

## Original Article

## Epidural Catheter Compared with Local Infiltration Analgesia for Postoperative Pain Relief in Total Knee Replacement

Mohammadreza Minator Sajjadi<sup>1</sup>, Mohammadreza Moshari<sup>2</sup>, Mohammad Ali Okhovatpour<sup>1</sup>, Reza Zandi<sup>1</sup> , Keyvan Jalali<sup>1</sup>

### Abstract

**Background:** This study compared the effects of epidural analgesia with infiltration analgesia in postoperative pain control for total knee arthroplasty.

**Methods and materials:** A total of 47 females and 13 males with an average age of 65.7 years were randomly allocated into epidural (EA; n=30) and local infiltration anesthesia (LIA; n=30) groups. All patients received spinal anesthesia and were inserted epidural catheter. In LIA group, 50mL of a mixture, containing bupivacaine, ketorolac, morphine sulfate, and epinephrine was injected in to periarticular tissue and in EA group normal saline was injected. In the EA group, after surgery, an epidural catheter was attached to the patient-controlled analgesia (PCA) infusion pump with 25cc bupivacaine diluted in 75mL of normal saline but in LIA group, the PCA pump of the epidural catheter contained 100cc of normal saline, and the pump was blocked.

**Results:** The difference in demographic data was not significant between the groups. The mean VAS score (Pain) of EA group was significantly higher than LIA group until 12 hours after surgery, At 24 hours, there was no significant difference between two groups, and pain of EA group was significantly lower than LIA group at 48 hours after the surgery. Drainage volume and hemoglobin drops were lower in LIA group. Knee range of motion in the LIA group was not superior to that of the EA group two weeks after surgery. The patients' ability to perform active straight leg raise had no significant difference between two groups one day after the surgery.

**Conclusion:** Local infiltration analgesia was better than epidural for postoperative pain control at first 12 hours. However, epidural analgesia could control postoperative pain more effectively at 48 hours after surgery. There was no significantly difference between two groups regard to patients ability to perform straight leg rising and Knee range of motion was similar in two groups.

**Keywords:** Epidural catheter, Local infiltration anesthesia, Total knee replacement, Analgesia, spinal anesthesia, Pain management

**Please cite this article as:** Minator Sajjadi M, Moshari M, Okhovatpour MA, Zandi R, Jalali K. Epidural Catheter Compared with Local Infiltration Analgesia for Postoperative Pain Relief in Total Knee Replacement. J Cell Mol Anesth. 2019;4(4):128-35.

1. Department of Orthopedics, Taleghani Hospital Research Development Committee, Shahid Beheshti University of Medical Sciences, Tehran, Iran

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

**Corresponding Author:** Reza Zandi, MD, Department of Orthopedics, Taleghani Hospital Research Development Committee, Shahid Beheshti University of Medical Sciences, Tehran, Iran

**Tel/Fax:** 00982122432580

**Email:** reza.zandi@sbum.ac.ir

## Introduction

Knee osteoarthritis is the most common joint disease, which affects more than 70% of adults aged 55-78 years (1). Total knee arthroplasty (TKA) is indicated when conservative treatments fail and severe disability impairs the patient's quality of life. Despite the effectiveness of TKA in the treatment of debilitating knee arthritis, postoperative pain may develop, affecting the patient's rehabilitation. The patients' clinical outcomes have significantly improved due to major progress in pain management using multimodal approaches. According to previous studies, pain control should be optimized in patients following TKA to increase their satisfaction and function.

It is known that inadequate postoperative analgesia is associated with poor rehabilitation, prolonged hospital stay, and increased risk of adverse events, such as pulmonary dysfunction, thromboembolism, myocardial ischemia, and urinary retention (6). Researchers have suggested a variety of methods for postoperative pain management and confirmed their remarkable efficacy; however, complications associated with the overuse of narcotics and nerve blockade are inevitable (7).

