Ultrasound-Guided 4 in 1 Block in Knee Surgery – An Observational Clinical Trial

Original Article

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ABSTRACT

Backgrounds: In this study, we aimed to investigate the effect of 4 in 1 block technique, which provides blockage of the saphenous, obturator, sciatic and the nerve to vastus medialis with a single injection without the need for position change, on postoperative analgesia in knee surgeries.

Our study was conducted in an observational, comperatively prospective study. A total of 62 patients who underwent knee surgery under spinal anesthesia were included in our study. In the recovery unit, they were divided into two groups according to the analgesia method; 4 in 1 block group and control group without any block. In the postoperative period, 2nd, 4th, 6th, 12th, 24th visual analog score (VAS), sensory block, rescue analgesics, quadriceps strength at 12th and 24th hours were questioned.

Results: The VAS value at the 2nd, 4th, 6th and 12th hours was found to be significantly lower in the block group compared to the control group. In terms of side effects, nausea-vomiting was low in the block group. A total of 10 of 16 patients with nausea were in the control group, and 4 patients with vomiting, and 1 patient with sedation were also in this group.

Conclusions: We observed that 4 in 1 block is effective on postoperative analgesia, reduces opioid consumption and related side effects in knee surgery. We believe that it can be used effectively as a part of multimodal analgesia in knee surgeries.

Key Words: 4 in 1 block, Knee surgery, Opioid, Postoperative pain, Visual analog scale.

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BACKGROUND

Today, there is an increase in knee surgeries such as total knee arthroplasty, arthroscopic anterior cruciate ligament and meniscus repair. Inadequate pain management may lead to cardiac, pulmonary or renal problems, endocrine, metabolic and inflammatory responses, which may lead to increased perioperative morbidity and mortality[1].

It is not possible to provide effective postoperative pain management with a single analgesic method. Therefore, multimodal analgesia methods have been developed. These methods may include oral and intravenous nonsteroidal anti-inflammatory drugs (NSAIDs), intravenous opioids, intra-articular local anesthetic applications, central and peripheral nerve blocks. It is aimed to provide better analgesia with the appropriate combination of these methods[2-5]. Central blocks have serious side effects such as motor block, urinary retention, hypotension, nausea and vomiting[6]. Due to these side effects, the application of peripheral nerve blocks has increased in recent years. Today, with the use of peripheral nerve blocks accompanied by ultrasound (US), complications are greatly reduced and effective anesthesia and analgesia are provided even in low volumes[7,8]. The most commonly used peripheral blocks for knee surgeries can be said femoral nerve block, sciatic nerve block, obturator nerve block, lateral femoral cutaneous nerve block, adductor canal block, IPACK block, and the combinations of these blocks[9].

There are some studies reporting that the newly defined ultrasound-guided (USG) 4 in 1 block provides blockage of the saphenous nerve, obturator nerve, sciatic nerve and the nerve to vastus medialis with a single injection in the supine position without the need for position change in knee surgeries[10-12]. In this study, we aimed to comparatively investigate the effect of US-guided 4 in 1 block technique on postoperative analgesia in knee surgeries.

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METHODS

For this prospective, observational study, approval was obtained from the Health Sciences University Kocaeli Derince Training and Research Hospital Clinical Research Ethics Committee on 14.01.2021 with the file approval number 2020-173. The patients were informed before the study and an informed consent form was signed. Clinical Trials No: Health Sciences University Kocaeli Derince Training and Research Hospital Clinical Research Ethics Committee. (https://clinicaltrials.gov/ct2/show/Health Sciences University Kocaeli Derince Training and Research Hospital Clinical Research Ethics Committee) (registration date; February 16, 2021).

A total of 62 patients who would undergo elective knee surgery under spinal anesthesia were included in the study. Inclusion criteria were determined as patients aged 18-80 years, with ASA I-II score, who were informed about the study in the preoperative period, volunteered to participate in the study, and whose informed consent was obtained.

