



# Comparison of Saphenous Nerve Block and Oral Oxycodone for Postoperative Pain Management in Total Knee Arthroplasty: A Randomized Clinical Trial

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Received 2020-12-14; Accepted 2021-08-19; Online Published 2021-10-19

## Abstract

**Introduction:** Post-operative pain management following total knee replacement (TKA) is crucial. The introduction of some available, inexpensive, and effective methods for post-operative pain management is necessary. Therefore, this randomized clinical trial was done comparing the analgesic effect of an oral low-cost drug (oxycodone) and ultrasound-guided nerve block (saphenous nerve block) to assess the best method for post-operative pain management after TKA surgery.

**Methods:** This single-blind, randomized, controlled, single-center clinical trial was performed from June 2017 to June 2018. There were 80 patients undergoing TKA randomly divided into two groups; group A received a single shot ultrasound-guided saphenous nerve block and, group B took oxycodone which started before and continued every 6 hours after surgery to control post-operative pain. The pain score by visual analog scale (VAS), nausea- vomiting, and diclofenac use were assessed postoperatively at 2, 6, 12, and 24 hours' post-spinal anesthesia administration. Data were analyzed by SPSS-21, Chi2, Fishers' exact test, and Mann-Whitney test were used for comparing data between the two groups.

**Result:** The pain intensity according to the visual analog scale at 2, 6, 12, and 24 h post-operative was  $1.25 \pm 1.37$ ,  $4.12 \pm 1.11$ ,  $5.25 \pm 0.89$ , and  $4.57 \pm 0.95$  in group A, and  $1.10 \pm 0.95$ ,  $3.77 \pm 0.99$ ,  $4.05 \pm 0.78$ , and  $2.95 \pm 0.78$  in the group B, respectively; this was significantly lower in group B at 12 and 24 hours ( $P < 0.05$ ). The mean diclofenac use was  $87.01 \pm 68.02$  mg in group B and  $262.04 \pm 92.05$  mg in the group A ( $P < 0.001$ ). Also, the incidence of nausea and vomiting was significantly higher in group B compared to group B ( $P < 0.001$ ).

**Conclusion:** Oral oxycodone can control post-operative pain better than saphenous nerve block in the management of post-operative pain and reducing total additional analgesic drug consumption. Although, adverse effects such as nausea and vomiting were lower in saphenous nerve block.

**Keywords:** Total knee arthroplasty, Post-operative pain, Saphenous Block, Oxycodone.

## Introduction

Osteoarthritis (OA), as the most frequent joint disease, has shown an important causative agent for chronic pain in the United States<sup>1</sup> and other countries<sup>2</sup>. TKA is one of the treatments which is done frequently in elderly patients. Severe pain is common following this surgery. The control of the pain is necessary for optimum functional recovery after TKA. So, pain control is a challenging topic in this field<sup>3,4</sup>.

Pain relief is an important aspect for optimal recovery after TKA<sup>3</sup>. Some studies have shown that one of the most crucial factors associated with persistent chronic pain after TKA is poor acute pain control immediately after the surgery<sup>5</sup>. The main goals of postoperative analgesia are to decrease pain, patient's analgesic needs, and analgesic-related complications until optimized rehabilitation is achieved<sup>6</sup>.

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Developing these outcomes has potential valuable impacts on the patient's morbidity and consent, the level of the required care in the post-operative period, as well as the economic aspects<sup>7</sup>.

In one guideline that published by the Korean knee society, to reduce acute pain after the TKA, several ways were noticed, including:

- Spinal and epidural continuous analgesia, known as the neuraxial technique, in which local anesthetics and/or opioids are injected.
- Peripheral nerve block, single-shot injection, or continuous infusion with a catheter
- Local periarticular infiltration analgesia
- Intraarticular injection of local anesthetics
- Administration of systemic analgesic drugs like NSAIDs, opioids, or Gabapentinoids<sup>8</sup>.

