



## Evaluation of Effectiveness of Periarticular Injection of Cocktail of Drugs in Pain Management in Total Knee Arthroplasty

Dr. Sanjay Kalani<sup>1</sup>, Dr. Ankita Meena<sup>2</sup>, Dr. Chiranji Lal Khedia<sup>3\*</sup>

<sup>1</sup>Senior Professor, Department of Anaesthesiology, GMC Kota, Rangbari Rd, Sector - A, Rangbari, Kota, Rajasthan 324010, India

<sup>2</sup>Senior Resident, Department of Anaesthesiology, GMC Kota, Rangbari Rd, Sector - A, Rangbari, Kota, Rajasthan 324010, India

<sup>3</sup>Assistant Professor, Department of Anaesthesiology, GMC Kota, Rangbari Rd, Sector - A, Rangbari, Kota, Rajasthan 324010, India

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\*Corresponding Author  
Dr. Chiranji Lal Khedia

Assistant Professor,  
Department of  
Anaesthesiology, GMC Kota,  
Rangbari Rd, Sector - A,  
Rangbari, Kota, Rajasthan  
324010, India

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### ABSTRACT

**Background:** Post-operative pain management is a major concern in TKA. Periarticular infiltration in TKA is a technique in which a cocktail of drug combination is injected into the periarticular soft tissues such as posterior capsule, medial and lateral collateral ligaments, quadriceps mechanism, and peripatellar tissue at the end of the surgery. Recent studies found that periarticular injection significantly improved pain relief from 24hr to 1wk and straight leg raise in the early postoperative period. Therefore in our study, we evaluated a combination of local anaesthetic (Ropivacaine), alpha agonist (clonidine), cox-2 inhibitor (ketorolac) as a multimodal analgesic to effect on various pain receptors. We also added epinephrine to reduce their absorption and prolongation of their effect (analgesics). **Methods:** This study was conducted on 80 patients who were randomly divided into 2 groups, group's 42 patients (received local infiltration analgesia) and group c 38 patients (received normal saline injection) based on software-derived random number sequence. The data was revealed to the investigators at the end of the study. The statistical analysis of the data set was performed with Kolmogorov-Smirnov test ( $p < 0.05$ ) for normality and an unpaired-t test was used to compare mean of the group for the significance of differences of outcome variable. Dichotomous data were analyzed using chi-square test or Fisher's exact test, as appropriate. A p-value of  $< 0.05$  was considered statistically significant. **Results:** We observed that the mean VAS score in Group S was lower (2.57) as compared to the Group C (4.66). Patients in group 'S' were more satisfied and felt less pain with increased range of motion and physiotherapy. The patients in group 'S' were discharged earlier as they had less pain on physiotherapy as well as on rest and also there is increased mobility of knee joint. **Conclusion:** Our study suggests that periarticular injection of cocktail of drugs is a safe and effective multimodal analgesia technique that can be used for the management of pain in patient of total knee arthroplasty. **Keywords:** Total knee arthroplasty, Periarticular infiltration, cocktail of drugs.

### INTRODUCTION

Total Knee Arthroplasty (TKA) also known as Total knee replacement (TKR), which is a surgical procedure in which the weight bearing surfaces of the knee joint are replaced with knee prosthesis to relieve pain and disability. Post-operative pain management is a major concern in TKA because in TKA postoperative pain interferes with patient's mobilization, which can lead to undesirable outcomes such as hospital acquired infection, deep vein thrombosis, unwillingness to participate in physiotherapy, prolongs hospital stay, increased readmission rates, revision surgeries and increased cost of care causes poor surgical outcome and lower patient satisfaction. Patients with total knee replacement experience moderate to severe pain on early post operative period and pain management on first postoperative day is challenging. So, for a successful outcome of surgery postoperative pain management is key factor following total knee arthroplasty [1, 2].

Various modalities of pain relief available like Patient education, administration of preemptive analgesics, neuraxial analgesia: epidural analgesia, peripheral nerve block: femoral nerve block along with or without sciatic or obturator nerve block, intraarticular injection, periarticular injection, patient controlled analgesia and oral analgesics.

