

# Multimodal Post-Operative Pain Management Using Intraoperative Periarticular Cocktail Injection In Total Knee Arthroplasties

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## ABSTRACT

**INTRODUCTION:** Total knee arthroplasty (TKA) is one of the best methods for end stage osteoarthritis of knee joint that relieves pain and improves joint function. Most important problem which the patient suffers is postoperative pain, which has harmful effects on patient's rehabilitation. The aim of our study was to assess the postoperative pain relief and functional outcome following use of combination of drugs which we used as intraoperative, periarticular cocktail injection.

**MATERIALS AND METHODS:** It is a prospective interventional study consisting of 40 TKA's done in a single unit. All patients underwent TKA under spinal anaesthesia and underwent standard postoperative protocol. Intraoperative periarticular cocktail consisting of Bupivacaine 0.5% (20ml), Adrenaline 0.3 ml (1:1000), ketorolac 30mg/1ml, methylprednisolone 40mg/1ml, cefuroxime 750mg/10ml with 27.7 ml of normal saline to make total of 60ml solution was given. Assessment of pain was done by visual analogue scale (VAS) and functional assessment by knee society score postoperatively. The number of rescue analgesia used was recorded.

**RESULTS:** Mean age of patients was 64 years (47-76) with females predominantly affected than males. Mean static VAS at 6 hours was 4.3 and dynamic VAS at 1<sup>st</sup> recording was 4.9. there was a strong correlation between Body Mass Index and Dynamic VAS at 1<sup>st</sup> and Dynamic VAS at 3<sup>rd</sup> recording with  $p < 0.05$ . Patient satisfaction and functional scores improved postoperatively and there was a statistically significant improvement in knee ROM ( $P < 0.05$ ). only 2 patients received more than 3 doses of rescue analgesia due to high BMI. No complications related to the infiltration of the local anaesthetic were observed.

**CONCLUSION:** In our study, the combination of drugs which we used as a cocktail for periarticular injection safely provided excellent postoperative pain control and accelerated functional recovery in the patients undergoing total knee arthroplasty

**KEYWORDS:** Osteoarthritis Knee, Visual Analogue Scale, Knee Society Score, Intraoperative Cocktail, Total Knee Arthroplasty

## INTRODUCTION

Total knee arthroplasty (TKA) is one of the most effective methods of treating end-stage osteoarthritis of the knee joint, relieving pain and improving joint function.

Approximately 80-90% of patients reported having a better function of the knee after total knee arthroplasty<sup>1</sup>, which improves the quality of life. The postoperative period is painful following TKA, unlike THA due to varied reasons. The pain hampers the postoperative rehabilitation which in turn leads to severe arthrofibrosis which in turn leads to reduced range of motion and decreased functional outcome.

So, to get optimum pain relief different pain management modalities are available which include epidural analgesia, femoral nerve blocks, intravenous analgesia, and opioids. However, epidural analgesia can cause nausea, vomiting, urinary retention, hypotension, and spinal headache. A femoral nerve block may lead to falls or postoperative femoral nerve neuritis<sup>2</sup>. Multiple studies have been done to introduce the concept of multimodal analgesia intraoperatively in patients undergoing TKA<sup>3</sup>, which includes cocktails containing opioids or non-opioids. Achieving the painless TKA is within reach using regional anesthesia and multimodal pain control measures that avoid unnecessary use of narcotics<sup>4</sup>.

We aimed to study the effectiveness of a combination of different classes of drugs in optimal doses as a cocktail at different sites of the knee to maximize the pain relief and aid in early rehabilitation

## PATIENTS AND METHODS

This is a prospective interventional study conducted at MGMCRI, Puducherry between November 2019 and June 2021 after obtaining institute of human ethical committee (IHEC) approval.

### Inclusion criteria:

- Patients with grade 3 or 4 primary or secondary osteoarthritis

- BMI < 40
- Failed conservative management

Exclusion criteria:

- Patients with hypersensitivity to NSAIDs or local anesthetic agents
- Abnormal kidney or liver functions
- History of peptic ulceration/GI hemorrhage/ Coagulopathies/ hyperkalemia
- Neurological disorders
- Patients who underwent bilateral TKA

40 TKA's was done in a single unit, among them 2 patients with BMI > 40, 2 patients with extra-articular deformity, 2 patients who underwent bilateral TKA, and 2 patients lost to follow-up were excluded from the study. The remaining 30 patients were included in the study.

