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ORIGINAL ARTICLE

# Multimodal Cocktail Injection relieves Postoperative Pain and improves Early Rehabilitation following Total Knee Replacement: A Prospective, Blinded and Randomized Study

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## ABSTRACT

**Objectives:** An effective postoperative analgesia following total knee arthroplasty (TKA) would shorten the rehabilitation period and improve patient satisfaction. The primary objective of the present study is to test the hypothesis that intraoperative multimodal cocktail injection can significantly reduce the consumption of analgesics and duration of time required to perform straight-leg raise, and improve range of motion (ROM) and patient satisfaction rate following TKA.

**Materials and methods:** A total of 126 osteoarthritic knees in patients with a mean age of 68 years (58–80 years) scheduled for primary TKA were prospectively randomized into three groups. Patients in all three groups received the same anesthesia and postprocedure pain control and rehabilitation protocol. The assessor was blind with regard to multimodal cocktail injection for the duration of study. Assessment was done preoperatively at 1, 2, 3, and 4 postoperative days, and at 1, 2, and 3 months postoperatively. The primary outcome was function measured with Western Ontario and McMaster Universities Arthritis Index. Pain and patient satisfaction rate were established using visual analog scale and Likert scale respectively. Consumption of analgesic during the postoperative days (1–4 days), hospital stay, and ROM were recorded and evaluated. Outcome measures were critically analyzed. The level of significance was set at <0.05.

**Results:** Pain, functional scores, and satisfaction rates were significantly better in cocktail group than in the control group ($p < 0.05$). Consumption of nonsteroidal anti-inflammatory drugs was significantly lower in groups with multimodal cocktail injection than in the control group ($p < 0.05$). Mean follow-up time was 3 months with no patient lost to follow-up. No complications related to the infiltration of the local anesthetic and/or steroids were observed.

**Conclusion:** Multimodal cocktail injection offered improved postoperative pain control, thus facilitating early rehabilitation.


**Keywords:** Likert scale, Nonsteroidal anti-inflammatory drugs, Total knee arthroplasty, Visual analog scale, Western Ontario and McMaster Universities Arthritis Index.

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## INTRODUCTION

Total knee arthroplasty (TKA) in patients with advanced knee arthritis is an undisputed option for relieving pain and improving joint function. The most important issue concerning patients is "immediate postsurgical pain",[1] which often results in day of surgery delays or cancellations.[2] Postoperative pain following TKA has only recently been recognized as an important issue and a potential origin of delayed surgical recovery. Unrelieved postoperative pain has detrimental effects besides patients' discomfort following surgery.[3,4] In turn, these effects can contribute to longer length of hospital stay, increased readmission rates, and increased cost of care.[3,5] Ineffective or inadequate management of postoperative pain may lead to higher degree of patients' dissatisfaction,[6] thus reducing patients' willingness to undergo further treatment if required in future.[7,8] It is therefore imperative that postoperative pain control is managed well, to ensure that the patient has adequate analgesia. Although there are several treatment options for postoperative pain which are often helpful, they are fraught with problems.[9-16] Furthermore, the choice of analgesic agents and/or technique influences pain in the immediate postsurgical period. In view of these critical concerns, Kehlet and Dahl[8] introduced the concept of multimodal analgesia. The rationale behind the concept is to capture the effectiveness of individual agents of different classes of analgesia in optimal doses and use different sites of analgesic administration to maximize pain relief with reduced analgesic-associated side effects. This important concept allows the agents that act by different mechanisms to act synergistically in preventing or treating acute pain while requiring minimal optimal dose. Multimodal analgesia will minimize the postsurgical pain and improve the postoperative

outcome. An editorial[17] title suggests that we need to walk many miles before satisfactory results concerning postoperative pain control are achieved. The primary objective of the present study is to test the hypothesis that intraoperative multimodal cocktail periarticular injection can significantly reduce the consumption of analgesics, facilitate early rehabilitation [duration of time required to perform active straight-leg raise (ASLR), range of motion (ROM)], and improve patient satisfaction rate following TKA.

## MATERIALS AND METHODS

### Study Design

The present study is a multicentric, prospective, controlled, randomized, single-blind, clinical analysis comparing intraoperative multimodal analgesia (treatment/cocktail group) with control group in patients undergoing TKA. The study was approved by the Scientific Review Committee and the Institutional Review Board (IRB) at Shalby Hospitals, Ahmadabad, Gujarat, India.

### Inclusion and Exclusion Criteria

Patients of either sex with grade III or IV osteoarthritis knees (Kellgren and Lawrence system[18]) scheduled for a primary TKA with no revisions were enrolled for the study. Exclusion criteria consisted of (1) active inflammatory or connective tissue disease (i.e., lupus, rheumatoid arthritis), (2) diabetes mellitus, (3) hypersensitivity to nonsteroidal anti-inflammatory drugs (NSAIDs) or local anesthetic agents, abnormal liver or kidney function tests, history of peptic ulceration and upper gastrointestinal hemorrhage, cancer, hyperkalemia, (4) contraindications to use of per rectal (PR) diclofenac sodium including history of asthma, (5) history of coagulopathies, hematological or neurological disorders, and/or (6) any other conditions that, in the opinion of the team, would make involvement not in the best interest of the cohort or could prevent or limit the protocol-specified outcome assessment.

