Original Article

Local Infiltration Analgesia Improves Functional Outcome after Total Knee Arthroplasty: A Randomized Controlled Trial

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Abstract

Background: Total knee arthroplasty (TKA) may be associated with severe postoperative pain, which requires prolonged hospital stay to provide effective analgesia. Increasing postoperative pain is associated with increased hospital stays and readmissions, lower patient satisfaction, longer time to rehabilitation and physiotherapy milestones and diminished range of motion (ROM). **Purpose:** This randomized controlled trial compared the functional outcome following the use of local infiltration analgesia (LIA) with combined spinal epidural analgesia (CSEA) versus CSEA alone in patients undergoing primary unilateral osteoarthritis of the knee. **Methods:** Between December 2017 and June 2019, a total of 30 patients undergoing primary unilateral TKA were included in the study. The patients were randomized into two groups, 15 patients each. Patients in Group A were administered LIA intraoperatively while patients in Group B were not. Both groups were given CSEA as their primary modality of anesthesia. Primary outcome was ROM of knee on 1st, 5th, and 14th postoperative days. Secondary outcomes were pain assessment using visual analog scale score on 6th, 24th, and 48th h postsurgery, total opioid consumption in 1st 48 h, and duration of hospital stay. **Results:** Mean ROM at 1st, 5th and 14th day was significantly higher in Group A compared to Group B ($P < 0.05$ for all). Mean pain score at 6 h, 24 h, and 48 h was significantly higher in Group B compared to Group A ($P < 0.05$ for all). Mean total opioid consumption was significantly higher in Group B (455.20 ± 38.84 g) compared to Group A (325.73 ± 50.18 g) ($P < 0.001$). Mean duration of hospital stay was significantly higher in Group B (7.07 ± 0.96 days) compared to Group A (5.73 ± 0.59 days) ($P < 0.001$). **Conclusion:** LIA provides significant pain relief in the early postoperative period and hence is associated with higher patient satisfaction. LIA also allows early and improved pain-free ROM at knee and contributes to achieving rehabilitation milestones earlier. It significantly reduces opioid requirement and thus reducing opioid-related side-effects.

Keywords: *Local infiltration analgesia cocktail, local infiltration analgesia, total knee arthroplasty*

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Introduction

Total knee arthroplasty (TKA) is a very commonly performed surgery all across the world for both primary and secondary osteoarthritis of the knee. TKA may be associated with severe postoperative pain, which requires prolonged hospital stay to provide effective analgesia.[1] Increasing postoperative pain is associated with increased hospital stays and readmissions, lower patient satisfaction, longer time to rehabilitation and physiotherapy milestones and diminished range of motion (ROM).[2]

Effective analgesia is the keystone of any surgical procedure. Parenteral narcotics and opioids have

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been associated extensively in the past as mainstay of treatment for acute postoperative pain with several side effects including nausea, vomiting, urinary retention, constipation, confusion, dizziness, sedation, and respiratory depression.[3] Continuous epidural, lumbar plexus, femoral and sciatic nerve blocks are associated with side effects like epidural bleeding especially with use of prophylactic anticoagulation therapy, diminished muscle control, urinary retention, and nerve damage.[4] Multimodal anesthesia/analgesia includes the use of pre-established analgesic and anesthetic techniques including peripheral nerve blocks and patient-controlled anesthesia in combination with a preemptive medication protocol (pre-/post-operative NSAIDS, narcotics, and neuropathic medications) in TKA patients to improve overall patient satisfaction and procedural outcomes.[5]

Providing local analgesia called local infiltration analgesia (LIA) in the form of peri- and intra-articular injections directly at the area of surgical trauma, target the site of pain generation and pain pathways directly, with no or minimal systemic side effects.[6] Multi-modal analgesia (MMA) has been considered to be superior to use of a single analgesic agent for LIA, as the use of multiple drugs target different areas of pain pathway and thus provide effective pain relief.