Conventional pain management is a unimodal way. It usually involves the administration of opioids (injectable) with or without nonsteroidal anti-inflammatory drugs as required. This often requires higher doses of opioids, with its potential side effects and the administration of drugs being dependent on nursing usually is delayed.

Intravenous patient-controlled analgesia (PCA) is a commonly used analgesic option. Opioids are the primary analgesic in PCA for TKA. However, opioids are associated with side effects such as nausea, drowsiness, constipation and Respiratory Depression that might have negative effects on the patient and may interfere with rehabilitation.

Epidural analgesia may provide better pain relief compared to systemic drugs. There are, however, many side effects such as perioperative hypotension, urinary retention and respiratory depression with this method.

Periarticular injection at the end of surgery is a novel method for postoperative pain control. Recent studies have shown that this approach has several

advantages over other methods of pain management. In a prospective randomized controlled study by Fajardo et al., an intraarticular mixture of morphine, bupivacaine, epinephrine, and ketorolac significantly reduced postoperative pain and increased the knee range of motion (8). However, findings regarding the importance of intraarticular injection of analgesics are controversial. In this regard, Joo et al., in a double-blind randomized controlled trial, studied the efficiency of multimodal drug injection following TKA (9). They concluded that the patients' satisfaction, pain, blood loss, and range of motion did not significantly improve after the intraoperative intraarticular injection of multimodal drugs into the knee in comparison with the controls.

Recently, the femoral nerve block (FNB) has been recommended as the most effective technique for postoperative pain management following TKA (10). Despite the positive analgesic outcomes of FNB, there are concerns among surgeons about the prolonged weakness of quadriceps (11). This complication occurs in about 2% of patients (12) and can lead to falls, fractures, and delays in ambulation (13). We postulated that postoperative epidural catheters could ameliorate pain more effectively than periarticular injection without incurring more complications.

## Methods

After the exclusion of 17 patients, we enrolled 60 patients (47 females and 13 males), with an average age of  $65.7 \pm 7.21$  years, who were candidates for primary TKA.

By using the "R Program to Generate Random Number", the patients were randomly allocated into epidural anesthesia (EA; n=30) and local infiltration anesthesia (LIA; n=30) groups. Before the study, written consent was obtained from each patient. The Institutional Ethics Committee of Taleghani Hospital, affiliated to Shahid Beheshti University of Medical Sciences, approved all the procedures, and the study was registered in the Iranian Registry of Clinical Trials (IRCT).

We included patients (age, 53-83 years), who were candidates for primary knee arthroplasty between April and July 2017. We excluded patients who were candidates for revision or bilateral TKA, those with a history of allergy to any of the test drugs, and those

with collagen vascular diseases (e.g., rheumatoid arthritis), neuromuscular diseases, hematological diseases, and coagulopathy. Moreover, changes in the intraoperative anesthesia method (3 patients), a non-functional epidural catheter (2 patients), and an unwillingness to complete the questionnaire were among the exclusion criteria.

**Anesthesia and surgical procedure:** all the patients received spinal anesthesia with 4 cc Marcaine 0.5%. The epidural catheter was inserted for all patients by the same anesthesiologist. In addition, a single surgeon performed the operations. The joint was approached through a medial parapatellar arthrotomy. Bone cuts and soft tissue balancing were performed in the same manner. In all patients, a posterior stabilized prosthesis was used. During the operation, all the patients had intravenous sedation with midazolam and fentanyl.

In the LIA group, 50 mL of a mixture, containing bupivacaine (4 mg), ketorolac (60 mg), morphine sulfate (20 mg), and epinephrine (1 mg/1000), was prepared. Before polyethylene implantation, 20 mL of the mixture was injected into a posterior joint capsule. After closing the joint capsule, the remaining mixture was injected into the periarticular tissue; our goal was to deliver an adequate amount of the substance into the tissues. The goal is to deliver as much of the fluid as possible into the tissues, where it will be most effective. Using small needles, such as 22 gauges, is the best choice. Aspiration before injection was performed especially in areas of potential danger such as the posterior midline of the knee. By using two syringes, the nurse was able to draw up the syringe as the surgeon injected the solution. Generally, the most effective injections are multiple, small, and slow.

