RESEARCH ARTICLE

A Randomized Double-Blind Prospective Study Comparing the Efficacy of Subperiosteal and Periarticular Injections of a Local Anesthetic for Postoperative Pain Management after Total Knee Arthroplasty

Reza Minaei, MD; **Mohammad** Salehpour, MD; **Emad** Kouhestani, MD; **Mahshid** Ghasemi, MD

Research performed at Akhtar Orthopedic Hospital, Tehran, Iran

Received: 29 May 2023 *Accepted: 23 October 2023*

Abstract

Objectives: Total knee arthroplasty (TKA) serves as an effective surgical treatment method for advanced osteoarthritis (OA). Nonetheless, it is associated with postoperative pain that can influence patients' functional outcome. This study aimed to compare the analgesic effect of subperiosteal and periarticular injection methods of a special local anesthetic in patients who underwent TKA.

Methods: This double-blind prospective clinical study was conducted on patients with advanced knee OA who underwent TKA. Patients were randomly divided into two groups, with a local anesthetic (21 ml) administered either in periarticular (P group) or subperiosteal (S group) forms prior to wound closure. The local anesthetic consisted of lidocaine 2% (15 cc), dexmedetomidine (1 cc), and marcaine 0.5% (5 cc). A study-blinded orthopedic resident recorded postoperative pain levels using a 10-point visual analogue score (VAS) (0 indicating no pain, 10 indicating worst pain) at 6, 12, 24, and 48 hours after surgery.

Results: A total of 40 patients (P and S group; n=20 each), consisting of 10 males (mean age=67.4 years old), were included in this study. The intensity of pain in the S group was significantly lower than in the P group 24 hours after surgery (mean VAS scores in the P group: 4±1 vs. the S group: 3.3±0.7, P=0.024). Furthermore, VAS scores at 6, 12, and 48 hours post-surgery were lower in the S group compared to the P group; however, the difference was not statistically significant (P>0.05).

Conclusion: Our study indicated that subperiosteal injection of lidocaine, dexmedetomidine, and marcaine is more effective than periarticular injection, providing effective postoperative pain management after TKA.

Level of evidence: II

Keywords: Osteoarthritis, Pain, Postoperative pain, TKA, Total knee arthroplasty

Introduction

Total knee arthroplasty (TKA) is a commonly performed surgical procedure for advanced knee osteoarthritis (OA) with high success rates.[1] Postoperative pain is among the main issues for patients who undergo TKA, and it is directly related to surgical trauma.[2,3] About 60% of patients undergoing TKA experience severe postoperative pain, and approximately 30% experience moderate pain.[3] Postoperative pain is associated with increased rates of complications, morbidity, and a delayed recovery process.[4-6] Early postoperative pain management can result in reduced hospital stays, increased patient satisfaction, and improved rehabilitation.[3,4] It also reduces the risk of postoperative complications such as pneumonia or deep vein thrombosis.[4,5] Pain control can be achieved in several ways, each with its own risks and benefits. Although epidural anesthesia is a commonly effective method for pain relief during the postoperative period, it hinders early

Corresponding Author: Emad Kouhestani, Bone Joint and Related Tissues Research Center, Akhtar Orthopedic Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Email: emadkouhestani@gmail.com

THE ONLINE VERSION OF THIS ARTICLE
ABJS.MUMS.AC.IR

movement and leads to complications such as hypotension, postoperative headache, and spinal infection.[7] Regional nerve blocks carry the risk of damaging neurovascular structures, hematoma formation, and infection.[5] Systemic opioids such as morphine or fentanyl can cause nausea, vomiting, drowsiness, respiratory depression, urinary retention, and constipation.[7,8]