Materials and Methods

The protocol was approved by the Institutional Ethics Committee vide reference number IEC/Oct/2017 dt October 12, 2017, before the commencement of the study. The trial was registered with Clinical Trials Registry of India (Trial no-CTRI/2018/05/014183). A total of 30 patients, who underwent unilateral TKA for primary osteoarthritis of the knee were enrolled in the study. All patients were provided with CSEA as their primary modality of anesthesia. Patients with BMI more than 30 kg/m^2, inflammatory arthritis of knee, peripheral vascular disease in the affected limb, deranged coagulation profile, major neurological deficit and uncontrolled angina, allergy to any of the component drugs of LIA cocktail, operative time of more than 120 min, bone defects or fractures were excluded from the study. In addition, patients who were provided with any alternative means of anesthesia, other than CSEA were also excluded.

Randomization

All patients were randomly assigned to two treatment groups by a lottery system, as described in the randomization flowchart in Figure 1. All patients were asked to choose one of the two sealed envelopes, labeled Group A and Group B, respectively. Patients in Group A were administered LIA intraoperatively whereas patients in Group B were not administered LIA. However, patients in both the groups received CSEA as their primary modality of anesthesia. Only the surgeon who infiltrated the drug was aware about the intervention. Both the patient and the observer were blinded for the same.

Surgical procedure

All patients were administered CSEA using 0.125% bupivacaine. All patients underwent cruciate sacrificing TKA with posterior stabilized implants, using a standard midline medial parapatellar approach by one of the two senior arthroplasty surgeons. An electronic pneumatic tourniquet was used which was kept elevated throughout the surgical procedure.

Local infiltration analgesia infiltration

The LIA mixture was prepared according to the composition described in Table 1 in a 50 ml syringe with a 16/18 G hypodermic needle for better application. The infiltration was done before implantation of final components to have better access to the posterior capsule and other soft tissues. The drug cocktail was first injected into the posterior capsule and deep tissues around the knee posteromedially and laterally including the deep collateral ligaments. Figure 2 shows infiltration of drug into the posterior capsule. In addition, the drug

Table 1: Composition of cocktail

Drug	Dose (concentration)	Volume (ml)
Adrenaline	30 µg	0.3
Morphine	8 mg	0.5
Methylprednisolone	40 mg	1
Ceftriaxone	750 mg	7.5
0.5% bupivacaine plain		24
Normal saline		14.5
Total		48

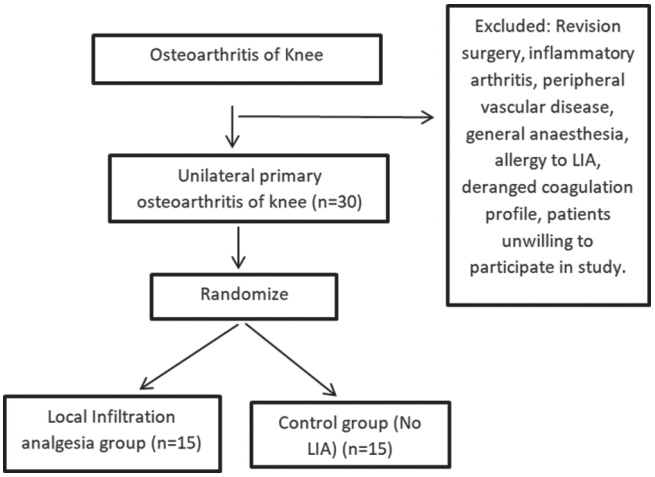

Figure 1: Randomization flowchart

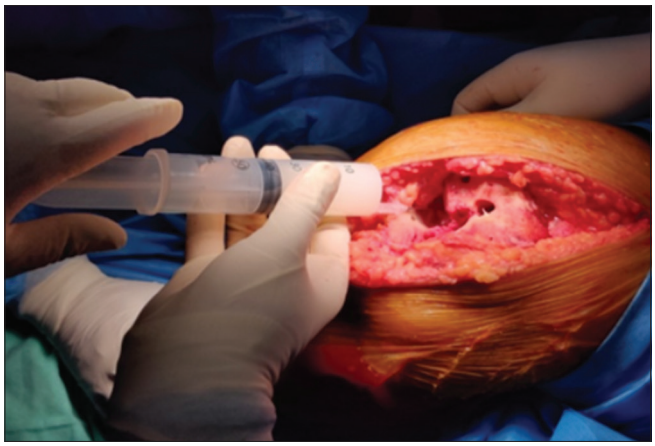

Figure 2: Infiltration of LIA cocktail

was also infiltrated in the peri-retinacular tissues and the quadriceps tendon. The remaining volume of drug was infiltrated later after placement of final components, into the subcutaneous tissue, just before wound closure.

