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## Single shot “3-in-1” femoral nerve blockade with 0.25% or 0.375% levobupivacaine provides similar postoperative analgesia for total knee replacement

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**Aim:** To compare postoperative analgesia provided by single shot “3-in-1” femoral nerve blockade using 0.25% or 0.375% levobupivacaine in preceding with spinal anesthesia for unilateral total knee replacement surgery.

**Materials and methods:** Forty consenting patients undergoing unilateral total knee arthroplasty were included in this prospective randomized study. Spinal anesthesia was achieved with 15 mg plain bupivacaine at the L3-4 or L4-5 interspace. After resolution of the spinal anesthesia, patients were randomized into 2 groups: “3-in-1” femoral nerve blocks were performed using 30 mL of 0.25% levobupivacaine (Group 1, n = 20) or 0.375% levobupivacaine (Group 2, n = 20). Pain was assessed by visual analogue scale (VAS). The total morphine consumption and the side effect profile were compared during the postoperative period.

**Results:** There were no significant differences between the 2 study groups with respect to characteristics or intraoperative variables. Furthermore, sensory block periods and time to first pain sensation, VAS, and morphine consumption for 24 h (Group 1: 19.7 ± 9.2, Group 2: 20.6 ± 12.1 mg) were similar. Pain scales and range of motion during rehabilitation period and side effects were also comparable.

**Conclusion:** Our results indicate that the augmenting concentration did not influence the clinical outcome when single shot “3-in-1” femoral nerve block was performed with 0.25% or 0.375% levobupivacaine in total knee arthroplasty.

**Key words:** Anesthetic techniques, regional, femoral nerve block, pain, postoperative, levobupivacaine

### Postoperatif analjezide % 0,25 veya % 0,375 levobupivakain ile tek doz 3'e 1 femoral sinir blokajı total diz protezi operasyonunda benzer analjezi sağlar

**Amaç:** Bu çalışmada tek taraflı total diz protezi cerrahisinde spinal anesteziyi takiben % 0,25 veya % 0,375 levobupivakain kullanılarak yapılan 3 e 1 femoral sinir bloğunun etkinliğinin karşılaştırılması amaçlandı.

**Yöntem ve gereç:** Çalışmaya tek taraflı elektif diz cerrahisi geçirmesi planlanan onamı alınmış kırk hasta dahil edildi. Spinal anestezi 15 mg düz bupivakain kullanılarak L3-4 veya L4-5 seviyesinden gerçekleştirildi. Spinal anestezinin ortadan kalkmasından sonra hastalar randomize olarak iki gruba ayrıldı: 3 e 1 femoral blok 30 mL % 0,25 levobupivakain (Grup 1, n = 20) veya % 0,375 levobupivakain (Grup 2, n = 20) kullanılarak gerçekleştirildi. Ağrı Vizüel Analog Skala (VAS) ile değerlendirildi. Postoperatif dönemde total morfin tüketimi ve yan etkiler belirlendi.

**Bulgular:** Her iki grup arasında hasta özellikleri veya intraoperatif değişimler açısından belirgin bir farklılık saptanmadı. Bundan öte, duyu bloğu süresi, ilk ağrı duyumu, VAS ve ilk 24 saatlik morfin tüketimi (Grup 1: 19,7 ± 9,2, Grup 2: 20,6 ± 12,1 mg) benzerdi. Ağrı skalaları, rehabilitasyon sırasındaki hareket genişliği ve yan etkiler benzerdi.

**Sonuç:** Bulgularımız % 0,25 veya % 0,375 levobupivakain kullanılarak yapılan tek doz 3 ü 1 yerde femoral sinir blokajında konsantrasyon artışının klinik sonucu etkilemediğini gösterdi.

**Anahtar sözcükler:** Anestezi teknikleri, rejyonel, femoral sinir bloğu, ağrı, postoperatif, levobupivakain

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## Introduction

Pain is one of the major contributors to morbidity in total knee replacement (TKR) surgery. Postoperative pain is considered to be severe and difficult to decrease with oral medications (1). Postoperative analgesia may influence the outcome including blood loss during this period (2), or quality of life (3). It has also been demonstrated that epidural analgesia may contribute to lower incidence of death after surgery (4).

