



A Randomized, Double-Blind, Comparative Study of the Analgesic Efficacy of Perineural Dexmedetomidine as Adjuvant to Ropivacaine versus Ropivacaine Alone in Ultrasound Guided Saphenous Nerve Block after Anterior Cruciate Ligament Reconstruction Surgery

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ABSTRACT

Background: The saphenous nerve block has been effectively used for pain treatment after knee surgeries, however, a single-shot saphenous nerve block with a long-acting local anesthetic usually provides a relatively short duration of postoperative analgesia. Dexmedetomidine is a highly selective alpha-2 adrenoceptors agonist and its perineural injection as an additive to local anesthetics has been shown to improve postoperative analgesia. The aim of this prospective, randomized double-blind study was to evaluate the effects of adding dexmedetomidine to ropivacaine on the quality of postoperative analgesia with ultrasound-guided saphenous nerve block after anterior cruciate ligament reconstruction surgery of the knee.

Methods: 40 ASA class I-II patients undergoing arthroscopic anterior cruciate ligament reconstruction surgery under general anesthesia were randomly divided into 2 groups of 20 patients each. At the end of surgery, ultrasound-guided saphenous nerve block was performed with either 10 ml ropivacaine 0.5% alone, or 1 µg/kg dexmedetomidine added to 10 ml of ropivacaine 0.5%. The total volume of injected solutions was increased to 12 ml by adding normal saline. The postoperative pain scores as well as fentanyl consumption through intravenous patient-controlled analgesia pump, hemodynamic parameters, sedation scores, and adverse effects were assessed every 1 hour to 6 hours and then every 2 hours to 24 hours.

Results: There were significantly lower postoperative pain scores in the ropivacaine plus dexmedetomidine group compared to ropivacaine alone group at all postoperative measured time points. The total amount of fentanyl consumption and sedation scores after surgery was significantly higher in group ropivacaine alone than in group ropivacaine plus dexmedetomidine. Systolic blood pressure and heart rate within 24 hours after surgery were significantly lower in the dexmedetomidine+ropivacaine group than in the ropivacaine alone group. However, no bradycardia and hypotension were detected in any of the patients.

Conclusion: Perineural administration of 1 µg/kg of dexmedetomidine as an adjuvant to ropivacaine 0.5% for ultrasound guided saphenous nerve block significantly reduced pain scores and opioid requirements in the first 24 h after ACLR surgery compared to ropivacaine alone without any significant side effects.

The authors declare no conflicts of interest.

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Arthroscopic anterior cruciate ligament reconstruction (ACLR) is one of the most commonly performed orthopedic operations. Effective post ACLR pain management is important for improving patient function, early mobilization, efficient rehabilitation, and fast recovery [1]. The saphenous nerve is the purely sensory terminal branch of the femoral nerve that provides sensory innervation to the knee joint and its block at the mid- thigh level has been shown to produce comparable analgesia to the femoral nerve block following ACLR surgery [2-3]. However, the saphenous nerve block (SNB) avoids the disadvantage of femoral block- related motor weakness as it preserves quadriceps muscle strength and therefore improves early ambulation of patients and decreases the risk of falling down [4-5]. However, a single-shot SNB with a long-acting local anesthetic (LA) usually provides a relatively short duration of postoperative analgesia. Furthermore, using higher doses of the LA for prolongation of the nerve block increases the risk of their related adverse effects. The reason for use of an adjuvant in nerve blocks is to extend the analgesia duration of a single-dose of LA [6-7].

Dexmedetomidine is a highly selective potent alpha-2 adrenoceptor agonist and its perineural injection as an adjuvant to different local anesthetics in various peripheral nerve blocks has been shown to shorten onset of the block, decrease postoperative pain intensity, prolong duration of postoperative analgesia, and reduce consumption of systemic opioids with minimal systemic adverse effects [8-11]. The peripheral analgesic effect of perineural dexmedetomidine is thought to be peripherally mediated by α_2 - adrenoceptors binding [8,10]. However, the use of dexmedetomidine for peripheral nerve blockade has not been widely evaluated and as far as we know, randomized clinical studies on its perineural effect as an adjuvant in SNB is limited.