Periarticular infiltration in Total Knee Arthroplasty is a technique in which a cocktail of drugs is infiltrated into the periarticular soft tissues such as peripatellar tissues, posterior capsule, medial and lateral collateral ligaments at the end of the Total Knee Arthroplasty. Though there is no standardized protocol in periarticular injection of cocktail of drugs for postoperative pain management following TKA, for post operative pain management a combination of long-acting local anesthetic drugs (bupivacaine, ropivacaine) along with steroids, opioids (morphine/fentanyl), and epinephrine is used. Steroids prevent local inflammation. Morphine blocks the three opiate receptors and epinephrine prolongs the action of local anesthesia by decreasing its absorption via its alpha-2 adrenergic effect. Injection of the mixture is avoided in the posterolateral corner of knee to prevent inadvertent injury to the peroneal nerve.

Recent studies [3, 4] found that infiltration of cocktail of drugs into periarticular soft tissues significantly improved pain relief from 24 hour to 1 week and straight leg raising in the early postoperative period.

Therefore we evaluated a combination of local anaesthetic (Ropivacaine), alpha agonist (clonidine), cox-2 inhibitor (ketorolac) as a multimodal analgesic to effect on various pain receptors. We also added epinephrine to reduce their absorption and prolongation of their effect (analgesics) as it was reported that epinephrine in doses (1:1000) 0.5ml, which we had used does not have any ill-effects on wound healing or tissue necrosis. We also added steroids in form of Methylprednisolone (MPS) as it had been suggested that MPS reduces local inflammation and thereby improve pain control. We evaluated the efficacy of these cocktail drugs in periarticular injection in patients posted for TKR in terms of post op analgesia, early mobility and rehabilitation as well as early discharge.

## Methods

Ethical clearance was obtained from the institute ethical committee of Govt. Medical College, Kota, Rajasthan, India with reference number No. F3(Acad/Ethical clearance/2019/1804 Dated 16/12/2019).

## Study Design:

It was a hospital based prospective double blinded randomized comparative analytical study (RCT).

## Participants:

This study was conducted in the Department of Anaesthesiology, Government Medical College and Associated Groups of Hospital Kota, Rajasthan. 100 Patients were assessed for a eligibility, out of 100 patients 20 patients did not meet the inclusion criteria and were excluded from the study (Figure A). A Hospital based prospective double blinded randomized comparative analytical study (RCT) was conducted on 80 patients, who had Osteoarthritis, Rheumatoid arthritis, Infective arthritis and Post traumatic severe knee deformity and demographic basis both sex and those who were between 50-80 years age belonging to ASA I and II were included, who were underwent total knee arthroplasty (TKA) under regional anaesthesia from January 2020 to April 2021. Written informed consent was taken from all patients. Patients were randomly divided them into two groups which was Group S 42 Patients (Received Local infiltration analgesia) and Group C 38 Patients (Received Normal Saline injection).

**Group S (N=42):** Patients was administered Ropivacaine 0.5% ( 30ml) + Ketorolac 1 ml (30mcg/ml) + Epinephrine 0.5ml (1:1000) + Clonidine 0.8 ml (120 µg) + Cefuroxime 750 mg + Methylprednisolone 40mg [Total volume made to 60 ml by adding normalsaline].

**Group C (N=38):** Control group received normal Saline injection.

Patient not giving consent, ASA III & IV, having history of allergy to any of the study drugs, drug abuse, uncontrolled hypertension, history of stroke or a major neurological deficit, uncontrolled angina or chronic medical illness, coagulation disorder skin infection at the puncture side, patients with bilateral TKR and patients who were having any deformity (more than 20° varus or flexion contractures) and restricted range of kneemovement were excluded from the study.

