Original Article

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Effect of Preemptive Femoral Nerve Block on Pain Control and Opioid Consumption After Total Knee Arthroplasty: A Randomized Controlled Trial

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Abstract

Aim: Peripheral nerve blocks, particularly femoral nerve blocks (FNBs), are a practical choice for relieving severe pain after total knee arthroplasty (TKA). We investigated the effectiveness of preemptive FNB on postoperative pain control and the reduction of opioid consumption.

Methods: This was a single-center, prospective, randomized controlled trial conducted at a tertiary care health center, Istanbul University-Cerrahpasa, Cerrahpasa Faculty of Medicine, Turkey. The study included 40 American Society of Anesthesiologists I-III patients scheduled for elective TKA surgery. Patients were studied in two groups. The FNB group (n=20) received preemptive single-injection FNB (15 mL of prilocaine 2% and 15 mL of 0.5% bupivacaine using a peripheral nerve stimulator) before general anesthesia (GA) as the study group and the control group (n=20) received standardized GA. The primary outcome measure was pain scores evaluated as numeric pain rating scale (0-10) at 2, 4, 8, 12, 16, 18, 20, and 24 h. Secondary outcome measures included opioid consumption with patient-controlled and perioperative hemodynamic changes.

Results: Pain scores and opioid consumption in the FNB group were significantly lower than those in the control group at every measurement time ($p<0.05$). Total perioperative morphine use was also lower in the FNB group ($p=0.023$). Regarding hemodynamic variables, the heart rate values at the beginning of surgery and tourniquet insufflation in the FNB group were significantly lower than those in the control group.

Conclusion: Using the FNB as part of any multimodal analgesia protocol to alleviate pain after TKA with less analgesic use would be beneficial.

Keywords: Femoral nerve block, orthopedic anesthesia, postoperative pain, preemptive, total knee arthroplasty

Introduction

Total knee arthroplasty (TKA) is associated with severe postoperative pain (1). However, adequate postoperative pain management increases patient comfort and allows for early physiotherapy (2). Numerous techniques have evolved, including neuraxial (NA) and general anesthesia (GA), both along with peripheral nerve blocks (PNB), local infiltration anesthesia, and oral medication regimens, within the concept of multimodal analgesia (3). The abundance of analgesic options for post-TKA pain comes with the price of uncertainty in defining the ideal approach. The American Society of Regional Anesthesia and Pain Medicine and the European Society of Regional Anesthesia and Pain Therapy demonstrated that standardized pathways are not identical in Europe or North America (4).

It is essential to design institutional protocols that are adapted to routine practice. A debate still exists about whether general or NA anesthesia is superior. In a recent consensus for anesthetic management of TKA, authors compared GA vs. NA and noted that NA was associated with fewer or no complications in all reported outcomes (5). Since then, NA has been recommended

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with a low level of evidence (5). On the other hand, the practice of PNB has gained popularity, but its effects as adjuncts to GA or NA still need to be studied (6). Thus, we investigated a protocol using GA with PNB. Previous studies suggest that femoral nerve block (FNB) is efficient for postoperative pain control after TKA, either stand-alone or as a part of multimodal regimens (7,8). Preemptive multimodal analgesia protocols have been shown to improve postoperative pain control, and the addition of a preemptive FNB to them could further improve their effect (9). In addition, different local anesthetics with various doses have been studied, mostly bupivacaine, ropivacaine, and liposomal bupivacaine, along with rapid-acting lidocaine. However, a preemptive FNB protocol containing a fast-acting local anesthetic agent to gain benefit during the intraoperative period has not been studied.

Determining the possibility of reducing pain scores and the amount of perioperative morphine consumption by adding a fast-acting local anesthetic agent, prilocaine, to FNB may bring a different dimension to clinical practice. This study compared the efficacy of a single-injection preemptive femoral nerve blockade with 2% prilocaine and 0.5% bupivacaine versus the control group in postoperative pain control after TKA.

Methods

Compliance with Ethical Standards

We screened adult patients planned for TKA at the Department of Orthopedics and Traumatology to be enrolled in the study. After the ethical approval of Istanbul University-Cerrahpasa, Cerrahpasa Faculty of Medicine, Clinical Research Ethics Committee (approval number: 83045809/6447, date: 18.03.2013), within which the work was undertaken, the study was conducted according to the provisions of the 1995 Declaration of Helsinki (as revised in Brazil in 2013). All subjects in the study provided informed consent, and patient anonymity was preserved.

