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Comparison of effectiveness of intraoperative subperiosteal versus periarticular analgesic cocktail injection for post operative analgesia in patients undergoing total knee arthroplasty

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ABSTRACT

Background: Early postoperative pain management is pivotal in patients undergoing Total knee arthroplasty. The advantage of Local infiltration analgesia is its ability to provide control of pain without interfering with motor strength of the lower extremity, thereby allowing early mobilization of patients. This study compares the effectiveness of local analgesic cocktail injection given through subperiosteal vs. periarticular routes.
Methods: The study included 30 patients admitted for primary total knee arthroplasty. They were grouped into two groups based on different injection sites. Group A included patients who received subperiosteal injection and Group B included patients who received periarticular injection, under spinal anaesthesia. The difference in pain among the two groups, using VAS at 12, 24, 48, and 72 hrs postoperatively, postoperative range of movements, and Functional outcome using IKDC score at the end of 6 months were assessed and compared between the two groups.
Results: The mean VAS scores at 12, 24, 48, and 72 hrs were 0.87±0.35, 1.47±0.52, 1.80±0.41, 1.07±0.46 in subperiosteal group and 2.00±0.53, 2.47±0.52, 2.80±0.56, 1.93±0.59 in periarticular group. The 6 months postoperative IKDC scores were 51.34±0.41 and 51.04±0.61 respectively.
Conclusions: Subperiosteal cocktail injection can significantly reduce the postoperative pain and result in early recovery of range of movements, compared with periarticular cocktail injection in patients undergoing Total knee arthroplasty. But the long-term functional outcomes were comparable among both the groups.

Keywords: Subperiosteal, Periarticular, Arthroplasty, Cocktail, Analgesia

INTRODUCTION

In patients with advanced knee arthritis, Total Knee Arthroplasty (TKA) has been found to be the most successful surgical procedure. But early postoperative pain management is important in reducing the hospital stay, increasing patient satisfaction, and for better rehabilitation. Postoperative pain management reduces the risk of complications such as pneumonia or deep vein thrombosis that may arise due to longer periods of immobilisation and hospital stay.[1] For postoperative analgesia following TKA, epidural analgesia, which combines an opioid with a local anaesthetic, has been a standard protocol. Epidural analgesia is associated with many adverse effects such as urinary retention, hypotension, pruritus, and motor block that may delay mobilization of the patient. Femoral or sciatic nerve blocks are associated with nerve injury, diminished muscle control, bleeding and infection.[2] The

advantage of Local infiltration analgesia is its ability to provide pain control without interfering with motor strength of the lower extremity, thereby allowing early mobilization of patients.[3] Periarticular cocktail injection was first used in Total Knee Arthroplasty by Bianconi et al in 2003.[4] These days cocktail injection is popular in which the drug is injected into the tissues surrounding the knee joint such as muscles, tendons, suprapatellar bursa, and subpatellar bursa. The internal surface of periosteum is rich in unmyelinated nerve fibres and small vessels, which are sensitive to local anaesthetics. Hence local analgesics given under the periosteum can effectively reduce pain in the immediate postoperative period. The patients will have prolonged narcotic-free postoperative period, and also reduced parenteral analgesics postoperatively. Also, it does not require any special technical skill for administration of cocktail. The analgesic cocktail used in our study was a modification of Ranawat orthopaedic centre cocktail (Figure 1).[5] Morphine stimulates all three opiate receptors (μ, δ, κ) in the joint with less adverse systemic effects and steroid prevent local inflammation. Epinephrine reduces blood loss and prolongs the action of local agents by decreasing the absorption by vasoconstriction via its α adrenergic effects. Cefuroxime was given for prevention of postoperative infection and sodium chloride was used as diluent. The purpose of this study was to compare the effectiveness of this analgesic cocktail injection given through subperiosteal vs periarticular routes, by means of VAS, speed of recovery of range of movements and IKDC score.