The cocktail drugs with methylprednisolone were prepared in a 60ml measuring jar by another resident other than the surgeon infiltrating the drugs and anaesthesiologist

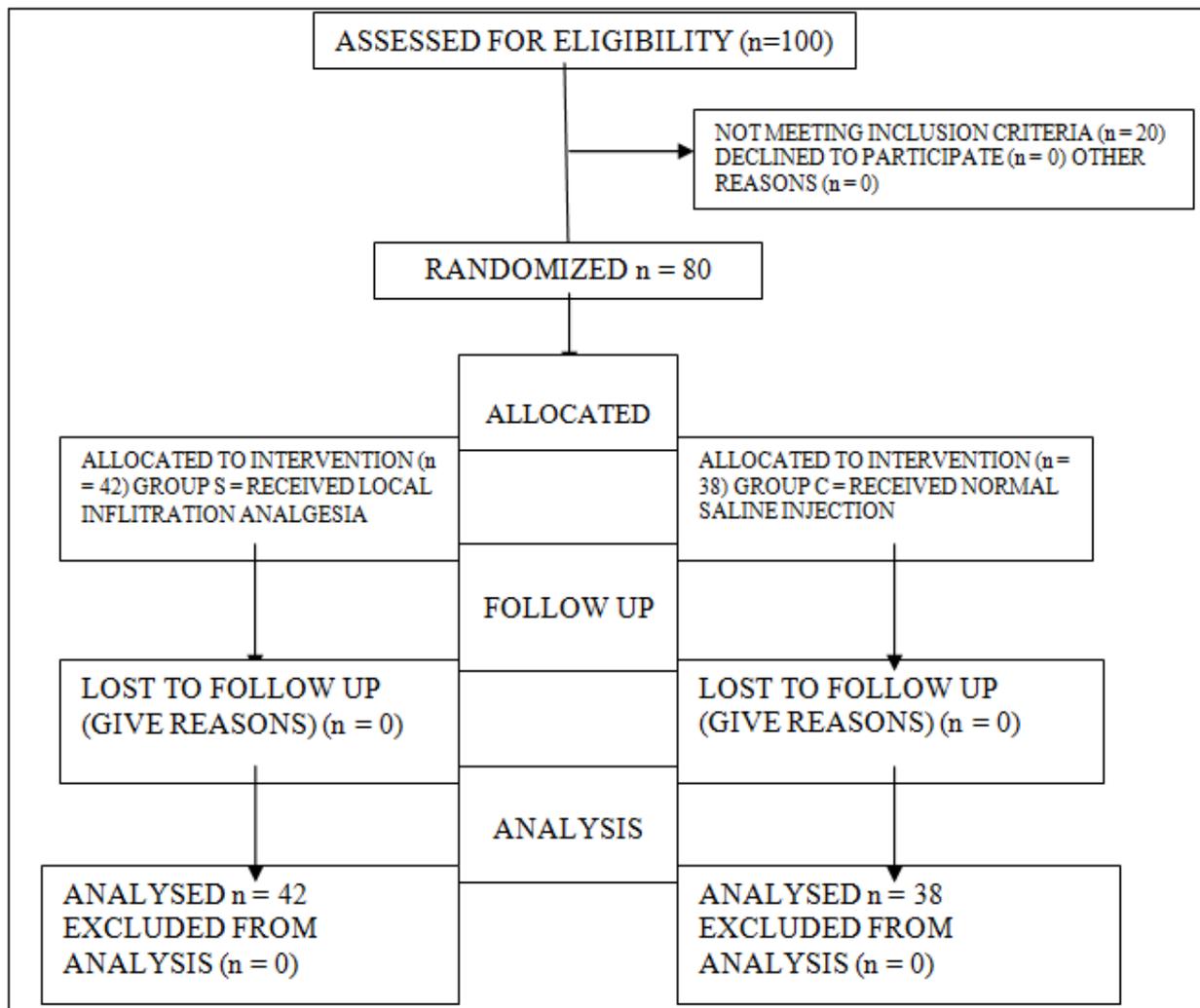
monitoring the patient to ensure blinding. The local infiltration and control solution (both colourless) were prepared and provided in identical disposable syringes tagged with number codes for all allocation concealment and blinding by the resident doctor. The third anaesthesiologist, who was unaware of the injected solution in periarticular soft tissues and recorded all the parameters (neither the patient nor the anaesthesiologist monitoring the patient knew about the group of the patient), Cardio-respiratory parameters of heart rate, blood pressure, and SpO<sub>2</sub> were monitored.

