Effect of Periarticular Injections of Triamcinolone Acetonide During Unicompartmental Knee Arthroplasty in the Perioperative Period: A Randomized Clinical Trial

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Abstract

Background: Unicompartmental knee arthroplasty (UKA) is a minimally invasive procedure that preserves most knee tissue, but can also cause moderate-to-severe pain. We investigated if triamcinolone acetonide (TA) addition to a “cocktail” of agents in a periarticular injection could reduce postoperative pain and the inflammatory response, and promote rapid recovery after UKA.

Methods: This was a prospective randomized clinical trial undertaken from March 2018 to October 2019. Patients were divided randomly into a control group (A) and TA group (B). In group A, a 50-mL cocktail lacking TA was injected in tissue around the joint cavity. In group B, a 50-mL cocktail containing TA was injected. Primary-outcome measurements were the visual analog pain score upon rest (VASR) and exercise (VASE), morphine consumption, range of motion (RoM), level of C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) in venous blood at different times. Complications were also monitored.

Results: Forty-five patients in group A and 46 patients in group B were assessed. At 6, 12 and 24 h postoperatively, VASR in group A was significantly higher than that in group B (P<0.05). At 6 and 12 h postoperatively, VASE in group A was significantly higher than that in group B (P<0.05). Morphine consumption in group A was significantly higher than that in group B at 0–24 h (P<0.05) and 0–48 h (P<0.05) after surgery. At postoperative day (POD)1–3, the RoM in group B was significantly higher than that in group A (P<0.05). There was a significant decrease in CRP level in group B vs. group A on POD1 (P<0.05) and POD3 (P<0.05). The ESR of group B was significantly lower than that of group B on POD3 (P<0.05) and POD5 (P<0.05). No serious complications occurred in either group.

Conclusion: TA addition to a cocktail of agents for periarticular injection effectively relieved pain, improved knee-joint function, reduced the inflammatory response, did not increase risk of complications, and promoted rapid recovery after UKA.

Introduction

In recent years, the effect of single-compartment osteoarthritis of the knee joint treated by unicompartmental knee arthroplasty (UKA) has improved significantly [1]. UKA involves replacement of only a single compartment. In this way, natural movement is retained, and proprioception is not destroyed. UKA also has the advantages of preserving the normal structure and bone mass of the knee, eliciting little surgical trauma and few complications, along with rapid recovery of joint function [2,3].

Although UKA is a minimally invasive procedure in which most knee tissue is preserved, it can also cause moderate-to-severe pain [4,5]. Pain management after UKA is also a focus of research [6]. In recent years, postoperative analgesia after joint replacement has changed gradually from using a single drug to using multiple drugs [7–9]. A periarticular multimodal injection consisting of a “cocktail” of agents is often used
after joint replacement, and is important for reducing pain and enhancing recovery after surgery \cite{10,11}. The ingredients of this cocktail are a popular research topic \cite{7,9,12}.

Glucocorticoids can alleviate swelling and pain by reducing the postoperative inflammatory response and immune regulation. They can also inhibit local vascular dilatation, as well as reduce capillary permeability, congestion, plasma exudation, leukocyte infiltration, and phagocytosis \cite{13}. Scholars have shown that addition of glucocorticoids to cocktails can reduce pain and the inflammatory response, as well as promote rapid recovery, after total knee arthroplasty (TKA) \cite{14,15}.

Whether addition of triamcinolone acetonide (TA) to a cocktail is also efficacious for UKA is not known. Hence, we conducted a randomized clinical trial to explore if TA addition to a cocktail could reduce pain and the inflammatory response, and promote rapid recovery, after UKA.

**Materials And Methods**

**Ethical approval of the study protocol**

The study protocol was approved by the Ethics Committee of our hospital. Procedures involving human participants were in accordance with the ethical standards set in the Declaration of Helsinki Ethical Principles for Medical Research by the World Medical Association. All patients provided written informed consent.

**Inclusion criteria**

The inclusion criteria were patients with: (i) unilateral and medial-compartment osteoarthritis; (ii) good stability of the knee; (iii) good function of the cruciate ligament and collateral ligament; (iv) degree of motion of the knee $> 90^\circ$; (v) flexion contracture $< 10^\circ$; (vi) varus deformity $< 15^\circ$ that could be corrected to a neutral position under passive stress.