METHODS

A longitudinal comparative study was conducted in 30 patients admitted for Primary total knee arthroplasty in Pushpagiri institute of medical sciences, Thiruvalla. The study was conducted during the period of February 2021 to March 2023. Patients were selected based on inclusion and exclusion criteria after obtaining informed consent and were randomly grouped into Group A and Group B. Inclusion criteria includes all patients undergoing unilateral primary total knee arthroplasty under spinal anesthesia, and patients willing to take part in the study. Patients with uncontrolled medical comorbidities which may delay or restrict postoperative mobilization (neurologic disorders, respiratory depression), prior surgeries or injuries in same lower limb within past 12 months, allergy to components of the cocktail and cognitive or language disorders were excluded from the study. Group A included 15 patients who received injection beneath the periosteum of the proximal tibia and distal femur (Subperiosteal route) and Group B included 15 patients who received injection into knee joint's muscles, tendons, suprapatellar bursa, and sub-patellar bursa (Periarticular route), before the bone cuts were taken. Preoperative IKDC scores were recorded for each patient. Cocktail composition was based on Ranawat orthopaedic centre cocktail (Figure 1) and included 0.5% Bupivacaine (24 cc), morphine sulphate (8 mg), 1:1000 epinephrine (300 μg), cefuroxime (750 mg) and sodium chloride diluted to a total volume of 100 ml.[5]

Medication	Strength/dose	Amount
First injection		
Bupivacaine	0.5% (200–400 mg)	24 cc
Morphine sulphate	8 mg	0.8 cc
Epinephrine (1:1000)	300 μg	0.3 cc
Methylprednisolone acetate	40 mg	1 cc
Cefuroxime	750 mg	10 cc (reconstituted in normal saline)
Sodium chloride	0.9%	22 cc
Second injection		
Bupivacaine	0.5%	20 cc
Sodium chloride	0.9%	20 cc

Clonidine transdermal patch applied in operating room (100 μg/24 hours). No steroid in diabetics, immunocompromised, elderly (> 80 years) or revisions. Vancomycin used if patient allergic to penicillin/cephalosporins.

Figure 1: Ranawat Orthopaedic centre cocktail.[5]

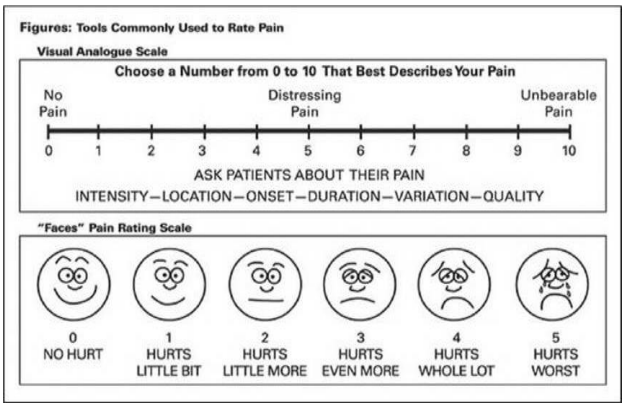

Figure 2: Visual analogue scale.[2]

Methyl prednisolone of Ranawat's cocktail was not included in the present study due to the possible risk of infection.[6,7] All the operations were performed by medial parapatellar arthrotomy approach under spinal anaesthesia and similar IV analgesics were used among the two groups in the postoperative period. Postoperatively serial follow up of pain using visual analogue scale (VAS) (Figure 2) at 12, 24, 48, and 72 hrs, postoperative range of movements at day 2, day 3, and day 4 and functional outcome using IKDC score at 6 months were done and compared among the two groups. Data was be analysed and the categorical data was be presented as frequency and percentage and continuous as descriptive (mean, SD, median and range). The median values of outcome variable (pain using VAS) between the groups were tested for statistical significance using Mann-Whitney U test. Range of motion and Length of hospital stay was be compared using Mann-Whitney U test. A p value of less than 0.05 was be considered as statistically significant. The data was analysed using SPSS software version 26.0

RESULTS

The participants were in the age group of 54-76 years. The mean age of the population was 64±6.3 years (Table 1). The majority of our study population were females (83.3%) (Figure 3).

Out of the total 30, 9 study participants, i.e., 30% were hypertensive and 3 out of 30, that is 10% were known cases of diabetes mellitus. It was found that 2 of the total 30 study participants (6.7%) were having both diabetes and hypertension. Another 2 of them, that is 6.7% were found to be suffering from diabetes, hypertension and dyslipidemia together (Table 2).

