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Research Article

# How Effective Is Intrawound periarticular Cocktail Injection and Postoperative Intravenous Paracetamol for Analgesia and Early Mobilization after Total Knee Arthroplasty (TKA)

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## Abstract

**Introduction:** Total knee arthroplasty (replacement) is a treatment of choice in severe osteoarthritis of knee joint and relieve knee pain and improves joint function, but still managing post-surgical pain after Total knee replacement (TKR) is a challenging and crucial step for early rehabilitation of patient and for better outcome. There are some reports demonstrate the 70 to 75% patients of total knee replacement complaint of moderate to severe chronic pain. Clinical practice guidelines recommend multimodal, therapy combining preoperative, intraoperative, and postoperative medications, such as opioids, nonsteroidal anti inflammatory drugs, gabapentin, pregabalin, and local anesthetics. Adequate pain relief is essential for early mobilization and good functional recovery.

Use of intravenous acetaminophen has seen recent enthusiasm as one component of a multimodal approach to pain management. However, there is a lack of literature examining the efficacy of intravenous acetaminophen for pain control in total knee replacement.

**Aims:** The purpose of this study was to evaluate the efficacy of intravenous acetaminophen with intraarticular cocktail injection as multimodal approach for pain management and its effect on early rehabilitation following total knee replacement.

**Material and Methods:** Total (n = 82) patent enrolled in the study who underwent total knee replacement. They were divided into two groups, Group A received epidural analgesia with intravenous (I.V) diclofenac and for any breakthrough pain Tramadol injection was given intravenously. Group B received periarticular injection of an anesthetic cocktail of drugs with antibiotic with intravenous acetaminophen (paracetamol) with diclofenac injection. Inclusion criteria was patient with age group of 50-80 years and underwent unilateral TKR. For outcome Knee society score (KSS) and Visual Analog scale (VAS) was used. For functional outcome Post-operative range of movement was also noted.

**Results:** The mean average KSS score of the study subjects were 52. Group A with epidural analgesic had a score of 58 when compared to 79 for group B where cocktail and IV acetaminophen was used. The mean average functional score was 61 for group A and 75 for group B. Both the scores were better in the analgesic cocktail group B. The mean pain score in group A was 5.2 and in group B was 2.1.

**Conclusion:** In Conclusion periarticular cocktail with Intravenous acetaminophen is effective in significantly reducing opioid/NSAID's requirements in the first 24 hours following primary total knee arthroplasty. Additionally, there is a clinically significant decrease in VAS pain scores in patients receiving this intervention.

**Keywords:** Total Knee Replacement; Pain Control; Early Rehabilitation; Local Infiltration Analgesia; Knee Society Score; Visual Analog Scale

## Introduction

Total knee arthroplasty (replacement) is a treatment of choice in severe osteoarthritis of knee joint and relieve knee pain and improves joint function. It is one of the commonest performed musculoskeletal surgery now adays. It is well documented in literature that effective pain management leads to a better and earlier functional recovery but still managing post-surgical pain after Total knee replacement (TKR) is a challenging and crucial step for early rehabilitation of patient and for better outcome [1-3]. There are some reports demonstrate the 70 to 75% patients of total knee replacement complaint of moderate to severe chronic pain [4,5].

With exploration of the mechanisms underlying postoperative pain in TKA, it has been verified that both peripheral and central mechanisms are involved. Therefore, monotherapy alone is not enough to provide satisfactory postoperative pain relief after TKA. At present, multimodal analgesia is considered as the optimal method for perioperative pain management of TKA through targeting numerous pain pathways. Multimodal analgesia requires an understanding of the molecular mechanisms of pain pathways. Postoperative pain is a consequence of tissue injury, nerve irritation and the resulting cascade of neurohumeral events that follow. After a painful stimulus, chemical mediators such as prostaglandins (PGE2) and bradykinin are released at the site of tissue injury [6].