**Exclusion criteria**

The exclusion criteria were patients with a history of acute and slow knee infection, or inflammatory joint disease (e.g., rheumatoid arthritis), pigmented villonodular synovitis, bone fusion, or severe deformity.

**Patients and procedures**

This was a prospective randomized clinical trial undertaken from March 2018 to October 2019. Patients scheduled for UKA were recruited to participate in our study.

UKA was performed in all patients using the third-generation Oxford® Unicompartmental Knee Replacement system (Biomet, Warsaw, IN, USA). All procedures were undertaken by the same senior surgeon.
Preoperatively, the envelope method of randomization was used to divide patients into two groups. Intraoperatively, all patients received spinal anesthesia.

In the control group (group A), a 50-mL intraoperative periarticular injection of cocktail of agents (ropivacaine (20 mL or 10 mL:100 mg), morphine (0.5 mL: 5 mg), epinephrine (0.1 or 1 mL; 1 mg), TA (1 mL: 40 mg), and physiologic (0.9%) saline (28.4 mL or 10 mL: 90 mg) was prepared in five 10-mL syringes. In the TA group (group B), a 50-mL intraoperative periarticular injection employing a cocktail using the same agents stated above but with addition of TA (1 mL: 40 mg) was employed. Before prosthesis implantation, 20 mL of the cocktail was injected into the posterior articular capsule. After the prosthesis had been implanted, 30 mL of the cocktail was injected into the synovium, medial collateral ligament, quadriceps femoris, fat, and surrounding patellar soft tissue (except the patellar tendon).

All patients were given a single dose of cefuroxime (1.5 g) 30 min before surgery and cefuroxime (1.5 g, b.d.) on postoperative day (POD)1 for prophylaxis. A drainage tube was placed intraoperatively, which was clipped routinely for 4 h after surgery, and was removed 24 h after surgery. Flurbiprofen (100 mg, b.d.) was used to relieve pain for POD1–3. Rivaroxaban (5 mg/day) was administered for 7 days to prevent deep-venous thrombosis (DVT).

**Outcome measurements**

The primary outcome measurements were: the visual analog pain score upon rest (VASR) and visual analog pain score on exercise (VASE) 6 h, 12 h as well as 1, 2, 3, 4 and 5 days after surgery; morphine consumption for patient-controlled anesthesia (PCA) for POD1 and POD2; range of motion (ROM; preoperative, and POD1, 2, 3, 4 and 5); level of C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) in venous blood (preoperative, and POD1, 3, and 5).

The secondary outcome measures were nausea, vomiting, infection, DVT, hematoma, and nerve injury.

**Statistical analyses**

SPSS v22.0 (IBM, Armonk, NY, USA) was employed for statistical processing. Data are the mean ± standard deviation. The independent-sample t-test and Mann–Whitney test were used for comparison of measurement data between groups. The χ² test was used for comparison of count data. P < 0.05 was considered statistically significant.

**Results**

Initially, 96 patients were enrolled, and randomized into two groups. Three patients were excluded from group A because they were switched to TKA (n = 2), or lost to follow-up (n = 1). Two patients were excluded from group B (one patient was switched to TKA and one patient was lost to follow-up). Finally, 45 patients in group A and 46 patients in group B were evaluated. The demographic characteristics of the study cohort are listed in Table 1: there was no significant difference in any parameter between the two groups.
Table 1
Demographic characteristics of the patient cohort

| Demographic     | Group A (n = 45) | Group (n = 46) | p    |
|-----------------|------------------|----------------|------|
| Gender (male/femal) | 11/34            | 7/39           | 0.269|
| Side (left/right)  | 22/23            | 27/19          | 0.185|
| Age (year)       | 67.56 ± 8.94     | 69.80 ± 6.95   | 0.185|
| Height (cm)      | 160.38 ± 4.108   | 161.37 ± 3.122 | 0.198|
| Weight (kg)      | 65.17 ± 8.183    | 66.09 ± 6.157  | 0.547|
| BMI (kg/m²)      | 25.34 ± 3.08     | 25.38 ± 2.31   | 0.943|
| Incision (cm)    | 8.56 ± 0.93      | 8.65 ± 1.01    | 0.545|