All the TKA were done by a single surgeon using a standard anterior midline incision with a medial parapatellar approach. Standard release and cuts were made for PS knees, and trials were checked. All the patient received Intraoperative periarticular injection consists of injections Bupivacaine 0.5% (20ml), Adrenaline 0.3 ml (1:1000), ketorolac 30mg/1ml, methylprednisolone 40mg//1ml, cefuroxime 750mg/10ml added with 27.7 ml of normal saline to make total of 60ml solution. Eight zones as described by Dye et al were chosen as injection sites because they have increased neurosensory sensitivity and a higher concentration of mechanoreceptors<sup>5</sup>. Infiltration of cocktail injection was given in the posterior capsule (Zone 5 and Zone 6) with 15ml of Cocktail in equal doses in the medial and lateral aspect of the capsule by a freehand technique using a 16G venflon needle. 5minutes of fixation time was allowed for the drug to fix into tissue after infiltration. While infiltrating the posterior areas of the knee, care was taken not to inject into the neurovascular structures. Cementing and Implantation were done. The remaining Cocktail (45ml) was infiltrated in the Suprapatellar and Quadriceps muscle (Zone1), Capsule, Subcutaneous tissue, Patellar Fat pad (Zone 2), medial and lateral meniscal capsular attachment (Zone 3 & 4), medial and lateral retinaculum (Zone 7 & 8) in equal doses (about 6ml at each zone). A suction drain was used in all cases. Postoperatively in paracetamol, 1g was given for 24 hours q6h along with etoricoxib 120mg and duloxetine 20mg. The standard postoperative and rehabilitative protocol was done. In the event of postoperative pain, the patient has been given Inj TRAMADOL 1mg/kg IV in 100ml normal saline as rescue analgesia. On a postoperative day, 0 Straight leg raising was started. From postoperative day 1 Static Quadriceps exercises, ankle pump exercises, pelvic lifting exercises, and full weight bearing mobilization with walker support were started. Range of movement exercises was started from Day 2 after Drain removal.

VAS was assessed as static at rest at 6, 12, 24, and 48 hours post-surgery and dynamic during mobilization, initial 4 recordings irrespective of time were documented, and the total number of rescue analgesia used was also recorded. Knee society score which included patient satisfaction score, patient expectation score, and patient functional activity score was assessed postoperatively at 3 and 6 months

## STATISTICAL ANALYSIS

SPSS, Confidence intervals were set at 95%, and a p-value  $\leq$  of 0.05 was considered statistically significant. Descriptive statistics were applied for demographic detail & Categorical variables are presented in the form of a frequency table. Continuous variables are presented in the Mean  $\pm$  SD/ (Min, Max) form. Paired t-test was applied to compare pre-operative and post-operative Knee range of motions and scoring system. Pearson's Correlation was applied to check the effect of Body Mass Index on Visual Analog Scores.

## RESULTS

Among 30 patients the average age was 64 years (range 47-76) with 14 males and 16 females. The mean BMI of the participants was 26 of which 50% of the participants were Obese (25-29.9) and 26.7% of the participants were overweight (23-24.9). 60% of the participants had comorbidities of which 33.3% of the participants had diabetes. There was a strong correlation between Body Mass Index and Dynamic VAS at 1<sup>st</sup> and Dynamic VAS at 3<sup>rd</sup> recording with  $p < 0.05$  (Table 1).

Static visual analog scores were observed highest at 6 hours  $4.30 \pm 0.988$ , followed by 12 hours  $3.67 \pm 5.081$ , 24 hours  $3.30 \pm 0.651$  and 48 hours  $2.57 \pm 0.626$  which was lowest. Dynamic visual analog scores at 1<sup>st</sup> were observed highest at  $4.90 \pm 0.960$ , followed by 2<sup>nd</sup> reading at  $4.17 \pm 0.648$ , 3<sup>rd</sup> reading at  $3.63 \pm 0.928$ , and 4<sup>th</sup> reading at  $3.47 \pm 0.90$  which was lowest. Two patients required rescue Analgesia, one 3 doses and the other 4 doses due to high BMI.

In all the patients Patient Satisfaction Score was highest at 6 months  $34.90 \pm 5.081$  compared to 3 months which was  $32.20 \pm 3.418$ . there was not much difference with Patient Expectation Score at 6 months  $14.67 \pm 0.758$  and at 3 months  $14.47 \pm 5.081$ . and Patient Functional Activity was highest at 6 months at  $80.60 \pm 14.25$  compared to 3 months which was  $73.03 \pm 5.288$ .