Local pain control represents an innovative approach to pain management due to its lower complication rates and rapid-acting effects. This achievement has been facilitated through local intra-articular or periarticular injections of analgesic compounds that exhibit high effectiveness, affordability, and ease of prescription, all without impeding movement. Furthermore, it does not necessitate any specialized technical skills.[9] Several studies have reported promising results regarding periarticular injections of various drug combinations, including ketorolac, ropivacaine, bupivacaine, morphine sulfate, epimorphine, methylprednisolone, cefuroxime, epinephrine, and normal saline.[10-12] Lidocaine, dexmedetomidine, and marcaine are among the safe and effective pain relief methods that have demonstrated efficacy in controlling pain following various orthopedic procedures.[13-17] However, to the best of our knowledge, no research has evaluated the analgesic effect of a combination of these drugs in patients undergoing TKA. Additionally, it remains unknown whether subperiosteal or periarticular approaches induce stronger patient-related outcomes, including pain relief. Therefore, this study aims to compare pain scores using special local anesthetics containing lidocaine 2% (15 cc), dexmedetomidine (1 cc), and marcaine 0.5% (5 cc) applied via either subperiosteal and periarticular methods, in two groups of patients undergoing TKA. We hypothesized that there is no significant difference in pain intensity between subperiosteal and peri-articular injections of the local anesthetic after TKA.

Materials and Methods

This study was a double-blind, prospective investigation conducted from April 2022 to February 2023 at Akhtar Orthopedic Hospital in Tehran, Iran. The study comprised 40 patients with 40 knees OA who were undergoing TKA. Inclusion criteria encompassed individuals aged between 50 and 85 years, categorized as American Society of Anesthesiologists (ASA) physical status I or II, possessing a body mass index (BMI) ranging from 20 to 35. Additionally, participants were required to possess a comprehensive understanding of the study objectives and provide their consent for participation. Exclusion criteria were as follows: patients with a known allergy to the drugs employed in this study, usage of analgesics or non-steroidal anti-inflammatory drugs (NSAIDs) within 24 h before surgery, individuals with chronic kidney disease or chronic liver disease, uncontrolled diabetes, those ineligible for spinal anesthesia, and individuals with a history of addiction. Prior to engaging in the study, written consent was obtained from all the participants.

After transferring the patients to the operating room, peripheral oxygen saturation, non-invasive blood pressure, and electrocardiogram monitoring were conducted. Spinal anesthesia was induced using marcaine 7.5 mg/mL. The surgery was performed with the application of a tourniquet. All patients underwent the procedure through an anterior midline incision. The patients were randomly divided into two groups using the sealed-envelope method:

1. Group S - Subperiosteal injection of lidocaine 2% (15 cc), dexmedetomidine (1 cc), and marcaine 0.5% (5 cc) before wound closure using a 21-gauge needle.
2. Group P - Periarticular injection of lidocaine 2% (15 cc), dexmedetomidine (1 cc), and marcaine 0.5% (5 cc) before wound closure using a 21-gauge needle.

The above local anesthetic was formulated by a pain specialist based on their clinical experience and previous studies.[18-20] the periarticular injections were administered into the posterior capsule, medial capsule/synovium/periosteum, quadriceps tendon, and lateral capsule/synovium/periosteum after implantation. The subperiosteal injections were administered to the subperiosteal of the distal femur and proximal tibia. All surgeries and local anesthetic injections were performed by the same surgeon at our hospital. One surgeon (RM) participated in all surgeries. None of the patients received patient-controlled analgesia or a peripheral nerve block. In all cases, a prosthesis with an incised posterior cruciate ligament was utilized. The same prosthesis was used for all patients.

During the postoperative period, Acetaminophen (Exir Pharmaceutical Company, Tehran, Iran) (1000 mg) was administered intravenously every 12 h for the first two days, followed by 25 mg of methadone in the initial 6 h after surgery, and Acetaminophen (Dana Pharmaceutical Company, Tehran, Iran) 500 mg capsules were taken three times a day for the subsequent 10 days. While hospitalized, patients after surgery were prescribed 40 mg of subcutaneous Enoxaparin prophylaxis once daily and then 81 mg of oral aspirin every 12 h for six weeks. Patients began using a walker 12 h after surgery, and a full range of motion (ROM) and isometric exercises were initiated. All patients were observed until discharge and received regular follow-up.