### Procedures

Potentially eligible patients were screened. A medical and demographic history was taken, and patients were examined. After informed consent was obtained, patients received detailed instructions from the team concerning the treatment/procedure. Patient involvement was entirely voluntary and each patient had an opportunity to refuse the surgery as well as the additional education at any point during the study duration. Following IRB approval, 126 patients scheduled for total knee replacement under spinal anesthesia were randomized by means of sealed envelopes into three groups: Group I did not receive any cocktail injection and acted as control; group II received cocktail injection: Inj. Ducati (cefuroxime) 1.5 gm diluted with 20 mL inj. NS + inj. Bupitroy (bupivacaine hydrochloride 0.5%) 20 mL; group III received cocktail injection: Inj. Ducati (cefuroxime) 1.5 gm diluted with 20 mL inj. NS + inj. Bupitroy (bupivacaine hydrochloride 0.5%) 20 mL + inj. Depomedrol (methylprednisolone acetate) 40 mg/mL. Routine baseline parameters including age, gender, and severity of diseases (Kellgren and Lawrence system), deformity, and comorbidity, if any, were recorded preoperatively (Table 1). All the operations were performed by the senior author or under his direct supervision. All patients underwent TKA using standard midline incision with medial parapatellar arthrotomy without tourniquet. Standard release and cuts were made. Patellar resurfacing was done in all cases. Trial checking was done. The patients received cocktail injection prior to cementing. Eight zones were identified as site for injections as these have increased neurosensory sensitivity and elevated concentration of mechanoreceptors.[19] Approximately 2 to 3 mL of cocktail is injected into the suprapatellar pouch/synovium around quadriceps tendon (Zone 1; Fig. 1), patellar fat pad (Zone 2; Fig. 2), medial meniscus capsular attachment (Zone 3; Fig. 3), lateral meniscus capsular attachment (Zone 4; Fig. 4), posteromedial capsule (Zone 5; Fig. 5), posterolateral capsule (Zone 6; Fig. 6), medial retinaculum (Zone 7; Fig. 7), and lateral retinaculum (Zone 8; Fig. 8). We only allow 3 to 4 mL of cocktail to diffuse per pass. All had posterior stabilized metal-backed TKA. A three-layered

**Table 1:** Demographic and clinical variables

| *Sl. no.* | *Characteristics* | *Group I* | *Group II* | *Group III* | *p-value* |
|---|---|---|---|---|---|
| 1 | Age (years) | 68.20 ± 1.21 | 68.19 ± 2.33 | 68.31 ± 1.30 | p > 0.05 |
| 2 | Sex | 32 females (76.19%)<br>10 males (23.80%) | 33 females (78.57%)<br>9 males (22.428%) | 32 females (76.19%)<br>10 males (23.80%) | $\chi^2$ = 0.09<br>p = 0.956 |
| 3 | Severity of disease (Kellgren and Lawrence system) | 33 grade IV (78.57%)<br>9 grade III (22.428%) | 33 grade IV (78.57%)<br>9 grade III (22.428%) | 34 grade IV (80.95%)<br>8 grade III (19.04%) | $\chi^2$ = 0.097<br>p = 0.953 |
| 4 | Deformity (varus/valgus) | 18.7 ± 1.33 | 19.2 ± 1.22 | 18.8 ± 1.21 | p > 0.05 |
| 5 | Flexion angle | 110.2 ± 1.20 | 109.8 ± 1.31 | 110.5 ± 1.23 | p > 0.05 |
| 6 | Comorbidity (HTN, IHD) | 14.7% (n = 35) | 14.28% (n = 34) | 14.7% (n = 35) | $\chi^2$ = 0.11<br>p = 0.946 |

No significance regarding demographic variables (p > 0.05); HTN: Hypertension; IHD: Ischemic heart disease