The present study was conducted to assess the effect of adding dexmedetomidine to ropivacaine on the quality of postoperative analgesia in ultrasound-guided saphenous nerve block following ACLR surgery. The primary outcome measure was numerical rating scale (NRS) of pain scores during the first 24 hours after surgery. The secondary outcome measure was postoperative fentanyl consumption, hemodynamic parameters, and sedation score.

Methods

This prospective double-blinded randomized clinical trial was conducted at Akhtar Hospital affiliated to Shahid Beheshti University of Medical Sciences and its protocol was approved by the Research Ethics Committee of the University in Tehran, Iran (ethics code of ir.sbm.u.Retech.Rec.1396.215). Forty patients aged 15 to 50 years with American Society of Anesthesiologists

physical status I -II, scheduled for elective ACLR surgery were included in the study after obtaining informed consent. Patients with allergy to local anesthetics, age less than 15 and more than 50 years, bleeding disorders, opium addiction, infection over the block site, BMI>30, and neuropathy over area of saphenous nerve supply were excluded from the study. Uncooperative patients and those who regularly took painkillers for chronic pain were also excluded. Eligible participants were randomly assigned to two equal groups of ropivacaine alone (R) and ropivacaine plus dexmedetomidine (RD) with an allocation concealment method by using a random allocation software. The allocation sequences were separately concealed in numbered, opaque, sealed envelopes. In the operating room, monitoring consisted of electrocardiogram, pulse oximetry, and noninvasive blood pressure. General anesthesia was induced with fentanyl, midazolam, propofol and atracurium and was maintained with infusion of propofol and remifentanyl and atracurium boluses. An appropriate size of laryngeal mask airway was inserted to secure the airway. At the end of the operation and before awakening the patient, based on the order of patient entry to the operating room, the related envelope was opened by a staff with no involvement in the trial and assigned group of the participant was identified. SNB was performed under the guidance of ultrasound (SonoSite S-Nerve, Bothell, WA, USA) using a 6-13 MHz linear transducer and a 22G-bevel 30°, 85 mm block needle (Visioplex®, Vygon, Ecouen, France). The knee on the operative side was slightly flexed and leg externally rotated. The transducer was placed in the short axis view on the anteromedial side of the mid- thigh until the sartorius muscle, the femoral artery and the hyperechoic saphenous nerve near the femoral artery was visualized. The block needle was inserted in-plane in a lateral to medial direction. After proper needle positioning, 10 ml of 0.5% ropivacaine hydrochloride (L. Molteni & C. dei F.lli Alitti Societa di Esercizio SpA, Italy) + 2 ml normal saline was injected in the R group. In the RD group, 10 ml of 0.5% ropivacaine hydrochloride plus 1 $\mu\text{g}/\text{kg}$ of dexmedetomidine (Precedex dexmedetomidine HCl, Hospira, Lake Forest, USA) was injected. The total volume of injected solution in the RD group was reached to 12 ml by adding normal saline, if needed. Adequate spread of the drug around the femoral artery was confirmed in both groups. The patients were extubated and transferred to the recovery room. Postoperatively, all patients received IV fentanyl patient-controlled analgesia (PCA) pump for 24 hours, allowing to deliver boluses of 50 μg fentanyl, with a lockout interval of 15 min, with no background opioid infusion. Pain intensity was assessed every hour to 6 hours and then every 2 hours up to 24 hours after surgery with a 0-10 NRS (0 =no pain and 10=the worst possible

pain). The values of heart rate, systolic blood pressure, sedation degree, PCA fentanyl consumption, and side effects were recorded at the same time intervals. Sedation was evaluated with the 6-points Ramsay score (1. irritable; 2. quiet, cooperative and with good orientation; 3. drowsy, but still responsive to commands; 4. light sleep, but still active when tapping the forehead; 5. sleep, and dull to the forehead tapping stimulation; 6. deep sleep, having no response to the forehead tapping stimulation). Hypotension was defined as systolic blood pressure < 90 mmHg, bradycardia as heart rate <60 bpm.

Randomization and assignment of patients was done by a staff who was not involved in the study. Patients, surgeons, anesthesiologist who performed the block and ward nurses were unaware of group allocations. Peri-neural medication was prepared according to the randomized protocol by anesthesiology assistants who were not involved in the study. The anesthesiology staff who assessed postoperative outcomes in two groups was also kept blinded.