Postoperative pain in each knee was separately recorded by a study-blinded orthopedic resident using a 10-point visual analogue score (VAS) ranging from 0 to 10, where 0 indicated no pain, and 10 represented the worst imaginable pain, at 6, 12, 24, and 48 h postoperatively. The VAS is a commonly utilized tool in various research studies, particularly in the field of pain assessment.[21,22] This subjective measure provides researchers with valuable insights into the individual's pain perception, allowing for a quantitative assessment of pain severity and enabling comparisons across different interventions, conditions, or populations.[21,22]

Adverse events, including allergic reactions, nausea, vomiting, urinary retention, or respiratory depression, were monitored until patients were discharged. Patient demographic information, including age, ethnicity, gender, body mass index, hemoglobin levels, and history of deep vein thrombosis or infection, as well as the length of hospital stay, was extracted from the patient's medical records. This study was approved by the Research Ethics Committee of Shahid Beheshti University of Medical Sciences (IR.SBMU.MSP.REC.1402.039), and written informed consent was obtained from all patients before participation in the study.

Statistical Analysis

Statistical analyses were performed using Statistical Package for the Social Sciences (SPSS, version 26). Continuous variables were presented as mean ± SD. To compare the means of two independent groups, an independent t-test was employed. Categorical data were analyzed using Fisher's Exact Test. The non-parametric Friedman's analysis of variance by ranks was utilized to assess differences among multiple related groups. For assessing within-subject effects over time, repeated measures Analysis of Variance (ANOVA) was performed.

To determine the sample size, a pilot study was performed with five participants in each group. Based on the mean and standard deviation of the VAS score at 24 h, we found that a minimum of 18 individuals per group is necessary. The following formula was used:

$n = [(Z1-\alpha/2 + Z1-\beta)^2 * \{ó12 + ó_2^2\}]/ (\mu1 - \mu2)^2$

- Significance level (Alpha): 0.05
- Study power (Beta): 0.8
- Standard deviation group 1: 1.1
- Standard deviation group 2: 0.7
- Mean group 1: 3.4
- Mean group 2: 2.7

A total of 63 participants were screened to assess eligibility. Out of 63 participants, 23 did not meet our inclusion criteria. The calculated sample size was 18 for each group; however, considering the dropouts, we decided to enroll 20 patients in each group.

Results

A total of 40 patients (10 male and 30 female) were included in our study. [Figure 1] indicates the patient selection process. The mean age of participants in the P and S groups was 67.8 ± 5.6 and 67 ± 7.6, respectively. [Table 1] presents the demographic characteristics of patients in the S and P groups. No significant differences were observed across all demographic variables except BMI (P=0.033) between the P and S groups.

