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### RESEARCH ARTICLE

#### “EFFICACY OF LOCAL INFILTRATION ANALGESIA IN POST OPERATIVE PAIN MANAGEMENT AND EARLY REHABILITATION IN TOTAL KNEE ARTHROPLASTY”

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##### Manuscript History

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#### Abstract

TKR is a surgical procedure in which an artificial joint or prosthesis replaces a damaged knee joint. The primary indication for TKR is pain, followed by functional limitation. Usually, a person's daily activities must be substantially affected by pain and functional limitations for him or her to be considered a candidate for TKR. The most common risks and complications associated with TKR are deep venous thrombosis, infection, stiffness, loosening, and osteolysis. To prevent deep venous thrombosis, patients are treated with heparin prophylactically and/or given support stockings to wear. Patients are also given antibiotics for 24 hours after surgery to minimize the risk of infection. Stiffness is another associated complication. In most patients, it can be avoided by keeping the knee moving in the days and weeks following surgery.

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#### Introduction:-

TKR is a surgical procedure in which an artificial joint or prosthesis replaces a damaged knee joint. The primary indication for TKR is pain, followed by functional limitation. Usually, a person's daily activities must be substantially affected by pain and functional limitations for him or her to be considered a candidate for TKR.

The most common risks and complications associated with TKR are deep venous thrombosis, infection, stiffness, loosening, and osteolysis. To prevent deep venous thrombosis, patients are treated with heparin prophylactically and/or given support stockings to wear. Patients are also given antibiotics for 24 hours after surgery to minimize the risk of infection. Stiffness is another associated complication. In most patients, it can be avoided by keeping the knee moving in the days and weeks following surgery.

Factors influence the post-arthroplasty pain

1. Anesthetic technique,
2. Patient pain threshold,
3. Residual effects of perioperative analgesia,
4. The use and duration of tourniquet exsanguinations,
5. Pre-operative pain level,
6. Volume of drug injected,
7. Surgical trauma involved,
8. The sex of the patient,
9. The experience of the surgeons, and finally,
10. The postoperative activity level of the patients.

**Material Method:-**

A periarticular cocktail injection consisting of 90 mL of normal saline, 17.5 mL of 5% bupivacaine, 2 mL of inj. ketorolac (30 mg), and 0.5 mL of adrenaline (total volume: 110 mL) was given to the right knee of all the patients involved in the study. The infiltration was performed using a 21-gauge needle and syringe. The aforementioned cocktail injection was formulated by the orthopaedic surgeon based on his or her clinical experience and past clinical studies.

The cocktail was injected at the following 7 anatomical zones

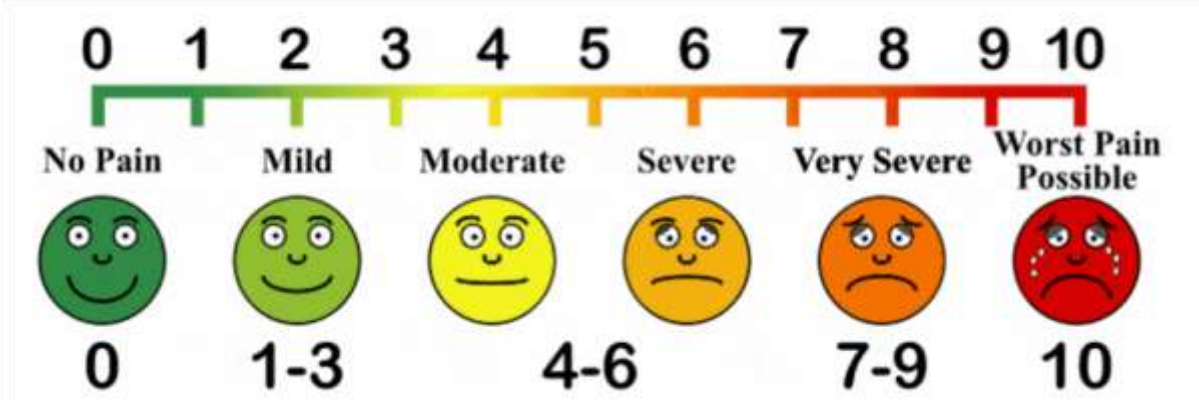
- Zone 1: medial retinaculum
- Zone 2: medial collateral ligament and medial meniscus capsular attachment
- Zone 3: posterior capsule
- Zone 4: lateral collateral ligament and lateral meniscus capsular attachment
- Zone 5: lateral retinaculum
- Zone 6: patellar tendon and fat pad
- Zone 7: cut ends of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





**Measurement of outcome:-**

Using a 10-point VAS at 6, 12, 24, and 48 hours postoperatively.