**Outcome measures:**

Outcome measure include VAS score at rest and on movement, range of motion (ROM), Quadriceps muscle strength, length of hospital stay and incidence of complication. Participants was followed-up at 6h, 12h and 24hours for 1<sup>st</sup> 24 hours after surgery then every 12 hourly for next 48 hours (3 Days). Assessment was conducted post-operatively, daily during the hospital stay.

**Primary outcome measure:**

Post operative pain: Pain intensity was evaluated in three periods-prior to surgery, at 6h, 12h and 24hours for 1<sup>st</sup> 24 hours after surgery then every 12 hourly for next 48 hours (3 Days), using Visual Analogue Score (VAS) of 0 – 10.



**Figure A: Consort Flow Chart**

**Secondary outcome measures:**

- A. Range of Motion
- B. Quadriceps muscle strength
- C. Length of hospital stay
- D. Complications
- E. Patient acceptance & level of satisfaction

**Statistical Analysis**

The statistical analysis was done using Kolmogorov-Smirnov test ( $p < 0.05$ ) for normality and an unpaired-t test was performed to compare mean of the group for the significance of differences of outcome variable. Dichotomous data were analyzed using chi-square test and Fisher's exact test. A p-value of  $< 0.05$  was considered statistically significant.

## RESULTS

Demographic data like age and sex were comparable in both the groups (Table 1 & 2). It was observed that in Group S and Group C the majority of the patients belonged to the age group of 61 to 70 years. Majority of the patients were female in Group S and C respectively and in our study both the groups were comparable.

**Table 1: Age distribution of the patients**

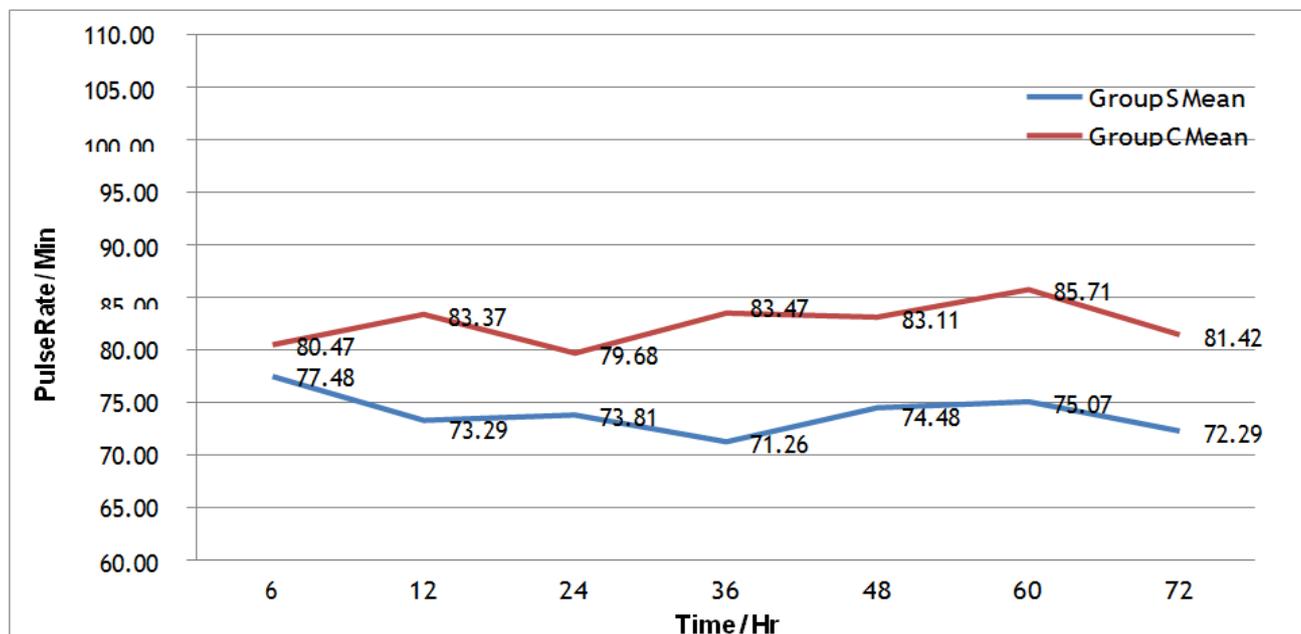
Age in years	Group S (n=42)	Group C (n=38)
50 TO 60	13	6
61 TO 70	17	21
71 TO 80	12	11
MEAN (S.D.)	65.17 (7.92)	66.74 (6.31)
P value	0.5164 (NS)*	