Study Population

Patients with ASA physical status I-III between 30 and 75 years of age were recruited for the study. Exclusion criteria included allergy to prilocaine, bupivacaine, morphine, or dexketoprofen trometamol, previous history of narcotic abuse, a pre-existing neurological deficit in the lower extremity, inability to use patient control analgesia (PCA), bleeding disorders, a local or systemic infection, patients who underwent procedures in both legs, uncontrolled hypertension or a history of severe arrhythmia, and patients with severe hepatic or renal insufficiency. All patients were preoperatively informed about the procedures and trained using the numeric pain rating scale [(NPRS) as 0 meaning no pain, 10 being the worst pain ever felt], along with a PCA pump (Bodyguard 323; pfm Medical).

Procedure

We assessed the 60 patients scheduled for TKA (Figure 1). After screening for eligibility and signing the

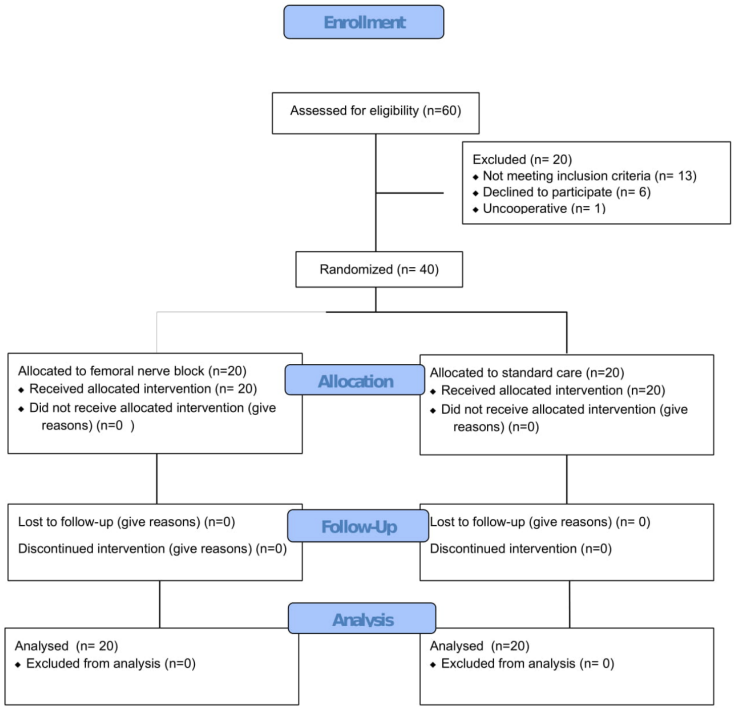

Figure 1. Consort flow diagram

informed consent form,the corresponding anesthesiologist randomized the patients using the research randomizer application with the allocation ratio 1:1 into two groups: the control group and the FNB group to receive the preemptive FNB.

Femoral nerve block was performed in the pre-operative care room under standard monitoring and according to the rules of asepsis. The femoral nerve was identified with the aid of a peripheral nerve stimulator (HNS11, B. Braun Medical Inc., Pennsylvania, USA) with confirmation of quadriceps muscle contraction (patellar dance) at 0.2-0.5 mA intervals, after which 15 mL of 2% prilocaine (Citanest; Zenica Medical) and 15 mL of 0.5% bupivacaine (Buvasin 0.5%; Vem Medical) were injected using a 50-mm needle (Simplex A-50, B. Braun Medical Inc., Pennsylvania, USA) (Figure 2). An anesthesia resident performed all blocks with at least two years of experience under the supervision of an anesthesiologist trained in regional anesthesia with electrostimulation. Fifteen minutes later, the anesthesiology attendant confirmed sensory and motor blockade using a pinprick test and the Bromage scale.

All patients (the FNB and the control group) received standardized GA with propofol (1.5-2 mg/kg), atracurium (0.5 mg/kg), sevoflurane (target 2% MAC), and morphine (0.1 mg/kg) as analgesia. If the heart rate (HR) and mean arterial pressure (MAP) raised over 20% of the baseline values (values measured at the entry of the surgical room) of the patient, we administered 2 mg of IV morphine (with a maximum value of 0.1 mg/kg morphine). At the end of the surgery, residual neuromuscular block was reversed with atropine (0.01 mg/kg) and neostigmine (0.02 mg/kg). All patients included in the study were operated on by the same surgical team using the same surgical technique.