Patients requiring intensive care with ASA III-IV score, under the age of 18 and over the age of 80, receiving general anesthesia, pregnant or breastfeeding,with emergency surgery, having a history of local anesthetic or analgesic allergy, with bleeding diathesis and infection in the area to be blocked in which regional interventions are contraindicated, with neurologic deficit in the same leg, and those who did not agree to participate in the study were not included (Figure 1).

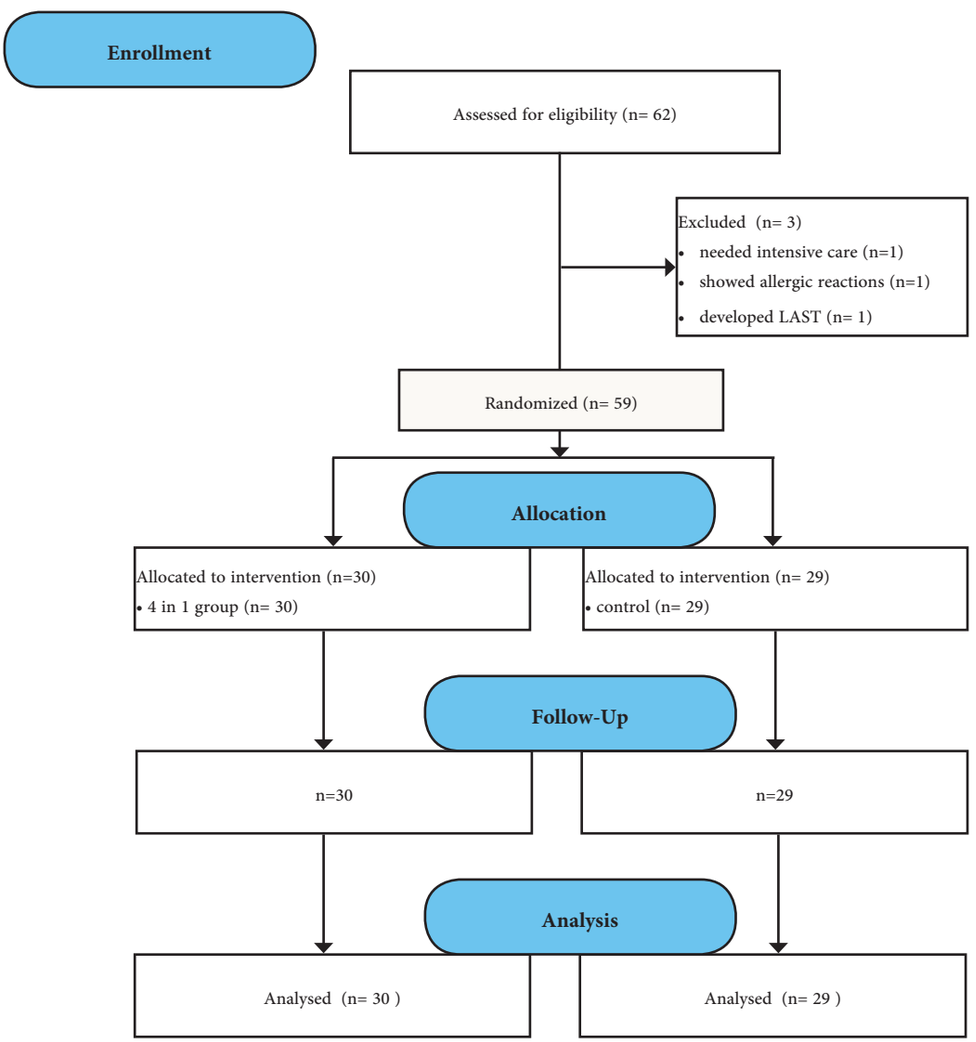

Fig. 1: CONSORT 2010 Flow Diagram.

Preoperative management:

After the preoperative anesthesia examination, the consent of the patients who were planned to be operated under spinal anesthesia and who would be included in the study and who were informed about the study were taken. Demographic data such as age, gender, ASA score, height, weight, and the planned surgery were recorded, and they were taken to the operating room. The patients were not intervened with in the preoperative period by the researcher.

Postoperative care unit:

The postoperative analgesia method applied to the patient was learned from the perioperative anesthesia form in the postoperative recovery unit, and the patient was included in the block group if 4 in 1 block was applied, and in the control group if systemic analgesics was planned without a block.