NS\* - Not Significant

**Table 2: Sex distribution of the patients**

Sex	Group S (n=42)	Group C (n=38)	Total
Male	18	16	34
Female	24	22	46

When both the groups were compared for changes in postoperative pulse rate, it was observed that in groups 'S' the pulse rate remained stable. This was observed up to 72 hours postoperatively. This might be due to adequate pain relief postoperatively. The group 'C' patients shown some changes in mean pulse rate and found to be statistically increased (Figure 1).



**Fig 1: Changes in postoperative mean pulse rate**

We studied postoperative changes in the systolic blood pressure (SBP) and diastolic blood pressure (DBP) in Group S and C at 6 hr, 12 hr, 24 hr, 36 hr, 48 hr, 60 hr and 72 hours. In our study we observed that mean systolic blood pressure and diastolic blood pressure was higher in group 'C' as compared to group 'S' postoperatively and we found that in group 'S', the mean systolic blood pressure and diastolic blood pressure were stable and both the groups were statistically comparable (Table 3 & 4).

**Table 3: Changes in postoperative mean systolic blood pressure**

Time / Hr	Group S		Group C		P Value	Statistical Sign
	Mean	SD	Mean	SD		
6	126.76	6.27	131.16	5.30	0.0142	S
12	129.60	5.72	132.05	6.52	0.0815	NS
24	131.71	5.61	134.00	5.96	0.6649	NS
36	126.71	8.88	132.32	5.51	0.0066	S
48	129.86	7.10	132.18	8.58	0.5526	NS
60	124.71	7.74	131.45	6.66	0.0071	S
72	126.40	9.39	128.37	6.44	0.1757	NS

SD – Standard Deviation, S – Significant, NS – Non Significant

**Table 4: Changes in postoperative mean diastolic blood pressure**

Time / Hr	Group S		Group C		P Value	Statistical Sign
	Mean	SD	Mean	SD		
6	73.24	4.04	81.63	5.88	0.0001	S
12	74.29	3.58	80.97	6.84	0.0002	S
24	79.45	9.03	79.55	6.08	0.0628	NS
36	75.05	5.10	81.11	6.47	0.0003	S
48	78.74	6.48	80.21	8.81	0.6460	NS
60	72.62	3.44	81.79	8.32	0.0001	S
72	72.76	3.50	78.97	7.34	0.0001	S

SD – Standard Deviation, S – Significant, NS – Non Significant

The mean VAS (Visual Analog Scale) Score was assessed according to age groups in male and female variables. In age group of 71-80 years VAS score mean was low in female as compare to male. We also found low VAS score in group ‘S’ at all the time period postoperatively in comparison to group ‘C’ (Table 5 & 6).

**Table 5: VAS score mean according to age group in males**

Age in Groups	Group S							Group C						
	6hr	12hr	24hr	36hr	48hr	60hr	72hr	6hr	12hr	24hr	36hr	48hr	60hr	72hr
50 TO 60	0.00	0.60	1.20	1.40	2.20	2.40	2.60	2.00	2.50	3.50	3.50	3.50	4.00	5.00
61 TO 70	0.43	0.57	1.00	1.43	2.14	2.57	2.71	1.38	2.38	3.38	3.75	4.13	4.75	4.88
71 TO 80	1.00	0.33	1.00	1.83	2.50	2.50	2.67	1.50	2.83	3.67	3.83	4.17	4.50	4.67

