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Enhanced Post Total Knee Replacement Recovery by Using Intraarticular Intraoperative Cocktail Injections

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Author`s Contribution

[1,2,3]Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; [2,4,5]Drafting the work or revising it critically for important intellectual content,[1,5,6]Final approval of the version to be published [1,6]Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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ABSTRACT

Objective: To assess the advantages of a specific cocktail combination in TKR patients, focusing on postoperative pain relief and enhanced recovery of knee mobility.

Methodology: This prospective, double-blinded, placebo-controlled study was conducted at Akbar Niazi Teaching Hospital, Islamabad, from January 2022 to December 2024. Sixty consecutive patients underwent unilateral TKR were enrolled, with 30 receiving an intraoperative intraarticular cocktail injection (intervention) and 30 receiving normal saline (control). Postoperative pain for each knee was assessed using visual analog scale (VAS), and time required to attain 90° of knee flexion was recorded for both groups. The collected data were analyzed utilizing SPSS v 23. Changes in pain scores within the groups across follow-up periods were analyzed using repeated measures ANOVA

Results: The patients were between 55 and 85 years old (mean was 63.2±9.2 years), and males were 66.7%. Patients who received the cocktail injection experienced significantly less pain than the control group during the first 48 hours and achieved 90° of knee flexion in a significantly shorter time.

Conclusion: Intraoperative intraarticular cocktail injection significantly alleviates early postoperative pain and enhances early knee mobility.

Keywords: Arthroplasty, Replacement, Knee; Injections, Intra-Articular; Pain; Range of Motion, Articular; Visual analog scale.

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Introduction

Total knee replacement (TKR) is recognized as the most effective surgical procedure for patients with advanced knee arthritis. Effective early postoperative pain management is crucial for shortening hospital stays, enhancing patient satisfaction, and improving rehabilitation outcomes. It also minimizes the risk of postoperative complications, including deep vein thrombosis (DVT) and pneumonia by early pain free mobilization.[1] Around 60% of TKR patients experience severe postoperative pain, while approximately 30% report moderate pain.[2]

Pain management can be achieved via various approaches, each has its own risks and benefits. Epidural anesthesia is a widely used method for postoperative pain relief; however, it delays early mobilization and may cause

complications like spinal infections, hypotension, and postoperative headaches. Regional nerve blocks carry a risk of neurovascular injury, infection, and hematoma formation.[3] Systemic opioids like fentanyl or morphine may lead to vomiting, nausea, drowsiness, urinary retention, respiratory depression, and constipation.[4]

The patient control analgesia (PCA) is also an effective method of pain control. However, it is hospital based and the patient cannot be discharged early. Several studies on intracapsular injections have shown promising results using different drug combinations, including ropivacaine, ketorolac, bupivacaine, epimorphine, morphine sulfate, methylprednisolone, epinephrine, cefuroxime, and normal saline.[5-8] The patients had an extended narcotic-free postoperative time and required less parenteral analgesia after surgery.[9]

This study objectives were to compare the pain score postoperatively in patients underwent unilateral TKR, with one group receiving an intraoperative intraarticular cocktail injection including antibiotics (intervention) and the other receiving an equivalent volume of normal saline with antibiotics (control). This study also seeks to compare the duration (days) needed to attain 90° of active knee flexion postoperatively using a specific cocktail combination of Inj. Bupivacaine, Toradol (ketorolac) & Methylprednisolone. Comparing pain score between the groups helped eliminate confounding factors like systemic analgesia and individual differences in pain tolerance.

Methodology

Patients underwent unilateral TKR at Akbar Niazi Teaching Hospital, Islamabad, between January 2022 and December 2024 were included in the study. To ensure uniformity, only patients who received spinal anesthesia were included. Sixty (n=60) consecutive patients, both gender and aged ≥ 55 years, meeting the inclusion criteria were enrolled in the study. All patients had a clear understanding of 10 points visual analog scale (VAS) for pain assessment.

Patients were excluded if they had a history of allergy to the study medications, abnormal liver or renal function, uncontrolled diabetes, or were ineligible for spinal anesthesia. Also, the revision total knee arthroplasties for any cause were excluded from the study.

This study was a prospective, double-blinded, and placebo-controlled. All participants provided informed consent, and the study methods were approved by the ethics committee of the institute (Ref. No: 130/IMDC/IREB-2022).

Thirty patients served an intraoperative intraarticular cocktail injection in operative knee, while the other 30 served as the control group, receiving an equal volume (34 mL) of normal saline with antibiotics. Patients were unaware of whether they given cocktail injection. All patients underwent spinal anesthesia using a 0.5% bupivacaine. Antibiotic prophylaxis consisted of a 1 g cefazolin injection and gentamycin 80 mg injection administered 30 minutes before the incision.

A single surgeon (first author) performed all surgeries and administered the cocktail injections using the medial parapatellar arthrotomy method.