Adding a peripheral nerve block like a saphenous nerve block to a systemic analgesic regimen provides better pain control<sup>9,10</sup> and decreases the length of hospitalization than neuraxial techniques like epidural or intravenous patient-controlled analgesia (PCA) solely<sup>11-13</sup>.

Saphenous nerve block (SNB) is superior to femoral nerve block (FNB) regarding postoperative pain management following TKA because the possibility of motor block is lower in this technique<sup>14</sup>. However, extended motor block after FNB is about 2%, but there is a risk of patient falls that is very dangerous. Fast-track total joint replacement that is gaining popularity needs to maintain motor strength for rapid mobilization after surgery. With ultrasound, the adductor canal that contains the saphenous nerve is the easily attainable indirect vision at the mid-thigh, allowing successful SNB<sup>15</sup>. Although, ultra-sonography machines and special nerve-block needles are very expensive and are not under the cover of the insurance company, so they are not available in most hospitals in developing countries like Iran.

One of the effective medications used for moderate to severe pain after surgery is opioids. Oral opioids are absorbed gradually from the GI system and can provide extended pain relief without giving extra medication than is needed. Oxycodone tablet is an inexpensive and available drug that can be used as an analgesic.

Until the design of this study, no randomized clinical trial has been done to compare SNB and oral oxycodone following TKA. We tested the hypothesis which single-shot SNB and oral oxycodone would provide better

analgesia and lesser side effects in patients who underwent TKA.

### Methods

This single-blind, randomized, controlled, single-center clinical trial was performed in Baghiatallah Hospital, Tehran, Iran from June 2017 to June 2018.

The 80 participants by Convenience Sampling undergoing elective TKA in Baghiatallah Hospital were included in the study after obtaining written informed consent. They were assigned to two groups: group A received ultrasound-guided saphenous nerve block, and group B had an oral intake of oxycodone to control the post-operative pain with 1:1 allocation as well as a parallel trial design by a randomization table. Using opaque envelopes, which were opened following allocation, the assignments were concealed. Inclusion criteria were elective unilateral TKA, planned spinal anesthesia, those aged 15- 75 years and capable of observing the research protocol, and American Society of Anesthesiologists (ASA) physical status I - II. Exclusion criteria were also contraindications to neuraxial anesthesia (spinal and epidural), long-term opioid usage (daily or almost daily using opioids over three months), hypersensitivity, and/or allergic reactions against local anesthetics, using intravenous anesthetics intraoperatively, pre-existing neuropathies on the operative extremity, contraindication for SNB, allergic reactions against the used medicines, and the ASA physical status III or more. All Surgeries were done by an orthopedic surgeon, and patients' anesthesiology was done by anesthesiologists.

The participants' demographic characteristics such as age, sex, and medical history were recorded. Two groups received standard cardiovascular and pulse oximetry monitoring. Furthermore, sedation before anesthesia was done by Midazolam 0.15 mg/kg as well as Fentanyl 1 µ/kg, intravenously. Group A received 15 ccs of bupivacaine 0.5% + 5 µg/ml of epinephrine, by a 22-gauge, Stimuplex needle (4 inches) (B. Braun Medical Inc., Germany) at the level of the midthigh through a high-frequency linear ultrasound transducer (10 to 12 Hz; eZono® 4000; Medical technology manufacturer in Jena, Germany). The transducer was held in a transverse position on the anteromedial thigh at the junction between the middle and distal third of the thigh. The needle was introduced with an in-plane approach, and local anesthetic spread lateral toward the femoral artery and deep to the sartorius muscle. The

occurrence of the block was measured using pinprick and temperature discrimination by the blunt needle and an alcohol swab in the saphenous nerve distribution than the non-operative side. If the block was not successful, the patient would be excluded from the study, and if the block was positive, she/he continued the study. In group B, Oxycodone tablet (5mg, Faran Shimi Pharmaceutical Co.) was taken orally, 2 hours before the surgery, and continued every 6 hours following surgery. Spinal anesthesia was administered, in both groups with 3cc of bupivacaine 0.5% as the intrathecal agent by the same anesthesiologist with the same median L4-L5 interspinous approach. All operations were done by one surgeon using a similar technique. Patients' pain was measured and recorded based on the visual analog scale (VAS) in 2, 6, 12, and 24 hours' post-operative. VAS was explained for participants as a ruler that is numbered from 0 to 10<sup>16</sup>. A score of zero indicates painlessness, and a score of 10 indicates unbearable pain imaginable by the patients. In both groups, if patients had extra pain with VAS more than 4, diclofenac 100 mg could be prescribed. The total dose of diclofenac as an extra analgesic used during the 24 hours after surgery was recorded.