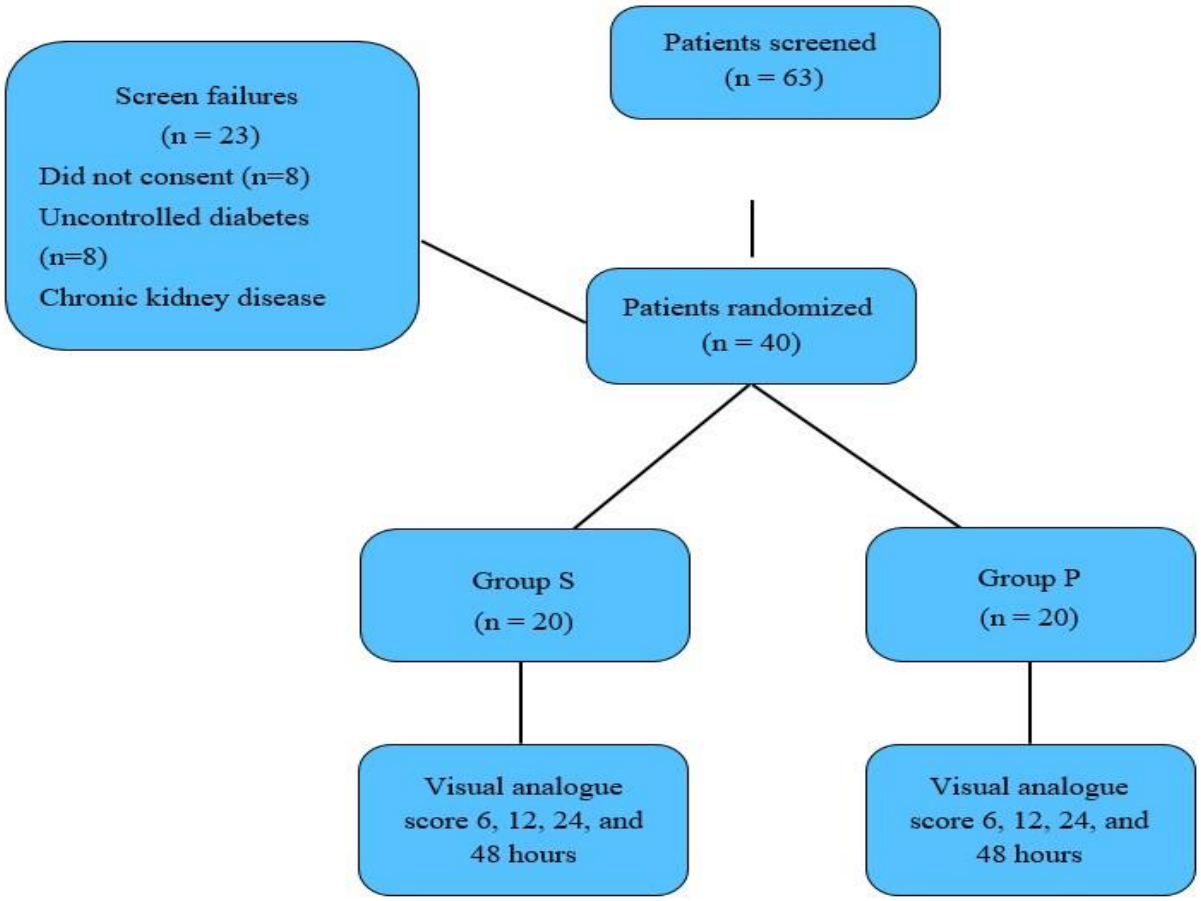

Figure 1. Study flow diagram

Table 1. Participants demographic characteristics

Variable	P group (n=20)	S group (n=20)	P-value
Age, y (mean±SD)	67.8±5.6	67±7.6	0.689
Gender, male (n, %)	3 (15%)	7 (35%)	0.273
BMI (kg/m2) (mean±SD)	26.6±2.5	25±2.2	0.033
DM (n, %)	5 (25%)	7 (35%)	0.731
HTN (n, %)	12 (60%)	10 (50%)	0.525

BMI: body mass index, DM: diabetes mellitus, HTN: hypertension

In the P group, two patients were unable to perform full weight bearing (FWB) by the end of the first or second postoperative day. In the S group, all patients were able to achieve FWB on the first or second postoperative day. However, the difference in FWB rates between the two groups was not statistically significant (P=0.487). Thirty percent of the patients in the P group and twenty percent of the patients in the S group required a blood transfusion, and this difference between the two groups was not significant (P=0.716).

The VAS values for both groups are presented in [Table 2]. The pain intensity at 6, 12, and 48 h following surgery was lower in the S group compared to the P group; however, the difference between the two groups was not statistically significant (P>0.05). Furthermore, the VAS score was significantly lower in the S group compared to the P group 24 h following surgery (3.3±0.7 vs. 4±1; P=0.024). The results of the repeated measures ANOVA provide insights into the dynamic changes in pain scores over time and between the two study groups. With a calculated *P*-value of 0.21, the observed trends in pain relief did not appear to demonstrate a statistically significant divergence between group S and group P [Figure 2, Table 2].

We observe no complications due to injection in our study. None of the patients developed any adverse events, including infections.

Table 2. Visual analogue scale values for both groups

VAS values	P group	S group	*P*-value
6 h, mean±SD	5.2±1.2	4.9±1	0.445
12 h, mean±SD	4.8±1.6	4.9±1.3	0.529
24 h, mean±SD	4±1	3.3±0.7	0.024
48 h, mean±SD	2.4±0.8	2.2±0.8	0.369