At 6, 12, and 24 h postoperatively, there were significant differences between the two groups for VASR (4.05 ± 1.545 vs. 3.00 ± 1.664, P = 0.007; 4.21 ± 1.718 vs. 2.93 ± 1.207, P = 0.009; 3.53 ± 0.841 vs. 2.43 ± 0.514, P = 0.00, respectively) (Fig. 1). At 6 h and 12 h postoperatively, there were significant differences between two groups for VASE (6.00 ± 1.453 vs. 4.57 ± 1.342, P = 0.007; 5.32 ± 0.82 vs. 4.50 ± 1.019, P = 0.029, respectively) (Fig. 2). Thereafter, a significant difference was not observed between the two groups. Morphine consumption for PCA in group A was significantly higher than that in group B at 0–24 h (5.62 ± 2.41 vs. 3.17 ± 1.81, P = 0.016) and 0–48 h (10.25 ± 1.62 vs. 6.25 ± 1.77, P = 0.016) after surgery (Fig. 3).

At POD1, 2 and 3, the RoM of group B was significantly higher than that of group A (33.95 ± 12.313 vs. 47.86 ± 14.239, P = 0.004; 51.58 ± 17.001 vs. 65.71 ± 16.036, P = 0.022; 69.21 ± 16.772 vs. 83.57 ± 14.469, P = 0.016, respectively). Although there was no significant difference in knee flexion mobility between the two groups at POD4 and POD5, we observed from the curve that the RoM of group B was superior to that of group A (Fig. 4).

The mean level of CRP and ESR preoperatively as well as on POD0, 1, 3 and 5 for the two groups are displayed in Fig. 5A and B. There was a significant decrease in the CRP level for group B vs. group A on POD1 (41.67 ± 23.95 vs. 26.92 ± 11.279, P = 0.047) and POD3 (52.00 ± 25.74 vs. 26.37 ± 11.79, P = 0.001). The ESR of group B was significantly lower than that in group B on POD3 (50.20 ± 17.67 vs. 35.67 ± 14.606, P = 0.041) and POD5 (43.00 ± 15.91 vs. 27.00 ± 12.46, P = 0.005).

Mild-to-moderate nausea and vomiting occurred in four patients in group A and in three patients in group B. There was no significant difference in the prevalence of nausea and vomiting between the two groups. Their symptoms were relieved after metoclopramide (i.m.) administration. No patients had symptoms of infection (redness, swelling, heat, pain) around the wound. One patient in group A was found to have an intramuscular thrombus on POD5. No patients developed DVT.
Discussion

Efficacious pain management is necessary for effective recovery after arthroplasty \[16\]. Traditionally, pain control after TKA has been achieved through epidural analgesia or peripheral nerve blocks \[17\]. However, these methods are often costly, technically difficult, and can have side-effects. Some studies have shown that local injection of anesthetic agents into soft tissues can reduce pain scores and the amount of opioid analgesics used \[18–20\]. Toftdahl and colleagues compared the effect of local periarticular and intra-articular infiltration of agents with that of a continuous femoral nerve block. They found that patients receiving local infiltration of agents had better postoperative pain relief, faster recovery, and no increased risk compared with control group \[21\].

Fan and colleagues \[22\] injected ropivacaine, ketorolac, morphine, and epinephrine around the joints of patients undergoing knee arthroplasty. They found that the pain score decreased significantly, the patient satisfaction score increased, and the demand for intravenous controlled analgesia decreased within 24 h after surgery. In another randomized trial, local injections of bupivacaine, fentanyl, and methylprednisolone were given to patients undergoing simultaneous bilateral knee arthroplasty. Patients who received local injections after surgery had significantly lower pain scores and significantly improved knee motion than those who received contralateral knee arthroplasty \[23\]. Maheshwari et al. \[24\] emphasized the importance of periarticular injections in multimodal pain management. In view of the high incidence of the side-effects of systemic opioid use, local injection of cocktails has been used to replace intravenous controlled analgesia. Lamplot and collaborators \[25\] reported that injection of a cocktail of agents around joints could reduce the pain score (with fewer adverse reactions), significantly reduce use of anesthetic drugs, and lead to higher postoperative patient satisfaction and faster recovery.

Pain after joint replacement can be caused by soft-tissue injury or bone injury \[6, 26\]. Some scholars believe that there are opioid receptors in the synovial membrane of the knee \[27–29\]. Vendittoli et al. \[30\] reported that intraoperative local injection around the joint could target injured tissues and nerve endings accurately and alleviate postoperative pain. In addition, the drug was released slowly in soft tissue, thereby extending the postoperative duration of analgesia effectively \[8, 29\]. In addition to its direct effect, local injection can enhance the postoperative analgesic effect by inhibiting the response of neuroendocrine stress to surgery \[31\].

