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Original Article

Continuous intraarticular and periarticular levobupivacaine for management of pain relief after total knee arthroplasty: A prospective randomized, double-blind pilot study

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ABSTRACT

Background: Total knee arthroplasty (TKA) can result in major postoperative pain which can impact the recovery and rehabilitation of patients and for this reason the use of a pain-control infusion pumps (PCIP) enhances analgesia for TKA.

Purpose: To investigate whether a PCIP of levobupivacaine would reduce pain in patients following TKA.

Methods: This was a prospective, randomized, controlled study conducted in 55 patients. Criteria for participation were unilateral TKA for osteoarthritis and no allergies to levobupivacaine. The primary outcomes measured were postoperative pain intensity on Visual Analogue Scale (VAS) score measured at 24 h and 48 h. Other measures included amount of narcotics, presence of adverse events, and length of hospital stay.

Results: PCIP-treated patients ($n = 28$) showed significant reductions in VAS score at any time versus control ($p < 0.01$). Amount of narcotics, presence of adverse events, and length of hospital stay were significantly less with the PCIP versus control (each $p < 0.01$).

Conclusion: The use of a mix of levobupivacaine, ketoral-trometamina, and adrenalin provides a safe and effective means in post-operative pain relief in patients undergoing TKA.

Level of evidence: Level II therapeutic study.

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1. Introduction

Orthopedic surgery is reportedly among the most painful surgical procedures.⁵ Surgical damage following major

orthopedic surgery often involves a large, deep incision with considerable tissue dissection and muscle, bone, and vascular exposure.

Total knee arthroplasty (TKA) is billed as a pain relieving procedure, but patients experience immense discomfort in the

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immediate postoperative period to attain this benefit. High postoperative pain levels decrease knee range of motion, increase narcotic analgesic use, and increase hospital length of stay.⁸

The growing trend toward quicker recovery following orthopedic procedures has stimulated the development of a variety of techniques focused on improving postoperative pain management. Postoperative pain relief after TKA can be achieved by a variety of techniques such as intravenous analgesia, epidural analgesia, and peripheral nerve block techniques.

Hoenecke et al.⁷ found that postoperative pain was decreased (4.0 versus 2.7 on a scale of 0–10) and narcotic use was reduced by 37% after ACL reconstruction using a continuous, 48 h intraarticular infusion of bupivacaine. Knee range of motion (100° versus 70° at discharge) and hospital stay (7 days versus 9 days) have also been shown to improve with continuous infusions of ropivacaine and morphine in a non-randomized trial of primary total knee replacements.¹²

There is a paucity of literature on continuous intraarticular bupivacaine infusion in the primary TKA population, with no published randomized controlled trials. We chose to conduct a randomized controlled trial (RCT) pilot study to assess the efficacy of a 48-h continuous infusion of intraarticular levobupivacaine versus placebo in decreasing morphine consumption and postoperative pain levels following primary TKA.

The aim of this study was to evaluate the efficacy of intra- and extraarticular anesthetic infusion in patients undergoing TKA by determining postoperative (1) pain, (2) narcotic consumption, and (3) leg of hospital stay.

2. Materials and methods

This was a prospective, randomized, controlled trial conducted in 57 patients. All procedures took place at the same institution, San Salvatore Hospital L'Aquila, and were performed using the same standard surgical procedure. Criteria for participation were unilateral TKA for osteoarthritis and a preoperative hemoglobin level >13 g/dL. Patients with inflammatory arthritis, allergies to local anesthetic, and metals were excluded from the study. The study was approved by the local ethics committee and conducted according to the Declaration of Helsinki; the patients gave their informed consent prior to their inclusion. Between January 2010 and January 2012, 57 consecutive patients undergoing elective primary TKR for osteoarthritis at San Salvatore Hospital L'Aquila who met the inclusion criteria were enrolled. The sample size was calculated by a power analysis and participants were allocated to treatment group by the surgeon, using a computer-generated list of random numbers. The study dataset was derived from a randomized, double-blind study with approval of the local ethics committee and patients were followed up according to the pre-defined study protocol. The trial is registered at Hospital S. Salvatore L'Aquila (BCG:2656), and full details of the trial protocol can be found in the Department of Orthopaedic Surgery, San Salvatore Hospital, via Vetoio, N°1, 67100 L'Aquila, Italy.

We tested the hypothesis that the application of pain pump with a multihole catheter 19 Ga (length 15 cm) which instilled

10 cc/h for the first 30 h and 5 cc/h for the subsequent of a mix of levobupivacaine (200 mg), ketoral-trometamina (30 mg), and adrenalin (0.1 mg) for a total volume of 40 ml in the intra- and extraarticular prosthesis space reduces pain following TKA.