To prevent bias, an additional questionnaire was completed in the post-operative stage by an assistant who was blinded to the analgesia technique. The

complications such as drowsiness, nausea, vomiting were recorded in all participants. Based on the frequency of nausea and vomiting, the severity of the symptoms was divided into three groups: low (0 to 1 time), moderate (2 to 3 times), and severe (more than four times). The itching was reported as occurring or not occurring in the first 24 hours after surgery. The hypotension was considered, as more than a 20% reduction in the blood pressure of the initial pressure. The volume of required additional analgesic (Diclofenac) was recorded in milligrams for each patient within the first 24 hours after surgery.

The research protocol was confirmed by the Ethics Committee of Baghiatallah University of Medical Sciences and registered with the Iranian Registry of Clinical Trials (IRCT20170826035905N3). All patients gave written informed consent.

Data were analyzed by SPSS-21. Mean, standard deviation, frequency, and percent were presented for the description of data. Chi<sup>2</sup>, Fishers' exact test, and Mann-Whitney test were used for comparing data between two groups. A P-value less than 0.05 was considered statistically significant.

## Results

The participants were divided into two groups (n=40/each; 21 males and 19 females in group A and 23 males and 17 females in group B) (Fig 1).

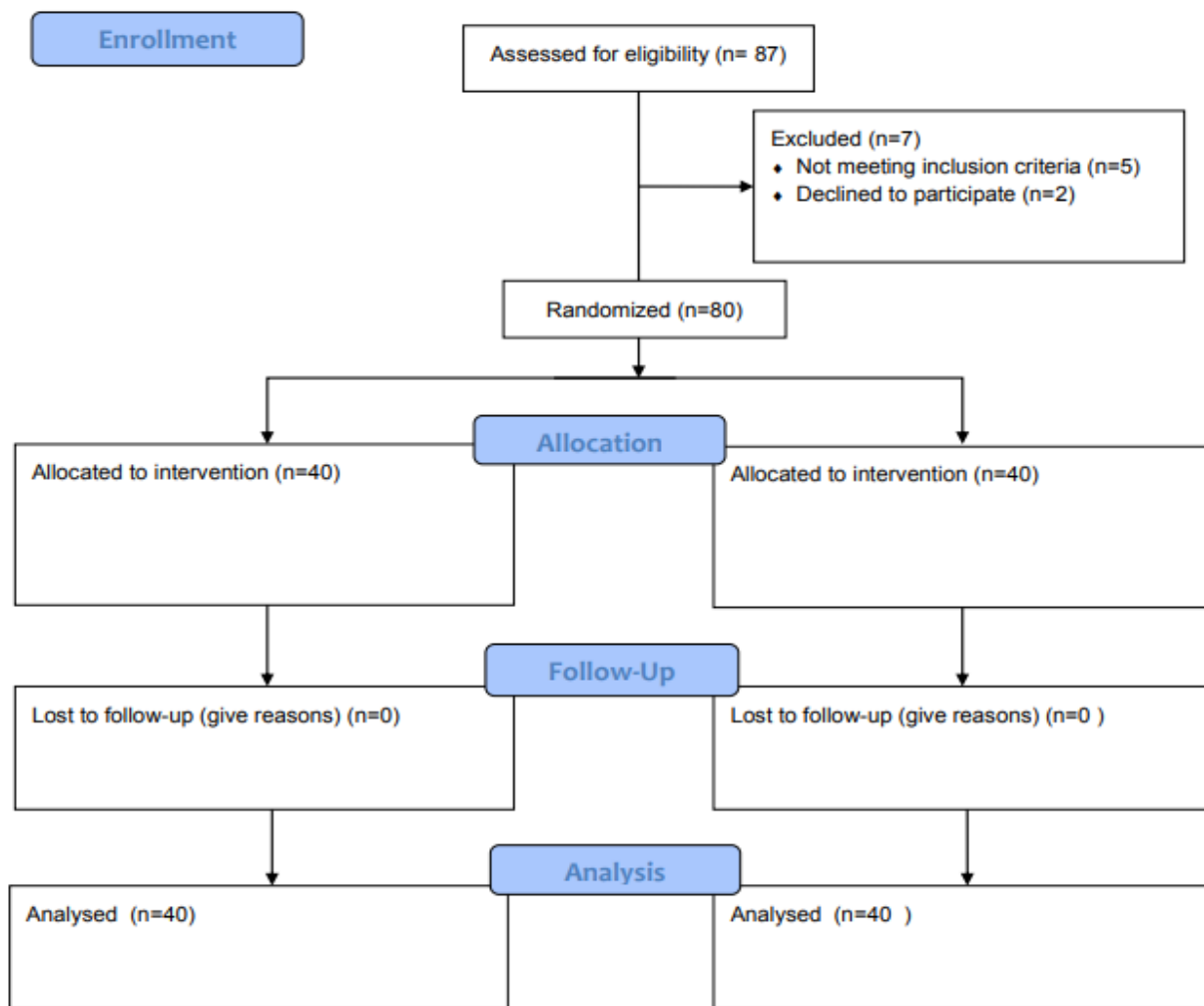


Fig 1: Flowchart diagram

The average age obtained  $68.0 \pm 9.4$  years (range 50-75) in group A and  $67.6 \pm 11.3$  (range 48-75) in group B, respectively ( $p=0.043$ ).

Both groups showed no significant difference regarding pain severity according to VAS at 2 and 6 hours after surgery ( $p=0.996, 0.125$ , respectively). However, there were significant differences at 12 and 24 hours after surgery (Table 1).