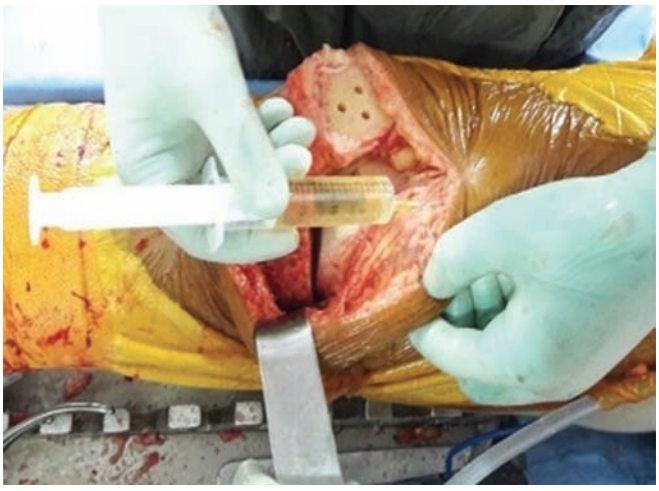

**Fig. 1:** Suprapatellar pouch/synovium around quadriceps tendon (Zone 1)

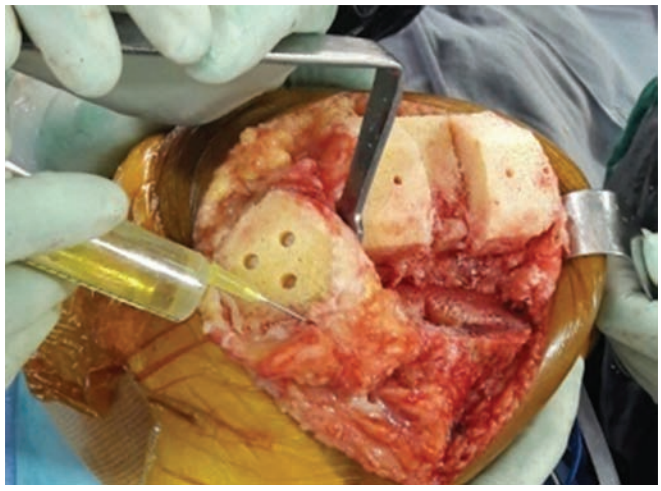

**Fig. 2:** Patellar fat pad (Zone 2)

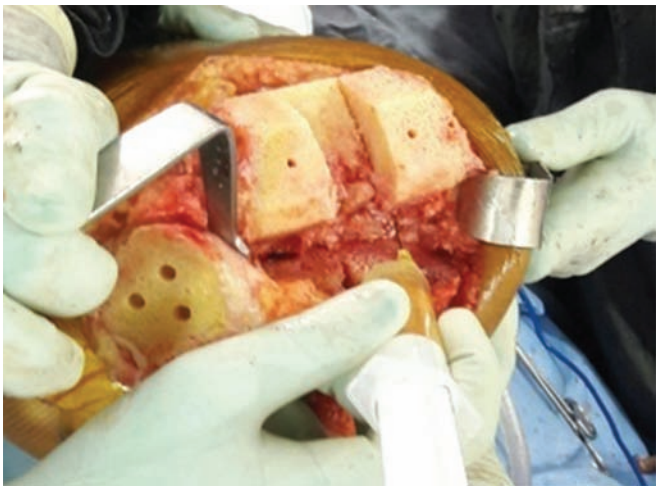

**Fig. 3:** Medial meniscus capsular attachment (Zone 3)

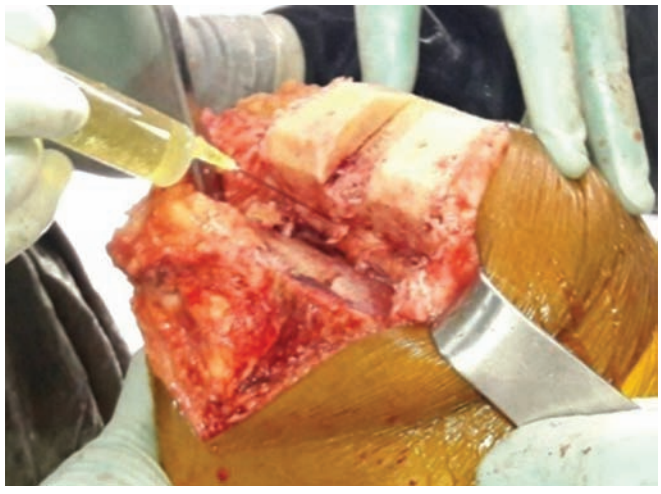

**Fig. 4:** Lateral meniscus capsular attachment (Zone 4)

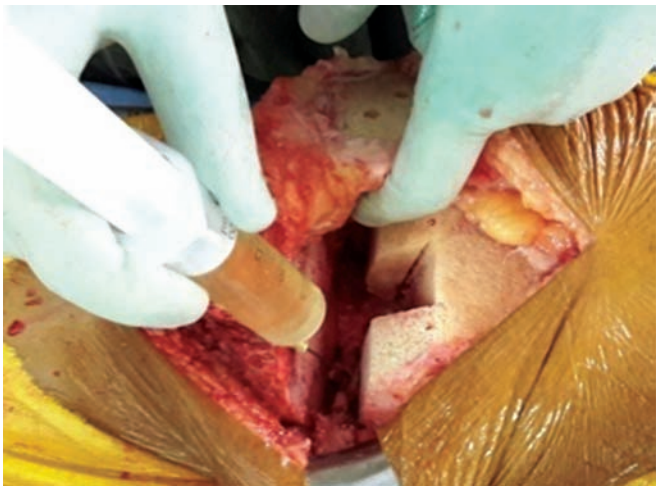

**Fig. 5:** Posteromedial capsule (Zone 5)

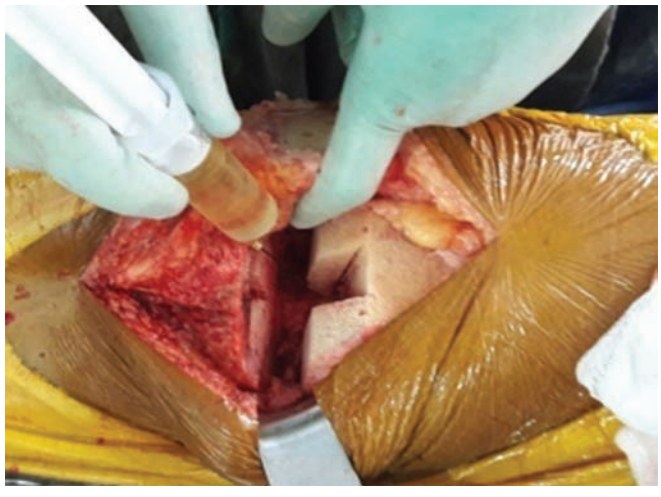

**Fig. 6:** Posterolateral capsule (Zone 6)

closure was done. No drains were used in any group. All the three groups received a similar anesthetic procedure, postsurgical pain control, and rehabilitation protocol. Analgesia during the postoperative days (1–4) was standardized for all patients and consisted of diclofenac suppositories 50 mg PR 6 hourly until discharge. No parenteral narcotics were used. Patients who reported moderate to severe pain [i.e., visual analog scale (VAS) greater than 3] were given intravenous 1 gm acetaminophen as rescue medication. Postoperative ankle pumps and standing

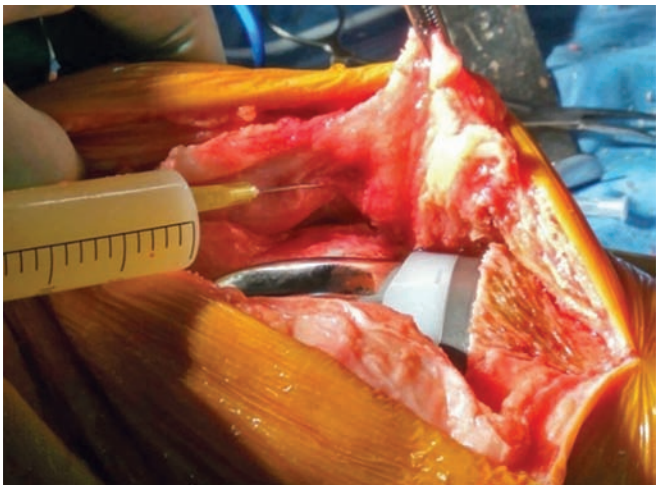

**Fig. 7:** Medial retinaculum (Zone 7)

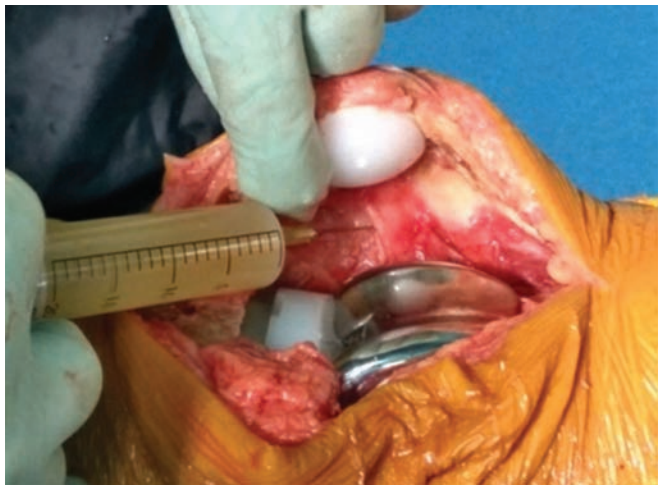

**Fig. 8:** Lateral retinaculum (Zone 8)

were started the same evening. Static quadriceps and high sitting were allowed from the next morning. Straight-leg raise (SLR) was permitted whenever the patient was comfortable. The range of movement of operated knee was documented daily by a physiotherapist using a goniometer. Following discharge, all patients were given a standard discharge analgesic medication and rehabilitation protocol. All the data were collected by the assessor who was blind to the multimodal cocktail injection for the duration of the study. Assessment was performed preoperatively, on the first four postoperative days, and at 1, 2, and 3 months. Complications, such as postsurgical infection and tendon rupture were documented.