Intraarticular cocktail comprising Inj. Bupivacaine 50 mg (10 ml), Inj. Toradol (ketorolac) 30 mg (1 ml), Inj. Methylprednisolone 80 mg (1 ml), Inj. Vancomycin 1 g (20 ml), Inj. Gentamycin 80 mg (2 ml), total of 34 ml solution. The injection was administered using a 21G needle. The trained scrub nurse formulated the cocktail based on prior clinical expertise. The injections were prepared under strict aseptic protocols. The injections filling needle was discarded and new needle was used to inject.

The cocktail was administered using 34 mL via the anterolateral approach. Injection was given after closing the medial parapatellar arthrotomy (capsular closure). It was made sure that the closure was air tight, and no spilling of the injection was seen out of the joint. The subcutaneous tissue and midline skin incision closed subsequently. Cemented post stabilizing (PS) implants were utilized in all cases. The tourniquet was released, and no drains were placed.

Postoperatively, systemic analgesics included intravenous ketorolac (30 mg) and tramadol (100 mg) accompanied by ondansetron (4 mg) as per needed for three days, followed by a ten-day regimen of oral Piroxicam (20 mg) and a combination of paracetamol and orphenadrine (700 mg). Oral pregabalin (75 mg) was administered to patients who either were not tolerated or not achieved adequate pain relief with the standard medications.

In addition to mechanical DVT prophylaxis, such as manual massage and ankle pumping, patients received Inj. Enoxaparin (Clexane) on day one post operatively followed by a daily dose of oral aspirin (150 mg) for six weeks. Within 3 to 4 hours post-surgery, patients began ambulation using a walker on the same day, accompanied by the initiation of isometric exercises and range of motion

(ROM) activities. Patients were closely monitored until discharge and remained under regular follow-up.

A nurse or an educated attendant unaware of the study, separately recorded postoperative pain the operated knee using 10 points VAS score at 6, 12, 24, and 48 hours, followed by daily assessments until fourth postoperative day. The VAS is a 10 cm scale where 0 represents no pain, and 10 signifies the worst impossible pain.

A physiotherapist, also unaware of the study, separately recorded the postoperative active knee flexion range daily the operated knee until the fourth postoperative day.

Monitoring of vital signs encompassed oxygen saturation, blood pressure, and heart rate. Adverse reactions, including allergies, vomiting, nausea, respiratory depression, and urinary retention, were monitored until patient discharge.

The collected data were analyzed utilizing SPSS v 23. Descriptive stats were presented as mean and SD. Independent t test was conducted to assess the association between intervention and control patients. Changes in pain scores within the groups across follow-up periods were analyzed using repeated measures ANOVA. A post hoc analysis was performed to determine significance between the two time points.

Results

Overall 30 patients were selected with an overall mean age of 47 years, of whom 63.3% were female and 36.7% were male. Before the surgery, 66.7% of patients were using hypoglycemic drugs and more than half (53.3%) were on insulin therapy. Overall mean preoperative HbA1c was 8.85%, which progressively decreases to 8.17% on the 3rd postoperative day, 7.07% after 2 weeks, and 5.92% at 6 months after surgeries. Additionally, the plasma glucose levels also improved from a mean of 202.7 mg/dL on the 3rd postoperative day to 138.4 mg/dL at 2 weeks, and 100.8 mg/dL at 6 months after surgeries. The EWL also noted steady improvement, increasing from 4.05% at the study included 60 patients, accounting for 60 TKR. Osteoarthritis was the primary condition in 90% (n=54) of patients, while the remaining had rheumatoid arthritis. The patient's mean age was 63.2±9.2 years. Among 60 patients, 66.7% (n=40) were male, while 33.3% (n=20) were female.

The mean VAS score at 6, 12, 24, and 48 hours, as well as on the 3rd and 4th postoperative days for both groups, are presented in Table I and Figure 1. The cocktail-injected group showed a significantly lower pain score than the control at 6, 12, 24, and 48 hours ($p < 0.001$). While, the difference in mean pain score between two groups on third ($p = 0.573$) and fourth ($p = 0.140$) postoperative days was insignificant.

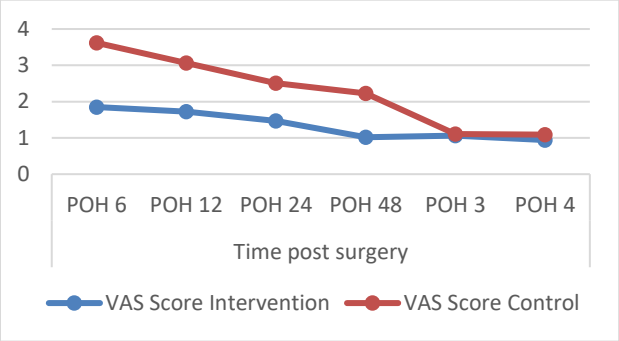

Figure 1. VAS comparison. (n=60)

The average duration to achieve 90° knee flexion was 1.6 days in intervention patients and 2.7 days in control patients. The difference was significant ($p < 0.001$).