**Table 6: VAS score mean according to age group in females**

Age in Groups	Group S							Group C						
	6hr	12hr	24hr	36hr	48hr	60hr	72hr	6hr	12hr	24hr	36hr	48hr	60hr	72hr
50 TO 60	0.00	0.50	1.13	1.38	2.13	2.38	2.50	1.75	2.25	3.25	3.50	3.50	4.00	4.75
61 TO 70	0.00	0.40	0.90	1.30	2.00	2.40	2.60	1.31	2.23	3.46	3.54	3.62	4.46	4.54
71 TO 80	0.00	0.00	0.83	1.17	1.33	2.17	2.33	1.40	2.40	3.40	3.60	3.80	4.20	4.40

SD – Standard Deviation, S – Significant

We observed that mean VAS score was higher in group ‘C’ as compared by group ‘S’ postoperatively and we found that in group ‘S’, the mean VAS score was near to baseline and normal. This was observed up to 72 hours postoperatively. The group ‘C’ patients shown increased changes in VAS score and found to be statistically significant postoperatively (Table 7).

**Table 7: Changes in postoperative mean VAS score**

Time/Hr	Group S		Group C		P Value	Result
	Mean	SD	Mean	SD		
6	0.21	0.42	1.45	0.50	0.0001	
12	0.40	0.50	2.39	0.50	0.0001	S
24	1.00	0.49	3.45	0.50	0.0001	S
36	1.40	0.50	3.63	0.49	0.0001	S
48	2.05	0.54	3.82	0.56	0.0001	S
60	2.40	0.50	4.42	0.50	0.0001	S
72	2.57	0.50	4.66	0.48	0.0001	S

The range of motion was assessed by measuring postoperative knee flexion with a goniometer by the physiotherapist. On the 1<sup>st</sup> day, 23 patients in group ‘S’ showed early flexion of the knee in the range of 30°-60° as compared with group ‘C’. On the 2<sup>nd</sup> day, 40 patients in group ‘S’ showed improved flexion of the knee in the range of 30°-60° and 61°-90° as compared with group ‘C’. This might be due to better pain relief in group ‘S’. On the 3<sup>rd</sup> day, 28 and 12 patients in the range of 91°-120° and 61°-90° showed improved flexion of the knee in Group ‘S’ as compared with group ‘C’. This might be due to better pain relief in group ‘S’ (Table 8).

**Table 8: Range of motion on 1<sup>st</sup>, 2<sup>nd</sup> and 3<sup>rd</sup> postoperative day**

Patients		Range of motion achieved in degree		
		91-120	61-90	30-60
1 <sup>st</sup> Post Operative day	Group S	0	0	23
	Group C	0	0	1
2 <sup>nd</sup> Post Operative day	Group S	2	24	16
	Group C	0	1	12
3 <sup>rd</sup> Post Operative day	Group S	28	12	1
	Group C	6	9	23

There was significant difference for patient satisfaction with pain between the two groups. The mean VAS score in Group S was lower (2.57) as compared to the Group C (4.66). Patients in group ‘S’ were more satisfied and felt less pain with increased range of motion and physiotherapy (Table 9).

**Table 9: Patient satisfaction with pain**

Patient satisfaction with pain		
Mean VAS score	Group S	Group C
	2.57	4.66

We observed that in the ‘S’ group, 22/42 patients were discharged during the 4<sup>th</sup> postoperative day, 14/42 on 5<sup>th</sup> postoperative day and 4 on 6<sup>th</sup> postoperative day as compared to 3/38 on 5<sup>th</sup> postoperative day, 15 on 6<sup>th</sup> and 20 on 7<sup>th</sup> postoperative day in the ‘C’ group. The patients in group ‘S’ were discharged earlier as they had less pain on physiotherapy as well as on rest and also there is increased mobility of knee joint (Table 10).

**Table 10: Hospital discharge days**

Patients	Hospital discharge days			
	Day 4	Day 5	Day 6	Day 7
Group S	22	14	4	2
Group C	0	3	15	20

## DISCUSSION

The preferred prospective randomized controlled trial was done to assess the effectiveness of periarticular injection of cocktail of the drug to reduce postoperative pain following TKA, as well as to compare the need for postoperative analgesic requirement. We also did this study to know whether patient of TKA following periarticular infiltration, had early mobility, improved range of motion, and also their cooperation in physiotherapy. We also compare the length of hospital stay because of pain etc.