Table 1: Age of study participants.

Variable	N	Minimum	Maximum	Mean	SD
Age	30	54	76	64.27	6.291

Table 2: Comorbidities of study participants.

Comorbidity	N	%
Hypertension (HTN)	9	30.0
Diabetes Mellitus (DM)	3	10.0
CAD, OAD, HTN, DLP, Hypothyroidism	1	3.3
DM, DLP	1	3.3
DM, HTN	2	6.7
DM, HTN, Hypothyroidism	1	3.3
DM, HTN, DLP	2	6.7
DM, HTN, Hypothyroidism	1	3.3
HTN, BPH	1	3.3
HTN, DLP	1	3.3
HTN, DLP, Hypothyroidism	1	3.3
HTN, DM	1	3.3
HTN, DM, Hypothyroidism, OAD	1	3.3
HTN, Hypothyroidism	1	3.3
HTN, Hypothyroidism, DLP	1	3.3
HTN, OAD	1	3.3
Hypothyroidism, DLP	1	3.3
OAD	1	3.3
Total	30	100.0

Table 3: Comparison of VAS at different time intervals.

Group Statistics					
Route		**N**	**Mean**	**SD**	**P value**
VAS at 12 hrs	Periarticular	15	2.0000	0.53452	0.001
	Subperiosteal	15	0.8667	0.35187	
24 hrs	Periarticular	15	2.4667	0.51640	0.001
	Subperiosteal	15	1.4667	0.51640	
48 hrs	Periarticular	15	2.8000	0.56061	0.001
	Subperiosteal	15	1.8000	0.41404	
72 hrs	Periarticular	15	1.9333	0.59362	0.001
	Subperiosteal	15	1.0667	0.45774	

Table 4: Comparison of IKDC Score among the different routes.

Group statistics					
Routes		**N**	**Mean**	**SD**	**SEM**
IKDC Score preoperatively	Periarticular	15	35.53333	2.3924484	0.901
	Subperiosteal	15	35.63333	1.9263832	
IKDC Score 6 months postoperatively	Periarticular	15	51.040	0.6139	0.12
	Subperiosteal	15	51.340	0.4120	

Table 5: Comparison of range of movements among different routes.

Routes		N	Mean	SD	P value
Flexion-Pre-op	Periarticular	15	100.00	10.690	0.463
	Subperiosteal	15	102.67	8.837	
Flexion-day 2	Periarticular	15	76.67	8.997	0.001
	Subperiosteal	15	90.00	5.345	
Flexion-day 3	Periarticular	15	82.00	8.619	0.001
	Subperiosteal	15	98.67	6.399	
Flexion-day 4	Periarticular	15	87.33	9.612	0.001
	Subperiosteal	15	102.67	7.037	
Extension LAG-Pre-op	Periarticular	15	5.00	6.547	0.667
	Subperiosteal	15	4.00	6.036	
Extension LAG-day 2	Periarticular	15	11.33	5.815	0.001
	Subperiosteal	15	3.33	4.499	
Extension LAG-day 3	Periarticular	15	8.67	6.114	0.001
	Subperiosteal	15	1.00	2.803	
Extension LAG-day 4	Periarticular	15	6.67	4.880	0.001
	Subperiosteal	15	0.00	0.000	