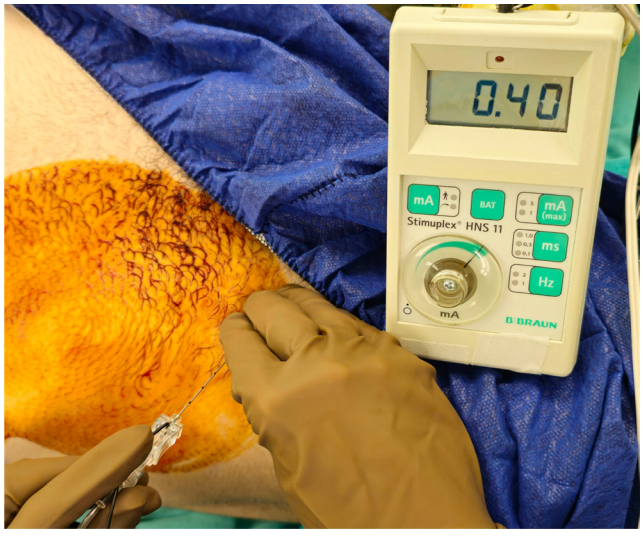

Figure 2. The femoral nerve block procedure

All patients received IV PCA pumps postoperatively for 24 hours. Patient control analgesia solution was prepared as 100 mg of morphine in 100 mL of isotonic saline. The device was set to administer a bolus dose of 1 mg on demand, with a lockout period of 7 minutes. In addition, all participants received 50 mg of dexketoprofen and trometamol (two per day, intravenous) until discharge from the hospital.

Data Collection

Patients were followed at the orthopedic post-anesthesia care unit (OPACU) for 24 hours, and all data were collected at the OPACU, from time "0" as entry to the postoperative 24th hour as discharge from the OPACU (0-4-8-12-16-20-24 hours). Data were collected by an orthopedic ward nurse blind to patient randomization.

The primary outcome measure was the pain score (NPRS) (0-10), evaluated at predetermined intervals. Secondary outcome measures included the total amount of opioid consumed via PCA (in mg), perioperative hemodynamic changes, the development of side effects, and complications.

Patient control analgesia values were recorded separately as demand and delivery (the demanded number is the total amount of patient requests; the delivery number is the total amount of drugs given, limiting patient requests with the lockout setting). We also saved the perioperative total amount of morphine usage.

Intraoperative hemodynamic data (HR, systolic, and diastolic blood pressures) were collected at admission to the surgical room, induction of anesthesia, intubation, tourniquet insufflation, beginning of the surgery, tourniquet deflation, and extubation.

We evaluated side effects using a questionnaire filled out by a nurse blinded to the groups. The questionnaire investigated the following items: the presence of nausea or vomiting, pruritus, sedation (with the Modified Observer's Assessment of Alertness and Sedation scale), respiratory depression (<8), hypotension (MAP<65), urinary retention, and signs of local anesthetic toxicity (circumoral or tongue numbness, metallic taste, lightheadedness, and visual and auditory disturbances).

The presence of motor blockade was assessed using the Bromage score; we evaluated sensory and motor deficits on the third postoperative day before hospital discharge and observed any quadriceps weakness or falls at the first physiotherapy session (24 hours postoperatively) before discharge from OPACU.

Statistical Analysis

We used the clinical sample size calculator (https://clincalc.com/stats/samplesize.aspx) to calculate the sample size. After examining previous studies, as in Szczukowski

et al. (8), we calculated a sample size of 18 patients per group with alpha equal to 0.05 (two-sided) and a power of 0.80. We increased our sample size to 20 patients per group to compensate for possible dropouts. Statistical analyses were performed using the Number Cruncher Statistical System 2007 and Power Analysis and Sample Size 2008 Statistical Software (Utah, USA). Descriptive statistical methods (average, standard deviation, median, frequency, ratio, minimum, maximum), Student's t-test (for the two-group comparisons of parameters showing a normal distribution), and Mann-Whitney U test (for two-group comparisons of parameters that did not show a normal distribution) were used. Significance was evaluated at $p<0.01$ and $p<0.05$ levels.

Results

We screened sixty patients and enrolled forty, all of whom completed the study protocol. There were no differences between the groups regarding demographic data, duration of surgery, or tourniquet time (Table 1). The weight and height values of the intervention group were higher than those of the control group, but the body mass index values showed no statistical difference.

The NPRS values of the femoral group at each control hour for 24 hours were significantly lower than those of the control group. A statistically significant difference was found at all hours between the NPRS measurements of the patients according to the groups (Figure 3).