Multimodal local infiltration analgesia technique involves infiltration of a large volume of diluted solution of a long-acting local anaesthetic agent (Bupivacaine or Ropivacaine) alone or along with adjuvants like Epinephrine, Ketorolac, and opioid in the periarticular soft tissues during surgery provides better analgesia in postoperative period. All the adjuvants which are used have different modes of action on the pain pathway and hence their effect is multimodal. This technique of postoperative pain management in patients of TKA provides optimal pain relief and it permits early rehabilitation and recovery thus allowing reduction in hospital stay [5, 6].

This study was specifically designed to investigate the efficacy of LIA on postoperative pain management following TKA. Secondly, its effect on range of motion, length of hospital stay and overall patient satisfaction with pain was also noted. The active ingredients of the infiltration mixture that were used in the present study were Ropivacaine, Ketorolac, Epinephrine, Clonidine and Methylprednisolone administered intraoperatively in volume of around 60ml. While in this study Ropivacaine has been used instead of Bupivacaine, to avoid possible toxicity of Bupivacaine as it is less cardiotoxic. NSAID (Ketorolac) was used to optimize the anti-inflammatory and analgesic effect of the ‘cocktail’ solution. Ketorolac 30 mg [5] which is a directly acting injectable formulation was used, in

addition to Epinephrine. Steroid (Methylprednisolone) was also used in the cocktail solution to decrease inflammation[7].

In our group study we found very significant result as compared group S and group C. Table: 13 revealed the patients VAS pain score, and were lower in group S than in group C ( $p < 0.0001$ ) at 6, 12, 24, 36, 48, 60, and 72 hrs, and also patients had lower VAS during rest during or physiotherapy. In other study, Krenzelet *et al.*, [8] performed a randomised double blind study (66 patients) and compared local Ropivacaine infiltration with placebo along with femoral nerve block, found out that there was a decrease in the pain score in the early post operative period but did not discuss the impact on discharge from the hospital. In previous study RajuVaishyaet *et al.*, [9] they recorded visual analog scores (VAS) for pain (at rest and during activity), patient satisfaction and range of motion postoperatively. They concluded that patients who had received the periarticular injection used significantly less Patient Controlled Analgesia (PCA) after the surgery as compared to the control group and they also had lower VAS for pain during rest and activity and higher visual analog scores for patient satisfaction 72 hours postoperatively.

In our study the postoperative knee flexion on 1<sup>st</sup>, 2<sup>nd</sup>, and 3<sup>rd</sup> postoperative day was improved in the group S. The mean range of motion in the S group was 58° as compared to 40° in the C group, on 1<sup>st</sup> post-operatively day. The mean range of motion in the S group was 79° as compared to 55° in the C group, on 2<sup>nd</sup> post-operatively day. The mean range of motion in the S group was 91° as compared to 57° in the C group, on 3<sup>rd</sup> post-operatively day. In other study, RajuVaishyaet *et al.*, [10] they recorded postoperative knee flexion on 3<sup>rd</sup> postoperative day was improved in the infiltration group. The mean range of motion in the infiltration group was 90° as compared to 59° in the control group.

The average LOS was significantly lower ( $p < 0.0001$ ) in S group compared to C group (Table 18). In the S group, 22/42 patients were discharged during the 4<sup>th</sup> postoperative day, 14/42 on 5<sup>th</sup> postoperative day and 4 on 6<sup>th</sup> postoperative day as compared to 3/38 on 5<sup>th</sup> postoperative day, 15 on 6<sup>th</sup> and 20 on 7<sup>th</sup> postoperative day in the C group. The capacity of local infiltration analgesic to provide adequate pain relief and allowing early mobilization without prolonging recovery was also assessed. Since several factors can affect duration of hospital stay, an objective method to assess the criteria for discharge was used. In other study Lombardi *et al.*, [10] did not find any significant difference in length of hospital stay and range of motion despite claiming good pain relief after Local Infiltration of Anaesthetics. Adequate pain control in early postoperative period is one of the main contributory factors in reducing length of hospital stay. The results of this study have shown that there was a substantial reduction in duration of hospital stay without having a negative effect on patient satisfaction, which are similar to other published reports [6, 7].