Postoperative range of active flexion was noted each day till the fourth postoperative

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.

**Selection Of Cases-**

An informed written consent will be taken from all the patients/relatives/guardian after the approval of institutional ethics committee.

Thirty patients undergoing primary total knee replacement were included in the study. A total of 30 knees were randomized either to receive a periarticular intra-operative injection containing adrenaline, bupivacaine, ketorolac, normal saline (Group A) and other not receiving any intra articular injection (Group B) The perioperative and post-operative analgesic regimens were standardized. All patients received the same standard analgesia protocol. Visual analog scores for pain, knee range of motion and quadriceps function were recorded on the day of surgery, first post-operative day, second post-operative day, day of discharge. The need for rescue analgesic requirement and adverse effects to the cocktail injection were also noted during the study period.

We included patients who underwent simultaneous TKR from from April 2021 to December 2022 in our institute. For uniformity, we included only the patients for whom spinal anesthesia was the mode of anesthesia. 30 patients who satisfied the inclusion criteria were selected for the study. All the patients had a full understanding of the 10-point visual analog pain scale (VAS).

**Source Of Data –**

Patients of grade III OA admitted to Sri Aurobindo institute of medical sciences & P.G Institute, Indore (M.P) for TKR

**Mode Of Selection Of Cases-**

All the patients fulfilling the inclusion criteria and giving consent will be included.

**Study Design –**

prospective observational

**Inclusion Criteria**

1. Primary grade III OA undergoing TKR
2. Age >55 years

**Exclusion Criteria**

1. Other associated disease or comorbidities



S.NO.	IPD NO.	NAME	AGE /SEX	SIDE	COMPLICATIONS IF ANY	VAS SCORE ( HOURLY)			
1			F	R	NONE	6	12	24	48
2			F	R	NONE	7	6	6	4
3			M	R	NONE	8	5	5	5
4			M	L	NONE	9	7	7	6
5			F	L	NONE	6	5	5	4
6			F	L	NONE	6	4	4	4
7			F	L	NONE	7	7	5	5
8			F	R	NONE	6	6	5	5
9			F	R	NONE	7	7	6	6
10			F	R	NONE	7	6	6	6
11			M	R	NONE	8	8	7	7
12			M	R	NONE	9	9	9	5
13			M	L	NONE	7	7	6	6
14			M	L	NONE	9	9	5	4
15			M	L	NONE	7	7	6	5
16			F	R	INCREASED DRAIN	9	8	8	5
17			F	R	INCREASED DRAIN	7	7	6	6
18			F	L	PAIN	8	7	6	6
19			M	L	PAIN	10	9	7	7
20			M	L	NAUSEA	8	8	7	7
21			F	L	NAUSEA	7	7	6	3
22			M	L	VOMITING	8	8	6	5
23			F	R	VOMITING	9	9	8	7
24			F	R	NONE	7	7	5	5
25			M	L	NONE	8	8	6	5
26			M	R	NONE	10	8	8	6
27			F	L	NONE	9	8	6	6
28			F	R	NONE	7	7	5	5
29			M	L	NONE	8	8	6	6
30			F	L	NONE	9	9	8	7

2. Exclusion criteria were patients with a history of allergy to the medications used in this study abnormal renal or liver function, uncontrolled diabetes, and those who could not receive spinal anesthesia.

### Sample Size

The sample size of approximately 30 patients will be taken.

### Results:-

A total of 30 patients were included in the study.

The mean pain scores (VAS) at 6, 12, 24, and 48 hours in table .When compared with the control knee, a statistically significant reduction in pain score was noted in the cocktail injected knee at 6, 12, 24, and 48 hours ( $P < .001$  in all cases).

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

Postoperative duration	Group	Mean	Standard deviation	Standard error mean	P value
6 h	Control	3.73	1.927	.193	<.001 a
	Intervention	1.96	1.406	.141	

12 h	Control	3.17	1.770	.177	<.001 a
	Intervention	1.83	1.371	.137	
24 h	Control	2.62	1.362	.136	<.001 a
	Intervention	1.58	.654	.065	
48 h	Control	2.34	1.056	.106	<.001 a
	Intervention	1.13	.825	.082	



Figure 1:- VAS comparison.