### Outcome

Outcome measures include VAS (measured by a 0–10 cm linear scale, where 0 cm represented "no pain" and 10 cm represented "worst possible pain"), Western Ontario and McMaster Universities Arthritis Index (WOMAC), ROM, duration of SLR, consumption of total hospital NSAIDs, stay in hospital, and patient satisfaction rate. The total amount of diclofenac administered was defined as the amount of analgesics used. Pain was evaluated from the day of surgery to 4 days after surgery than during the follow-up period using VAS. For satisfaction rate, four items/criteria, determined by an expert consensus panel were chosen to evaluate the level of postsurgical satisfaction experienced by patients who have undergone TKA. The satisfaction questionnaire included four questions (each with four possible answers)[20]: Patients' overall satisfaction with the procedure, the extent of pain relief, mental health (ability to enjoy life as before), and the ability to perform routine work. These are scored on a 4-point Likert scale[21] with response categories comprising very satisfied (100 points), somewhat satisfied (75 points), somewhat dissatisfied (50 points), and very dissatisfied (25 points). Face validity was assessed by having the scale reviewed by a board of independent experts in the field of orthopedics. The internal consistency or reliability of the scale was evaluated using Cronbach's alpha coefficient. When assessing Cronbach's alpha, scores of 0.8 or greater are labeled "good" while scores >0.9 are "excellent."

### Satisfaction Rate

In the current study, the percentage distribution and frequency of the control and cocktail groups' satisfaction scores were recorded, analyzed, and compared.

### Statistical Analysis

Outcome measures were critically analyzed and expressed as mean (± standard deviation). Differences between the groups were analyzed by Student's t-test using $p < 0.05$ as the level of significance.

## RESULTS

The clinical and demographic variables of groups are summarized in tables and did not show any significant difference ($p > 0.05$) (Table 1). All the participating patients significantly experienced less pain than the baseline parameters ($p < 0.05$) following TKA. Patients in the cocktail groups have significantly lower VAS score than the control group during early postoperative days (1–4) ($p < 0.05$) (Table 2). Furthermore at the end of 3 months the groups did not show any significant difference ($p_1$ *vs* $p_2 = 0.3$, $p_1$ *vs* $p_3 = 0.15$, $p_2$ *vs* $p_3 = 0.59$). During early postoperative days (1–4) pain decreased in the cocktail groups compared with the control group ($p < 0.05$), while the scores of stiffness and impaired physical function were significantly improved in the cocktail groups ($p < 0.05$) compared with the control group. The improvement in the total WOMAC score was sharper in the cocktail groups compared with the control group (52.36 ± 2.10, 50.26 ± 3.13 *vs* 62.26 ± 2.13; $p_1$ *vs* $p_2 < 0.0001$, $t = 21.449$;

**Table 2:** Visual analog scale score

| *Sample (n)* | *Tool* | *Baseline* | *Postoperative* | | | | | *Follow-up* | | |
|---|---|---|---|---|---|---|---|---|---|---|
| *Group I* | | | | | | | | | | |
| 42 | VAS score | | Immediate operative day | Postoperative day 1 | Postoperative day 2 | Postoperative day 3 | Postoperative day 4 | Month 1 | Month 2 | Month 3 |
| | | 6.66 ± 1.26 | 6.56 ± 1.22 | 6.33 ± 1.2 | 6.12 ± 1.23 | 6.0 ± 1.22 | 5.78 ± 1.3 | 4.72 ± 1.2 | 3.99 ± 1.32 | 2.1 ± 1.02 |
| t-value | | | 0.37 | 1.23 | 1.99 | 2.44 | 3.15 | 7.23 | 9.48 | 18.23 |
| p-value | | | 0.713 | 0.22 | 0.05 | 0.017 | 0.002 | <0.0001 | <0.0001 | <0.0001 |
| *Group II* | | | | | | | | | | |
| 42 | VAS score | | Immediate operative day | Postoperative day 1 | Postoperative day 2 | Postoperative day 3 | Postoperative day 4 | Month 1 | Month 2 | Month 3 |
| | | 6.06 ± 1.3 | 6.01 ± 1.22 | 5.23 ± 1.32 | 5.2 ± 1.23 | 4.9 ± 1.26 | 4.56 ± 1.23 | 3.01 ± 1.3 | 2.33 ± 1.23 | 1.89 ± 1.23 |
| t-value | | | 0.18 | 2.90 | 3.11 | 4.15 | 5.43 | 10.75 | 13.51 | 15.10 |
| p-value | | | 0.86 | 0.005 | 0.005 | 0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 |
| *Group III* | | | | | | | | | | |
| 42 | VAS score | | Immediate operative day | Postoperative day 1 | Postoperative day 2 | Postoperative day 3 | Postoperative day 4 | Month 1 | Month 2 | Month 3 |
| | | 6.56 ± 1.23 | 5.78 ± 1.20 | 5.03 ± 1.12 | 4.9 ± 1.32 | 4.9 ± 1.5 | 4.11 ± 1.02 | 2.99 ± 1.26 | 2.01 ± 1.23 | 1.75 ± 1.20 |
| t-value | | | 2.94 | 5.96 | 5.96 | 5.54 | 9.94 | 13.14 | 16.95 | 19.51 |
| p-value | | | 0.004 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 |