These chemical mediators stimulate nociceptors, peripheral pain receptors that respond to trauma and high temperatures. Multimodal analgesia includes preoperative, intraoperative, and postoperative analgesic regimens, aiming to maximize the analgesic efficacy through the combination of several analgesic regimens, while minimizing undesired adverse effects. Adequate preemptive analgesia could prevent pain nociceptors from entering a state of hyperalgesia, and make acute postoperative pain easier to control, ultimately reducing opioid consumption. Intraoperatively, Local infiltration analgesia is performed by a surgeon near the conclusion of a procedure that directly prevents the generation and conduction of pain signals from incision [6]. Clinical practice guidelines recommend multimodal, therapy combining preoperative, intraoperative, and postoperative medications, such as opioids, nonsteroidal antiinflammatory drugs, gabapentin, pregabalin, and local anesthetics. Adequate pain relief is essential for early mobilization and good functional recovery.

Use of intravenous acetaminophen has seen recent enthusiasm as one component of a multimodal approach to pain management. However, there is a lack of literature examining the efficacy of intravenous acetaminophen for pain control in total knee replacement. The purpose of this study was to evaluate the efficacy of intravenous acetaminophen with intraarticular cocktail injection as multimodal approach for pain management and its effect on early rehabilitation following total knee replacement.

## Material and Methods

### Study design and period

This is a retrospective study on (n = 82) patients who underwent total knee replacement from year June 2020 to December 2022. Patient were divided into two groups of (n = 41) patients each. Group A received epidural analgesia with intravenous (I.V) diclofenac and for any breakthrough pain Tramadol injection was given intravenously. Group B received periarticular injection of an anesthetic cocktail of drugs with antibiotic with intravenous acetaminophen (paracetamol) with diclofenac injection. Preoperative medication and post-operative rehabilitation were same in both the groups. All cases were done by senior joint replacement surgeon and with our multimodal approach for fast rehabilitation. The patients were thoroughly informed and consented for the procedures.

### Inclusion criteria

- Patient undergoing unilateral TKR with only degenerative osteoarthritis.
- Age group 50-80 years.
- Both Sex.

### Exclusion criteria

- Patient undergoing TKR due to inflammatory, post traumatic, septic and neuropathic knee.
- Revision TKR.
- Patient with chronic kidney diseases.

### Method

In the present study, preoperative knee assessment was done using knee society score[7,8]. Range of movement was measured preoperatively. Extensor lag if any was also noted. Xrays were reviewed and the deformity present documented. Informed valid consent was obtained from patients who were willing to participate in the study. History of diabetes mellitus and rheumatoid arthritis if any was taken. Parameters such as walking distance, aids used, preoperative pain score was noted with visual analog scale (VAS) [9].

### Pre-operative protocol

Patient was given Tab Pregabalin 75mg, Tab Celecoxib 200mg, Tab Alprazolam 0.5mg and Tab Pantoprazole and Domperidone 40mg following a protocol made for all knee replacement surgeries. All the patients were advised and trained for preoperative

quadriceps strengthening and VMO (vastus medialis Obliquus) strengthening physiotherapy by orthopaedic surgeon of the team.

## Operative procedure

In all cases, Pre-operative antibiotic was given 30min before incision. Patients are typically placed supine on the operative table standard midline incision with a medial parapatellar arthrotomy is used. soft tissue release is performed medially for varus knees and sometime lateral soft tissue release is required, infrapatellar fat pad removed followed by medial and lateral meniscus and anterior cruciate excision. All knees were Posterior cruciate sacrificing. Measured resection technique is used where femur cuts and sizing were done followed by tibial cut and then trial is done. Once knee is properly balanced then final cementing and component placement is done. Once knee is properly balanced then final cementing and component placement is done.

Tranexamic acid 10-15 mg/kg dose was injected intravenously for control of blood loss starting approximately 15 min before tourniquet release. A tourniquet was used for all patients, and it was set to a pressure between 280 mm of Hg (Mercury) and 350 mm of Hg depending on the patient's systolic blood pressure before skin incision and deflated before wound closure. The mean time for tourniquet was (Mean = 92) minutes.

The cocktail was injected at the following 7 anatomical zones [6]

- Zone 1: medial retinaculum
- Zone 2: medial collateral ligament and medial meniscus capsular attachment
- Zone 3: posterior capsule Zone
- Zone 4: lateral collateral ligament and lateral meniscus capsular attachment
- Zone 5: lateral retinaculum Zone
- Zone 6: patellar tendon and fat pad Zone
- Zone 7: cut ends of quadriceps muscle and tendon.