Table 1: Mean and standard deviation of pain in the two groups studied over a 24-hour period

Pain	Oxycodone	SNB	P-value
2 Hour	$1.10 \pm 0.95$	$1.25 \pm 1.37$	0.996
6 Hour	$3.77 \pm 0.99$	$4.12 \pm 1.11$	0.125
12 Hour	$4.05 \pm 0.78$	$5.25 \pm 0.89$	<0.001
24 Hour	$2.95 \pm 0.78$	$4.57 \pm 0.95$	<0.001

Group B showed a greater frequency of nausea considerably within 24 hours after surgery. Also, the amount of analgesic supplement (Diclofenac) consumed after surgery in group A was significantly more than group B ( $262.04 \pm 92.05$  versus  $87.01 \pm 68.02$  mg, respectively;  $p < 0.001$ ).

The mean of diclofenac used during 24 hours in group B was significantly lower in comparison to group A (87 versus 262 respectively;  $P < 0.001$ ).

The incidence of nausea (55% vs. 30%) and vomiting (22.5% vs. 2.5%) was considerably higher in patients receiving oral oxycodone ( $P < 0.001$ ) (Table 3).

The incidence of hypotension was not significantly different between the two groups in the 24 hours ( $P = 0.432$ ) (Table 3).

Table 2: Incidence of nausea and vomiting in the patients of the two groups after 24 hours

Group		Oxycodone	SNB	P-value
Nausea and Vomiting	No	18 (45.0%)	28 (70.0%)	<0.001
	Yes	22 (55.0%)	12 (30.0%)	
Vomit	No	31 (77.5%)	39 (97.5%)	<0.001
	Yes	9 (22.5%)	1 (2.5%)	

Table 3: Incidence of hypotension in the two groups of patients over a period of 24 hours

Group	Oxycodone	SNB	Total	P-value
Hypotension				
No	35 (87.5%)	38 (95.0%)	73 (91.2%)	0.432
Yes	5 (12.5%)	2 (5.0%)	7 (8.8%)	
Total	40	40	80	

### Discussion

The present research aimed to compare the effect of oral oxycodone as well as saphenous nerve block on post-operative pain after knee replacement. The two methods had been used to determine pain control, hemodynamic status, level of consciousness, amount of additional drugs for controlling pain, and their side effects in the first 24 hours' post-surgery.