Postoperative management

Postoperative pain management consisted of a continuous epidural infusion with 0.125% bupivacaine plus 2 µgm/ml fentanyl (opioid) with a total volume of 300 ml in an infusion pump, over the *in situ* epidural catheter. The rate of infusion was regulated between 3 and 5 ml/h, depending on patient's complaints of pain. In addition, injection paracetamol was made available to all the patients in a dose 1 g injected intravenously every 8 h, for the first 48 h. The epidural catheter was removed between 48 and 72 h. After 48 h, pain was managed with oral paracetamol tablets 1 g every 8 h, with rescue pain relief using tablet Tramadol 50 mg on SOS basis till discharge.

The drain was removed after 24 h of surgery in all the patients. Postoperative intravenous antibiotics were given for 48 h. Venous thromboembolism prophylaxis was started using injection low molecular weight heparin 60 mg (1 mg/kg) dose subcutaneously once daily starting from the first postoperative day (POD) till the day of discharge. After discharge, oral thromboprophylaxis was continued using Tab Disprin 350 mg once a day till 04 weeks from the date of surgery. Patients were encouraged to sit with legs hanging outside the edge of the bed in the morning following the surgery. Full weight-bearing ambulation with assistance of a walker was started on the 1st POD. Patients were usually discharged on the 5th/6th POD unless wound complication occurred for which patient required regular dressings/ intravenous antibiotics.

Postoperative evaluation

The functional outcome was assessed using the following variables:

ROM at knee joint-assessed by measuring postoperative knee flexion using a standard goniometer on 1st, 5th, and 14th PODs.

Visual analog scale (VAS) score-Postoperative pain was measured using VAS scoring at 6 h, 24 h, and 48 h postoperatively, using a numeral rating scale from 0 to 10 or an animated facial pain scale.

Total consumption of opioids (Fentanyl in µgm) through continuous epidural infusion at 48 h-by calculating the volume of continuous epidural infusion used in the infusion pump at the end of 48 h. Fentanyl was used in a volume of 2 µg/ml. Hence, the total consumption of fentanyl in µg was equal to volume of epidural used ×2.

The duration of hospital stay calculated in number of days, from the patient's date of surgery till date of discharge.

The time to discharge was decided based on the following criteria:

- Patient was ambulant with walker and was able to use toilet on his own
- Had VAS score <3 on oral analgesics
- No wound complications
- No symptoms suggestive of thromboembolic phenomenon.

Statistical analysis

The inter-group statistical comparison of distribution of categorical variables is done using Chi-Square test or Fisher's exact probability test. The inter group statistical comparison of means of continuous variables is done using independent sample *t*-test. Intragroup comparison of means of continuous variables is done using paired *t*-test. In the entire study, the $P < 0.05$ is considered to be statistically significant. All the hypotheses were formulated using two-tailed alternatives against each null hypothesis (hypothesis of no difference). The entire data are statistically analyzed using Statistical Package for Social Sciences (SPSS version 21.0, IBM Corporation, USA) for MS Windows.

Observation and Results

Mean pain score (visual analog scale)

The distribution of mean pain score at 6-h, 24-h and 48-h among the cases studied is significantly higher in Group B compared to Group A ($P < 0.05$ for all). Inter-group distribution of mean pain scores is described in Figure 3.

Mean range of motion

The distribution of mean ROM at 1-Day, 5-Day, and 14-Day among the cases studied is significantly higher in Group A compared to Group B ($P < 0.05$ for all). Inter-group distribution of mean pain scores is described in Figure 4.

Duration of hospital stay

The distribution of mean duration of hospital stay among the cases studied is significantly higher in Group B compared to Group A ($P < 0.001$). Inter-group distribution of mean duration of hospital stay is described in Figure 5.

Opioid consumption

The distribution of mean Total opioid consumption among the cases studied is significantly higher in Group B compared to Group A ($P < 0.001$). Inter-group distribution of mean total opioid consumption is described in Figure 6.