## Post-operative protocol

Group A (n = 41) received epidural analgesia in 4 total doses starting from first dose at pre-operative period followed by second dose in 12 hours after surgery and then last two doses 24 hours apart with 1ml intravenous diclofenac TID for 5days. For breakthrough pain INJ Tramadol 50mg intravenous in 100ml normal saline was given. Group B (n = 41) received periarticular cocktail which includes anesthetic agents and antibiotic (Table 1) followed by I.V acetaminophen Injection 1-gram TID (three times a day) for 5days with Inj. diclofenac 1ml TID (three times a day) for 5 days. No other analgesia was given for breakthrough pain relief. All patients were encouraged to perform foot pump exercises in bed as soon as patient is comfortable.

| Drugs | Concentration | Dose |
|---|---|---|
| INJ Ropivacaine | 0.2% | 60ml |
| INJ Ketorolac | 60mg | 2ml (*avoid if S. creatine is>1.2) |
| INJ Adrenaline | 0.5mg | 0.5ml |
| INJ Methyl Prednisolone | 40 mg | 1ml |
| INJ Cefuroxime | 750mg | |
| Normal saline | 0.9% | 36.5ml |
| Total | | 100ml |

**Table 1:** Pericapsular cocktail of anesthetic drugs used for pain control includes.

On the 2nd day, they were encouraged to sit with the legs out of the bed, and do active quadriceps strengthening. Amount of knee flexion possible and the lag on extension when sitting from the second postoperative day were also documented. Later, all were encouraged to walk with a walker after the drain was removed. They were started on active and passive range of movement exercises by sitting at bedside.

Range of motion was measured post operatively from day 2 onwards till hospital stay of the patient. Average hospital stay was 6 days.

## Outcome Measurements

Knee society score (KSS) [7] was used for primary outcome, it is an objective knee score to evaluate the knee and a subjective patient function score. Knee score includes three main constructs: pain, knee stability, and ROM [7,8]. Of the maximum 100 points, a possible 50 points are assigned to pain, 25 points to stability, and 25 points for ROM with deductions for deformity and malalignment of the native joint and knee arthroplasty [7,8]. A well-aligned knee with no pain, 125° of motion, and good AP and mediolateral instability will achieve a KSS of 100 points. The maximum function score is also 100 points and consists of patient-reported outcomes that measure walking distance (50 points) and the ability to ascend and descend stairs (50 points) with deductions for the use of assistive devices such as canes or walkers [7,8].

Visual Analog score (VAS) [9] was used for pain evaluation. Scores are based on self-reported measures of symptoms that are recorded with a single handwritten mark placed at one point along the length of a 10-cm line that represents a continuum between the two ends of the scale-"no pain" on the left end (0 cm) of the scale and the "worst pain" on the right end of the scale (10 cm) [9,10] (VAS; 0 = no pain to 10 = worst possible pain). Pain scores

were then collected at 12-hour intervals post operatively till post-operative day (POD) 5.

The assessment was done with the help of visual analogue scale (VAS). The VAS score at rest was recorded every 6 hrs for first 24 hrs, from time zero, when the patients were awake. After this 24-h time period, the VAS score was recorded every 12 hrs for further 120 Hrs (5 days).

Vitals monitoring included blood pressure, heart rate, and oxygen saturation. Any adverse reactions including allergic reactions, nausea, vomiting, urinary retention, or respiratory depression were also monitored till the patients were discharged. Range of movement was measured by the Knee society scoring system. The data were collected during the hospital stay (from day one to five after surgery).

## Statistical analysis

The data were analyzed using a repeatedmeasure ANOVA to compare neuropathic pain scale for pain, range of movement, and postoperative functional rehabilitation capability.

## Results

Total of 82 patients were included in this study. Patient were divided into two groups. Group A included patient who received epidural analgesia with injectable diclofenac and group B received periarticular cocktail with IV acetaminophen post operatively with injectable diclofenac.

## Sex ratio

There was 37% males and 63% females in group A and 46% males and 54% females in group B(Table2).

## Age Distribution

Middle aged people formed most of the study group. The mean age of the study population was 59 years. The mean age of those patients who received epidural infiltration with I.V diclofenac in group A was 63 years and that of the analgesic cocktail with I.V paracetamol was 59 years (Table 2). The lowest age group studied being 52 years and the oldest being 76 years.