VAS: visual analogue scale

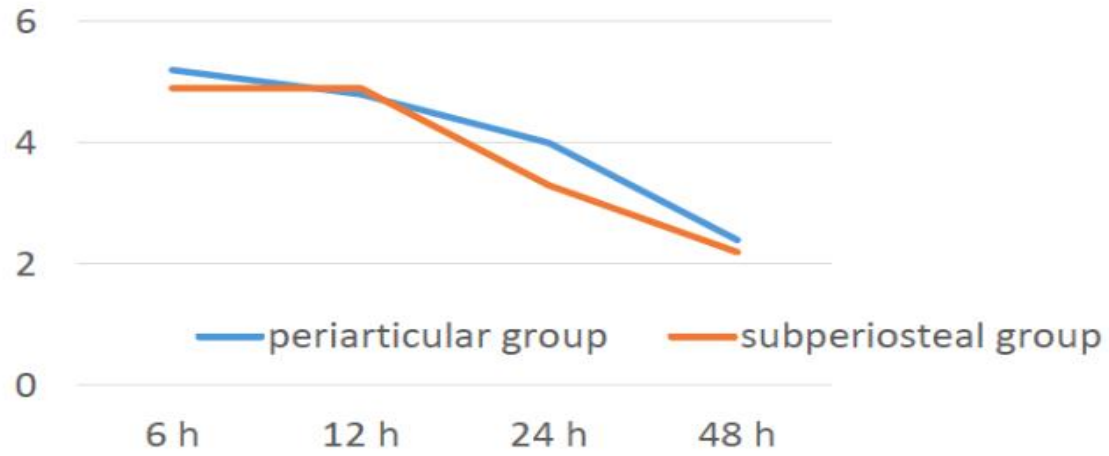

Figure 2. Figure 2. Visual analogue scale of both groups

Discussion

In this study, our objective was to compare the effectiveness of periarticular and subperiosteal injections of a special local anesthetic containing lidocaine, dexmedetomidine, and marcaine for managing postoperative pain, as measured by VAS scores at 6, 12, 24, and 48 h after TKA. The results of this study indicated that the subperiosteal injection of a special local anesthetic provides a significantly greater analgesic effect compared to periarticular injection at 24 h post-surgery. However, no significant difference in VAS scores was observed between the periarticular and subperiosteal groups at 6, 12, and 48 h after surgery. Furthermore, both types of injections were found to be safe, with no adverse events. To the best of the authors' knowledge, this study is the first research comparing periarticular and subperiosteal injection methods in TKA.

As mentioned, TKA is associated with postoperative pain, which can lead to an increased complication rate, lower quality of life, higher costs, and impaired overall functional outcomes.[3,23] Severe pain may also result in bone loss, severe deformity, and limited ROM.[24] Early postoperative management is crucial for rapid recovery, a reduced complication rate, patient satisfaction, and improved function.[25] The pain experienced after TKA is attributed to trauma to intra-articular and capsular structures during surgery, which stimulates free nerve endings and afferent nociceptors, leading to the release of inflammatory factors such as histamine.[23,26] Surgical trauma during TKA alters the central nervous system through peripheral and central sensitization.[26] Tourniquet use during TKA can also cause trauma to bones and soft tissues, as well as hyperperfusion.[18] Local anesthetics are considered more effective and safer than general anesthetics because they bypass systemic effects and target the source of pain in the subcutaneous layer, intra-articular, and capsular areas.[27] Several studies have demonstrated the efficacy of local anesthetics methods in orthopedic surgery.[10,28] For instance, Busch et al. found that patients who underwent TKA and received a periarticular injection had a significantly lower requirement for patient-controlled analgesia 12 h after surgery compared to patients who did not receive an injection.[10] No serious adverse events were reported during this study.[10]

The results of our study are consistent with previous studies that indicated subperiosteal local anesthetic injection is a more effective treatment method for pain management compared to periarticular injection.[5,29,30] This effectiveness could be attributed to the injection of the local anesthetic beneath the periosteum of the bone, which is rich in small blood vessels and unmyelinated nerve terminal.[31] Furthermore, the combination of anti-inflammatory agents, such as dexamethasone, with local anesthetics agents, as used in our study, may extend analgesic effects within the bone periosteum.[28] Although VAS scores were consistently lower in the S group in comparison with the P group across all time points, statistical significance was only achieved at the 24-hour post-surgery mark. This finding is similar to a study by Serbest et al. In which patients who received the subperiosteal local anesthetic injection exhibited lower pain scores on the first day after surgery.[32] notably, no serious adverse events were documented during this study.[32] we posit that this could be attributed to differing half-lives of medications employed in our local anesthetic. Specifically, the half-lives of lidocaine, dexmedetomidine, and marcaine are approximately 1.5 to 2 h, 2 h, and 2.7 h, respectively.[33-35]