Numerous methods are implicated to decrease pain in the postoperative period. Peripheral nerve blocks are widely accepted due to lower complication rates, and they provide efficient long-term analgesia during both for the operation and the postoperative period. They also offer earlier ambulation with shorter hospital stay (5,6). Femoral nerve block (FNB) is associated with lower side effects when compared with intravenous morphine and epidural analgesia (7,8). It was also demonstrated that FNB, when added to the epidural analgesia, significantly improved analgesia for 2 days (9). Continuous FNB offers the advantages of less nausea and vomiting but has higher analgesic consumption than with continuous epidural analgesia (10).

Although rare, serious complications might be detected with peripheral nerve blocks due to the requirement of high volume of local anesthetic solutions. Cardiovascular complications might be observed with accidental vascular entry during drug disposition or rapid absorption from the injected site. When compared to the racemic form, intravenous levobupivacaine has been demonstrated to produce significantly less effects on cardiovascular function including negative inotropic effect in particular (11). On the other hand, the optimal concentration of levobupivacaine for FNB has never been determined in patients undergoing total knee arthroplasty for postoperative analgesia.

This study aimed to compare postoperative analgesia of single shot "3-in-1" FNB using 0.25% or 0.375% levobupivacaine in combination with spinal anesthesia for unilateral TKR surgery in order to determine the optimal initial levobupivacaine concentration for bolus dose.

## Materials and methods

After obtaining approval from the local ethics committee and written informed consent, 40 American Society of Anesthesiologists (ASA) class I and II adult patients undergoing knee arthroplasty were enrolled in the study. Exclusion criteria were patient refusal, age < 18 years or > 85 years, body mass index over 45 kg/m<sup>2</sup>, infection at the injection site, coagulation disorders or therapy, pre-existing neurological disorder involving a lower extremity, sepsis and any systemic illness that corresponds to ASA class III or more. The study protocol, randomization procedure, pain control, and assessments were explained at least 1 day before the operation during the preoperative visit. Patients were randomly assigned into 2 groups using sealed envelopes chosen before the operation.

Patients were monitored with ECG and peripheral O<sub>2</sub> saturation continuously, and non-invasive arterial blood pressure was determined and recorded every 5 min during the perioperative period and in the recovery (Cardicap 5 Datex-Ohmeda, Helsinki, Finland). A large bore cannula was inserted to the peripheral vein and pre-hydration with crystalloid solution was started with a dose of 10 mL kg<sup>-1</sup> administered within 15 min. Spinal anesthesia was performed using 15 mg plain bupivacaine at L<sub>3-4</sub> or L<sub>4-5</sub> interspace with 25 gauge pencil-point needle (B. Braun; Melsungen, Germany). After resolution of the spinal anesthesia, which was assessed with pinpricks during the recovery period, FNBs were performed for postoperative analgesia.

The insertion point was classically determined as 1 to 1.5 cm lateral to the pulsation of the femoral artery and just below the iliac crest using a short beveled 5 cm long Stimuplex cannula (B. Braun; Melsungen, Germany). Drug dilutions with labeled syringes were prepared immediately before the surgery in the Pharmacy Department. A peripheral nerve stimulator was attached to the cannula with settings at 2 Hz and pulse width of 0.1 s. While contractions in the quadriceps femoris muscle were still elucidated under 0.5 mAmp with a nerve stimulator (HNS 11., B. Braun Melsungen, Germany), 30 mL of either 0.25% levobupivacaine (Group 1, n = 20), or 0.375% levobupivacaine (Group 2, n = 20) was injected with increments and gentle aspirations. The

success of the block was determined with pain sensation using pinpricks at the distribution area of all nerves and muscle strength according to ability to raise the leg. Insufficient analgesia to the pinpricks or no change in motor strength in the 30 min observation period was accepted as failed block and excluded from further analysis.

Pain was assessed with a standard plastic scale according to the patient's expression defined as Visual Analogue Scale (VAS), from 0 = no pain to 100 = worst imaginable pain determined at 4 h intervals on the first postoperative day. Pain during passive movements were also determined and assessed during physiotherapy.

Patient-controlled analgesia (PCA) device (Provider, Abbott, Chicago, USA) was attached to the peripheral vein with a stopcock and set at 1 mg morphine with 5-min lockout interval. Total morphine consumption and the side effect profile were compared for 48 h and assessed every 4 h. Analgesia in the postoperative period was provided with a PCA device. Analgesic requirements, time to first analgesic, and sum of the analgesics were recorded for both study groups. Time to first analgesic was determined as first analgesic requirement with PCA from 3-in-1 block noted by the patient or relatives. Analgesia and analgesic requirements were assessed every 4 h.