**Pain assessment and management:** Postoperative pain was assessed using VAS, which was completed by patients who were informed preoperatively. The VAS score ranges from zero (no pain) to 10 (worst pain possible), which was measured at 1, 6, 12, 24, and 48 hours postoperatively.

**Blood loss assessment:** hemoglobin drops (preoperatively/postoperatively) and drainage volume 24 hours after the surgery were considered as the indices of blood loss. The need for transfusion in the two groups was also recorded.

**Functional outcomes assessment:** Functional

outcomes assessment

Regarding the functional outcomes, the patients' ability to perform SLR was examined by the surgeon one day after surgery, and the surgeon measured the knee range of motion two weeks following the surgery.

**Demographic characteristics and length of hospital stay:** demographic information, including gender, age, and body mass index (BMI), was compared between the two groups as possible factors that might affect the results. The length of hospital stay was also considered as a factor affecting the cost-effectiveness of the surgery.

**Statistical analysis:** Statistical analyses were done with SPSS software version 14 (SPSS Inc., Chicago, IL, USA) on a Microsoft Windows-based computer. Continuous variables, such as age, BMI, hospital stay, VAS score, hemoglobin drops, and drainage volume were compared by independent-sample t-tests between the two groups. Categorical variables such as gender and SLR were analyzed with Chi-square and Fisher's exact test. The P-value of less than 0.05 considered a statistically significant difference.

## Results

**Demographic characteristics:** the demographic characteristics of all patients were compared between the two groups. The mean age of patients in the Epidural group was  $66 \pm 6.55$  and in Local group was  $65.3 \pm 7.92$ . In the epidural group, 23 females and 7 males and in the LIA group, 24 females and 6 males were assessed. No statistically significant difference was observed in the clinical characteristics, including gender, age, and BMI, between the two groups (Table 1). The demographic characteristics of all patients (30 patients in group EA and 30 patients in group LIA) were compared (table 1). No significant difference was observed among the two groups in the patients' characteristics, including gender, age, and BMI (Table 1).

**Pain:** pain was primary outcome of this study was calculated by a VAS ruler within 48 hours after the surgery to evaluate the pain intensity experienced by the patients. The mean VAS score of EA group was significantly higher than LIA group at 1 hour (P-value=0.009), 6 hours (P-value=0.003) and 12 hours (P-value=0.0001) after the surgery. At 24 hours, there

**Table 1:** Demographic characteristics of patients in both groups.

Study Groups		Epidural Anesthesia (N=30)	Local Infiltration Anesthesia (N=30)	P value
Gender	Male	7 (23.3)	6 (20)	0.754
	Female	23 (76.7)	24 (80)	
Age		66 ± 6.55	65.3 ± 7.92	0.71
BMI		29 ± 2.57	29.5 ± 2.37	0.487

was no significant difference between two groups regarding VAS score (P-value=0.068). VAS score was lower in the EA group ( $4.3 \pm 0.65$ ), compared to the LIA group ( $4.73 \pm 0.64$ ) at 48 hours postoperatively (P-value = 0.012) (Table 2; Figure 1).

**Blood loss:** blood loss was measured by drainage volume postoperatively. It was lower in the LIA group 24 hours after the surgery, and the difference was statistically significant (P-value = 0.0001). Hemoglobin drops was also lower in LIA group compared to EA group three days after the surgery (P-value =0.0001) (Table 3).

**Knee range of motion:** the knee range of motion in

the LIA group was not superior to that of the EA group two weeks after the surgery (P-value=0.499). The patients' ability to perform active straight leg raise was measured by the surgeon one day after the surgery. More patients in the LIA group could perform SLR one day after the surgery but the difference between the two groups was not significantly different (P-value=0.1) (Table 4).