Group 4 in 1 (*n*:30):

Patients who underwent 4 in 1 block for postoperative analgesia (30ml 0.25% bupivacaine plus 4mg dexamethasone).

Control Group (*n*:29):

Patients receiving only systemic analgesics without any block.

Three patients who were included in the study in the preoperative period, needed intensive care in the postoperative period, showed allergic reactions, developed local anesthetic systemic toxicity (LAST) and were intervened with intravenous lipid solution were excluded from the study. Analyzes were performed on 59 patients.

Application of the 4 in 1 Block:

4 in 1 block cases performed after the surgery was completed before the effects of spinal anesthesia wore off are included. The patient lies in the supine position and the leg to be operated is externally rotated, slightly abducted and the knees are slightly flexed (frog leg position). The medial femoral condyle is marked. A linear high-frequency ultrasound probe (6-13Hz) is used, it is placed on the femoral condyle, the vastus medialis muscle is identified and scanned proximally. The junction of the vastus and sartorius (anteromedial intermuscular septum) is determined and the probe is shifted proximally until the superficial femoral artery is visible in the adductor hiatus. The injection point is determined by slowly sliding the probe proximally until the genicular artery is visible from the pattern branching from the superficial femoral artery in the hiatus. This point is 8-10cm above the femoral condyle. Under all aseptic precautions, the needle is guided straight from lateral to medial to reach the perivascular area, guided by US, 0.25% bupivacaine 30ml± adjuvants are injected after negative aspiration. It is observed that the femoral artery is pushed posteriorly. After the block, it is observed that the drug spreads to the perivascular area around the sciatic nerves in the popliteal fossa as well as the adductor canal[10,11] (Figure 2).

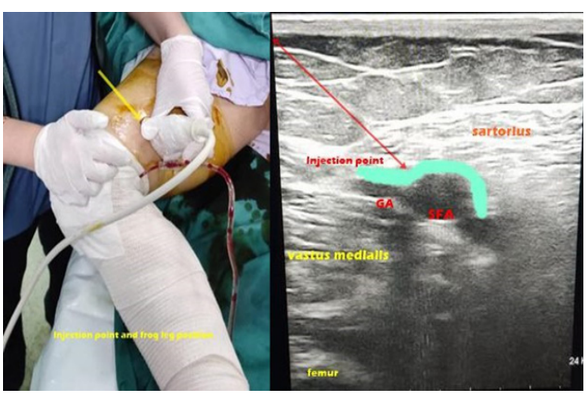

Fig. 2: Application of the 4 in 1 Block.

Postoperative follow-up: The patients were visited by the researcher in the orthopedic service at the 2nd, 4th, 6th,

Table 1: Demographic data (without group distinction and between groups):

		Without group distinction (*n*/%)	4 in 1 (*n*/%)	Control (*n*/%)	*P** (4in1 & control)
(mean±sd)		49,7±18,0	50,8±18,4	48,6±18,0	0,518
Sex	female	23(39.0)	12 (40,0)	11 (37,9)	0,542
	Male	36(61.0)	18 (60,0)	18 (62,1)	
Total		59	30	29	
BMI group	<25	23(39.0)	13 (43,3)	10 (34,5)	
	25,1–30,0	23(39.0)	12 (40,0)	11 (37,9)	0,574
	>30,1	13(22.0)	5 (16,7)	8 (27,6)	
Total		59	30	29	
BMI (mean±sd)		26,6±3,5	26,4±2,9	26,8±4,0	0,158
operation	arthroscopy	29(49.2)	14 (46,7)	15 (51,7)	0,698
	arthroplasty	30(50.8)	16 (53,3)	14 (48,3)	
Total		59	30	29	
Group	4 in 1	30(50.8)			
	control	29(49.2)			

*: Chi-Square Tests.

