**Original research article**

# A Study on Post TKR Pain Management Surgical Cocktail Vs Nerve Blocks

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**Abstract**

Pain control after total knee replacement (TKR) is pivotal in postoperative rehabilitation. Usage of epidural analgesia or parenteral opioids can cause undesirable side effects hampering early recovery and rehabilitation. These side effects can be avoided by infiltration of an analgesic cocktail locally. Our study was performed to evaluate the benefits of a particular cocktail combination in patients undergoing TKR with respect to pain and knee motion recovery.

**Materials and Methods:** Fifty consecutive patients who underwent simultaneous bilateral TKR were enrolled and received an intraoperative periarticular cocktail injection in the right knee (intervention) and normal saline in the left knee (control). Postoperative pain was recorded using the visual analog scale for each knee, and the time taken to achieve 90◦ of knee flexion was noted for each side. Data collection about post of pain and ROM was double blinded.

**Results:** The cocktail injected knee had significantly less pain when compared with the control knee during the first 48 hours and significantly shorter period to achieve 90◦ of knee flexion.

**Conclusions:** The use of intraoperative periarticular cocktail injection significantly reduces early post- operative pain and provides better early knee motion.

## Introduction

In patients with advanced knee arthritis, total knee replacement (TKR) has been found to be the most successful surgical procedure. However, early postoperative pain control is pivotal in reducing the hospital stay, increasing patient satisfaction, and for better reha- bilitation. It also reduces the potential for postoperative compli- cations such as pneumonia or deep vein thrombosis [1]. Severe postoperative pain is experienced in approximately 60% of the patients and moderate pain in approximately 30% of patients un- dergoing TKR [2]. Control of pain is achievable through multiple ways, and each has its own risks and benefits. Epidural anesthesia is a common modality for providing effective pain relief during the postoperative period, but it hinders early mobilization and leads to complications such as hypotension, postoperative headache, and spinal infection. Regional nerve blocks pose the risk of injuring neurovascular structures, he- matoma formation, and infection [3]. Systemic opioids such as morphine or fentanyl can cause nausea, vomiting, drowsiness, res-

piratory depression, urinary retention, and constipation [4]. An innovative approach to pain management is to aim at con- trolling local pain pathways and receptors within the knee. This has been possible through local intraarticular or periarticular injection of analgesic combinations which has good efficacy, is cost-effective, and is easy to administer without causing motor blockade. Also, it does not require any special technical skill for administration [5]. Various studies about periarticular injection have reported promising results from various combinations of drugs such as ketorolac, ropivacaine, bupivacaine, morphine sulfate, epi- morphine, methylprednisolone, cefuroxime, epinephrine, and normal saline [6-11]. The patients experienced a prolonged narcotic-free postoperative period and also a reduced parenteral analgesia postoperatively [12,13].

## Material and methods

We included patients who underwent simultaneous bilateral TKR from July 2017 to Jan 2023 in our institute. For uniformity, we included only the patients for whom spinal anesthesia was the mode of anesthesia. fifty consecutive patients who satisfied the inclusion criteria were selected for the study. All the patients had a full understanding of the 10-point visual analog pain scale (VAS). Exclusion criteria were patients with a history of allergy to the medications used in this study, abnormal renal or liver function, uncontrolled diabetes, and those who could not receive spinal anesthesia.

**Content of local infiltration-Single**

| WEIGHT < 70 Kg | WEIGHT > 70 Kg |
|---|---|
| • Ropivacaine 300 mg (40cc*0.75% ropin)<br>• Adrenalin 0.3 cc<br>• Clonidine 0.6 cc<br>• NS 19 cc<br>• Ketorolac 2cc<br><br>Total volume 60 cc | • Ropivacaine 405 mg (54cc*0.75% ropin)<br>• Adrenaline 0.3cc<br>• Clonidine 0.8 cc<br>• NS 25 cc<br>• Ketorolac 2cc<br><br>Total volume 80 cc |

Data collection about post of pain and ROM was double blinded- need to mention about this