**Length of hospital stay:** no significant difference was found in the length of hospital stay between the groups ( $4.4 \pm 0.93$  days in the EA group versus  $4.57 \pm 0.77$  days in the LIA group); (P-value=0.44).

**Table 2:** Visual analogue scale (VAS) in epidural group and Local infiltrative group.

Study Groups	Epidural Anesthesia (N=30)	Local Infiltration Anesthesia (N=30)	P value
1 hour after Surgery	8.3 ± 1.02	7.63 ± 0.89	0.009*
6 hour after Surgery	8.77 ± 0.86	8.13 ± 0.73	0.003*
12 hour after Surgery	7.27 ± 0.87	6.4 ± 0.77	0.0001*
24 hour after Surgery	5.77 ± 0.82	5.4 ± 0.72	0.068
48 hour after Surgery	4.3 ± 0.65	4.73 ± 0.64	0.012*

**Table 3:** Drainage volume 24 hours after the surgery and hemoglobin drop 3 days after the surgery.

Study Groups	Epidural Anesthesia	Local Infiltration	P value
	(N=30)	Anesthesia (N=30)	
Hemoglobin drops	2.76 ± 0.28	2.01 ± 0.2	0.0001
Drainage Volume	188 ± 43.5	122 ± 32.9	0.0001

## Discussion

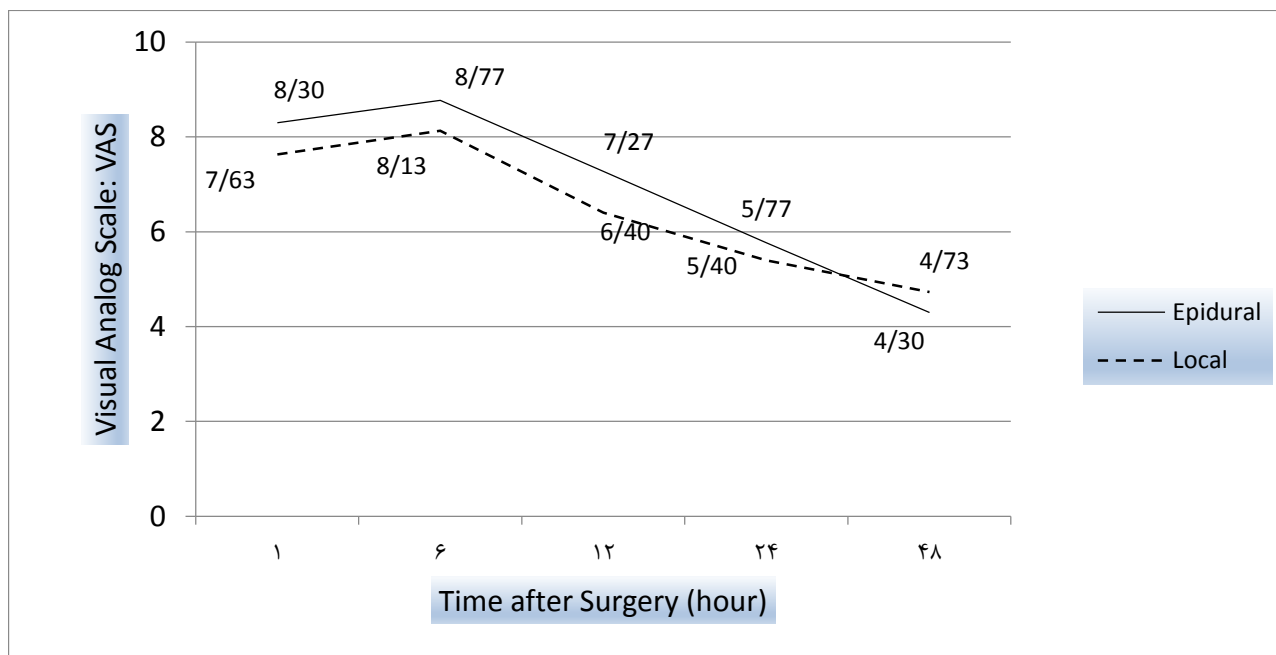
The aim of this study was to compare the functional outcomes, pain intensity, and blood loss between the LIA and EA groups, who underwent TKA under spinal anesthesia with a pain control infusion pump. The two groups were not different in terms of age and male-to-female ratio; therefore, these factors had no significant effects on the results. BMI was measured because it was assumed to be effective in postoperative pain and blood loss; however, the results did not confirm this assumption. The mean VAS score of the EA group was significantly higher than the LIA group at 1 hour, 6 hours and 12 hours after the surgery. At 24 hours, there was no significant difference between the two groups regarding the VAS score. However, the VAS score was lower in the EA group, compared to the LIA group at 48 hours postoperatively.