There was a statistically significant difference between Preoperative Knee ROM (range 30-120) and Postoperative Knee ROM (range 0-120) i.e  $p < 0.05$  (Table 2).

## DISCUSSION

In our study, we used bupivacaine, ketorolac, methylprednisolone, cefuroxime, and adrenaline as an intraoperative periarticular cocktail injection, which did not include any opioid, showed effective pain control and enhanced functional activity in terms of knee ROM postoperatively which was in line studies by Shah et al<sup>6</sup>, Shi and dang et al<sup>1</sup> and TC Kelley et al<sup>7</sup> where no opioid analgesic was used and good pain control and functional activity was obtained but with different combinations of drugs.

The rationale for employing this analgesic cocktail was to aid smooth muscles lining arterioles to contract more easily, conceivably reducing intraarticular hemorrhage and extending the time that the drugs need to operate locally.

In our study, the mean age of the participants was 64 years and the highest prevalence was mentioned amongst the 51-60 years of age group i.e., 26.7%, similar findings were

reported in the study by Jordan JM et al<sup>8</sup>. In one of the studies, it was mentioned that among adults above 65 years reporting chronic knee pain, only 50% had radiographic evidence of knee osteoarthritis<sup>9</sup> whereas, in a study done by Felson DT et al<sup>10</sup>, the prevalence of knee osteoarthritis in 1420 subjects aged 60 and higher was evaluated

In this study, females were suffering more from severe osteoarthritis as compared to males and had undergone TKA which was in line with current existing literature<sup>11-13</sup>. According to data, higher hormone levels at specific times of the menstrual cycle can induce joint laxity, leading to injury and joint instability, which might be linked to women's predisposition to osteoarthritis<sup>14-16</sup>. In addition, women's knees have lesser cartilage than men<sup>17</sup>. Body mass index was higher in 50% of our study population (obese I). Iseki T et al<sup>11</sup> discussed that body mass index amongst two groups, periarticular injection and other with no injection was significant according to authors. 60% of patients were having co-morbidities of which 33.3% of the population was suffering from diabetes mellitus. similar findings were reported by Tsukada S et al<sup>12</sup> and Iseki T et al, that history of diabetes mellitus is non-significant.

In our study pain was assessed at the interval of 6, 12, 24, and 48 hours as static VAS and dynamic VAS during 1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup>, and 4<sup>th</sup> recordings done during mobilization. It showed no statistically significant difference in static VAS whereas; there was a strong correlation between Body Mass Index and Dynamic VAS in the 1<sup>st</sup> and 3<sup>rd</sup> recordings. In our study, the mean VAS at 6 hours was  $4.3 \pm 0.988$  whereas in a study conducted by Shah et al<sup>6</sup> mean VAS on the immediate postoperative day was  $5.78 \pm 1.2$  where the intraoperative cocktail they used was more or less the same combination. The study by Tsukada S et al<sup>12</sup> and Iseki T et al<sup>11</sup> reported VAS for postoperative pain at rest where they found the p-value as statistically significant only in the recovery room.

In our study, we reported that more than 3 doses of rescue analgesia were required only twice, this finding is not reported by other authors. A study by Tsukada S et al<sup>12</sup> reported several suppositories employed as rescue analgesia between superficial injection in the early stage and late stage of surgery respectively; where they found a nonsignificant difference in rescue analgesia between both groups. Another study by Iseki T et al<sup>11</sup> reported suppositories as rescue analgesia between periarticular injection and no injection group, where they reported usage of diclofenac sodium suppository as a rescue treatment in similar amounts for both the groups.

In our study, we have discussed Postoperative Patient Functional Activity and Patient Satisfaction which was found to be highest at 6 months compared to 3 months which indicates the patient is having good functional outcomes and rehabilitation. Fan JC<sup>13</sup> discussed patient function activity and that a statistically significant difference was observed in functional scores between the cocktail and control group.

In our study, we have compared pre-operative and post-operative knee range of motion (ROM), which was found to be statistically significant. A study by Zhang et al<sup>18</sup> found no significant difference in pre and postoperative knee ROM.

In our study, we have introduced the newer cocktail combination for patients undergoing Total Knee Arthroplasty (TKA), where patients are getting the best therapy for severe osteoarthritis with minimal postoperative pain and no post-operative complications. The limitations of our study were the smaller sample size and the need a comparative group to substantiate our findings in assessing the effectiveness of intraoperative periarticular cocktails. As spinal anesthesia was used due to lower risk for TKR, it could have masked the pain score in the postoperative period due to the additives.