The anti-inflammatory effects of glucocorticoids include varying degrees of disruption of prostaglandin and cyclooxygenase pathways \[32–34\]. Glucocorticoids act directly on nuclear steroid receptors, and control the rate of mRNA/protein synthesis. They also cause inhibition of phospholipase A2, as well as changes in T- and B-cell functions, white-blood-cell activity, cytokine levels, and enzyme levels, and result in reduction of levels of the proinflammatory derivatives of arachidonic acid. Thus, injection of glucocorticoids into the soft tissues around the joint can reduce the inflammatory response at the site of the surgical wound, thereby relieving pain effectively. In addition, by reducing production of prostaglandins (especially vasodilators), postoperative blood loss can be reduced. Studies have
demonstrated that injection of hormones into the local infiltration around a joint does not increase the risk of complications such as joint infection, tissue atrophy, or osteonecrosis. Through strict aseptic operation/control and strict indications, Noticewala et al. [2] found that glucocorticoid replacement in local injections into a single condyle did not increase the risk of complications.

TA is an insoluble synthetic glucocorticoid that has anti-inflammatory effects and is intended for intra-articular use. Its effects last several weeks, longer than that of methylprednisolone. Studies have shown that at a single dose of TA (60–100 mg, i.m.) leads to adrenal suppression within 24–48 h that returns to normal gradually within 30–40 days [35–37]. In our study, patients receiving a periarticular injection of TA had significantly improved knee RoM in the early postoperative period compared with that of group A.

Our study had two main deficiencies. First, the study cohort was small. Studies with large sample sizes carried out at multiple centers are needed, and postoperative complications should be investigated further. Second, the duration of follow-up was short.

Conclusions

TA addition to a cocktail of agents for periarticular injection effectively relieved pain, improved knee-joint function, reduced the inflammatory response, did not increase risk of complications, and promoted rapid recovery after UKA.

List Of Abbreviations

Unicompartmental knee arthroplasty (UKA)

Triamcinolone acetonide (TA)

Total knee arthroplasty (TKA)

Visual analog pain score upon rest (VASR)

Visual analog pain score exercise (VASE),

Range of motion (ROM),

C-reactive protein (CRP) and

Erythrocyte sedimentation rate (ESR)

Postoperative day (POD)

Deep-venous thrombosis (DVT)

Patient-controlled anesthesia (PCA)
Declarations

All procedures performed in studies involving human participants were in accordance with the ethical standards of World Medical Association Declaration of Helsinki Ethical Principles for Medical Research Involving Human Subjects. The Ethics Committee of Aviation General Hospital approved this study. All patients agreed to participate in it.

All authors agree to publish “Effect of Periarticular Injections of Triamcinolone Acetonide During Unicompartmental Knee Arthroplasty in the Perioperative Period: a Randomized Clinical Trial” in Journal of Orthopaedic Surgery and Research.

Data and materials availability statement:

All data and materials used to support the findings of this study are included within the article.

We declare that we do not have any commercial or associative interest that represents a conflict of interest in connection with the work submitted.

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HG and YLZ collect data and write articles; JAY did the surgery; XZG, RDW, BL, QS, WYL, JC and YNL were responsible for literature review. All authors read and approved the final manuscript.

This article conforms to the journal style.

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Figures

![Figure 1](image)

**Figure 1**

Curve for VASR. Data are the mean ± SD. The asterisk indicates a significant difference (P < 0.05) between the two groups.
Figure 2

Curve for VASE. Data are the mean ± SD. The asterisk indicates a significant difference (P < 0.05) in the composition ratio between the two groups.
Figure 3

Comparison of morphine consumption between two groups. Data are the mean ± SD. The asterisk indicates a significant difference (P < 0.05) between the two groups.
Figure 4

Curve for RoM. Data are the mean ± SD. The asterisk indicates a significant difference (P < 0.05) between the two groups.

Figure 5

Curve for CRP level. Data are the mean ± SD. The asterisk indicates a significant difference (P < 0.05) between the two groups.
Figure 6

Curve for ESR. Data are the mean ± SD. The asterisk indicates a significant difference (P < 0.05) between the two groups.