The findings of this study indicated that oral oxycodone administration was effective in post-operative pain management than single-shot blockage of saphenous nerve at 12 and 24 h after TKA. In the present study, between 2 and 6 hours after surgery, both groups showed no significant difference regarding pain score. Although, at 12 and 24 hours after surgery, the mean pain in the oxycodone group was lower compared to the saphenous block group. A significant difference was found between using additional analgesic drugs in our study groups. In the oxycodone group, the 24-hour cumulative diclofenac dose was significantly lower than the saphenous block group,

and this difference increased with time from the end of the operation. Regarding the hemodynamic status, no significant difference was observed in the hypotension incidence between the two groups. Moreover, the complications of nausea and vomiting in the oxycodone group were higher compared to the saphenous block group.

Previously, epidural analgesia has been known as a routine post-operative analgesic prescription for cases with TKA, consisting of a local anesthetic agent and an opioid<sup>17</sup>. Epidural analgesia showed post-operative analgesia with less nausea, vomiting, and pruritus. But, some studies revealed that epidural anesthesia is related to adverse effects such as urinary hypotension, retention, pruritus, and motor block. Peripheral nerve blockade is used to manage postoperative pain of TKA<sup>18-20</sup>. Peripheral nerve blockade can decrease the use of opioids, and also it can reduce opioid-associated adverse effects. It can improve mobilization and the time of hospitalizations. A femoral nerve block is one of the most popular pain management methods after TKA<sup>21</sup>. Some studies showed that femoral nerve block can be related to some serious complications such as damage adjacent major blood vessels and nerves itself, and reduces quadriceps muscle strength, which limits the extension of the knee and increases the risk of falls post-operatively<sup>22-24</sup>. Therefore, SNB is an alternative analgesic regimen to femoral nerve block. The saphenous nerve is the most extensive sensory branch of the femoral nerve to the knee, while spare the main motor branches of the femoral nerve<sup>21</sup>. Consequently, SNB can produce post-operative pain management as femoral nerve block without damage of quadriceps muscle strength. Besides better quadriceps muscle power, some studies reported that patients with saphenous nerve block have better early rehabilitation, higher ambulation distance, and reduce the length of hospital stay matched with the femoral nerve block method<sup>24-25</sup>.

A meta-analysis study showed SNB has an advantage in pain management at an active flexion

of the knee and rest after TKA <sup>26</sup>.

Patient-controlled analgesia is generally utilized for pain relief in patients after TKA <sup>21</sup>. Patient-controlled analgesia is related to some adverse effects led opioids, including respiratory depression, nausea, vomiting, and urinary retention <sup>27</sup>.

Hithem et al. (2020) assessed saphenous nerve block with continuous infusion of bupivacaine compared to an incremental dose of intravenous morphine after TKA surgery in a randomized, double-blind trial on 54 patients. The SNB group revealed better postoperative pain relief, lower uses of intravenous morphine consumption, and lower frequency of nausea and vomiting <sup>28</sup>. The present study confirmed the results of the previous study regarding a lower incidence of nausea and vomiting in the SNB group. Nausea and vomiting are common side effects of opiates, which is also predictable in this study. Although, it can be controlled using anti-nausea drugs such as ondansetron, which is prescribed for patients when it is needed. However, in the current study, the oxycodone group VAS was lower than the saphenous block group, 12 and 24 hours after surgery, mean pain in the oxycodone group was lower compared to the saphenous block group. It showed single-shot saphenous block for more extensive hours, for early post-operation pain control, is insufficient, and another adjuvant method or continuous block should use for this purpose.