12th and 24th hours postoperatively, and visual analogue scale (VAS: pain intensity between 0 and 10; 0- no pain, 10 - very severe pain), sensory block (pinprick test: no sensation, touch, stinging) were evaluated and recorded. In addition, undesirable effects such as nausea, vomiting, itching, and sedation developed in the patient were noted. Quadriceps strength of our patients was examined at 12th and 24th hours, especially since we were able to bring our arthroplasty patients to a sitting position under supervision at the 12th postoperative hour, in consultation with our orthopedic doctors.

In the orthopedic ward of our hospital, Tenoxicam 20mg 2*1 (orally) is applied to patients who routinely undergo knee surgery. After the operation, arthroplasty patients are additionally administered 100mg of contramal intravenously and when the effect of spinal anesthesia is close to wear off, intramuscular diclofenac sodium is given. All patients are, if necessary, given outside the routine rescue analgesia with pethidine, tramadol, dexketoprofen, diclofenac, tenoxicam and paracetamol, upon the recommendation of the orthopedic doctor. The routine postoperative analgesia method of the ward was not interfered with, only the additional analgesics were recorded.

Quadriceps strength: Sitting position:

1. No contractions.
2. Slight contraction.
3. Moves only in the horizontal plane, unable to resist gravity.
4. Liftes against gravity but unable to perform additional pressure.
5. Performs both antigravity lifting and moderate pressure.
6. Normal healthy movement.

The primary aim of the study is the comparison of postoperative VAS values.

Secondary purposes are to determine independent factors such as age, gender, body mass index (BMI), type of surgery that may affect VAS values, and to observe the difference between quadriceps strength loss and postoperative complications.

Statistical analysis

In the study of Roy *et al*.[10], it was observed that 90% effective analgesia was provided in the first 36 hours in 4 in 1 block. However, this study is not a comparative study. In our study, on the other hand, according to the calculation we made by predicting that the analgesia success in the first 24 hours would be 60% more successful than the traditional method, it was determined that the type 1 error rate was 0.05, and when the power was considered as 80, 31 patients in each group and 62 patients in total should be included. SPSS 21.0 statistical package program was used for statistical analysis. Pearson's chi-square test and Fisher's exact test were used to compare qualitative data as well as descriptive statistical methods (frequency, percentage, mean, standard deviation).

RESULTS

The mean age of the 59 patients included in our study was 49.7±18.0 years, and there was no difference in age between the groups. 61% of the patients included in the study were male and the number of male patients was higher in the groups. Only 13 patients (22%) had a body mass index (BMI) of 30 and above, and there was no difference between the groups. While 50.8% of the patients had undergone arthroplasty, the other half had undergone arthroscopic surgery. There was no difference between the ASA values of the patients (Table 1).

When the VAS values were compared according to the time, which is the primary aim of the study, the VAS values were significantly lower in the 4 in 1 block group from the 4th hour, and rescue analgesia was applied to only 4 patients in the first 24 hours because the VAS was above 5 (Figure 3, $p<0.005$).

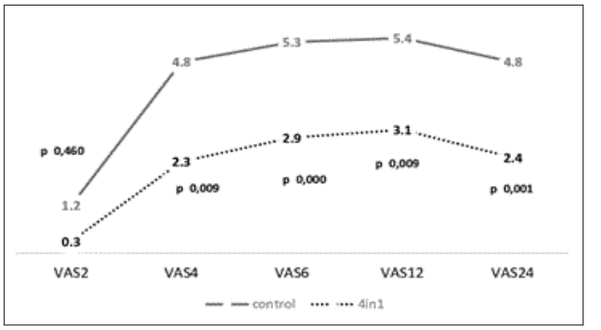

Fig. 3: VAS values between groups over time.

Considering the loss of quadriceps strength, which is one of the expected complications especially in the group with block in the postoperative period, it was found that strength loss was observed in the group with block at the postoperative 12th hour, but there was no loss of strength in the group without block. (p: 0.006) On the other hand, 10 of 16 patients with nausea were in the control group, and 4 patients with vomiting, and 1 patient with sedation were also in the control group who were given systemic analgesics. Table (2) Sedation was observed after pethidine was given to 1 patient. In one patient who underwent block, itching was observed at the 2nd hour, but only vomiting was statistically significant. There was no difference between the groups in the pinprick measurements of the patients.