Morphine consumption with PCA in the femoral group at each control hour for 24 hours was significantly lower than that in the control group. A statistically significant difference between the groups was found, except in the 0th hour. Likewise, the total morphine used perioperatively was significantly lower in the FNB group (p=0.023) (Table 2).

There were no significant changes in the blood pressure values for intraoperative hemodynamic variables. However, we found statistically significant differences between the patients' HR values at the beginning of surgery and tourniquet insufflation (p=0.036, p=0.011). The HR values at the beginning of surgery and tourniquet insufflation in the intervention group were significantly lower than those in the controls. Moreover, although HR values at extubation were not statistically different, they were remarkably lower in the femoral group (p=0.073) (Table 3).

Table 1. Demographic data

	Group A	Group B	p-value
	Mean ± SD	Mean ± SD	
Age (year)	67.50±6.66	61.85±11.80	**0.070**
ASA	2.10±0.55	1.90±0.45	**0.216**
Weight (kg)	83.40±11.50	72.80±15.53	**0.019***
Height (cm)	162.45±7.96	156.95±8.65	**0.043***
BMI	31.74±4.91	29.63±6.03	**0.234**
Duration of surgery (minute)	130.00±32.44	140.50±50.57	**0.439**
Tourniquet time (minute)	115.15±23.60	104.65±21.52	**0.150**

Student's t-test, *p<0.05
ASA: American Society of Anesthesiologists, BMI: Body mass index, SD: Standard deviation

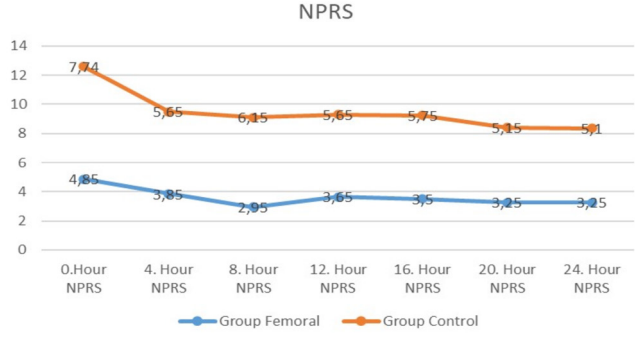

Figure 3. Numeric pain rating scale values

Table 2. Morphine consumption

	Group A	Group B	p-value
	Mean ± SD (Median)	Mean ± SD (Median)	
Total morphine 0. hour	1.65±1.46 (1.0)	2.70±1.98 (2.0)	**0.069**
Total morphine 4. hour	5.15±4.60 (4.5)	9.20±7.18 (6.5)	**0.010***
Total morphine 8. hour	6.75±4.99 (5.0)	12.45±7.69 (10.0)	**0.004****
Total morphine 12. hour	8.10±5.58 (7.0)	15.00±8.77 (13.0)	**0.005****
Total morphine 16. hour	9.65±6.39 (8.0)	17.50±9.93 (15.5)	**0.005****
Total morphine 20. hour	11.65±8.12 (10.0)	21.55±11.12 (19.5)	**0.003****
Total morphine 24. hour	15.65±11.38 (13.0)	24.95±12.64 (22.0)	**0.023***
Peroperative morphine (mg)	15.65±11.38 (13.0)	24.95±12.64 (22.0)	**0.023***

Mann-Whitney U test, *p<0.05, **p<0.01
SD: Standard deviation

Table 3. Heart rate values			
	Group A	Group B	p-value
	Mean ± SD	Mean ± SD	
HR entrance	80.85±14.88	86.45±15.89	0.257
HR induction	77.60±14.77	83.85±14.40	0.183
HR entubation	77.65±11.82	85.42±13.41	0.062
HR tourniquet insufflation	70.35±11.11	81.45±15.02	0.011*
HR surgical beginning	71.30±11.88	80.65±15.09	0.036*
HR tourniquet desufflation	74.40±12.77	82.65±17.24	0.093
HR extubation	81.05±16.31	89.80±13.61	0.073

Student's t-test, *p<0.05
SD: Standard deviation, HR: Heart rate

No side effects or complications developed in any patient in either group. In addition, none of the patients, including the femoral group, fell due to quadriceps weakness.

Discussion

Our study demonstrates that NPRS values and morphine consumption in patients submitted to FNB after TKA decreased compared with controls. We also demonstrated less hemodynamic variability during induction and tourniquet insufflation in the femoral group.