In this study, we used ketamine with bupivacaine for local infiltration anesthesia. Ketamine is an analgesic drug (used as general or local

anesthesia) that can interact with several types of receptors (as an antagonist), including adrenergic, serotonergic, muscarinic, opioids, and N-methyl D-aspartate (NMDA) (14). This drug can be used for the management of pre-, intra- and postoperative pain (15). Adam et al (16) concluded that small doses of ketamine (0.5 mg/kg) might improve the knee range of motion following TKA. Bupivacaine is typically used for intra-articular (IA) analgesia because of its extended period of effectiveness (4–7 h) or long-lasting anesthetic properties. Furthermore, ketamine has been reported to be more efficient when combined with bupivacaine. It induces fewer adverse effects and does not affect any motor function. Inanoglu et al (17) concluded that ketamine and bupivacaine (multimodal regimen) could effectively control the postoperative pain following tonsillectomy. Furthermore, Batra et al (18) in their pilot study indicated that ketamine and bupivacaine could provide better pain relief following arthroscopic knee surgery by evaluating visual analog scale (VAS) and opioids consumption in arthroscopic knee surgery.

**Table 4:** Patient ability to perform SLR the day after the surgery and knee range of motion 2 weeks after the surgery.

Study Groups		Epidural	Local Infiltration	P value
		Anesthesia (N=30)	Anesthesia (N=30)	
SLR	Yes	7 (23.3)	13 (43.3)	0.1
	No	23 (76.7)	17 (56.7)	
knee Range of motion		94.8 ± 10.4	93 ± 10.1	0.499



**Figure 1.** Visual analogue scale trend in epidural group and Local infiltrative group.

There are different methods for the decrease of postoperative pain after total knee replacement. In the unimodal conventional method, injectable opioids with or without non-steroidal anti-inflammatory drugs can be used. However, this method has some side effects such as nausea, drowsiness, constipation and respiratory depression that might have negative effects on the patient.

The femoral nerve block (FNB) with local anesthetics provides superior pain relief and results in fewer side effects compared with conventional IV PCA with opioids. Compared with epidural analgesia, FNB does not have a motor blockade in the opposite leg. FNB also avoids the risk of epidural hematoma, which is associated with the anticoagulants used to prevent vascular thromboembolism and has a lower risk of postoperative hypotension and urinary difficulty, but this method needs an expert anesthesiologist and also, it may produce femoral quadriceps muscle weakness, which interfere with ambulation and risk of falling. (19, 20).

The LIA method is suitable for pain control due to its simplicity, unlike epidural catheter insertion, which requires equipment. In addition, LIA can be performed faster and easier compared with the femoral nerve block procedure. Moreover, it is associated with less motor function impairment, compared with cases

of a femoral nerve block (21). Although there are numerous studies confirming the effectiveness of LIA in postoperative pain management following TKA (22-24), studies comparing EA with LIA are scarce. In this regard, Li et al. reviewed the results of seven studies in a systematic review and reported similar efficacy to EPA in terms of pain control after TKA; on the other hand, a reduction in nausea and length of hospital stay, besides an increase in the range of motion, was observed (25).