When the significant difference in VAS values between the groups is evaluated in terms of gender, BMI, and operation type, it was determined that the VAS values were high in women and this difference was especially significant in the control group ($p<0.05$). Again, it was determined that

Table 2: Comparison of the groups in terms of the relationship between gender and surgery type and VAS and Secondary variables between groups:

	4 in 1		*P*	Control		*P*
	Female	**Male**		**Female**	**Male**	
VAS2	0,0±0,0	0,5±1,4	0,250	2,7±3,0	0,2±0,9	0,004*
VAS4	2,9±1,5	1,8±1,8	0,120	6,3±1,9	3,8±2,9	0,019*
VAS6	3,8±1,9	2,2±1,6	0,028*	6,9±2,1	4,4±2,2	0,008*
VAS12	3,4±2,1	2,8±1,8	0,478	6,6±2,5	4,7±1,7	0,021*
VAS24	3,7±1,2	1,6±1,1	0,000	6,1±1,8	4,0±1,9	0,006*
	arthroscopy	arthroplasty		arthroscopy	arthroplasty	
VAS2	0,5±1,6	0,0±0,2	0,233	0,3±1,0	2,1±2,9	0,033*
VAS4	1,5±1,9	2,9±1,3	0,032*	3,3±2,4	6,4±2,3	0,002*
VAS6	1,6±1,6	4,0±1,4	0,000*	3,9±2,0	6,9±2,0	0,000*
VAS12	2,9±1,6	3,2±2,2	0,635	4,5±1,7	6,4±2,3	0,018*
VAS24	1,7±1,5	3,1±1,4	0,014	3,4±1,4	6,3±1,7	0,000*
Q12	7			0		0,006**
Q24	0			0		
Nausea	6			10		0,211
Vomiting	0			4		0,035**
Itching	1			1		0,981
Sedation	0			1		0,305

*: Student *t* test; **: Chi square; Q12, Q24:12th-24th Hour Quadriceps strength.

Table 3: Comparison of the groups in terms of the relationship between BMI and VAS values:

	4 in 1				control			
BMI	<25	25,1-30,0	>30,1		<25	25,1-30,0	>30,1	
VAS2	0,5±1,6	0,1±0,5	0,0±0,0	p^1: 0,434 p^2: 0,791 p^3: 0,389	0,1±0,3	1,1±2,3	2,6±3,1	p^1: 0,264 p^2: 0,164 p^3: 0,021*
VAS4	2,0±1,8	2,3±1,8	3,0±1,4	p^1: 0,646 p^2: 0,490 p^3: 0,298	3,5±2,1	4,8±3,3	6,5±2,0	p^1: 0,267 p^2: 0,185 p^3: 0,025*
VAS6	2,3±1,8	3,1±2,3	3,6±0,8	p^1: 0,324 p^2: 0,679 p^3: 0,245	4,3±1,9	5,1±2,5	7,0±2,5	p^1: 0,399 p^2: 0,108 p^3: 0,023*
VAS12	3,4±1,7	2,5±1,8	3,4±2,7	p^1: 0,277 p^2: 0,444 p^3: 0,953	5,0±1,9	5,2±2,0	6,2±2,8	p^1: 0,782 p^2: 0,355 p^3: 0,249
VAS24	1,92±1,2	2,6±1,8	3,4±1,5	p^1: 0,248 p^2: 0,389 p^3: 0,086	4,1±1,8	4,9±2,5	5,6±1,9	p^1: 0,400 p^2: 0,483 p^3: 0,149

p^1: <25 and 25,1-30,0; *: Oneway ANOVA; p^2: 25,1-30,0 and >30,1; p^3: <25 and >30,0.

VAS scores were lower in arthroscopic surgeries compared to arthroplasty, but high VAS values were observed in both surgeries if no block was performed. In the control group, arthroplasties had significantly higher VAS scores. (Table 2, $p<0.05$)

While BMI and VAS scores did not change in the 4 in 1 block group, statistically significantly higher VAS values (Table 3), and the need for additional analgesics were found in patients with high BMI in the control group who were given systemic analgesics.

