al. noted that when fentanyl and dexmedetomidine were used as an adjuvant to ropivacaine for brachial plexus block, there was no difference in the duration of analgesia and motor blockade in both the groups.²⁴ Also confounding factor may be the longer duration of action of ropivacaine compared to bupivacaine.²⁴

In our study, in group D, the mean time taken to raise up from the bed at 6 hours was 108.63 seconds, and in group F it was 183.90 seconds with a standard deviation of 35.88 seconds and the p value was 0.0001 seconds, which is highly significant. We have found that in group D the time taken to raise up was much less compared to group F.

CONCLUSION

In our study, we observed that dexmedetomidine when used as an adjuvant with bupivacaine showed better analgesia compared to fentanyl. The number of steps walked by the patients after 6 hours was more in patients administered dexmedetomidine

Table 4: Heart rate

<i>Time</i>	<i>Group</i>	<i>Heart rate</i>	<i>Standard deviation</i>	<i>Standard error of mean</i>	<i>p value</i>
Basal	Group D	75.60	6.41	1.17	0.5605
	Group F	74.50	8.05	1.47	
10th minute	Group D	67.20	7.30	1.33	0.0001
	Group F	77.63	7.64	1.34	
20th minute	Group D	66.63	7.32	1.34	0.001
	Group F	78.27	7.80	1.42	
30th minute	Group D	67.13	7.80	1.42	0.001
	Group F	79.57	7.59	1.39	
40th minute	Group D	69.97	7.49	1.37	0.0005
	Group F	77.33	7.86	1.43	
50th minute	Group D	72.57	6.89	1.26	0.0724
	Group F	75.97	7.49	1.37	
1 hour	Group D	75.23	5.66	1.03	0.7569
	Group F	74.73	6.75	1.23	
2 nd hour	Group D	79.07	8.36	1.53	0.8913
	Group F	79.33	6.58	1.20	
3rd hour	Group D	76.43	4.99	0.99	0.939
	Group F	76.53	5.13	0.94	
4th hour	Group D	75.27	5.86	1.07	0.2812
	Group F	77.03	6.69	1.22	
5th hour	Group D	75.53	5.70	1.04	0.2635
	Group F	77.30	6.40	1.17	
6th hour	Group D	77.57	5.37	0.98	0.8073
	Group F	78.80	6.20	1.13	
10th hour	Group D	77.43	4.64	0.85	0.935
	Group F	77.83	6.92	1.24	
14th hour	Group D	75.40	6.79	1.24	0.1970
	Group F	77.77	7.25	1.320	
18th hour	Group D	77.90	4.91	0.90	0.4525
	Group F	79.03	6.58	1.20	
24th hour	Group D	76.03	5.11	0.93	0.324
	Group F	77.70	7.64	1.39	
30th hour	Group D	78.70	7.38	1.35	0.5292
	Group F	79.93	7.71	1.41	
36th hour	Group D	75.30	7.24	1.32	0.1621
	Group F	77.97	7.35	1.34	
48th hour	Group D	82.23	15.17	2.77	0.319
	Group F	85.23	6.14	1.12	

and the mean time taken to raise up from the supine position was less in dexmedetomidine group compared to the fentanyl group. In addition, less VAS scores were observed in dexmedetomidine group, which promoted early ambulation and less local anesthetic requirements. Hence, we can use ACB with dexmedetomidine as an adjuvant in the postoperative pain management of patients undergoing total knee replacement, which in turn promotes early ambulation with minimal or no pain, thereby reducing the complications related to delayed ambulation.

REFERENCES

- Jiang X, Wang Q-Q, Wu C-A, et al. Analgesic efficacy of adductor canal block in total knee arthroplasty: a meta-analysis and systematic review. *Orthopaedic Surgery* 2016;8(3):294–300. DOI: 10.1111/os.12268.
- Bansal P. Dexmedetomidine as an adjuvant to local anaesthetic agents in peripheral nerve blocks: a review. *Journal of Clinical and Diagnostic Research* 2019;13(1):UE01–UE07. DOI: 10.7860/JCDR/2019/38311.12494.
- Patel AA, Buller LT, Fleming ME, et al. National trends in ambulatory surgery for upper extremity fractures: a 10-year analysis of the US national survey of ambulatory surgery. *Hand (NY)* 2015;10(2): 254–259.
- Cozowicz C, Poeran J, Zubizarreta N, et al. Trends in the use of regional anaesthesia: neuraxial and peripheral nerve blocks. *Reg Anaesth Pain Med* 2016;41(1):43–49. DOI: 10.1097/AAP.0000000000000342.
- Packiasabapathy S, Kashyap L, Arora M, et al. Effect of dexmedetomidine as an adjuvant to bupivacaine in femoral nerve