The mean time taken for achieving 90° flexion in the intervention and control knees were 1.70 and 2.82 days, respectively. The difference was found to be statistically significant (P < .001).

Within the intervention group, there was a significant difference in the pain scores over different time points (Table 2). A post hoc analysis showed no significant difference within various time points on the first day (6, 12, and 24 hours) after surgery. However, a statistically significant difference in the pain scores was noted at 48 hours (P < .001).

Table 1:- Within-group repeated-measures ANOVA.

Group	Mean	Standard deviation	N	P value
Control				
6 h	3.73	1.927	100	<.001
12 h	3.17	1.770	100	
24 h	2.62	1.362	100	
48 h	2.34	1.056	100	
Intervention				
6 h	1.96	1.406	100	<.001
12 h	1.83	1.371	100	
24 h	1.58	.654	100	
48 h	1.13	.825	100	

ANOVA, analysis of variance.

Within the control group, there was a significant difference in pain scores over different time points. However, a post hoc analysis showed that there was no significant difference within various time points on the first day (6, 12, and

24 hours) after surgery, and statistically significant improvement was found only after 72 hours ( $P < .001$ ) and 96 hours ( $P < .001$ ), compared with the 24-hour value.

**Discussion:-**

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

The rationale for using the analgesic cocktail was to facilitate contraction of the smooth muscles that line the arterioles to potentially minimize intraarticular bleeding and prolong the time the agents would act locally. The component epinephrine in the cocktail is especially conspicuous in this regard

The component ketorolac not only acts as antiinflammatory and analgesic but also possesses synergistic activity when given along with other oral nonsteroidal antiinflammatory drugs, such as acetaminophen and gabapentin, thereby reducing the requirement of these systemic agents.

Significant pain relief was obtained when intraarticular ketorolac was given along with bupivacaine and epinephrine as a cocktail combination in previous studies

According to Badner et al. addition of an opioid like morphine in the cocktail mixture did not provide any significant additional advantage when compared to cocktail mixtures without opioids with respect to postoperative pain relief

In accordance with their study, our study also excluded the use of opioids in the cocktail mixture.

According to Christensen et al. , addition of steroids to multimodal periarticular cocktail injection only minimized the length of hospital stay in patients undergoing TKR. It did not improve pain relief or early postoperative ROM. They also posed an increased risk of postoperative infection.

Although the existing randomized controlled trials have confirmed the safety of steroids, many surgeons still hesitate to use a drug which is thought to increase the risk of catastrophic complications such as infection and patellar tendon rupture [

For the aforementioned reasons, steroids were not added to the cocktail mixture in our study.

The results of immediate postoperative pain control by various authors are promising. Mullaji et al. used bupivacaine, fentanyl, methylprednisolone, and cefuroxime in their intraarticular cocktail. Badner et al. used a combination of bupivacaine and epinephrine. Andersen et al. used subcutaneous ropivacaine, and Vaishya et al. used bupivacaine, adrenaline, morphine, ketorolac, and gentamycin. All of them demonstrated significant pain relief, increased early postoperative knee movements, and quadriceps function.

We included consecutive TKR patients belonging to a particular time frame.

In our study, the cocktail injection was given in a periarticular manner. Significant reduction in pain (by VAS) was recorded over the knee where the injection was given (right side) compared with the patient in whom cocktail injection was not given at 6, 12, 24, and 48 hours ( $P < .001$ ). This is in comparison with the study by Fu et al. which showed VAS score at rest was significantly lower at 6, 10, 24, and 36 hours postoperatively in the trial group compared with the control group, although the difference was insignificant at 24 hours postoperatively, and at days 2, 7, and 15 between the 2 groups. VAS score during activity was also lower in the trial group at 24 and 36 hours postoperatively than that in the control group, although the difference was insignificant at days 2, 7, and 15

Busch et al. noted that patients who received a periarticular intraoperative injection containing ropivacaine, ketorolac, epimorphine, and epinephrine used significantly less PCA during the first 24 hours postoperatively

Vaishya et al. , in their study comparing 2 groups of 40 knees each, reported that the cocktail injected patients reported significantly less PCA and postoperative pain recordings at 6, 24, 48, and 72 hours after TKR.