Statistical analysis

SPSS software version 21 was used for data analysis. A sample size of 20 patients in each group was calculated with a power of 80%, a significant level of 5%, and a pain score of 2.2 ± 2.2 in the ropivacaine and 0.7 ± 0.8 in the ropivacaine plus dexmedetomidine groups. Student t-test or Mann-Whitney non-parametric test was used to

compare quantitative variables and chi-square or Fisher's exact tests to compare the qualitative variables between the two groups. Repeated Measures ANOVA was used to compare quantitative variables at different time points between the groups. Data are expressed as mean \pm standard deviation and number. A p value less than 0.05 was considered significant.

Results

Forty patients (20 patients in each group) were entered into the study. Patients' characteristics were similar in two groups (Table 1). The mean pain scores at all postoperative measured time points were significantly higher in the R group compared with the RD group (Figure 1). The amount of fentanyl usage via PCA was significantly higher in the R group than in the RD group on the second and third hours after surgery (Figure 2). The total consumption of PCA fentanyl was also significantly higher in the R group than in the RD group (Table 1). Systolic blood pressure and heart rate within 24 hours after surgery were significantly lower in the RD group than in the R group. However, no bradycardia and hypotension were detected (Figure 3). The degree of sedation in the first 12 hours and at 16 and 22 hours after surgery was significantly higher in the RD group compared to R group (Figure 4).

Table 1- Patients' characteristics and anesthesia data in two groups. Data are presented as mean \pm SD and numbers.

	R group n=20	RD group n=20	P value
Age (yrs.)	32.55 \pm 6.82	30.45 \pm 6.35	0.320
Gender			>0.999
Female	9(45.0%)	9(45.0%)	
Male	11(55.0%)	11(55.0%)	
Height(cm)	169.55 \pm 7.01	171.15 \pm 6.18	0.449
Weight (Kg)	75.15 \pm 14.14	73.85 \pm 14.74	0.777
BMI	26.27 \pm 4.72	24.90 \pm 4.18	0.336
ASA			>0.999
I	13(65.0%)	13(65.0%)	
II	7(35.0%)	7(35.0%)	
Intraoperative fentanyl (μ g)	239.15 \pm 86.42	209.30 \pm 52.32	0.194
Intraoperative remifentanyl (mg)	36.54 \pm 8.73	36.55 \pm 6.95	0.998
Duration of surgery (min)	54.10 \pm 12.92	50.50 \pm 15.21	0.425
Postoperative total PCA fentanyl (μ g)	4.15 \pm 4.6	2.05 \pm 2.63	<0.001*

*There was significant difference between ropivacaine alone (R) group and ropivacaine with dexmedetomidine (RD) group.: patient-controlled analgesia.

Figure 1- Ropivacaine with dexmedetomidine (RD) group had statistically significant lower postoperative pain scores than ropivacaine alone (R) group at all measured time points in the first 24 hours postoperatively. NRS: numerical rating scale.

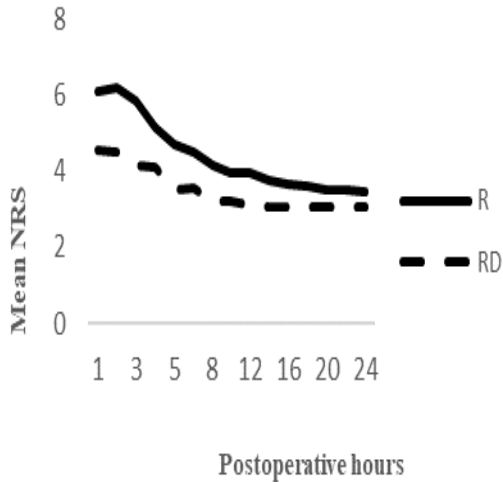


Figure 2- Mean consumption of patient-controlled analgesia (PCA) fentanyl in the second and third hours after surgery was significantly higher in the ropivacaine alone (R) group than in the ropivacaine with dexmedetomidine (RD) group