## Pre-operative pain score

Average preoperative pain score in group A was 7.8 (P = 0.2114) compared to 6.4 (P = 0.2513) in the group B. The maximum pain experienced by the epidural group was nine and of the analgesic cocktail was eight. The minimum pain score was three and one. There was no significant statistical difference in the preoperative pain scores between the two groups on analysis.

| Variables | Group A (n = 41) | Group B (n = 41) | P value |
|---|---|---|---|
| Age (years)* | 63 (mean) | 59 (mean) | 0.338 |
| Sex male/Female | 15/26 (37%/63%) | 19/22 (46%/54%) | 0.501 |
| Varus/Valgus Knee | 33/8 80%/20%) | 35/6 (85%/15%) | 0.769 |
| FFD<5*/>5* | 26/15 (63%,37%) | 29/12 (71%,29%) | 0.638 |
| Recurvatum deformity | 3 | 2 | |
| KSS (Knee society score) * | 45 | 47 | |
| VAS (Visual analog scale) * | 7.23 | 8.32 | |

**Table 2:** Demographics (variables in * there values are in mean).

## Post-operative knee society score

The mean average KSS score of the study subjects were 52. Group A with epidural analgesic had a score of 58 when compared to 79 for group B where cocktail and IV acetaminophen was used. The mean average functional score was 61 for group A and 75 for group B. Both the scores were better in the analgesic cocktail group B, but the difference was not statistically significant (P = 0.426) (Table 3).

## Post-operative pain score

The mean score on the 1st day in the epidural group A was 8.2(P = 0.0456) and in the analgesic cocktail group B it was 6.3(P = 0.1638). On the 2nd day and 3rd day, it was 7.5, 6.4 and 5.7, 4.3 respectively. In the initial days analgesic cocktail group shows better pain control and as the days go by the pain equals in both the groups. (Graph 1).

Pain score on the day of surgery was 8 in group A and in group B it was around 7. This study shows that the use of periarticular cocktail injection with 1gram I.V acetaminophen TID combined with 1ml diclofenac I.V TID helps in improving post-operative pain after TKR which can easily see in difference in VAS score (p = 0.786) (Table 3) specially in first 24 hours compare to group A (P = 0.0987) and even after 24 hours when the effect of cocktail wear of, group B shows constant pain reduction compare to group A due to continues acetaminophen infusion with diclofenac coverage. It was also seen that in epidural group A where diclofenac was also used for pain control, beside this there was need of I.V tramadol for breakthrough pains, whereas there was no need of supporting analgesic in group B.

### Range of movements

There was marked difference in the range of movement between the groups with mean range of movement in the epidural group A being 95 degrees when compared to 109° in the analgesic cocktail group B.

| Variable | Group A (n = 41) | Group B (n = 41) | P value |
|---|---|---|---|
| KSS (Part one) | 58 | 79 | 0.426 |
| KSS Functional | 61 | 75 | 0.301 |
| VAS score | 5.2 | 2.1 | 0.786 |
| Range of movements | 95 | 109 | 0.314 |

**Table 3:** Results (values are in mean).

**Figure 1:** Periarticular cocktail infiltration.

**Graph 1:** Visual Analog Scale 12 hourly charting.

## Discussion

Our study was aimed at comparing the combination of intravenous acetaminophen with periarticular infiltration of a cocktail of drugs with diclofenac injection without epidural analgesia in controlling pain and enabling early functional recovery after TKA for those patients presenting to a tertiary hospital with degenerative arthritis.

Total of 82 patients were included in this study. Patient were divided into two groups. Group A included patient who received epidural analgesia with injectable diclofenac and group B received periarticular cocktail with IV acetaminophen post operatively with injectable diclofenac.

Mean Preoperative knee society score was 45 in group A and 47 in group B, whereas pre-operative VAS score was 7.26 and 8.32 in group A and B respectively.

Pain score on the day of surgery was 8 in group A and in group B it was around 7. This study shows that the use of periarticular cocktail injection with 1gram I.V acetaminophen TID combined with 1ml diclofenac I.V TID helps in improving post-operative pain after TKR which can easily see in difference in VAS score (p = 0.786) specially in first 24 hours and even after 24 hours when the effect of cocktail wear of, group B shows constant pain reduction compare to group A due to continues acetaminophen infusion with diclofenac coverage. It was also seen that in epidural group A where diclofenac was also used for pain control, beside this there was need of I.V tramadol for breakthrough pains, whereas there was no need of supporting analgesic in group B.