In a clinical trial conducted by Binici, the patients were assessed in two groups. Group 1 (n=15), 72 mL of 0.9% NaCl and 48 mL of bupivacaine were administered postoperatively for 24 hours using an epidural catheter. On the other hand, group 2 (n=15), an ON-Q infiltration pump was used. At 30 minutes, 8 hours, and 12 hours post-operation, the mean VAS scores were not significantly different. However, group 2 had significantly higher VAS scores at 60 minutes and 2 hours post-operation in comparison with group 1 (26). In our study, the VAS score was not significantly different at 24 hours postoperatively, but the VAS score was significantly lower in the epidural group between 48 hours.

In a Cochrane review by Choi et al. (27), the efficacy of epidural analgesia in pain management was examined after knee or hip replacement. According to



VAS scores, the pain was lower at rest in patients with epidural analgesia in comparison with patients on systemic analgesia; nevertheless, at 18 to 24 hours post-operation, the effect was found to be insignificant. The extent of pain relief needs to be compared with the frequency of adverse events.

The femoral nerve block provides excellent pain relief, but it causes some problems, such as weakness of the quadriceps and unblocking the popliteal fossa; it requires an expert anesthesiologist for catheter insertion (28). In a study by Chaumeron et al., it was found that pain control in LIA was similar to a femoral nerve block, although in this method, the motor block was prevented, and there were no negative functional effects. According to the findings, it can be a suitable option for replacing the femoral nerve block (29). Nevertheless, epidural analgesia has multiple side effects, such as urinary retention, perioperative hypotension, respiratory depression, and pruritus (30). Moreover, in the non-operated leg, ambulation and sensation seem to be affected; accordingly, early physiotherapy may be interrupted after TKA due to these adverse effects. In addition, anticoagulation therapy, which is used to prevent thromboembolic events, may be delayed due to epidural analgesia.

Increased bleeding is associated with delayed recovery, increased complications, increased costs, and decreased patient satisfaction. In our study drainage volume and hemoglobin drops was significantly lower in the LIA group. The difference might be related to the vasoconstrictive effects of epinephrine employed in the local injection cocktail. We inserted in both groups intra-articular catheters and analgesic drugs were infiltrated in the periarticular soft tissue in the LIA group. Therefore, the intraarticular drain could not decrease the volume of analgesic drugs.

Knee function was assessed by straight leg raise ability and knee range of motion, as mentioned previously. In this regard, spinal LIA group had a greater ability to perform active straight leg raise on the first postoperative day but the difference was not significant between two groups statistically. This suggests less interference of LIA with quadriceps muscle function, which is similar to the results reported by Chaumeron et al. (29) but more numbers of patients may be needed.

In this study, low-molecular-weight heparin was

injected day after the surgery. For preventing epidural hematoma, on the second day after the surgery, catheters removed 12 hours following the dose of LMWH, and the next dose is held for at least 2 hours following catheter removal. The current guidelines recommend waiting 12 h after the last prophylactic dose of LMWH before CNB or epidural catheter removal (31, 32). Administration the evening before surgery, or after operation, is therefore appropriate. After CNB or catheter removal, a period of 2–4 h should elapse before LMWH administration.

## Conclusion

Based on the results of this study, local infiltration analgesia was better than epidural analgesia for postoperative pain control in the first 12 hours. However, epidural analgesia could control postoperative pain more effectively at 48 postoperative hours. Knee range of motion and patients' ability to perform straight leg rising were similar in two groups.

## Acknowledgment

The authors would like to thank all the study participants and the staff of Taleghani Hospital Department of Orthopedics for their help in preparing this paper.

## Conflicts of Interest

The authors declare that they have no conflict of interest.