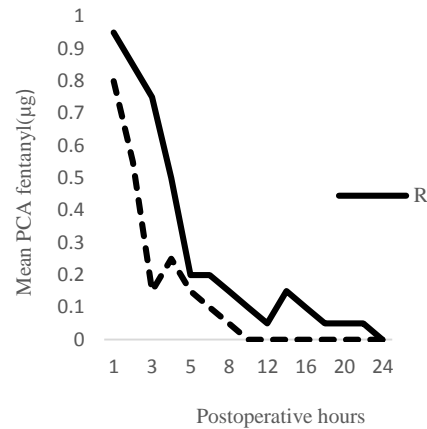


Figure 3- Postoperative mean systolic blood pressure (SBP) and heart rates (HR) were significantly lower in the RD group than in the R group at all measured time points within the first postoperative 24-h. Rh: HR in ropivacaine alone group. Rb: SBP in ropivacaine alone group. RDh: HR in ropivacaine with dexmedetomidine group. RDb: SBP in ropivacaine with dexmedetomidine group.

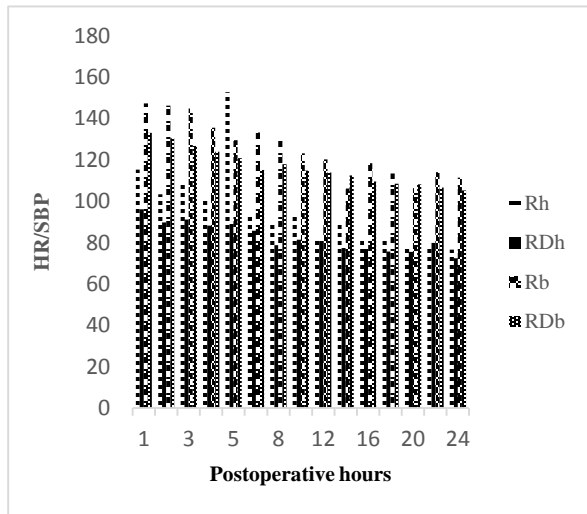
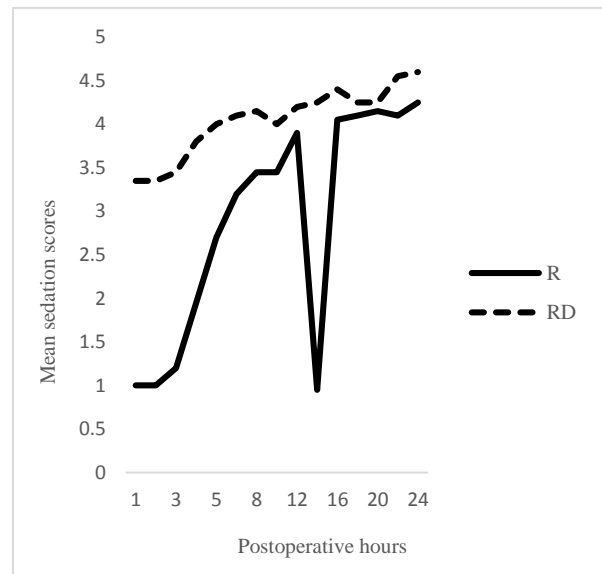


Figure 4- Postoperative mean Ramsay sedation scores in the first 12 hours and at 16th and 22th hours after surgery was significantly higher in the ropivacaine with dexmedetomidine (RD) group compared to ropivacaine alone (R) group.



Discussion

According to the results of the present study, addition of 1 µg/kg of dexmedetomidine to ropivacaine 0.5% in the ultrasound-guided block of saphenous nerve significantly decreased the pain intensity and opioid

usage in the first 24 hours after ACLR surgery compared to ropivacaine alone and without any adverse effects.

The saphenous nerve is the largest cutaneous branch of the femoral nerve. It separates from the femoral nerve in the proximal third of the thigh and descends with the femoral artery in the adductor canal between the sartorius and gracilis muscles in the anterior thigh [12].

The ultrasound-guided blockade of saphenous nerve in the middle of thigh has been suggested as an alternative to femoral block in the treatment of pain after knee surgery while it lacks the disadvantage of quadriceps strength impairment associated with the femoral block [2,4-5]. Moreover, blockade of the infrapatellar branch of the saphenous nerve can be achieved with SNB that is beneficial for pain relief after knee joint procedures [13].