No significance at 3 months ($p > 0.05$); Significance during postoperative days (1–4) between groups ($p < 0.05$)

**Table 3:** Total WOMAC score

| *Sample (n)* | *Tool* | *Baseline* | *Postoperative* | | | | | *Follow-up* | | |
|---|---|---|---|---|---|---|---|---|---|---|
| *Group I* | | | | | | | | | | |
| 42 | Total WOMAC | | Immediate operative day | Postoperative day 1 | Postoperative day 2 | Postoperative day 3 | Postoperative day 4 | Month 1 | Month 2 | Month 3 |
| | | 71.65 ± 2.23 | 70.70 ± 2.20 | 65.26 ± 3.13 | 64.78 ± 3.01 | 64.78 ± 3.01 | 62.26 ± 2.13 | 24.30 ± 1.26 | 24.25 ± 1.23 | 15.01 ± 1.20 |
| t-value | | | 1.96 | 10.78 | 11.88 | 11.86 | 19.73 | 119.80 | 120.621 | 144.95 |
| p-value | | | 0.053 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 |
| *Group II* | | | | | | | | | | |
| 42 | Total WOMAC | | Immediate operative day | Postoperative day 1 | Postoperative day 2 | Postoperative day 3 | Postoperative day 4 | Month 1 | Month 2 | Month 3 |
| | | 70.91 ± 3.05 | 62.70 ± 2.34 | 55.26 ± 2.13 | 54.78 ± 3.11 | 54.78 ± 3.01 | 52.36 ± 2.10 | 20.30 ± 2.26 | 18.25 ± 2.23 | 14.92 ± 2.20 |
| t-value | | | 13.84 | 27.26 | 24.0 | 24.39 | 32.46 | 86.40 | 90.3396 | 96.49 |
| p-value | | | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 |
| *Group III* | | | | | | | | | | |
| 42 | Total WOMAC | | Immediate operative day | Postoperative day 1 | Postoperative day 2 | Postoperative day 3 | Postoperative day 4 | Month 1 | Month 2 | Month 3 |
| | | 71.05 ± 3.23 | 60.28 ± 3.20 | 52.26 ± 3.13 | 52.26 ± 3.13 | 52.26 ± 3.13 | 50.26 ± 3.13 | 19.78 ± 1.26 | 18.32 ± 1. 23 | 14.80 ± 1.23 |
| t-value | | | 13.35 | 27.07 | 27.07 | 27.07 | 29.96 | 95.84 | 98.87 | 105.47 |
| p-value | | | < 0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 |

No significance at 3 months ($p > 0.05$). Significance during postoperative days (1–4) between groups ($p < 0.05$)

**Table 4:** Nonsteroidal anti-inflammatory drugs

| | | *Amount of NSAIDs (diclofenac suppository) (PODs 1–4)* | | | |
|---|---|---|---|---|---|
| | *Groups* | *POD 1* | *POD 2* | *POD 3* | *POD 4* |
| | I | 161.4 ± 21.30 mg | 158.52 ± 27.30 mg | 143.23 ± 31.30 mg | 129.79 ± 24.83 mg |
| | II | 114.28 ± 35.41 mg | 109.52 ± 37.02 mg | 107.14 ± 37.56 mg | 102.38 ± 38.1 mg |
| | III | 77.380 ± 33.49 mg | 73.80 ± 31.69 mg | 66.66 ± 23.855 mg | 52.380 ± 10.77 mg |
| *t- and p-values* | | | | | |
| | I *vs* II | t = 7.39; p < 0.0001 | t = 6.90; p < 0.0001 | t = 4.78; p < 0.0001 | t = 3.91; p < 0.0001 |
| | I *vs* III | t = 13.65; p < 0.0001 | t = 13.13; p < 0.0001 | t = 12.61; p < 0.0001 | t = 18.54; p < 0.0001 |
| | II *vs* III | t = 4.85; p < 0.0001 | t = 4.75; p < 0.0001 | t = 5.90; p < 0.0001 | t = 8.18; p < 0.0001 |

Significance between groups; POD: Postoperative day

$p_1$ *vs* $p_3 < 0.0001$, t = 20.54) (Table 3). Patients under group III showed significant improvement in total WOMAC score in comparison to patients in group II (50.26 ± 3.13 *vs* 52.36 ± 2.10; $p_2$ *vs* $p_3$ = 0.0005, t = 3.6). There was a clear trend for increased NSAIDs doses in the control group up to postoperative day 4. The mean total hospital NSAIDs consumption on the 4th postoperative day was significantly reduced in the treatment groups II and III compared with the control group (group I) (102.79 ± 38.1; 52.380 ± 10.77 mg *vs* 129.79 ± 24.83 mg respectively; $p_1$ *vs* $p_2 = 0.0002$, t = 3.9061; $p_1$ *vs* $p_3 < 0.0001$, t = 18.53) (Table 4). Patients under group II showed significantly reduced consumption of NSAIDs when compared with group III ($p_2$ *vs* $p_3 < 0.0001$, t = 8.18). Also, more percentage of patients in the control group asked for rescue medicine than the cocktail groups [95.23% (n = 40) *vs* 9.52% (n = 4), 2.3% (n = 1), $\chi^2 = 97.69$, $p < 0.0001$] (Table 5). No difference was demonstrated in postoperative nausea and vomiting between the groups ($p > 0.05$). On the 4th postoperative day, patients in the cocktail groups (groups II and III) achieved more degree of flexion than the control group (group I) ($p_1$ *vs* $p_2 = 0.0003$, t = 3.818; $p_1$ *vs* $p_3 < 0.0001$, t = 11.97) (Table 6). Group III patients achieved satisfactorily high degrees of flexion after TKA than group II patients (118.6° ± 1.12° *vs* 116.5° ± 1.32°; $p_3$ *vs* $p_2 < 0.0001$, t = 2.10). At the end of 3 months, the cocktail groups had significantly higher degree of flexion than the control group (122.8° ± 1.23°, 122.2° ± 1.21° *vs* 120.2° ± 1.32°). Significantly more patients in the cocktail group (98%) were able to do ASLR on postoperative day 1 than in the control group ($p < 0.05$). Times to start ASLR (11.47 ± 2.339 hours, 7.42 ± 4.20 hours *vs* 22.9 ± 0.54 hours; $p_1$ *vs* $p_2 < 0.0001$, t = 21.45; $p_1$ *vs* $p_3 < 0.0001$, t = 20.43) (Table 7) and to discharge (4.26 ± 0.54 days, 4.02 ± 0.15 *vs* 5.92 ± 0.777; $p_1$ *vs* $p_2 < 0.0001$, t = 11.37; $p_1$ *vs* $p_3 < 0.0001$, t = 15.56) (Table 8) were statistically significant in the cocktail groups (groups II and III) than in the control group (group I). Furthermore, patients under group III significantly started ASLR (7.428 ± 420 hours *vs* 11.47 ± 2.339 hours; $p_2$ *vs* $p_3 < 0.0001$, t = 5.45) and were discharged (4.02 ± 0.15 *vs* 4.26 ± 0.54 days; $p_2$ *vs* $p_3 = 0.007$, t = 2.77) little earlier than group II.