## References

1. Aweid O, Haider Z, Saed A, Kalairajah Y. Treatment modalities for hip and knee osteoarthritis: A systematic review of safety. *J Orthop Surg (Hong Kong)*. 2018;26(3):2309499018808669.
2. Zhang W, Moskowitz RW, Nuki G, Abramson S, Altman RD, Arden N, Bierma-Zeinstra S, Brandt KD, Croft P, Doherty M, Dougados M, Hochberg M, Hunter DJ, Kwoh K, Lohmander LS, Tugwell P. OARSI recommendations for the management of hip and knee osteoarthritis, part I: critical appraisal of existing treatment guidelines and systematic review of current research evidence. *Osteoarthritis Cartilage*. 2007;15(9):981-1000.
3. Fang R, Liu Z, Alijiang A, Jia H, Deng Y, Song Y, Meng Q. Efficacy of Intra-articular Local Anesthetics in Total Knee Arthroplasty. *Orthopedics*. 2015;38(7):e573-81.
4. Kurosaka K, Tsukada S, Seino D, Morooka T, Nakayama H, Yoshiya S. Local infiltration analgesia versus continuous femoral nerve block in pain relief after total knee arthroplasty: a randomized

- controlled trial. *J Arthroplasty*. 2016;31:913-7.
5. Goyal N, McKenzie J, Sharkey PF. The 2012 Chitranjan Ranawat award: intraarticular analgesia after TKA reduces pain: a randomized, double-blinded, placebo-controlled, prospective study. *Clin Orthop Relat Res*. 2013;471(1):64-75.
6. Moucha CS, Weiser MC, Levin EJ. Current strategies in anesthesia and analgesia for total knee arthroplasty. *J Am Acad Orthop Surg*. 2016;24(2):60-73.
7. Sharma S, Iorio R, Specht LM, Davies-Lepie S, Healy WL. Complications of Femoral Nerve Block for Total Knee Arthroplasty. *Clin Orthop Relat Res*. 2010;468(1):135-40.
8. 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.
9. Joo JH, Park JW, Kim JS, Kim YH. Is Intra-Articular Multimodal Drug Injection Effective in Pain Management After Total Knee Arthroplasty? *J Arthroplasty*. 2011;26(7):1095-9.
10. Fischer HB, Simanski CJ, Sharp C, Bonnet F, Camu F, Neugebauer EA, Rawal N, Joshi GP, Schug SA, Kehlet H; PROSPECT Working Group. A procedure-specific systematic review and consensus recommendations for postoperative analgesia following total knee arthroplasty. *Anaesthesia*. 2008;63(10):1105-23.
11. Kandasami M, Kinninmonth AW, Sarungi M, Baines J, Scott NB. Femoral nerve block for total knee replacement - a word of caution. *Knee*. 2009;16(2):98-100.
12. Beaulieu P, Babin D, Hemmerling T. The pharmacodynamics of ropivacaine and bupivacaine in combined sciatic and femoral nerve blocks for total knee arthroplasty. *Anesth Analg*. 2006;103(3):768-74.
13. Ilfeld BM, Duke KB, Donohue MC. The association between lower extremity continuous peripheral nerve blocks and patient falls after knee and hip arthroplasty. *Anesth Analg*. 2010; 111(6):1552-4.
14. Jouguelet-Lacoste J, La Colla L, Schilling D, Chelly JE. The use of intravenous infusion or single dose of low-dose ketamine for postoperative analgesia: a review of the current literature. *Pain Med*. 2015;16(2):383-403.
15. Zhang Y, Lin H and Yi WB: Evaluation of the effects of ketamine on spinal anesthesia with levobupivacaine or ropivacaine. *Exp Ther Med*. 2016 Oct;12(4):2290-2296.
16. Adam F, Chauvin M, Du Manoir B, Langlois M, Sessler DI, Fletcher D: Small-dose ketamine infusion improves postoperative analgesia and rehabilitation after total knee arthroplasty. *Anesth Analg*. 2005;100(2):475-80.