The mean average KSS score of the study subjects were 52. Group A with epidural analgesic had a score of 58 when compared

to 79 for group B where cocktail and IV acetaminophen was used. The mean average functional score was 61 for group A and 75 for group B. Both the scores were better in the analgesic cocktail group B, but the difference was not statistically significant (P = 0.426).

Study by Mullaji., *et al*. [20] on the effectiveness of a mixture of opioid, corticosteroid and a local anesthetic for periarticular injection in patients undergoing bilateral TKR showed significantly lower pain scores and better quadriceps recovery on the side that had periarticular injection of the anesthetic cocktail, were mean KSS score was 53 in cocktail and 46 in epidural group and mean functional score was 53 in whole study whereas in this study group A where epidural was used KSS was 58 whereas group b where cocktail plus IN acetaminophen was used KSS was 79 which clearly shows how acetaminophen improves overall pain control after TKR.

Post-operative analgesia in total joint arthroplasty presents multiple challenges including the need to balance adequate pain control with avoidance of undesirable medication side effects. Common side effects of post-operative narcotics include excessive sedation, bowel and bladder retention, nausea, and respiratory depression [28].

Since Kerr and Kohan published one of the earliest reports of the benefits of an local infiltration analgesia pain protocol in 2008, a growing body of literature has supported this concept, along with a multimodal oral regimen that includes preemptive analgesics, and many studies have reported substantial improvements in patient recoveries with this regimen after TKR [9-12]. Preemptive analgesia is another potentially useful strategy that seeks to moderate postoperative pain by decreasing sensitization of pain pathways caused by surgical trauma [18,19].

Other studies by Busch., *et al*. [21] Vendittoli., *et al*. [22] and Toftdahl., *et al.* [23] in which patients received either peri or intraarticular treatment or patientcontrolled analgesia with opioid or femoral nerve blocks in total knee replacement shows marked reduction in post-operative pain, mean VAS score in there study was 6.6 in epidural group and 4.7 in cocktail group where as in this study mean VAS score is 5.2 in Group A and 3.1 in group B.

Tammachote., *et al.* [31], compared the pain control effect of intrathecal morphine and multimodal drug injections in patients undergoing TKA. They found that though initially there was no difference between the two modalities, 12-16h postoperatively, the intrathecal group consumed significantly more Ketorolac and that the side effects of nausea and vomiting was also more in this group compared to the group treated with multimodal drug injections.

Several more recent studies examine the use of intravenous acetaminophen in patients undergoing total joint arthroplasty with varying results. Murata-Ooiwa., *et al.* performed a prospective double blind randomized placebo controlled trial comparing intravenous acetaminophen versus placebo for patients undergoing total knee arthroplasty and found lower pain scores at post-operative day (POD) 1 and less need for rescue analgesia in the form of diclofenac suppository on POD 2 [29]. Two additional recent trials compare oral versus intravenous formulations of acetaminophen for total knee replacement. O'Neal., *et al.* found no difference in a prospective randomized double-blind placebo trial for patients receiving either intravenous acetaminophen compared to oral acetaminophen versus a control placebo group [30].

The purpose of this study was to evaluate the efficacy periarticular cocktail with intravenous acetaminophen in pain management and its effect on early rehabilitation following total knee replacement. Early rehabilitation leads to decrease venous stasis and decreased quadriceps inhibition. This leads to decrease chance of Deep Vein thrombosis.

## Conclusion

Pain management is a critical component for patients undergoing total joint replacement. Effective pain control allows for maximum physical therapy and early rehabilitation efforts. The combination of an effective, well-delivered periarticular cocktail injection, in addition to a multimodal supplemental pain management drugs has revolutionized the post-operative recovery after total knee replacement. Patient satisfaction is extremely high with multimodal approach in pain management. Enhanced pain control and early rehabilitation are desired by patients and surgeons alike. Although there are numerous methods to achieve these goals, the above combination has been found to be safe and extremely effective, with no apparent risks.

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