## **CONCLUSION:**

This study concludes that the combination of drugs that was used as a cocktail for periarticular injection safely provided excellent postoperative pain control and accelerated functional recovery in the patients undergoing total knee arthroplasty. It can be substituted for conventional pain control alternatives like femoral blocks and epidural analgesia with minimal adverse effects.

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**Informed consent (Patient/Guardian):** Informed consent was taken from the patient/guardian for all the participants.

**Institutional Ethical Committee Approval:** Institutional human ethical committee clearance was taken from IHEC, SBV university.

**Authors' contribution:** **Dr. Kailash Karur:** Formal analysis, Writing – Original draft, Investigation **Dr. Nandakumar Rengarajan:** Conceptualization, Validation, Supervision **Dr. Santhosh Kumar:** Methodology, Data curation, Visualization **Dr. Sripriya R:** Project administration.

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## **TABLES**

**TABLE 1: CORRELATION OF BODY MASS INDEX WITH PAIN**

	<b>Body Mass Index</b>
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<b>Static VAS at 6 hrs</b>	Pearson Correlation	.235
	p-value	0.211
	N	30
<b>Static VAS at 12 hrs</b>	Pearson Correlation	-.075
	p-value	0.693
	N	30
<b>Static VAS at 24 hrs</b>	Pearson Correlation	.111
	p-value	.560
	N	30
<b>Static VAS at 48 hrs</b>	Pearson Correlation	-.060
	p-value	.754
	N	30
<b>Dynamic VAS 1<sup>st</sup></b>	Pearson Correlation	-.401
	p-value	0.028*
	N	30
<b>Dynamic VAS 2<sup>nd</sup></b>	Pearson Correlation	-.206
	p-value	.274
	N	30
<b>Dynamic VAS 3<sup>rd</sup></b>	Pearson Correlation	-.383
	p-value	0.037*
	N	30
<b>Dynamic VAS 4<sup>th</sup></b>	Pearson Correlation	-.202
	p-value	0.284
	N	30

**TABLE 11: DESCRIPTIVE STATISTICS**

<b>Variables</b>	<b>Minimum</b>	<b>Maximum</b>	<b>Mean</b>	<b>Std. Deviation</b>
Preop PSS	0	20	7.13	5.056
Preop PES	9	15	13.40	1.632
Preop PFA	0	54	20.23	11.941

Static VAS at 6 hrs	2	6	4.30	.988
Static VAS at 12 hrs	2	5	3.67	.711
Static VAS at 24 hrs	2	5	3.30	.651
Static VAS at 48 hrs	1	4	2.57	.626
Dynamic VAS 1 <sup>st</sup>	2	6	4.90	.960
Dynamic VAS 2 <sup>nd</sup>	3	5	4.17	.648
Dynamic VAS 3 <sup>rd</sup>	2	7	3.63	.928
Dynamic VAS 4 <sup>th</sup>	2	6	3.47	.900
Rescue Analgesia	0	4	.77	1.040
PSS at 3 months	22	36	32.20	3.418
PES at 3 months	12	15	14.47	.900
PFA at 3 months	65	86	73.03	5.288
PSS at 6 months	10	38	34.90	5.081
PES at 6 months	12	15	14.67	0.758
PFA at 6 months	8	90	80.60	14.255

**TABLE 13: DISTRIBUTION OF RESCUE ANALGESIA**

Rescue Analgesia	Number	Percentage
0	16	53.1
1	8	26.7
2	4	13.4
3	1	3.4
4	1	3.4
Total	30	100

**TABLE 2: COMPARISON OF PRE AND POST KNEE RANGE OF MOTION (ROM)**

	<b>Knee range of motion (ROM)</b>	<b>Mean <math>\pm</math> Std. Deviation</b>	<b>p-value</b>
<b>Pair 1</b>	PreOp Knee ROM Minimum	12.83 $\pm$ 11.03	0.001*
	PostOp Knee ROM Minimum	0	
<b>Pair 2</b>	PreOp Knee ROM Maximum	90.67 $\pm$ 10.80	0.001*
	PostOp Knee ROM Maximum	106.33 $\pm$ 7.18	



**FIGURE: POSTEROLATERAL CAPSULAR INFILTRATION**



**FIGURE: MEDIAL RETINACULUM COCKTAIL INFILTRATION**