Our results indicated that there may not be a statistically significant difference in pain relief trends between the two groups over the measured time periods. This outcome suggests that the initial observed reduction in pain levels for the S group at the 24 h post-surgery mark may not be consistently maintained across subsequent time points. While this particular P-value does not meet the conventional threshold for statistical significance, it is important to note that the clinical significance of the observed pain score differences may still hold relevance. Further investigation and consideration of clinical implications are necessary to fully interpret these findings.

This study had several limitations. Most importantly, it lacked a control group. The absence of a control group was attributed to the limited availability of a sufficient number of patients for inclusion in the study. Consequently, we opted to solely compare subperiosteal and periarticular injection methods, as previous studies indicated the analgesic efficacy of the compounds within the local anesthetic, but their relative superiority remained unknown.[14-16] Another limitation pertained to the small sample size and short follow-up period. Additionally, we did not measure VAS separately at rest, motion, and nighttime. Future studies with large sample sizes and proper control groups are essential to further evaluate the analgesic effect of this local anesthetic and compare the subperiosteal and periarticular methods.

Conclusion

In conclusion, the findings of our study demonstrated that subperiosteal injection of a local anesthetic containing idocaine, dexmedetomidine, and marcaine provides more effective postoperative analgesia than periarticular injection 24 h following TKA. Furthermore, larger prospective randomized comparative studies using these agents in both periarticular and subperiosteal injections are needed to confirm our results.

Acknowledgement

The authors thank all the patients for participating in the study.

Conflict of interest: None

Funding: None

Reza Minaei MD [1,2]
Mohammad Salehpour MD [1]
Emad Kouhestani MD [1,2]
Mahshid Ghasemi MD [3]

1 Department of Orthopedic Surgery, Shahid Beheshti University of Medical Sciences, Tehran, Iran

2 Bone Joint and Related Tissues Research Center, Akhtar Orthopedic Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran

3 Anesthesiology Research Center, Shahid Beheshti University of Medical Sciences,Tehran, Iran

References

1. Lowe CJM, Barker KL, Dewey M, Sackley CM. Effectiveness of physiotherapy exercise after knee arthroplasty for osteoarthritis: systematic review and meta-analysis of randomised controlled trials. BMJ.2007; 335(7624):812. doi: 10.1136/bmj.39311.460093.BE.
2. Paul JE, Arya A, Hurlburt L, et al. Femoral nerve block improves analgesia outcomes after total knee arthroplasty: a meta-analysis of randomized controlled trials. Anesthesiology.2010; 113(5):1144-62. doi: 10.1097/ALN.0b013e3181f4b18.
3. Fard AB, Jabalameli M, Khorrami AM, Ghaderi MT, Mohammadpour M, Gharanizadeh K. The Effect of Adding Corticosteroid to the Periarticular Injection Cocktail for Pain Control after Total Hip and Total Knee Arthroplasty: A Double-Blinded Randomized Clinical Trial. Arch Bone Jt Surg.2022; 10(12):1049-1055. doi: 10.22038/ABJS.2022.50610.2509.
4. Galimba J. Promoting the use of periarticular multimodal drug injection for total knee arthroplasty. Orthop Nurs.2009; 28(5):250-4; quiz 255-6. doi: 10.1097/NOR.0b013e3181b822ed.
5. Fu P, Wu Y, Wu H, Li X, Qian Q, Zhu Y. Efficacy of intra-articular cocktail analgesic injection in total knee arthroplasty—a randomized controlled trial. Knee.2009; 16(4):280-4. doi: 10.1016/j.knee.2008.12.012.
6. Abdulwahab T, Meshram P, Althani S, Albelooshi A. Comparison of Intraarticular Versus Combined Intravenous and Intraarticular Tranexamic Acid Administration in Patients Undergoing Primary Unilateral Total Knee Arthroplasty: A Randomized Controlled Trial in the Middle Eastern Patient Population. Arch Bone Jt Surg.2022; 10(12):1037-1043. doi: 10.22038/ABJS.2022.67705.3210.
7. Fajardo M, Collins J, Landa J, Adler E, Meere P, Di Cesare PE. Effect of a perioperative intra-articular injection on pain control and early range of motion following bilateral TKA. Orthopedics.2011; 34(5):354. doi: 10.3928/01477447-20110317-11.
8. Yuenyongviwat V, Pornrattanamaneewong C, Chinachoti T, Chareancholvanich K. Periarticular injection with bupivacaine for postoperative pain control in total knee replacement: a prospective randomized double-blind controlled trial. Adv Orthop.2012:2012:107309. doi: 10.1155/2012/107309.
9. Dalury DF. A state-of-the-art pain protocol for total knee replacement. Arthroplast Today.2016; 2(1):23-25. doi: 10.1016/j.artd.2016.01.004.
10. Busch CA, Shore BJ, Bhandari R, et al. Efficacy of periarticular multimodal drug injection in total knee arthroplasty: a randomized trial. J Bone Joint Surg Am.2006; 88(5):959-63. doi: 10.2106/JBJS.E.00344.
11. Parvataneni HK, Shah VP, Howard H, Cole N, Ranawat AS, Ranawat CS. Controlling pain after total hip and knee