**Table 5:** Rescue analgesia

| *Sl. no.* | *Groups* | *Number of patients using rescue medicine (PODs 1–4)* | $\chi^2$ *and p-values* |
|---|---|---|---|
| 1 | I | 95.23% (n = 40) | $\chi^2 = 97.69$ $p < 0.0001$ |
| 2 | II | 9.52% (n = 4) | |
| 3 | III | 2.3% (n = 1) | |

Significance between groups; POD: Postoperative day

Of the entire sample in the control group, as seen in Table 9, when reporting overall satisfaction with surgery procedure during postoperative days (1–4), 85.75% (n = 36) of patients noted that they were "somewhat satisfied" and 14.25% (n = 6) of patients answered that they were "somewhat dissatisfied." With regard to pain relief/improving or alleviating pain, 47.61% (n = 20) of patients stated that they were "somewhat satisfied" while 52.38% (n = 22) stated they were "somewhat dissatisfied." When patients reported their satisfaction with their ability to perform routine work, 47.61% (n = 20) of patients stated that they were "somewhat satisfied" and 52.38% (n = 22) stated they were "somewhat dissatisfied." And finally, when expressing satisfaction with their ability to perform recreational activities (mental health), 47.61% (n = 20) of patients noted they were "somewhat satisfied" while 52.38% (n = 22) of patients were "satisfied." At 12 weeks, with regard to overall satisfaction with surgery, ability to perform routine work, and ability to perform leisurely activities, 95.23% (n = 40) stated they were very satisfied and 92.85% (n = 39) stated they were very satisfied with the outcome of procedure for improving/alleviating pain. The majority of patients at 12 weeks were "very satisfied" or "somewhat satisfied" and no patients in the control group ever gave a response of "very dissatisfied" irrespective of the question.

The patients under group II (cocktail group), as seen in Table 10, during early postoperative days (1–4 days) revealed that 92.85% (n = 39) of patients were "somewhat satisfied" and 7.14% (n = 3) of patients were "somewhat dissatisfied" with regard to overall satisfaction with the procedure. With regard to pain relief/improving or alleviating pain, 85.75% (n = 36) of patients stated that they were "somewhat satisfied" and 14.28% (n = 6) stated they were "somewhat dissatisfied." When patients reported their satisfaction with their ability to perform routine work,

**Table 6:** Range of motion

| Sample (n) | Tool | Baseline | Postoperative | | | | Follow-up | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| *Group I* | | | | | | | | | | |
| 42 | ROM | | Immediate operative day | Postoperative day 1 | Postoperative day 2 | Postoperative day 3 | Postoperative day 4 | Month 1 | Month 2 | Month 3 |
| | | 110.2 ± 1.20 | 110.2 ± 1.20 | 112.2 ± 1.21 | 112.2 ± 1.21 | 112.2 ± 1.21 | 115.4 ± 1.32 | 118.6 ± 1.21 | 120.2 ± 1.32 | 120.2 ± 1.32 |
| | t-value | | 0 | 7.61 | 7.61 | 7.61 | 18.89 | 31.94 | 36.33 | 36.33 |
| | p-value | | 1.0 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 |
| *Group II* | | | | | | | | | | |
| 42 | ROM | | Immediate operative day | Postoperative day 1 | Postoperative day 2 | Postoperative day 3 | Postoperative day 4 | Month 1 | Month 2 | Month 3 |
| | | 109.8 ± 1.31 | 112.2 ± 1.21 | 115.4 ± 1.32 | 115.4 ± 1.22 | 115.4 ± 1.23 | 116.5 ± 1.32 | 120.2 ± 1.20 | 120.2 ± 1.33 | 122.2 ± 1.21 |
| | t-value | | 3.27 | 14.29 | 14.84 | 14.79 | 18.12 | 32.47 | 30.90 | 39.61 |
| | p-value | | 0.0016 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 |
| *Group III* | | | | | | | | | | |
| 42 | ROM | | Immediate operative day | Postoperative day 1 | Postoperative day 2 | Postoperative day 3 | Postoperative day 4 | Month 1 | Month 2 | Month 3 |
| | | 110.5 ± 1.23 | 113.5 ± 1.26 | 115.5 ± 1.26 | 116.5 ± 1.32 | 116.5 ± 1.32 | 118.6 ± 1.12 | 120.2 ± 1.20 | 121.4 ± 1.20 | 122.8 ± 1.23 |
| | t-value | | 8.46 | 15.83 | 19.04 | 19.04 | 28.83 | 33.94 | 38.47 | 43.22 |
| | p-value | | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 |

No significance at 3 months ($p > 0.05$); Significance during postoperative days (1–4) between groups

**Table 7:** Straight leg raise

| Sl. no. | Groups | Hours after surgery | t- and p-values |
|---|---|---|---|
| 1 | I | 22.9 ± 2.54 | 1 *vs* 2: t = 21.45; p <0.0001 |
| 2 | II | 11.47 ± 2.339 | 1 *vs* 3: t = 20.43; p <0.0001 |
| 3 | III | 7.428 ± 4.20 | 2 *vs* 3: t = 5.45; p <0.0001 |

Significance between groups ($p < 0.05$)