## Results

A total of 50 patients were included in the study. Osteoarthritis was the underlying condition in 47 patients, while the rest of them had rheumatoid arthritis The mean pain scores (VAS) at 6, 12, 24, and 48 hours, and at third and fourth days in both knees are enumerated in Table 1 . When compared with the control knee, a statistically significant reduction in pain score was noted in the cocktail injected knee at 6, 12, 24, and 48 hours ($P < .001$ in all cases). However, the difference in the mean pain scores between both knees at the third ($P$ ¼ .684) and fourth ($P$ ¼ .251) days were not significant. The mean time taken for achieving 90° flexion in the intervention and control knees were 1.70 and 2.82 days, respectively. The difference was found to be statistically significant ($P < .001$). Within the intervention group, there was a significant difference in the pain scores over different time points (Table 2). A post hoc analysis showed no significant difference within various time points on the first day (6, 12, and 24 hours) after surgery. However, a statistically significant

difference in the pain scores was noted at 48 hours ($P < .001$), 72 hours ($P < .010$), and 96 hours ($P < .001$), compared with the 24-hour score. Within the control group, there was a significant difference in pain scores over different time points (Table 2). However, a post hoc analysis showed that there was no significant difference within various time points on the first day (6, 12, and 24 hours) after surgery, and statistically significant improvement was found only after 72 hours ($P < .001$) and 96 hours ($P < .001$), compared with the 24-hour value.

**Table 1: Between-group comparison.**

| Postoperative duration | Group | Mean | Standard deviation | Standard error mean | *P* value |
|---|---|---|---|---|---|
| 6 h | Control | 3.73 | 1.927 | .193 | <.001[a] |
| | Intervention | 1.96 | 1.406 | .141 | |
| 12 h | Control | 3.17 | 1.770 | .177 | <.001[a] |
| | Intervention | 1.83 | 1.371 | .137 | |
| 24 h | Control | 2.62 | 1.362 | .136 | <.001[a] |
| | Intervention | 1.58 | .654 | .065 | |
| 48 h | Control | 2.34 | 1.056 | .106 | <.001[a] |
| | Intervention | 1.13 | .825 | .082 | |
| 3 d | Control | 1.22 | 1.050 | .105 | .684 |
| | Intervention | 1.16 | 1.032 | .103 | |
| 4 d | Control | 1.10 | 1.010 | .101 | .251 |
| | Intervention | .95 | .821 | .082 | |

[a] Significant at $P < .05$.

**Table 2**
Within-group repeated-measures ANOVA.

| Group | Mean | Standard deviation | N | *P* value |
|---|---|---|---|---|
| Control | | | | |
| 6 h | 3.73 | 1.927 | 100 | <.001 |
| 12 h | 3.17 | 1.770 | 100 | |
| 24 h | 2.62 | 1.362 | 100 | |
| 48 h | 2.34 | 1.056 | 100 | |
| 3 d | 1.22 | 1.050 | 100 | |
| 4 d | 1.10 | 1.010 | 100 | |
| Intervention | | | | |
| 6 h | 1.96 | 1.406 | 100 | <.001 |
| 12 h | 1.83 | 1.371 | 100 | |
| 24 h | 1.58 | .654 | 100 | |
| 48 h | 1.13 | .825 | 100 | |
| 3 d | 1.16 | 1.032 | 100 | |
| 4 d | .95 | .821 | 100 | |

ANOVA, analysis of variance.

## Discussion

During TKR, trauma to the tissues exaggerates the neurological responsiveness to pain by reducing the threshold of afferent nociceptive neurons and by central sensitization of excitatory neurons. This contributes to increased sensitivity to postoperative pain [11]. Hence, a multimodal approach for postoperative pain control has been particularly effective not only in relieving post- operative pain but also in facilitating earlier rehabilitation and improving postoperative ROM. It also reduces the complications of other modalities of pain management such as patient-controlled anesthesia (PCA), continuous epidural anesthesia, and femoral nerve block [2,11,16]. The rationale for using the analgesic cocktail was to facilitate contraction