arthroplasty using a multimodal protocol with local periarticular injections: a prospective randomized study. J Arthroplasty.2007; 22(6 Suppl 2):33-8. doi: 10.1016/j.arth.2007.03.034.
12. Maheshwari AV, Blum YC, Shekhar L, Ranawat AS, Ranawat CS. Multimodal pain management after total hip and knee arthroplasty at the Ranawat Orthopaedic Center. Clin Orthop Relat Res.2009; 467(6):1418-23. doi: 10.1007/s11999-009-0728-7.
13. Packiasabapathy SK, Kashyap L, Arora MK, 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.
14. Gousheh M, Akhondzadeh R, Rashidi M, Olapour A, Moftakhar F. Comparison of dexmedetomidine and morphine as adjuvants to bupivacaine for epidural anesthesia in leg fracture surgery: A randomized clinical trial. Anesth Pain Med.2019; 9(4):e91480. doi: 10.5812/aapm.91480.
15. Kalamaras AB, Aarnes TK, Moore SA, et al. Effects of perioperative saphenous and sciatic nerve blocks, lumbosacral epidural or morphine–lidocaine–ketamine infusion on postoperative pain and sedation in dogs undergoing tibial plateau leveling osteotomy. Vet Anaesth Analg.2021; 48(3):415-421. doi: 10.1016/j.vaa.2021.02.004.
16. Modir H, Moshiri E, Azami M, Zad MJ, Hashiani AA. Comparative efficacy of ketamine, lidocaine, acetaminophen, and dexmedetomidine combined with morphine patient-controlled analgesia in treating opium-addicted patients undergoing tibia fracture surgery: A randomized clinical trial. Journal of Acute Disease. 2022; 11(5):181.
17. Jain N, Tada S, Sethi SK, Patodi V, Jain K, Garg DK. Dexmedetomidine with 0.5% lignocaine enhances postoperative analgesia in patients undergoing upper limb orthopedic surgeries under intravenous regional anesthesia. Journal of Dr NTR University of Health Sciences. 2021; 10(1):8.
18. Frisch NB, Darrith B, Hansen DC, Wells A, Sanders S, Berger RA. Single-dose lidocaine spinal anesthesia in hip and knee arthroplasty. Arthroplast Today.2018; 4(2):236-239. doi: 10.1016/j.artd.2018.02.011.
19. Hagar AD, Fang CJ, Dannenbaum JH, Smith EL, Bono JV, Talmo CT. Reducing narcotic usage with 0.5% bupivacaine periarticular injections in total knee arthroplasty. J Arthroplasty.2022; 37(5):851-856. doi: 10.1016/j.arth.2022.01.026.
20. Yang Q, Ren Y, Feng B, Weng X. Pain relieving effect of dexmedetomidine in patients undergoing total knee or hip arthroplasty: a meta-analysis. Medicine (Baltimore).2020; 99(1):e18538. doi: 10.1097/MD.0000000000018538.
21. Gutman MJ, Patel MS, Weintraub MT, Singh A, Padegimas EM, Abboud JA, Namdari S. Can Patients Accurately Recall their Preoperative Pain and Functional Scores Following Rotator Cuff Repair and Total Shoulder Arthroplasty? Arch Bone Jt Surg.2023; 11(3):160-165. doi: 10.22038/ABJS.2021.61260.3006.