Within intervention group, pain score varied significantly across different times (Table 2). Post hoc test revealed insignificant difference in pain score among the different times on 1st day postoperatively (6, 12, and 24 hrs.). While, the difference in pain score was observed significantly at 48 hrs ($p < 0.001$), 3rd day ($p < 0.020$), and 4th day ($p < 0.001$) compared to 24 hrs.

Within control group, pain score varied significantly across different times (Table I). Post hoc test revealed insignificant difference in pain score among the different times on 1st day postoperatively (6, 12, and 24 hrs). While, the difference in pain score was observed significant at 3rd day ($p < 0.001$), and 4th day ($p < 0.001$) compared to 24 hrs.

Table I: Comparison between groups. (n=60)

Postoperative duration	Intervention (n=30) Mean±SD	Control (n=30) Mean±SD	Std. Error mean	p-value
6 h	1.85±1.39	3.62±1.81	.167	.001
12 h	1.72±1.26	3.06±1.66	.157	.001
24 h	1.47±0.54	2.51±1.25	.101	.001
48 h	1.02±0.71	2.23±1.04	.094	.001
3 d	1.06±1.02	1.11±1.04	.104	.573
4 d	0.94±1.39	1.09±1.0	.092	.140

No patient had infection from both the groups. Impaired wound healing, marked by bloody and serous discharge, was observed in 1 patient from intervention group and 2 patients from control group. These patients wound swabs showed no bacterial growth, and healing was achieved with frequent cleaning and dressing. No instances of hematoma formation were clinically observed in either group. Not a single patient developed symptomatic DVT or experienced allergic reactions.

Table II: Comparison within groups repeated measures ANOVA. (n=60)

Groups	Mean±SD	N	p-value
Control			
6 h	3.62±1.81	30	.001
12 h	3.06±1.66	30	
24 h	2.51±1.25	30	
48 h	2.23±1.04	30	
3 d	1.11±1.04	30	
4 d	1.09±1.0	30	
Intervention			
6 h	1.85±1.39	30	.001
12 h	1.72±1.26	30	
24 h	1.47±0.54	30	
48 h	1.02±0.71	30	
3 d	1.06±1.02	30	
4 d	0.94±1.39	30	

Discussion

The analgesic cocktail was utilized to induce smooth muscle contraction in the arterioles, aiming to minimize intraarticular bleeding and prolong the local effects of the agents.[10]

Shetty reported that adding an opioid to cocktail did not offer significant benefit in postoperative pain relief compared to opioid-free cocktail mixtures.[11] Consistent with his findings, our study also excluded opioids from the cocktail mixture. Shah et al reported that adding steroids to cocktail primarily reduced the hospital stay in TKR patients.[12] It is not enhanced pain relief and ROM after surgery. Although existing literature have validated the steroids safety, various surgeons remain hesitant to utilize them due to concerns about potential complications, including infection and patellar tendon rupture.[13] However we have safely used steroid injection in our cocktail group with no above-mentioned complications.

Various authors have reported promising results regarding immediate postoperative pain control by the steroid use.[14] By comparing the outcomes, our study ensured that physiotherapy regimen and systemic medications (such as anti-inflammatories, antibiotics, and analgesics) remained consistent for both groups, effectively eliminating these factors as potential confounders. We included consecutive patients undergone unilateral TKR within a specific time frame.

In our study, the cocktail injection was administered intraarticular after closing the capsule and before closure of skin. A significant reduction in pain was observed in the intervention group compared to the control group at 6, 12, 24, and 48 hours ($p < .001$). This aligns with the study by Nair et al which demonstrated that the study patients exhibited significantly lower VAS scores at rest than control patients at 6, 12, 24, and 48 hrs postoperatively. However, the difference across the patients was insignificant on postoperative days 3 and 4.[1] During activity, the VAS score was also lower in the study patients than in the control patients at 24 and 36 hrs postoperatively, though the difference was not significant at 2, 7, and 15 days.[15] Vaishya et al in their study comparing two groups, found that patients who received the cocktail injection had significantly lower postoperative pain score at 6, 24, 48, and 72 hrs following TKR.[16]

In our study, the control group took significantly longer to attain 90° of knee flexion postoperatively compared to the intervention group. According to Martin et al study, a 24 to 72 hours intracapsular injection of ropivacaine significantly improved ROM and reduced the hospital stay.[17]

This study has certain limitations. A pilot analysis was not conducted prior to the study, and patient inclusion was based on a specific time frame. The ideal concentration of each component in the cocktail remained undetermined, and additional research is needed to evaluate the comparative effectiveness of each component. An ongoing debate is whether normal saline infiltration in control patients might mechanically trigger pain, despite the assumption that normal saline is presumed to lack local pharmacological effects. This study did not evaluate patients' long-term clinical outcomes.

Conclusion

The findings of this study clearly demonstrate that intraarticular cocktail injection in TKR not only alleviates pain but also facilitates early recovery and rehabilitation.

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