of the smooth muscles that line the arterioles to potentially minimize intraarticular bleeding and prolong the time the agents would act locally. The component epinephrine in the cocktail is especially conspicuous in this regard [3,5,11,17]. The component ketorolac not only acts as antiinflammatory and analgesic but also possesses synergistic activity when given along with other oral nonsteroidal antiinflammatory drugs, such as acet- aminophen and gabapentin, thereby reducing the requirement of these systemic agents [5]. Significant pain relief was obtained when intraarticular ketorolac was given along with bupivacaine and epinephrine as a cocktail combination in previous studies [3,11,17]. According to Badner et al. [15], addition of an opioid like morphine in the cocktail mixture did not provide any significant additional advantage when compared to cocktail mixtures without opioids with respect to postoperative pain relief [18]. In accordance with their study, our study also excluded the use of opioids in the cocktail mixture. According to Christensen et al. [19], addition of steroids to multimodal periarticular cocktail injection only minimized the length of hospital stay in patients undergoing TKR. It did not improve pain relief or early postoperative ROM. They also posed an increased risk of postoperative infection [12,19]. Although the existing randomized controlled trials have confirmed the safety of steroids, many surgeons still hesitate to use a drug which is thought to increase the risk of catastrophic complications such as infection and patellar tendon rupture [15,20-22]. For the aforementioned reasons, steroids were not added to the cocktail mixture in our study. The results of immediate postoperative pain control by various authors are promising. Mullaji et al. [23] used bupivacaine, fentanyl, methylprednisolone, and cefuroxime in their intraarticular cocktail. Badner et al. [15] used a combination of bupivacaine and epinephrine. Andersen et al. [24] used subcutaneous ropivacaine, and Vaishya et al. [25] used bupivacaine, adrenaline, morphine, ketorolac, and gentamycin. All of them demonstrated significant pain relief, increased early postoperative knee movements, and quadriceps function. Since our study compared the results of each knee of the same patient, the physical therapy regime and systemic medications (including antiinflammatories, analgesics, and antibiotics) would be the same for each knee of a particular patient, thereby elimi- nating these confounding factors during the comparison. Even though a power analysis was not performed before commencing the study, the number of knees included in our comparison (100 patients with 200 knees) was higher compared with the previous similar studies [2-4,26]. We included consecutive bilateral TKR patients belonging to a particular time frame. In our study, the cocktail injection was given in a periarticular manner. Significant reduction in pain (by VAS) was recorded over the knee where the injection was given (right side) compared with the opposite side at 6, 12, 24, and 48 hours ($P < .001$). This is in comparison with the study by Fu et al. [2] which showed VAS score at rest was significantly lower at 6, 10, 24, and 36 hours post- operatively in the trial group compared with the control group, although the difference was insignificant at 24 hours post- operatively, and at days 2, 7, and 15 between the 2 groups. VAS score during activity was also lower in the trial group at 24 and 36 hours postoperatively than that in the control group, although the difference was insignificant at days 2, 7, and 15 [2,8]. Busch et al. noted that patients who received a periarticular intraoperative injection containing ropivacaine, ketorolac, epimorphine, and epinephrine used significantly less PCA during the first 24 hours postoperatively [11]. Vaishya et al. [25], in their study comparing 2 groups of 40 knees each, reported that the cocktail injected patients reported significantly less PCA and postoperative pain recordings at 6, 24, 48, and 72 hours after TKR. In our study, the time taken

to achieve 90° of knee flexion postoperatively was found to be significantly longer for the control side (mean 2.82 days) than that for the intervention side (mean 1.70 days). According to a comparative study by Rasmussen et al., use of 24- to 72-hour continuous intraarticular infusion of morphine plus ropivacaine showed a significant improvement in ROM and decreased the length of hospital stay [27]. According to the study by Fu et al., in which 80 patients were grouped into 2 groups namely trial and control, the time of being able to perform straight leg raise and reaching 90° knee flexion was significantly shorter in the trial intraarticular analgesic injection is helpful in early postoperative rehabilitation [2].

## Conclusions

The results of our study clearly show that periarticular cocktail injection in TKR not only helps in relieving the pain but also aids in early recovery and rehabilitation.We must lead with evidence-based research designs and publications so that broader adoption can benefit most joint arthroplasty patients. Value-based health care improvements will always benefit from safer and more effective postoperative pain control strategies that avoid prolonged patient recoveries and narcotic addictions. Pericapsular injections with prolonged acting agents, coupled with tourniquet-less and tissue-sparing surgical techniques might well emerge as some of the brightest stars on our joint reconstructive horizon.

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