- block for perioperative analgesia in patients undergoing total knee replacement arthroplasty: a dose-response study. *Saudi J Anaesth* 2017;11(3):293–298. DOI: 10.4103/sja.SJA_624_16.
6. Jæger P, Koscielniak-Nielsen ZJ, Schrøder HM, et al. Adductor canal block for postoperative pain treatment after revision knee arthroplasty: a blinded, randomized, placebo-controlled study. *PLoS One*. 2014;9(11):e111951. DOI: 10.1371/journal.pone.0111951.
 7. Lund J, Jenstrup MT, Jaeger P, et al. Continuous Adductor-canal-blockade for adjuvant post-operative analgesia after major knee surgery: preliminary results. *Acta Anaesthesiol Scand* 2011;55(1): 14–19. DOI: 10.1111/j.1399-6576.2010.02333.x.
 8. Horn JL, Pitsch T, Salinas F, et al. Anatomic basis to the ultrasound-guided approach for saphenous nerve blockade. *Reg Anesth Pain Med* 2009;34(5):486–489. DOI: 10.1097/AAP.0b013e3181ae11af.
 9. Kapoor R, Adhikary SD, Siefiring C, et al. The saphenous nerve and its relationship to the nerve to the vastus medialis in and around the adductor canal: an anatomical study. *Acta Anaesthesiol Scand* 2012;56(3):365–367. DOI: 10.1111/j.1399-6576.2011.02645.x.
 10. Jaeger P, Nielsen ZJ, Henningsen MH, et al. Adductor canal block versus femoral nerve block and quadriceps strength: a randomized, double-blind, placebo-controlled, crossover study in healthy volunteers. *Anesthesiology*. 2013;118(2):409–415. DOI: 10.1097/ALN.0b013e318279fa0b.
 11. Jenstrup MT, Jaeger P, Lund J, et al. Effects of adductor-canal-blockade on pain and ambulation after total knee arthroplasty: a randomized study. *Acta Anaesthesiol Scand* 2012;56(3):357–364. DOI: 10.1111/j.1399-6576.2011.02621.x.
 12. Kirkpatrick JD, Sites BD, Antonakakis JG. Preliminary experience with a new approach to performing an ultrasound-guided saphenous nerve block in the mid to proximal femur. *Reg Anesth Pain Med* 2010;35(2):222–223. DOI: 10.1097/AAP.0b013e3181d24589.
 13. Schoenmakers KP, Wegener JT, Stienstra R. Effect of local anaesthetic volume (15 vs 40 mL) on the duration of ultrasound-guided single shot axillary brachial plexus block: a prospective randomized, observer-blinded trial. *Reg Anaesth Pain Med* 2012;37(3):242–247. DOI: 10.1097/AAP.0b013e3182405df9.
 14. Scott DB, Lee A, Fagan D, et al. Acute toxicity of ropivacaine compared with that of bupivacaine. *Anaesth Analg* 1989;69(5):563–569. DOI: 10.1213/00000539-198911000-00003.
 15. Vorobeichik L, Brull R, Abdallah FW. Evidence basis for using perineural dexmedetomidine to enhance the quality of brachial plexus nerve blocks: a systematic review and meta-analysis of randomized controlled trials. *Br J Anaesth* 2017;118(2):167–181. DOI: 10.1093/bja/aew411.
 16. Aboelela M, Kandeel AR, Elsayed U, et al. Dexmedetomidine in a surgically inserted catheter for transversus abdominis plane block in donor hepatectomy: a prospective randomized controlled study. *Saudi J Anaesth* 2018;12(2):297–303. DOI: 10.4103/sja.SJA_577_17.
 17. Brummett CM, Hong EK, Janda AM, et al. Perineural dexmedetomidine added to ropivacaine for sciatic nerve block in rats prolongs the duration of analgesia by blocking the hyperpolarization-activated cation current. *Anesthesiology* 2011;115(4):836–843. DOI: 10.1097/ALN.0b013e318221fcc9.
 18. Lanqvist PA. Alpha-2 adrenoceptor agonists as adjuncts to peripheral nerve blocks in children—is there a mechanism of action and should we use them? *Paediatr Anaesth* 2012;22(5):421–424. DOI: 10.1111/j.1460-9592.2012.03821.x.
 19. Keplinger M, Marhofer P, Kettner SC, et al. A pharmacodynamic evaluation of dexmedetomidine as an additive drug to ropivacaine for peripheral nerve blockade: a randomised, triple-blind, controlled study in volunteers. *Eur J Anaesthesiol* 2015;32(11):790–796. DOI: 10.1097/EJA.0000000000000246.
 20. Andersen JH, Grevstad U, Siegel H, et al. Does dexmedetomidine have a perineural mechanism of action when used as an adjuvant to ropivacaine? A paired, blinded, randomized trial in healthy volunteers. *Anesthesiology* 2017;126(1):66–73. DOI: 10.1097/ALN.0000000000001429.
 21. Goyal R, Mittal G, Yadav AK, et al. Adductor canal block for postoperative analgesia after simultaneous bilateral total knee replacement: a randomised controlled trial to study the effect of addition of dexmedetomidine to ropivacaine. *Indian J Anaesth* 2017;61(11):903–909. DOI: 10.4103/ija.IJA_277_17.
 22. Rajkhowa T, Das N, Parua S. Fentanyl as an adjuvant for brachial plexus block: a randomized comparative study. *Int J Clin Trials* 2016;3:64–67. DOI: 10.18203/2349-3259.ijct20160996.
 23. Bharti N, Sardana DK, Bala I. The analgesic efficacy of dexmedetomidine as an adjunct to local anesthetics in supraclavicular brachial plexus block: a randomized controlled trial. *Anesth Analg* 2015;121(6): 1655–1660. DOI: 10.1213/ANE.0000000000001006.
 24. Farooq N, Singh RB, Sarkar A, et al. To evaluate the efficacy of fentanyl and dexmedetomidine as adjuvant to ropivacaine in brachial plexus block: a double-blind, prospective, randomized study. *Anesth Essays Res* 2017;11(3):730–739. DOI: 10.4103/aer.AER_30_17.