Hanson et al. (2014) in a randomized, double-blind trial on 80 patients, compared continuous ultrasound-guided adductor canal block with a sham catheter for TKA. They showed a continuous adductor canal block for TKA decreases pain and opioid consumption compared with that of placebo in the first 48 hours after surgery <sup>29</sup>. The findings in the present study agreed with the previous study. Though, the present study follow-up patients for adverse effects for 24 hours' post-operative.

The present results were also confirmed by the study of Abdallah et al. (2016) on 100 patients

comparing the effect of adductor canal block with femoral nerve block by using 20 ml ropivacaine 0.5% in the two groups. They tested the analgesic efficacy using a VAS pain scale score, and they found that adductor canal block is effective to femoral nerve block regarding pain scores in the first 24 h <sup>30</sup>. Both investigations showed lower adverse effects at 24 h post-operative.

Kim et al. (2014) compared the effect of adductor canal block with the femoral nerve block on the pain control after surgery afterward knee replacement. They showed that the strength of quadriceps muscle in the saphenous block at 6 and 8 hours after operation returned earlier, and pain and narcotic used were similar in both groups. It indicated the preference of the adductor canal or saphenous nerve block to the femoral nerve block regarding pain control after knee replacement <sup>14</sup>. Based on these findings we performed the saphenous nerve block instead of the femoral block in our study. Other studies reported approximately complications such as quadriceps weakness, increased risk of falling of the patient after surgery, disturbances in the sense of balance, and femoral neuritis after using the femoral nerve continuous block <sup>14, 22-24, 29</sup>.

Several clinical trials have been conducted on pain control after knee replacement. The positive effects of various methods, such as the continuous and single-shot blockage of femoral nerve or saphenous nerve, intrathecal morphine injection of anesthetics, plus or minus of the morphine in the knee joint, or infiltration around the joint, the use of gapapentoids and NSAIDs have been performed. However, to the best of our knowledge, the preferred method has not been introduced in this regard, and further studies and especially the comparisons of different controlled procedures are required.

The results of this study are consistent with the findings of other studies and show that although the saphenous nerve block, which is the femoral nerve sensory branch, can be effective to reduce the pain after surgery following a knee replacement, it is

less effective in comparison with oral oxycodone. It is also cost-effective to use oral oxycodone instead of sono-guided block. It eliminates the need for expensive ultrasound devices and skills in performing the sono-guided block, especially in developing countries. Short-term use of oral narcotics with low complications and high safety is an effective, easy, and economical method for reducing pain after TKA surgery.

The analgesia duration of the single-shot SNB is not sufficient, and it's better to use a peripheral nerve catheter for continuous block by infusion of local anesthetics. Future studies are needed to pursue using additives, like dexmedetomidine and dexamethasone. The most important target should be prolonging sensory block for quicker ambulation of patients that cause to going home earlier. However, we showed that oxycodone considers as an effective beneficial alternative to the single-shot SNB, further studies are needed for comparing the continuous SNB with the oral opioids. We studied the patient only for 24 hours, and longer follow-ups could be done to investigate the rehabilitation outcomes.

### Conclusion

Oral oxycodone can control post-operative pain better than saphenous nerve block in the management of post-operative relief and reducing total additional analgesic drugs consumption. But, adverse effects such as nausea and vomiting were lower in saphenous nerve block than oral oxycodone.

### Acknowledgments

We thank all our cooperation who help us to conduct this study.

### Conflict of Interest Disclosures

The authors declare that they have no conflicts of interest.

### Funding Sources

None

### Authors' Contributions

Study design: Naderali Nazemyanyazdi and Abasali Delavari; Data gathering and analysis: Naderali Nazemyanyazdi, Abasali Delavari, Masood Saghafinia, Mohamad Kazem Emami; preparing manuscript: Naderali Nazemyanyazdi and Abasali Delavari

### Ethical Statement

The research protocol was confirmed by the Ethics Committee of Baghiatallah University of Medical Sciences and registered with the Iranian Registry of Clinical Trials (IRCT20170826035905N3). All patients gave written informed consent.

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