22. Joyce CD, Stoll KE, Harper TM, Sherman M, Botros J, Getz CL, Namdari S, Davis DE. Shoulder Synovitis does not Affect Pain after Arthroscopic Rotator Cuff Repair. Arch Bone Jt Surg.2022; 10(12):1013-1019. doi: 10.22038/ABJS.2022.64501.3101.
23. Li Jw, Ma Ys, Xiao Lk. Postoperative pain management in total knee arthroplasty. Orthop Surg.2019; 11(5):755-761. doi: 10.1111/os.12535.
24. Petersen KK, Simonsen O, Laursen MB, Nielsen TA, Rasmussen S, Arendt-Nielsen L. Chronic postoperative pain after primary and revision total knee arthroplasty. Clin J Pain.2015; 31(1):1-6. doi: 10.1097/AJP.0000000000000146.
25. Haegerstam GA. Pathophysiology of bone pain: a review. Acta Orthop Scand.2001; 72(3):308-17. doi: 10.1080/00016470152846682.
26. Wylde V, Beswick A, Bruce J, Blom A, Howells N, Gooberman-Hill R. Chronic pain after total knee arthroplasty. EFORT Open Rev.2018; 3(8):461-470. doi: 10.1302/2058-5241.3.180004.
27. Dennis DA. Evaluation of painful total knee arthroplasty. J Arthroplasty.2004; 19(4 Suppl 1):35-40. doi: 10.1016/j.arth.2004.03.003.
28. Beyzadeoglu T, Yilmaz C, Bekler H, Gokce A, Sayin MM. Intraarticular tramadol plus pericapsular incisional bupivacaine provides better analgesia than intraarticular plus pericapsular incisional bupivacaine after outpatient arthroscopic partial meniscectomy. Knee Surg Sports Traumatol Arthrosc.2007; 15(5):564-8. doi: 10.1007/s00167-006-0221-8.
29. Altay N, Sarıkaya B, Karahan MA, et al. Comparison of efficacy between combined periarticular and incisional injections versus periarticular injection alone of bupivacaine for pain control after total knee arthroplasty: A prospective randomized controlled trial. Acta Orthop Traumatol Turc.2020; 54(4):402-407. doi: 10.5152/j.aott.2020.20212.
30. Gibbs D, Green T, Esler C. The local infiltration of analgesia following total knee replacement: a review of current literature. J Bone Joint Surg Br.2012; 94(9):1154-9. doi: 10.1302/0301-620X.94B9.28611.
31. Akizuki S, Yasukawa Y, Takizawa T. A new method of hemostasis for cementless total knee arthroplasty. Bull Hosp Jt Dis.1997; 56(4):222-4.
32. Serbest S, Tiftikçi U, Çoban M, Çirpar M, Daglar B. Knee pain and functional scores after intramedullary nailing of tibial shaft fractures using a suprapatellar approach. J Orthop Trauma.2019; 33(1):37-41. doi: 10.1097/BOT.0000000000001337.
33. Bhana N, Goa KL, McClellan KJ. Dexmedetomidine. Drugs.2000; 59(2):263-8; discussion 269-70. doi: 10.2165/00003495-200059020-00012.
34. Dunn LK, Durieux ME. Perioperative use of intravenous lidocaine. Anesthesiology.2017; 126(4):729-737. doi: 10.1097/ALN.0000000000001527.
35. Moore DC, Mather LE, Bridenbaugh LD, Thompson GE, Balfour RI, Lysons DF, Horton WG. Bupivacaine (Marcaine®): an evaluation of its tissue and systemic toxicity in humans. Acta Anaesthesiol Scand.1977; 21(2):109-21. doi: 10.1111/j.1399-6576.1977.tb01201.x.