Both the treatment and control groups used a commercially available pain pump (Painfusor Catheter Baxter®).

The outcomes were postoperative pain score, narcotic consumption, knee motion all measured at 24 h, 48 h, 72 h, and length of hospital stay.

Low contact stress uncemented rotating platform prostheses (Depuy, Leeds, UK) without patellar resurfacing were used for all implants.

The TKA surgery was performed under a standardized spinal anesthetic with 10–15 mg of 0.75% or 0.5% plain bupivacaine and 20 µg of fentanyl. In addition, patients were sedated with intravenous midazolam and propofol titrated at the discretion of the case anesthesiologist.

2.1. Surgical procedure

All operations were performed in a bloodless field with use of a pneumatic tourniquet. In all cases, the drill hole created for the intramedullary guide rod was occluded with bone prior to implantation of the femoral component in order to reduce blood loss. After insertion of the prosthesis without cement, the tourniquet was deflated and hemostasis was achieved.

Before closure of the joint to all patients, a multihole catheter 19 Ga (Painfusor Catheter Baxter®) was placed in the intra- and extraarticular subfascial space for the infusion of the local anesthetic, the distal part of the catheter was adhered to the capsule, and the proximal was placed subcutaneously. The catheter was tested with a saline solution also to eliminate the air therein. The drains were positioned intraarticular space inside the joint.

All study patients received identical standard adjunctive pain control.

The rescue analgesic medication includes the following drugs: ketorolac 30 mg to a maximum dose of 120 mg daily if NSR between 3 and 4 and in case of persistent pain or NSR >4, morphine hydrochloride 5 mg subcutaneously repeated no earlier than one hour from the previous administration (maximum dose 10 mg in 8 h). In both patient groups, drains were used in the joint and connected to a high-vacuum, suction-drain bottle for 24 h. The knee joint was then closed in layers. All patients received low-molecular-weight heparin (4000 U.I. enoxaparin sodium) as thromboprophylaxis 12 h before the operation, and every 24 h postoperatively.

2.2. Statistical analysis

Data analyses were performed using the Student's t-test, the chi-squared test, and Pearson's correlation coefficient. A p-value of 0.05 or less was considered to be statistically significant for all analyses performed.

3. Results

Patients scheduled for unilateral TKA between January 2010 and January 2012 were included in this study. Of 57

Table 1 – Baseline patient characteristics for pain pump group (A) and control groups (B).

	Pain pump group (A) (n = 28)	Control group (B) (n = 29)
Age (years)	66.1 ± 7.3 (55–78)	71.9 ± 5.5 (59–82)
Mean height (cm)	172.6	164.6
Mean weight (kg)	74.1	72.2
Pain score (V.A.S.)	70 ± 5	72 ± 4

randomized patients, 28 were allocated to treatment with pump within pain drugs, and 42 were allocated to treatment with the pump without pain drugs (control group). All 57 patients completed the study. Patient demographics and baseline characteristics are presented in Table 1. There were no significant differences between the pain pump drugs (Group A) and control (Group B) groups for demographics.

3.1. Postoperative pain score at rest and during mobilization

In orthopedic unit, pain was assessed using Visual Analogue Scale (VAS). Changes in pain score at rest and during mobilization following surgery for pain pump drugs and control groups are shown in Table 2.

The mean (±SD) value in pain at rest 24 h after TKA was lower in the pain pump drugs group than the control group (26 ± 3 versus 46 ± 4), at 48 h (10 ± 5 versus 20 ± 6) and at 72 h (0 versus 11 ± 3).

The mean (±SD) pain score during mobilization at 24, 48, and 72 h are shown in Table 2. Levels were lower in the pain pump drugs group than the control group for each time control (36 ± 4 versus 45 ± 6), (18 ± 2 versus 36 ± 4), and (5 ± 1 versus 24 ± 6).

3.2. Narcotic consumption

Narcotic consumption during the first 24 h was significantly reduced in Group A relative to Group E. This difference in

narcotic consumption persisted during the whole period of observation (Table 2).

3.3. Complications

Two patients from the control group developed a superficial wound infection; these infections were treated successfully with oral antibiotics. No deep infections were observed. One patient in the Group A received intravenous antibiotics for a chest infection following surgery. One female patient from the Group B developed a femoral deep vein thrombosis (DVT) and another from the same group suffered a pulmonary embolism. There were no fatalities.

4. Discussion

TKA can result in major postoperative pain which can impact on the recovery and rehabilitation of patients and also require expensive and prolonged rehabilitation. This prospective, randomized controlled study evaluated the efficacy pain pump drugs in TKA.