Similarly, Wang et al. (10) studied a single dose of FNB but used 40 mL of 0.25% bupivacaine differently and applied it to 15 patients after surgery. Szczukowski et al. (8) used 30 mL of 0.5% bupivacaine plus epinephrine (1:200,000) and performed the block preoperatively. Both had similar results with lower visual analogue scale scores, concluding that single-injection FNB is effective for postoperative analgesia and early ambulation. Unlike previous studies, we added a fast-acting local anesthetic to the FNB application and thus provided intraoperative analgesia and hemodynamic stability.

Different multimodal analgesia protocols are available for TKA (3,4). However, timing seems to play an important role, and the effect of preemptive analgesia should not be underestimated. Preventing central sensitization can improve postoperative analgesia and reduce the risk of persistent postoperative pain (1). Furthermore, preemptive use of PNB attenuated the surgical-induced stress response, resulting in lower pro-inflammatory cytokine levels (IL-6), better cardiovascular stability during surgery, and improved postoperative pain control (11).

The contribution of FNB to post-TKA pain relief is not devoid of controversy. While motor blockage and sensory block contribute to pain relief with resolved postoperative quadriceps muscle spasms, they may also lead to muscle weakness (12). However, we did not encounter such an effect in our study. Moreover, several meta-analyses have compared an alternative sole sensory block, the adductor canal block (ACB), with FNB. They suggested equal analgesia, better ambulation, and faster recovery with ACB (13). However, other randomised controlled trials (RCTs) failed to show significant differences in ambulation with preserved quadriceps strength at each block (14,15). Besides, a few cases exist in the literature showing that ACB can result in significant quadriceps muscle weakness, and its technique mandatorily requires ultrasonography (USG) (6,16).

Although it results in prolonged analgesia, we did not choose a continuous FNB technique (17). Our main concerns were infection, prolonged muscle weakness, and technique skill (6,18); therefore, we chose a single-injection FNB and searched for methods to improve its effects within preemptive and multimodal analgesia.

Trained physicians capable of using USG and the technology itself were limited. USG has been the standard tool for peripheral nerve blockage; however, the use of a concurrent nerve stimulator is advised (19). Our study has the disadvantage of using only a nerve stimulator. However, using this technique may increase the effectiveness of FNBs, especially when the possibilities are limited. It should be noted that the nerve stimulator can be used as a physiological monitoring device while applying nerve blocks. As the American Society of Regional Anesthesia recently advised, combining USG with a nerve stimulator would ensure safer clinical practice, and recent studies seem to appreciate it (20,21).

Multimodal analgesia protocols are essential for enhanced recovery after surgery in patients undergoing total joint arthroplasty (22). These protocols consist of PNB and non-opioid drug combinations with the target of reducing perioperative opioid consumption, as demonstrated in our study. The amount of opioids used has been emphasized for the quality of patient care because higher amounts are directly related to postoperative chronic opioid use in patients undergoing TKA (23).

Study Limitations

Our study has some limitations. We could only follow the patients until discharge on postoperative day 3. In addition, we could not note pain scores during physiotherapy sessions. Rebound pain could also be evaluated in the femoral group, but the concept is relatively new. RCTs with a long-term follow-up of up to 3 months after surgery could be valuable to evaluate persistent postsurgical pain and possible rebound pain related to PNBs (24). Despite these limitations, the study's strength is presenting a traditional FNB block as a cost-effective, practical protocol based on the preemptive use of the moderate and long-acting local anesthetic combination, concluding both intraoperative

and postoperatively better outcomes. Future research must explore variations in effective multimodal protocols to ensure analgesia and ambulation without ignoring cost-effectiveness, practicality, and patient satisfaction.

Conclusion

Our study showed that FNB efficiently managed pain after TKA. We demonstrated that a single-injection FNB is adequate and can be reinforced with elements of preemptive and multimodal analgesia protocols. Selecting a local anesthetic mixture with different time intervals of action could potentiate favor perioperatively.

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Ethics

Ethics Committee Approval: This study was approved by the Istanbul University-Cerrahpasa, Cerrahpasa Faculty of Medicine, Clinical Research Ethics Committee (approval number: 83045809/6447, date: 18.03.2013), within which the work was undertaken, the study was conducted according to the provisions of the 1995 Declaration of Helsinki (as revised in Brazil in 2013).

Informed Consent: All subjects in the study provided informed consent, and patient anonymity was preserved.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: B.C., E.O.U., Concept: B.C., S.K., Design: B.C., E.O.U., S.K., Data Collection or Processing: B.C., Analysis or Interpretation: B.C., Literature Search: B.C., Writing: B.C.

Conflict of Interest: The authors have no conflicts of interest to declare.

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