DISCUSSION

Inadequate pain control after knee surgeries increases morbidity and mortality as a result of endocrine metabolic and inflammatory complications, and causes chronic postoperative pain, side effects due to opioid consumption, and prolongation of hospitalization by reducing mobilization. Therefore, effective postoperative analgesia methods are among the most researched subjects by researchers. In our study, we tried to show the effect of 4 in 1 block against systemic analgesics and its efficacy for postoperative

analgesia. It a new method which blocks the saphenous nerve, obturator nerve, sciatic nerve and the nerve to vastus medialis from a single injection point without the need for a position change.

In our study, we observed that the VAS score was significantly lower from the 4th hour in the 4 in 1 block group, and that only 4 patients in this group needed rescue analgesia within the postoperative 24 hours. In the control group, the VAS values were high and the intervention especially with opioid analgesics was excessive. This was supported by the findings of the other study. In studies comparing the patient groups who underwent peripheral nerve block and the patients who received IV analgesics, it was observed that the VAS scores in the first 24 hours were significantly lower in the groups that underwent peripheral nerve block. It has also been shown in many studies that the application of peripheral block after total knee arthroplasty (TKA) is effective in pain control and that the VAS scores followed in the 24-hour period are significantly lower[13-15]. Roy *et al*.,[10] observed that in the series of 100 cases consisting of patients who had undergone knee and below-knee surgery, VAS scores of all patients were 2 and below. These were similar to the results of our study.

Total knee arthroplasty is a major surgery and the postoperative period is very painful. It was found in studies that VAS values were between 4 and 8 in the early postoperative period[16,17]. However, in arthroscopic treatment, it is known that there is less pain as a result of less inflammatory response in the postoperative period compared to open surgery[18]. In our study, in parallel with the literature, it was found that VAS values were lower in arthroscopic surgeries compared to arthroplasty, but high VAS values were observed in both surgeries if no block was performed. In the control group, arthroplasties had significantly higher VAS scores.

It is thought that the pain threshold in women undergoing surgery is lower than in men[19]. Pope D. *et al*.,[20] and Cremeans-Smith *et al*.,[21] found that female patients had higher pain scores than male patients in patients who underwent total knee replacement (TKR). In our study, we found that the VAS values were high in female patients and this difference was especially significant in the control group.

With a high BMI, the pressure applied to the knee increases and the muscles need more traction to resist deformities after a surgery. In our study, we investigated the relationship between BMI and VAS scores and found that the VAS increased significantly in patients with high BMI in the control group, but in the block group, regardless of BMI, patients had low VAS scores and provided good analgesia. In the study of Qin *et al*., it was observed that as BMI increased, postoperative recovery was delayed and pain intensity increased[22].

It has been shown in the literature that lower extremity blocks, which hold an important place in the treatment of postoperative pain in orthopedic surgeries, cause undesirable postoperative effects such as loss of muscle strength and falling in the lower extremity. Early mobilization and rehabilitation is desirable after knee surgeries. Although lumbar plexus block provides effective analgesia, it has been shown in studies that it causes quadriceps muscle weakness and therefore delays in mobilization, and this has directed clinicians to more peripherally applied blocks[23]. In our study, quadriceps strength loss after block was evaluated. Considering the quadriceps strength loss in the postoperative period, especially in the block group, it was found that strength loss was observed in the block group until the postoperative 12th hour, but no strength loss was measured in the non-blocked group. No evidence of loss of strength or mobilization was mentioned in the study by Roy *et al*.,[11] Again, Roy *et al*., reported that no strength loss was observed in any patient in the series of 10 cases in which they separately blocked the nerve to vastus medialis and applied a modified 4 in 1 block[11]. However, this is not a comparative study and more studies are needed on this subject.