Thus, the main goal of our postoperative pain management in patients of TKA is to reduce postoperative pain and to provide preemptive analgesia using a multimodal analgesia protocol. This strategy of infiltration of cocktail of drugs in periarticular soft tissues enhances restoration of function by allowing patients to participate in the rehabilitation programs more easily and aids early recovery thus improving the overall postoperative outcome.

### Limitation

Our study is in a small number of cases with short duration and further follow up is necessitated. Dependent on the surgical team for infiltration of the cocktail, also due to the mixture of multiple agents used in the multimodal analgesia in the test group, it is difficult to ascertain the efficacy of any one particular drug.

### CONCLUSION

Our study suggests that periarticular injection of cocktail of drugs is a safe and effective multimodal analgesia technique that can be used for the management of pain in patient of total knee arthroplasty and it aids in early recovery and rehabilitation following TKA.

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**Conflicts of Interest:** There are no conflicts of interest.

### REFERENCES

1. Parvataneni, H. K., Shah, V. P., Howard, H., Cole, N., Ranawat, A. S., & Ranawat, C. S. (2007). Controlling pain after total hip and knee arthroplasty using a multimodal protocol with local periarticular injections: a prospective randomized study. *The Journal of arthroplasty*, 22(6), 33-38.
2. Chung, F., Ritchie, E., & Su, J. (1997). Postoperative pain in ambulatory surgery. *Anesthesia & Analgesia*, 85(4), 808-816.
3. Teng, Y., Jiang, J., Chen, S., Zhao, L., Cui, Z., Khan, M. S., ... & Xia, Y. (2014). Periarticular multimodal drug injection in total knee arthroplasty. *Knee Surgery, Sports Traumatology, Arthroscopy*, 22(8), 1949-1957.
4. Qian, W. W., Weng, X. S., Fei, Q., Li, Y., Zhai, J. L., & Bian, Y. Y. (2010). Application study of periarticular multimodal drug injection in total knee arthroplasty. *Zhonghua Yi Xue Za Zhi*, 90(37), 2593-2596.

5. Kerr, D. R., & Kohan, L. (2008). Local infiltration analgesia: a technique for the control of acute postoperative pain following knee and hip surgery: a case study of 325 patients. *Actaorthopaedica*, 79(2), 174-183.
6. Busch, C. A., Shore, B. J., Bhandari, R., Ganapathy, S., MacDonald, S. J., Bourne, R. B., ...&McCalden, R. W. (2006). Efficacy of periarticular multimodal drug injection in total knee arthroplasty: a randomized trial. *JBJS*, 88(5), 959-963.
7. Parvataneni, H. K., Ranawat, A. S., &Ranawat, C. (2007). The use of local periarticular injections in the management of postoperative pain after total hip and knee replacement: a multimodal approach. *Instructional course lectures*, 56, 125-131.
8. Krenzel, B. A., Cook, C., Martin, G. N., Vail, T. P., Attarian, D. E., &Bolognesi, M. P. (2009). Posterior capsular injections of ropivacaine during total knee arthroplasty: a randomized, double-blind, placebo-controlled study. *The Journal of arthroplasty*, 24(6), 138-143.
9. Vaishya, R., Wani, A. M., & Vijay, V. (2015). Local infiltration analgesia reduces pain and hospital stay after primary TKA: randomized controlled double blind trial. *ActaOrthopBelg*, 81(4), 720-729.
10. Lombardi Jr, A. V., Berend, K. R., Mallory, T. H., Dodds, K. L., & Adams, J. B. (2004). Soft tissue and intra-articular injection of bupivacaine, epinephrine, and morphine has a beneficial effect after total knee arthroplasty. *Clinical Orthopaedics and Related Research*®, 428, 125-130.