Our preliminary study and power analysis failed to determine any difference in morphine consumption and pain scale during the postoperative period. We, therefore, limited the number of subjects to 20 patients in each group. Demographic data were compared with  $X^2$  test. Nominal data, such as morphine consumption, were evaluated with one-way analysis of variance (ANOVA), and paired-t tests were used for statistical comparison. Ordinal data including pain scores were determined using Mann-Whitney U tests. Data were expressed as mean  $\pm$  SD and P value was considered as 0.05 for statistical significance.

## Results

Demographic characteristics of the study groups were the same, and there was no statistically significant difference ( $P > 0.05$ ). Moreover, tourniquet times, duration of surgery, time in recovery, and length of hospital stay were all similar ( $P > 0.05$ , Table 1).

Vital signs were stable throughout the operation and no medication was required. Analgesia was obtained from the distribution area of the nerves in all patients.

Times to first pain and rescue analgesic were similar between the study groups. There was also no

Table 1. Patients' characteristics, surgical data, and length of stay, (mean  $\pm$ SD).

	Group 1 (n = 20)	Group 2 (n = 20)	P
Age (year)	65.7 $\pm$ 8.1	62.0 $\pm$ 5.7	0.12
Weight (kg)	76.4 $\pm$ 11.0	81.1 $\pm$ 14.5	0.28
Height (cm)	159.3 $\pm$ 4.7	156.3 $\pm$ 6.7	0.19
Gender (F/M)	18 / 2	18 / 2	1.0
ASA class (I/II)	6 / 14	4 / 16	0.71
Tourniquet time (min)	63.7 $\pm$ 13.8	65.9 $\pm$ 16.3	0.18
Duration of surgery (min)	89.3 $\pm$ 10.9	83.7 $\pm$ 19.1	0.20
Time in recovery (min)	78.6 $\pm$ 25.3	81.4 $\pm$ 28.9	0.26
Length of stay (days)	3.9 $\pm$ 2.1	3.6 $\pm$ 2.4	0.61

ASA: American Society of Anesthesiology.

significant difference between morphine consumption after 12, 24, and 48 h periods (Table 2.). Pain scales during postoperative were comparable and no significant difference was determined during the observation period (Figure 1). No statistically significant difference between pain scores assessed with VAS during passive movement at the 6 h, 12 h, 24 h and 48 h time points (Figure 2).

Side effects in the postoperative period were similar ( $P > 0.05$ ). Mild nausea was observed in 3 patients in Group 1 and 4 patients in Group 2, which did not require medication. Mild itching was seen in 2 patients in Group 1 and 1 patient in Group 2, and also subsided without treatment.

No patients had residual numbness, dysesthesia, or weakness associated with spinal anesthesia or FNB.

### Discussion

In the present study, there was no significant difference between postoperative pain scores with 3-in-1 femoral nerve block using 0.25% or 0.375% levobupivacaine after TKR surgery. Morphine consumption, functional outcome and side effect profile between the study groups were also comparable. The possible outcome of our results is more important in the patients with comorbidities by limiting the dose requirements.

Ng et al. (12) demonstrated that there were no significant differences in postoperative pain scales and analgesic consumptions between 0.25% and 0.5% ropivacaine with 0.25% bupivacaine during intraoperative single shot 3-in-1 FNB in TKR surgery. According to the current literature, there is no study

Table 2. Time to first pain, analgesic and morphine consumption in the postoperative period (mean  $\pm$ SD).