We evaluated the side effects of the patients such as nausea, vomiting, dizziness and itching in the postoperative period and found that vomiting was significantly higher in the control group. In a study by Tomonori Tetsunaga *et al*., postoperative analgesic efficacy and side effects of epidural analgesia, PCA plus IV morphine infusion and 3 in 1 femoral block were compared after hip arthroplasty, and nausea-vomiting was significantly less in the group with a femoral block catheter[24]. Again, in a randomized controlled study conducted by Rafiq *et al*., they stated that the multimodal approach provided better analgesia than opioid-based analgesic administration and reduced the complaints of nausea and vomiting[25]. In a review by Albrecth *et al*., it was stated that perineural dexamethasone reduced nausea and vomiting[26]. In our study, opioid analgesic use was high in the control group, and we think that perineural dexamethasone administration also prevented nausea and vomiting, as the need for opioids decreased in patients with block.

Our study had some limitations. First of all, since it was an observational study and the analgesia method to be applied in the perioperative period and the rescue analgesia method was not interfered with in the postoperative period, the doses used in the block, whether PCA was used afterwards or analgesic types and the management of their doses were not in our hands. Therefore, the postoperative analgesia method could not be standardized. Secondly, our follow-up period was 24 hours, and since the quadriceps strength in the sitting position was examined at the 12th and 24th hours in this period, longer follow-up is required for parameters showing motor skills such as fall complications and walking distance. Third, since our study is not comparable with

another PNB (Peripheral Nerve Block), its superiority over other blocks cannot be evaluated. Additionally, since the study was planned to include all 4 in 1 blocks, both types of surgery were included. However, since there is a significant difference in pain intensity between different procedures, studies that include a single type of surgery may yield different results.

CONCLUSION

In our study, we observed that US-guided 4 in 1 block was effective in terms of postoperative analgesia, reduced opioid consumption and related side effects in patients undergoing knee surgery, and we think that it can be used effectively as a part of multimodal analgesia in knee surgeries. However, longer-term, comprehensive and comparative studies are needed for the effect of 4 in 1 block on postoperative analgesia and mobilization.

AUTHOR CONTRIBUTIONS

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by [seyran köksal], [merve yazıcı kara] and [ilke kupeli]. The first draft of the manuscript was written by [ilke kupeli] and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

CONFLICT OF INTERESTS

There are no conflicts of interest.

REFERENCES

1. Kehlet H. Surgical stress: the role of pain and analgesia. BJA: British Journal of Anaesthesia. 1989;63(2):189-95.

2. Tang R, Evans H, Chaput A, Kim C. Multimodal analgesia for hip arthroplasty. Orthopedic Clinics of North America. 2009;40(3):377-87.

3. Bauer MC, Pogatzki-Zahn EM, Zahn PK. Regional analgesia techniques for total knee replacement. Current Opinion in Anesthesiology. 2014;27(5):501-6.

4. Parvataneni HK, Ranawat AS, Ranawat CS. The use of local periarticular injections in the management of postoperative pain after total hip and knee replacement: a multimodal approach. Instructional course lectures. 2007;56:125-31.

5. Society KK. Guidelines for the management of postoperative pain after total knee arthroplasty. Knee surgery and related research. 2012;24(4):201.

6. Güler G, Atıcı Ş, Kurt E, Karaca S, Yılmazlar A. Current approaches in hip and knee arthroplasty anaesthesia. Turkish journal of anaesthesiology and reanimation. 2015;43(3):188.

7. Kurt E. Rejyonal Anestezide Ultrasonografi Kullanımı. Journal of the Turkish Anaesthesiology and Intensive Care Society-JTAICS/Türk Anestezi ve Reanimasyon Dergisi. 2010;38(2).

8. Akkaya A, Yildiz I, Tekelioglu U, Demirhan A, Bayir H, Ozlu T, *et al*. Dexamethasone added to levobupivacaine in ultrasound-guided tranversus abdominis plain block increased the duration of postoperative analgesia after caesarean section: a randomized, double blind, controlled trial. Eur Rev Med Pharmacol Sci. 2014;18(5):717-22.

9. Enneking KF, Chan V, Greger J, Hadžić A, Lang SA, Horlocker TT. Lower-extremity peripheral nerve blockade: essentials of our current understanding. Regional Anesthesia & Pain Medicine. 2005;30(1):4-35.

10. Roy R, Agarwal G, Pradhan C, Kuanardr D, Mallick DJ. Ultrasound guided 4 in 1 block–a newer, single injection technique for complete postoperative analgesia for knee and below knee surgeries. Anaesthesia, Pain & Intensive Care. 2018:87-92.