In our study, the time taken to achieve 90° of knee flexion postoperatively was found to be significantly longer for the control side (mean 2.82 days) than that for the intervention side (mean 1.70 days). According to a comparative study by Rasmussen et al., use of 24- to 72-hour continuous intraarticular infusion of morphine plus ropivacaine showed a significant improvement in ROM and decreased the length of hospital stay [

According to the study by Fu et al., in which 80 patients were grouped into 2 groups namely trial and control, the time of being able to perform straight leg raise and reaching 90° knee flexion was significantly shorter in the trial group than that in the control group. The mean ROM at day 15 was greater in the trial group than the control group, and the difference was insignificant at day 90 between the 2 groups, indicating that intraarticular analgesic injection is helpful in early postoperative rehabilitation

The only differences are that anterior cruciate ligament and posterior cruciate ligament attachment sites were not included for injection since we used cruciate-sacrificing type of implants. Cocktail injection to the cut ends of quadriceps tendon was given in addition.

In a study conducted by Nakai et al. postoperative nausea and vomiting was the least observed complication in the periarticular injection group compared with the other 2 groups where no injection or intraarticular injection was used. Femoral nerve blocks and epidural anesthesia have been reported to control pain with good efficacy. However, these procedures require a well-trained physician, and there are some complications that could result from these procedures.

Sharma et al. reported the rate of femoral neuropathy after femoral nerve block to be approximately 0.59%.

Vendittoli et al. reported that periarticular infiltration with ropivacaine, ketorolac, and adrenaline on the first postoperative day showed a reduction in narcotic requirements at 48 hours after the operation with minimal side effects when compared with the control group

In our study, 1 patient in the intervention group developed postoperative infection, followed by loosening. Two-staged revision was performed after the infection was controlled. Delayed wound healing characterized by bloody and serous discharge was encountered in 2 patients over the right side (intervention group) and 3 patients over the left side (control group). Their swabs were culture negative, and their wounds healed well on repeated cleaning and dressing. There were no cases of hematoma formation clinically in either group. None of the patients included in the study incurred symptomatic DVT, and there were no cases of allergic reactions.

There are a few limitations in our study. A power analysis was not performed before commencing the study, and we just included patients belonging to a particular time frame. The optimal concentration of the individual components of the cocktail could not be determined, and further effort is required to comment on the superiority of 1 component over the other. Another question of debate is whether the infiltration of normal saline to the control side itself could incite pain mechanically even though we presumed normal saline by itself has no local pharmacological effects. Our study did not attempt at evaluating long-term clinical outcomes of the patients.

### **Conclusions:-**

The patients who received the periarticular cocktail fared better in terms of pain scores and functional recovery. Additional rescue agents used were significantly less at 6 h, at 12 h, and over the first 24 h after the surgery in group A when compared with group B. No cardiac or central nervous system toxicity was observed.

Cemented cruciate-sacrificing implants were used for all the cases. After component placement and cement setting, tourniquet was released, and hemostasis was achieved before the wound was closed. drains were used.



During the postoperative period, systemic analgesics used were intravenous injection of diclofenac (75 mg) SOS and inj. tramadol (100 mg) along with inj. ondansetron (4 mg) every 12 hours for the first 2 days followed by tablet chymotrypsin- trypsin and with paracetamol (625 mg) for the next 10 days. Buprenorphine patch (10 mg) were used in patients for whom the aforementioned medications were insufficient in controlling pain or could not be tolerated. Postoperative pain over both the knees were separately recorded by using a 10-point VAS at 6, 12, 24, and 48 hours postoperatively, and The VAS consists of a 10-cm line, in which 0 indicates no pain and 10 indicates the worst imaginable pain [

Postoperative range of active flexion was noted each day till the fourth postoperative day on both the knees separately by the physiotherapist, who was also blinded about the study.

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.

Follow-up periods, we used repeated-measures analysis of variance. A post hoc test was conducted to assess the presence of any statistical significance between the 2 time points.

E. Carlos Rodriguez-Merchan, MD, PhD First Published February 1, 2018

Single Local Infiltration Analgesia (LIA) Aids Early Pain Management after Total Knee Replacement (TKR): An Evidence-Based Review and Commentary

Improvements in pain management techniques in the last decade have had a major impact on the practice of total knee replacement (TKR). Adequate postoperative analgesia with minimal side effects is essential for early mobilization and recovery in patients undergoing TKR. Local infiltration analgesia (LIA) with ropivacaine has been introduced as a popular method for decreasing postoperative pain after TKR. LIA is widely applied in patients undergoing TKR.