17. Inanoglu K, Ozbakis Akkurt BC, Turhanoglu S, Okuyucu S, Akoglu E: Intravenous ketamine and local bupivacaine infiltration are effective as part of a multimodal regime for reducing postsurgical pain. *Med Sci Monit*. 2009;15(10):CR539-543.
18. Batra YK, Mahajan R, Bangalia SK, Nagi ON, Dhillon MS. Bupivacaine/ketamine is superior to intra-articular ketamine analgesia following arthroscopic knee surgery. *Can J Anaesth*. 2005;52(8):832-6.
19. Ben-David B, Chelly JE. Continuous peripheral neural blockade for postoperative analgesia: practical advantages. *Anesth Analg*. 2003;96(5):1537.
20. Seet E, Leong WL, Yeo AS, Fook-Chong S. Effectiveness of 3-in-1 continuous femoral block of differing concentrations compared to patient controlled intravenous morphine for post total knee arthroplasty analgesia and knee rehabilitation. *Anaesth Intensive Care*. 2006;34(1):25-30.
21. Zhang LK, Ma JX, Kuang MJ, Ma XL. Comparison of Periarticular Local Infiltration Analgesia With Femoral Nerve Block for Total Knee Arthroplasty: a Meta-Analysis of Randomized Controlled Trials. *J Arthroplasty*. 2018;33(6):1972-8.
22. Kerr DR, Kohan L. Local infiltration analgesia: a technique for the control of acute postoperative pain following knee and hip surgery: a case study of 325 patients. *Acta Orthop*. 2008;79(2):174-83.
23. Moghtadaei M, Farahini H, Faiz SH, Mokarami F, Safari S. Pain Management for Total Knee Arthroplasty: Single-Injection Femoral Nerve Block versus Local Infiltration Analgesia. *Iran Red Crescent Med J*. 2014;16(1):e13247.
24. Quinn M, Deakin AH, McDonald DA, Cunningham IK, Payne AP, Picard F. An anatomic study of local infiltration analgesia in total knee arthroplasty. *Knee*. 2013;20(5):319-23.
25. Li C, Qu J, Pan S, Qu Y. Local infiltration anesthesia versus epidural analgesia for postoperative pain control in total knee arthroplasty: a systematic review and meta-analysis. *J Orthop Surg Res*. 2018;13(1):112.
26. Binici Bedir E, Kurtulmuş T, Başyigit S, Bakır U, Sağlam N, Saka G. A comparison of epidural analgesia and local infiltration analgesia methods in pain control following total knee arthroplasty. *Acta Orthop Traumatol Turc*. 2014;48(1):73-9.
27. Choi PT, Bhandari M, Scott J, Douketis J. Epidural analgesia for pain relief following hip or knee replacement. *Cochrane Database Syst Rev*. 2003;(3):CD003071.
28. Song SJ. Pain management and anesthesia in total knee arthroplasty. *Knee Surg Relat Res*. 2017 Jun 1;29(2):77-79.
29. Chaumeron A, Audy D, Drolet P, Lavigne M, Vendittoli PA. Periarticular injection in knee arthroplasty improves quadriceps function. *Clin Orthop Relat Res*. 2013;471(7):2284-95.
30. Markel DC, Doerr T, Lincoln D, Bass NF. Observational study on intrathecal and peridural changes after routine spinal and epidural anesthesia in patients undergoing total joint arthroplasty. *J Arthroplasty*. 2007;22(6):844-8.
31. Samama CM, Afshari A; ESA VTE Guidelines Task Force. European guidelines on perioperative venous thromboembolism prophylaxis. *Eur J Anaesthesiol*. 2018;35(2):73-76.
32. Gogarten W, Vandermeulen E, Van Aken H, Kozek S, Llau JV, Samama CM; European Society of Anaesthesiology. Regional anaesthesia and antithrombotic agents: recommendations of the European Society of Anaesthesiology. *Eur J Anaesthesiol*. 2010;27(12):999-1015.