11. Roy R, Agarwal G, Pradhan C, Kuanar D. Total postoperative analgesia for total knee arthroplasty: Ultrasound guided single injection modified 4 in 1 block. Journal of Anaesthesiology, Clinical Pharmacology. 2020;36(2):261.

12. Parthasarathy S. Ultrasound guided 4 in 1 block for managing postoperative pain in arthroscopic knee surgery. Sri Lankan Journal of Anaesthesiology. 2019;27(1):86-8.

13. Szczukowski Jr MJ, Hines JA, Snell JA, Sisca TS. Femoral nerve block for total knee arthroplasty patients: a method to control postoperative pain. The Journal of arthroplasty. 2004;19(6):720-5.

14. Wang H, Boctor B, Verner J. The effect of single-injection femoral nerve block on rehabilitation and length of hospital stay after total knee replacement. Regional Anesthesia and Pain Medicine. 2002;27(2):139-44.

15. Widmer BJ, Scholes CJ, Pattullo GG, Oussedik SI, Parker DA, Coolican MR. Is femoral nerve block necessary during total knee arthroplasty?: a randomized controlled trial. The Journal of arthroplasty. 2012;27(10):1800-5.

16. Hirst GC, Lang SA, Dust WN, Cassidy DJ, Yip RW. Femoral nerve block: single injection versus continuous infusion for total knee arthroplasty. Regional Anesthesia: The Journal of Neural Blockade in Obstetrics, Surgery, Pain Control. 1996;21(4):292-7.

17. Serpell M, Millar F, Thomson M. Comparison of lumbar plexus block versus conventional opioid analgesia after total knee replacement. Anaesthesia. 1991;46(4):275-7.

18. Gülman B. Artroskopik menisektomi ve açık menisektomilerin. Acta Orthop Traumatol Turc. 1992;26:322.

19. Sun L. Gender differences in pain sensitivity and responses to analgesia. The journal of gender-specific medicine: JGSM: the official journal of the Partnership for Women's Health at Columbia. 1998;1(1):28-30.

20. Pope D, El-Othmani MM, Manning BT, Sepula M, Markwell SJ, Saleh KJ. Impact of age, gender and anesthesia modality on post-operative pain in total knee arthroplasty patients. The Iowa orthopaedic journal. 2015;35:92.

21. Cremeans-Smith JK, Millington K, Sledjeski E, Greene K, Delahanty DL. Sleep disruptions mediate the relationship between early postoperative pain and later functioning following total knee replacement surgery. Journal of behavioral medicine. 2006;29(2):215-22.

22. Qin D, Chen W, Wang J, Lv H, Ma W, Dong T, *et al*. Mechanism and influencing factors of proximal fibular osteotomy for treatment of medial compartment knee osteoarthritis: a prospective study. Journal of International Medical Research. 2018;46(8):3114-23.

23. Memtsoudis SG, Danninger T, Rasul R, Poeran J, Gerner P, Stundner O, *et al*. Inpatient falls after total knee arthroplasty: the role of anesthesia type and peripheral nerve blocks. Anesthesiology. 2014;120(3):551-63.

24. Tetsunaga T, Sato T, Shiota N, Tetsunaga T, Yoshida M, Okazaki Y, *et al*. Comparison of continuous epidural analgesia, patient-controlled analgesia with morphine, and continuous three-in-one femoral nerve block on postoperative outcomes after total hip arthroplasty. Clinics in Orthopedic Surgery. 2015;7(2):164-70.

25. Rafiq S, Steinbrüchel DA, Wanscher MJ, Andersen LW, Navne A, Lilleoer NB, *et al*. Multimodal analgesia versus traditional opiate based analgesia after cardiac surgery, a randomized controlled trial. Journal of cardiothoracic surgery. 2014;9(1):1-8.

26. Albrecht E, Kern C, Kirkham K. A systematic review and meta-analysis of perineural dexamethasone for peripheral nerve blocks. Anaesthesia. 2015;70(1):71-83.