	Group 1 (n = 20)	Group 2 (n = 20)	P
Time to first pain (min)	322.3 $\pm$ 126.7	296.2 $\pm$ 69.6	0.23
Time to first analgesic (min)	349.7 $\pm$ 142.9	338.3 $\pm$ 56.1	0.54
Morphine consumption (mg)			
12 h	6.9 $\pm$ 4.7	6.4 $\pm$ 5.6	0.49
24 h	19.7 $\pm$ 9.2	20.6 $\pm$ 12.1	0.57
48 h	29.9 $\pm$ 13.4	31.3 $\pm$ 16.8	0.31

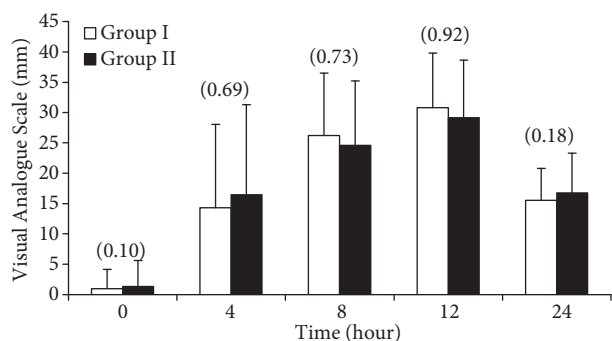


Figure 1. Postoperative pain during rest assessed with visual analogue scale, (p).

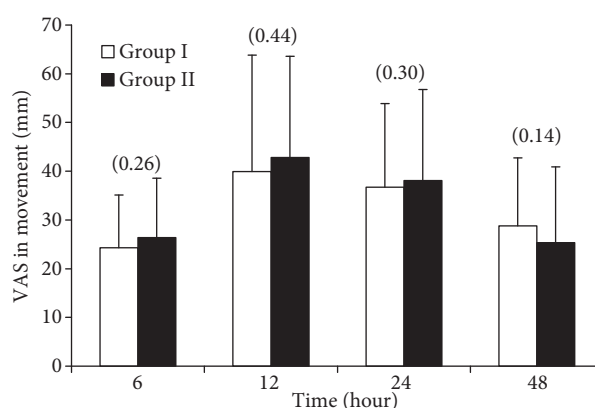


Figure 2. Visual analogue scale (VAS) in passive movement, (p).

comparing the different concentrations of levobupivacaine for postoperative analgesia using the same surgical model. Levobupivacaine has been largely accepted as a safe drug when compared to the racemic form. However, the potential of dose- and concentration-dependent nerve injury or myonecrosis has been implicated (13). Therefore, increasing the concentration is not recommended due to limited efficacy and to prevent potential complications.

When compared to the central neuroaxial blocks, contraindications of peripheral nerve blocks are rare due to lacks of hemodynamic side effects. The incidence of complication rate has also been found to be lower than general anesthesia and neuroaxial blocks. There is a tendency to use peripheral nerve blocks especially for postoperative analgesia in TKR (14). In addition to its simplicity and safety, 3-in-1 FNB has been demonstrated to be as efficient as posterior compartment (psoas) block in total knee arthroplasty (15), without possible nerve injury (16). Although the mean pain scores during rest and physical therapy and opioid consumptions were lower with continuous FNB when compared with single injection, there was no change in the outcome of hospital stay (17). It has also been demonstrated that a single injection of FNB provides equivalent analgesia with a reduction in side effects when compared with intrathecal morphine administration (18). We also recommend this safe technique using levobupivacaine in order to decrease morphine consumption at lower concentration. The combination of regional techniques and parenteral drugs with potentially fewer side effects might be an optional solution for pain therapy in TKR surgery (1).

Femoral and sciatic catheter is superior to femoral and psoas catheter with respect to reduced analgesic requirements; however, functional outcomes did not differ from those with continuous regional analgesia techniques (19). When compared with the FNB alone, combination of continuous femoral and sciatic nerve blocks improves analgesia while decreasing morphine consumption and postoperative nausea or vomiting (20,21). Macalou et al. (22) also indicated that obturator nerve block when added to the 3-in-1 FNB provides better analgesia. However, addition of any technique results in a risk of complications and possible confusion during the pain assessment. On the other hand, our results might be useful with limiting the total local anesthetic dose when combination of peripheral nerve block is required. Levobupivacaine might reach the toxic level when the combination of posterior lumbar plexus and sciatic nerve blocks are used for TKR. Authors also emphasize the difference between absorption of local anesthetics according to the region due to the vascularity (23).

Our results indicate that increasing the levobupivacaine concentration was not effective in 3-in-1 FNB possibly due to the vascular supply of the region. It might be helpful to decrease the local anesthetic dose during combination of peripheral nerve blocks and therefore possible toxicity or complications.

## Conclusion

Our results indicate that the augmenting concentration did not influence the clinical outcome when single shot "3-in-1" FNB was performed with 0.25% or 0.375% levobupivacaine in TKR.

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