The study has several limitations in that it included a relatively small number of patients and that every risk or complication associated with pain pump drugs treatment and TKA surgery could not be extensively explored. Further studies in a multicenter setting with a larger population of patients are warranted to support the current study. However, application of pain pump drugs to the wound site was found to lead to significant reductions in postoperative pain, as well as permanence in hospital and rehabilitation requirements. Poor control of postoperative pain after TKA may cause a series of adverse events that could negatively influence functional recovery and the final results and reports on the procedure.¹¹

Recent studies have examined continuous intraarticular infusion of local anesthetic in orthopedic surgery, concluding postoperative pain, the need for opioids as rescue medication, and mean length of hospital stay is reduced.^{2,9}

We found that the patients with the levobupivacaine pump had lower VAS scores during the first 3 days and had a reduction in the number of patients who required opioids for pain control during the first 3 days. In the patients who required opioids to control pain, there was a high percentage of adverse effects (e.g., nausea, vomiting, and dizziness). Opioid side effects, which are mainly nausea and vomiting, occur at an incidence of 30–80% and negatively influence patient satisfaction and well-being. They are sometimes reported to be one of the main negative factors, even more so than pain.³ In our study, the use of rescue medication was reduced and therefore opioid-related side effects were also decreased. The mean length of hospital stay was shorter in patients with the ropivacaine. Reduction of length of hospital stay is another of the noteworthy findings. The use of ropivacaine administered by a continuous infusion pump resulted in a mean reduction of length of stay of 1.5 days compared to the control group. This reduction in length of stay is similar to other reports which employ continuous infusion of anesthetics. In 2006, Vendittoli et al. studied 42 patients undergoing TKA who received deep and subcutaneous infiltration of 400 mg ropivacaine with added ketorolac

Table 2 – Postoperative pain score (V.A.S.) at rest and during motion, narcotic consumption during first 24 h in pain pump group (A) and control groups (B).

	Pain pump group (A) (n = 28)	Control group (B) (n = 29)
Pain score (V.A.S.) after 24 h	26 ± 3	46 ± 4
Pain score (V.A.S.) after 48 h	10 ± 5	20 ± 6
Pain score (V.A.S.) after 72 h	0	11 ± 3
Narcotic consumption during first 24 h (rescue analgesic medication)	50 ± 0.5/5 ± 1	80 ± 0.7/8 ± 1.2
ketorolac/morphine		
Pain score (V.A.S.) after 24 h during mobilization	36 ± 4	45 ± 6
Pain score (V.A.S.) after 48 h during mobilization	18 ± 2	36 ± 4
Pain score (V.A.S.) after 72 h during mobilization	5 ± 1	24 ± 6

and epinephrine, combined with one intraarticular injection of 150 mg ropivacaine. There was significant reduction in morphine consumption, increased pain relief, and reduced duration of nausea compared to the use of intravenous morphine.¹³

In contrast, recent studies note that the use of pain pump does not provide sustained postoperative pain relief in patients undergoing TKA, but our study differs for three reasons: the type of anesthetic, clamped drainage for the first 3 h, and catheter placement.

First is the choice and dose of the local anesthetic; using levobupivacaine, it is possible to increase the dosage and the flow, without any side effect, especially cardiotoxicity. In other studies, the type and flow rate were inadequate to pain relief following a mayor orthopedic procedure. Second, our recent study suggests that the use of hemostatic matrix in TKA not only reduces blood loss by drainage suction, but also by extravasation of blood into the tissues, and for this reason we decided to clamp the drainage for the first 3 h, allowing us to minimize the loss of local anesthetic.⁶ The potential benefits of effective hemostasis using hemostatic matrix include a decrease of total blood loss while maintaining higher hemoglobin levels reducing the rate of blood transfusion, faster functional rehabilitation, and lower rates of wound infection and finally decreasing the cost of each patient.^{4,10} Also, it is not recommended not to use the drain, because it increases the hemarthrosis, joint stiffness, and infection.

Third, little is known about the optimal catheter placement for total joint replacement procedures.¹ It is likely that the poor pain control could be explained by the inability of local anesthetic to reach nociceptors outside the joint; for this reason, we decided to locate the catheter in both compartments, in such a way to block periosteal and perifascial nociceptors. The potential benefits of effective hemostasis using hemostatic matrix include faster functional rehabilitation and lower rates of wound infection.^{4,10} The only two patients to develop superficial wound infections in this study were in the control groups.

These findings are not only significant with regard to patient care options, but also have important consequences with respect to the cost of patient care and suggest that future health-economic evaluations of surgical options in TKA should be considered. Future studies are also warranted to explore the use of Painfusor Catheter in situations additional to TKA, such as total hip arthroplasty and traumatology.

Ethical review committee statement

All human studies have been approved by the appropriate ethics committee and have been performed in accordance with the ethical standards of the Declaration of Helsinki.

Conflicts of interest

The authors have none to declare.

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