Perineural injection of dexmedetomidine as an adjuvant to LA seems to improve the effect of local anesthetics in peripheral nerve blocks. Analgesic effects of dexmedetomidine have been centrally mediated at the cerebral and spinal levels through an α_2 -receptor mechanism [14]. Several mechanisms have been proposed for the perineural effect of dexmedetomidine; One mechanism is that perineural dexmedetomidine prolong hyperpolarization of the nerve membrane and potentiate sensory analgesia. The other mechanism is an alpha-2 receptor inhibitory effect which decreases release of norepinephrine and lower the action potentials of nerve fibers and results in analgesia [10]. The study by Anderson et al. [8] supports the peripheral mechanism of perineural dexmedetomidine. They showed that perineural coadministration of dexmedetomidine and ropivacaine significantly prolong saphenous nerve block by a peripheral mechanism.

Most published studies have evaluated the effectiveness of adding dexmedetomidine to a LA in the brachial plexus blockade [15-19]. In the lower extremity, a significant number of studies have examined the perineural efficacy of dexmedetomidine in femoral nerve block for pain management after knee procedures. To our knowledge, there is only the study of Thapa et al. [20] that investigated the analgesic efficacy of perineural dexmedetomidine in ultrasound guided SNB after ACLR. Contrary to our results, that study showed that adding dexmedetomidine 0.5 $\mu\text{g}/\text{kg}$ to ropivacaine 0.5% had no impact on postoperative total morphine use and pain scores compared to ropivacaine alone during the first 24 hours following ACLR surgery. Their findings may be due to a lower dose of dexmedetomidine as compared to our study. In the study by Oritz-Gomez et al. [21], adding 100 μg dexmedetomidine as perineural adjuvant to levobupivacaine 0.375% resulted in similar effective pain relief and decreased rescue analgesic requirements in both femoral and adductor canal blocks after total knee arthroplasty. Sharma et al. [22] showed a similar finding in which addition of dexmedetomidine to ropivacaine in the femoral nerve block improve the quality and provide a longer duration of analgesia after total knee replacement surgery.

Some authors showed a dose-dependent increase in the duration of postoperative analgesia by adding dexmedetomidine to ropivacaine in a nerve block. Abdulatif et al. [23] assessed three different doses of perineural dexmedetomidine along with 0.5%

bupivacaine in ultrasound-guided femoral nerve block for pain control after arthroscopic knee surgery. According to their results, 75 and 50 μg of dexmedetomidine significantly shortened the block onset time, prolonged the duration of postoperative analgesia, and reduced postoperative morphine usage compared with 25 μg dose of dexmedetomidine. They concluded that 75 μg dexmedetomidine provided the best analgesia but was associated with increased risk of hypotension. Likewise, Packiasabapathy et al. [24] found that dexmedetomidine prolongs duration of femoral nerve block in a dose-dependent manner. They compared 2 $\mu\text{g}/\text{kg}$ and 1 $\mu\text{g}/\text{kg}$ dexmedetomidine as adjuvant to 0.25% bupivacaine and bupivacaine alone for pain after total knee replacement surgery. They showed significant lower pain scores and longer duration of analgesia with the higher dose of dexmedetomidine within 24 hours after surgery whereas postoperative morphine consumption was similar with both doses of dexmedetomidine. However, no significant side effects were detected with the two dosages. They also showed that adding dexmedetomidine is significantly superior to bupivacaine alone for postoperative pain relief.

The limitation of our trial was that we could not continue pain assessment for 48-72 hours after surgery due to staff shortages, and therefore, we could not evaluate the duration of postoperative analgesia in the two groups. We recommend that perineural dexmedetomidine in SNB for post-ACLR pain relief be further investigated in future studies.

Conclusion

In conclusion, perineural administration of 1 $\mu\text{g}/\text{kg}$ of dexmedetomidine as an adjuvant to 0.5% ropivacaine for ultrasound guided SNB significantly reduced pain scores and opioid requirements in the first 24 h after ACLR surgery compared to ropivacaine alone without any significant side effects.

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