**Table 8:** Hospital stay

| Sl. no. | Groups | Hospital stay (days) | t- and p-values |
|---|---|---|---|
| 1 | I | 5.92 ± 0.777 | 1 *vs* 2: t = 11.37; p <0.0001 |
| 2 | II | 4.26 ± 0.54 | 1 *vs* 3: t = 15.56; p <0.0001 |
| 3 | III | 4.02 ± 0.15 | 2 *vs* 3: t = 2.77; p = 0.007 |

Significance between groups ($p < 0.05$)

85.75% (n = 36) stated that they were "somewhat satisfied" and 14.28% (n = 6) stated they were "somewhat dissatisfied." And finally, when expressing satisfaction with their ability to perform recreational activities (mental health), 90.4% (n = 38) noted they were "somewhat satisfied" while 9.52% (n = 4) of patients were "satisfied." At 12 weeks, with regard to overall satisfaction with surgery, improving/alleviating pain, ability to perform routine work, and ability to perform leisurely activities, 97.61% (n = 41) noted that they were very satisfied.

The patients under group III (cocktail group), as seen in Table 11, during early postoperative days (1–4 days) revealed that 95.23% (n = 40) were "somewhat satisfied" and 4.76% (n = 2) were "somewhat dissatisfied," with regard to overall satisfaction with the procedure. With regard to pain relief/improving or alleviating pain, 95.23% (n = 40) of patients stated that they were "somewhat satisfied" and 4.76% (n = 2) stated they were "somewhat dissatisfied." When patients reported their satisfaction with their ability to perform routine work, 95.23% (n = 40) stated that they were "somewhat satisfied" and 4.76% (n = 2) stated they were "somewhat dissatisfied." And finally, when expressing satisfaction with their ability to perform recreational activities (mental health), 95.23% (n = 40) of patients noted they were "somewhat satisfied" while 4.76% (n = 2) were "satisfied." At 12 weeks, with regard to overall satisfaction with surgery, improving/alleviating pain, ability to perform routine work, and ability to perform leisurely activities, 97.61% (n = 41) noted that they were very satisfied.

During early postoperative period (1–4 days) the cocktail groups (groups II and III) consistently rated higher satisfaction percentages for each of the questions than the control group. Adverse events in the control group included nausea in four patients. Adverse events in the cocktail group included nausea in two each. No patient in either group experienced a serious adverse event, such as respiratory distress, infection, or local anesthetic

**Table 9:** Control group results (42 of 42 responded)

| | | | *Assessment (satisfaction)* | | |
|---|---|---|---|---|---|
| *Sl. no.* | *Items/criteria* | *4-Point Likert scale* | *PODs (1–4) (n = 42)* | *12 weeks (n = 42)* | *$\chi^2$ and p-values* |
| 1 | Overall satisfaction with surgery procedure | | | | |
| | | Very satisfied | – | 40 (95.23%) | $\chi^2 = 76.42$ |
| | | Somewhat satisfied | 36 (85.75%) | 2 (4.76%) | $p < 0.0001$ |
| | | Somewhat dissatisfied | 6 (164.28%) | – | |
| | | Very dissatisfied | – | – | |
| 2 | Satisfaction with the outcome of procedure for improving/alleviating pain | | | | |
| | | Very satisfied | – | 39 (92.85%) | $\chi^2 = 73.56$ |
| | | Somewhat satisfied | 20 (47.61%) | 3 (7.14%) | $p < 0.0001$ |
| | | Somewhat dissatisfied | 22 (52.38%) | – | |
| | | Very dissatisfied | – | – | |
| 3. | Satisfaction with the outcome of procedure for improving ability to do routine work | | | | |
| | | Very satisfied | – | 40 (95.23%) | $\chi^2 = 76.73$ |
| | | Somewhat satisfied | 20 (47.61%) | 2 (4.76%) | $p < 0.0001$ |
| | | Somewhat dissatisfied | 22 (52.38%) | – | |
| | | Very dissatisfied | – | – | |
| 4. | Satisfaction with the outcome of procedure for mental health (ability to enjoy life as before) | | | | |
| | | Very satisfied | – | 40 (95.23%) | $\chi^2 = 76.73$ |
| | | Somewhat satisfied | 20 (47.61%) | 2 (4.76%) | $p < 0.0001$ |
| | | Somewhat dissatisfied | 22 (52.38%) | – | |
| | | Very dissatisfied | – | | |

POD: Postoperative day

**Table 10:** Group II (42 of 42 responded)

| | | | *Assessment (satisfaction)* | | |
|---|---|---|---|---|---|
| *Sl. no.* | *Items/criteria* | *4-Point Likert scale* | *PODs (1–4) (n = 42)* | *12 weeks (n = 42)* | *$\chi^2$ and p-values* |
| 1 | Overall satisfaction with surgery procedure | | | | |
| | | Very satisfied | – | 41 (97.61%) | $\chi^2 = 80.10$ |
| | | Somewhat satisfied | 39 (92.85%) | 1 (2.38%) | $p < 0.0001$ |
| | | Somewhat dissatisfied 3 (7.14%) | – | – | |
| | | Very dissatisfied | – | – | |
| 2 | Satisfaction with the outcome of procedure for improving/alleviating pain | | | | |
| | | Very satisfied | – | 41 (97.61%) | $\chi^2 = 80.12$ |
| | | Somewhat satisfied | 36 (85.75%) | 1 (2.38%) | $p < 0.0001$ |
| | | Somewhat dissatisfied | 6 (164.28%) | – | |
| | | Very dissatisfied | – | – | |
| 3 | Satisfaction with the outcome of procedure for improving ability to do routine work | | | | |
| | | Very satisfied | – | 41 (97.61%) | $\chi^2 = 80.12$ |
| | | Somewhat satisfied | 36 (85.75%) | 1 (2.38%) | $p < 0.0001$ |
| | | Somewhat dissatisfied | 6 (164.28%) | – | |
| | | Very dissatisfied | – | – | |
| 4 | Satisfaction with the outcome of procedure for mental health (ability to enjoy life as before) | | | | |
| | | Very satisfied | – | 41 (97.61%) | $\chi^2 = 80.10$ |
| | | Somewhat satisfied | 38 (90.47%) | 1 (2.38%) | $p < 0.0001$ |
| | | Somewhat dissatisfied | 4 (9.52%) | – | |
| | | Very dissatisfied | – | – | |

POD: Postoperative day

intoxication. None of the patients reported disruption of the extensor mechanism.