Complications

Only minor or nonserious complications occurred. Five patients had nausea, 3 in Group A and 2 in Group B which lasted for the first 24 h in all except 1 in Group B which lasted for 48 h postsurgery. Two patients, from Group B had vomiting, which settled with injectable anti-emetic drugs. There were no other complications related to epidural analgesia. Only one patient had superficial SSI, who belonged to group B. He was managed with local wound care and parentral antibiotics. No other patient had any infection.

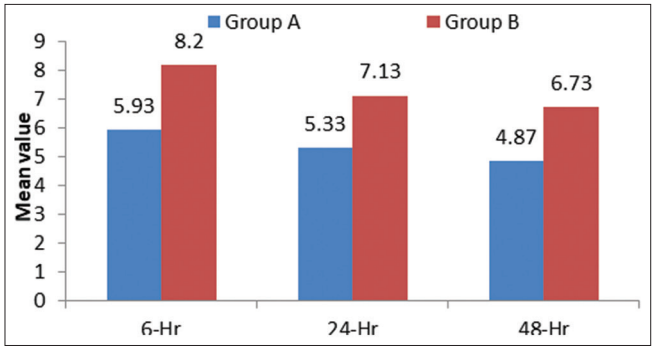

Figure 3: Inter-Group Distribution of Mean Pain Score

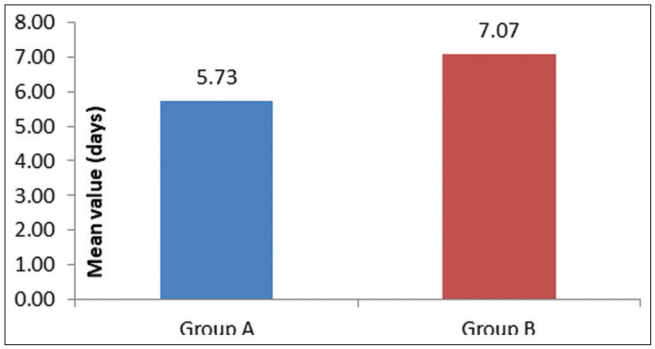

Figure 5: Inter-Group Distribution of Mean Duration of Hospital Stay

Discussion

Orthopedic procedures especially Joint arthroplasty, both knee and hip are considered to be amongst the most painful surgical procedures.[7] Postoperative pain has been directly linked to the surgical trauma to the bone and surrounding soft tissue and also to the hyper perfusion that occurs following tourniquet release.[8] It has been noted that more than half of the patients following TKR experience sub optimal pain control in the immediate and early postoperative period.[9] Postoperative rehabilitation is directly related to optimum pain control. Earlier mobilization and ambulation are associated with earlier return to normal gait, which is directly linked to adequate pain control.[10]

An effective postoperative pain management protocol which provides highest quality of patient satisfaction in terms of pain relief and improved function is desirable. With the advent of MMA, not only the pain pathways are tackled at multiple levels, there is improvement in patient satisfaction with respect to postoperative pain, with fewer side-effects due to overdose of a single analgesic agent.[11,12] The main aim of any analgesic regime is to provide the patient with a continuous pain-free period to prevent any peripheral or central sensitization of pain pathway.[13] It directly correlates with better sleep, early ambulation, better posture, gait

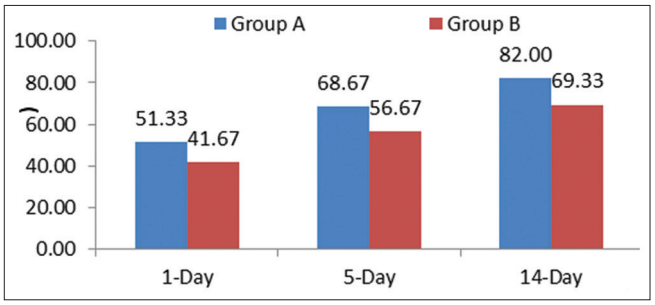

Figure 4: Inter-Group Distribution of Mean ROM

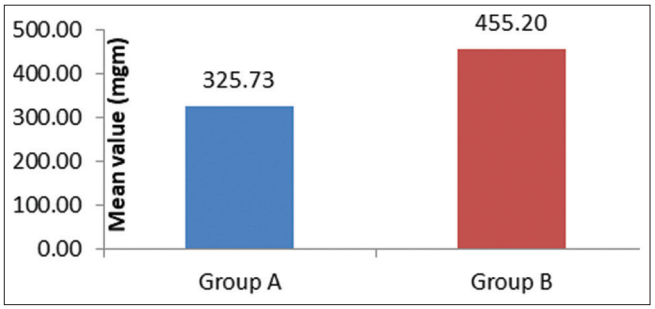

Figure 6: nter-Group Distribution of Mean Total Opioid Consumption

and better knee kinematics, which prolongs implant durability and longevity.