## DISCUSSION

Adequate postoperative analgesia facilitates early and effective rehabilitation after total knee replacement.[22,23] Total knee arthroplasty is an effective treatment for osteoarthritis and is performed with several goals, but the primary goals are pain relief and improvements in function. Despite excellent outcome following TKA, inadequate postoperative pain control limits the mobility, restricting patients' participation with physical therapy and causing disturbed sleep.[24,25] Pain has been found to be the third most common medical cause of delayed discharge after ambulatory surgery, and drowsiness and

**Table 11:** Group III (42 of 42 responded)

| | | | *Assessment (satisfaction)* | | |
|---|---|---|---|---|---|
| *Sl. no.* | *Items/criteria* | *4-Point Likert scale* | *PODs (1–4) (n = 42)* | *12 weeks (n = 42)* | *$\chi^2$ and p-values* |
| 1 | Overall satisfaction with surgery procedure | | | | |
| | | Very satisfied | – | 41 (97.61%) | $\chi^2 = 80.10$ |
| | | Somewhat satisfied | 40 (95.23%) | 1 (2.38%) | $p < 0.0001$ |
| | | Somewhat dissatisfied | 2 (4.76%) | – | |
| | | Very dissatisfied | – | – | |
| 2 | Satisfaction with the outcome of procedure for improving/alleviating pain | | | | |
| | | Very satisfied | – | 41 (97.61%) | $\chi^2 = 80.10$ |
| | | Somewhat satisfied | 40 (95.23%) | 1 (2.38%) | $p < 0.0001$ |
| | | Somewhat dissatisfied | 2 (4.76%) | – | |
| | | Very dissatisfied | – | – | |
| 3 | Satisfaction with the outcome of procedure for improving ability to do routine work | | | | |
| | | Very satisfied | – | 41 (97.61%) | $\chi^2 = 80.10$ |
| | | Somewhat satisfied | 40 (95.23%) | 1 (2.38%) | $p < 0.0001$ |
| | | Somewhat dissatisfied | 2 (4.76%) | – | |
| | | Very dissatisfied | – | – | |
| 4 | Satisfaction with the outcome of procedure for mental health (ability to enjoy life as before) | | | | |
| | | Very satisfied | – | 41 (97.61%) | $\chi^2 = 80.10$ |
| | | Somewhat satisfied | 40 (95.23%) | 1 (2.38%) | $p < 0.0001$ |
| | | Somewhat dissatisfied | 2 (4.76%) | – | |
| | | Very dissatisfied | – | – | |

POD: Postoperative day

nausea/vomiting. Unrelieved pain prolongs the stress response, adversely affecting patients' recovery rate.[26] Studies have reported a significantly lower satisfaction rate after TKA than after total hip arthroplasty due to postsurgical pain.[27-29] Postsurgical pain delays early rehabilitation and thus negatively affects patients' satisfaction rate. Postoperative pain is of concern for patients, and adequate analgesic countermeasures are necessary. Intraoperative cocktail injection of analgesia facilitates direct visualization and precise placement of the needle into the traumatized tissues and nerve endings. Furthermore, the local concentration of the cocktail agents within the soft tissue improved and prolonged the analgesic blockade and decreased the seepage from the wound.[30] Few studies have demonstrated improved pain scores and a decreased consumption of opiate analgesia with soft-tissue infiltration of local anesthetic agents,[30,31] while others fail to replicate these findings.[8,32-34] In the present study we have used two different cocktails for injection, one with local anesthetic bupivacaine and other with Depomedrol (methylprednisolone acetate). The use of 0.5% bupivacaine enhances pain relief both directly and indirectly by inhibiting the neuroendocrine stress response to operative procedure.[35] We have found no intraoperative or postoperative complication and/or toxicity related to injection. Steroids attenuate the stress response induced by an operative procedure. Currently, it is difficult to discern the exact underlying mechanism; a number of theories have been proposed for the favorable effects of steroids. Steroids inhibit phospholipase A2, thus reducing the levels of proinflammatory derivatives of arachidonic acid.[36,37] Infiltration of steroid enhances and prolongs pain relief by reducing the inflammatory response following surgery and by inhibiting the vasodilating effect of prostaglandin; it reduces blood loss and edema.[38] The results of the present study demonstrated that the use of intraoperative multimodal cocktail injection significantly reduced postsurgical pain ($p < 0.05$), postoperative in-hospital NSAID requirements ($p < 0.05$), and hospital stay ($p < 0.05$). Authors found that steroid was more effective at reducing pain during postoperative days when compared with bupivacaine. The enhanced and prolonged pain relief with the use of steroids in infiltration was in line with the results of other studies. [37-41] The significant reduction in postoperative pain seen with cocktail injection translates into reduction in hospital stay, facilitation of early rehabilitation, as well as increased patients' satisfaction. We found the cocktail to be effective and safe in postoperative pain control and early rehabilitation in TKA. In the present study, the addition of cocktail injection intraoperatively significantly reduces the consumption of NSAIDs, as also reported by Crowley et al.[42] By observing strict asepsis and stringent exclusion criteria, we found no infection during the early postoperative period and at follow-up. None of the patients in group III reported tendon rupture or disruption of extensor apparatus because we avoided injecting corticosteroid directly into the patella tendon. Peritendinous steroid injection may result in subsequent rupture.[43]

## CONCLUSION

The results of the current study successfully demonstrate that intraoperative multimodal cocktail injection safely provides excellent postoperative pain control and functional recovery and can be substituted for conventional pain control alternatives.

## LIMITATIONS

Small sample size and short follow-up period limit the generalization of the findings. Owing to low risk rate we have used spinal anesthesia for TKR; authors speculated that it could mask the pain score in postoperative period. Though none of the patients in the present study reported postsurgical infection especially after steroidal cocktail injection, a larger sample size with randomization would be needed to assess the impact of steroid on surgical site infection.

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