Infiltrating epidural space with drugs has advantage of providing perioperative analgesia as well as extended analgesia in the postoperative period, by means of an epidural catheter.[14] The analgesic effect can be extended till 24–72 h after surgery, until the catheter is removed, thus providing continuous pain relief and decreases the chances of breakthrough or incidental pain. Epidural infiltration however, can be associated with side effects such as nausea, vomiting, hypotension, pruritus, and poor muscle control.[15] It has also been associated with higher rates of postoperative nerve palsy including peroneal nerve palsy and gluteal compartment syndrome.[16] There is also a risk of epidural hematoma with use of deep vein thrombosis prophylaxis like heparin.[17] Hence, it is advised to stop the prophylaxis 8–12 h prior to removal of epidural catheter.[18]

LIA is a technique of delivering large volumes of local anesthetic agent along with adjuvants in a diluted form at the site of surgical insult to counter the effects of peripheral sensitization of pain pathway. The use of LIA is based on the fact that all pain after surgery arises as a result of damage to the local tissues at the surgical site.[19] LIA doesn't produce muscle weakness and does not cause systemic drug toxicity while providing adequate pain relief in the early postoperative period.[20,21] LIA has been shown to reduce requirements for postoperative analgesia, particularly opioids.[22] Few theoretical risks associated with LIA include systemic toxicity of local anesthetic agent, risk of infection at the injection site, though there is no literature to support the later.[23]

It can be safely concluded that administration of LIA reduces early postoperative pain for up to 48 h after surgery. Pain assessment based on single-shot LIA administration beyond 48 h is difficult as most of the drug is absorbed by then. The use an intra-articular catheter for LIA administration in the postoperative period can perhaps provide us with longer analgesia, though chances of introduction of infection into the knee joint must be outweighed with benefits of pain reduction. The better ROM can be directly attributed to the decrease in pain with use of LIA. The better ROM in the late postoperative period is possibly because of early gain in movements compared to the control group. Pain-free ROM at the knee also encouraged patients to be out of bed and ambulating at an earlier stage, thus reducing the complications of deep vein thrombosis and pulmonary embolism. Reduced hospital stay is associated with economic benefit to the patient. Furthermore, the use of LIA reduces requirement of other analgesics, further reducing the overall treatment cost. Only a very few patients had nausea which was present in both the groups. Two patients had vomiting in Group B which can be attributed to increase opioid consumption.[24] None of the patients in both groups had confusion, dizziness, sedation, pruritus, or respiratory depression.

Few limitations observed in the study are:

- The sample size was small for wider generalization of results. We recruited only those many patients as we deemed necessary for detecting a change in primary outcome
- The period of follow-up was very small and postoperative functional scores could not be recorded. A longer follow-up would have been more appropriate to assess the functionality and complications in the long run
- Due to the use of a mixture of drugs with multiple actions, it is difficult to determine the efficacy of individual drugs.

Conclusion

LIA is a simple, easily performed yet effective procedure for postoperative pain relief. LIA provides significant pain relief in the early postoperative period and hence is associated with higher patient satisfaction. LIA also allows early and improved pain-free ROM at knee and contributes to achieving rehabilitation milestones earlier. It significantly reduces opioid requirement and thus reducing opioid-related side effects. It reduces hospital stay, allows early discharge from hospital and decreases financial burden on patient. It is not associated with complications of wound healing and infections. The long-term effects of LIA use are yet to be studied.

Author contribution

All authors have contributed equally in the conception and design of this study, acquisition of data, data entry and analysis, initial drafting of the manuscript, critical revision, and final approval of the manuscript for publication.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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