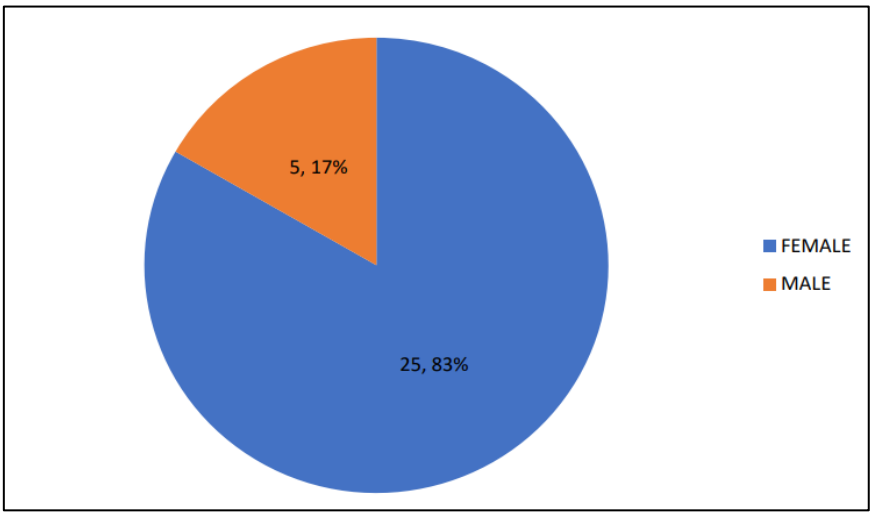

Figure 3: Gender distribution of patients.

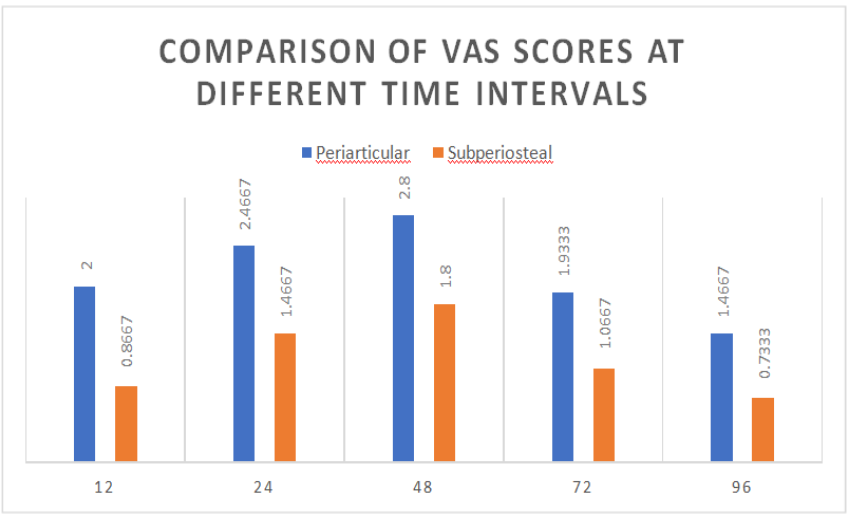

Figure 4: Comparison of VAS at different time intervals.

The mean postoperative VAS at 12, 24, 48 and 72 hrs were 0.866±0.351, 1.466±0.516, 1.800±0.414, 1.066±0.45 in subperiosteal group and 2.00±0.534, 2.466±0.516, 2.800±0.560, 1.933±0.593 among the periarticular group (Table 3, Figure 4).

The mean postoperative IKDC scores were 51.340±0.41 in subperiosteal group and 51.040±0.61 in periarticular group (Table 4). Range of movements (Table 5) of these patients are given below.

DISCUSSION

This comparative study was done among 30 patients who underwent total knee arthroplasty in a tertiary care hospital in South Kerala with the objectives of comparing the effect of subperiosteal and periarticular cocktail injection, in control of postoperative pain and on postoperative functional outcome. There were 15 patients included in each group. In the present study, the mean age of the study participants was found to be 64.3±6.3 years. Majority of them were females (83%). It was found that 30% of the study population were hypertensive.

The visual analogue scale (VAS) for pain were significantly higher among the periarticular injection group compared to the subperiosteal group at all intervals of time. This result had a statistically significant association at 12, 24, 48, and 72 hours postoperatively. Preoperatively there wasn't any significant difference in IKDC scores between periarticular and subperiosteal routes of cocktail injection. Post operatively also, there wasn't any significant difference in IKDC score between both the groups of cocktail administration.

On postoperative days 2, 3 and 4, there was significant difference between the groups in both flexion and extension as indicated by the p value, and the speed of recovery of range of movements was better among the subperosteal group. The results of present study are in agreement with those of a non-randomized trial by Wang et al in 2020.[2] Their study had revealed that subperiosteal cocktail injection can significantly reduce pain and blood loss compared with periarticular cocktail injection after TKR. As per their study, on the first postoperative day, the mean VAS was comparatively lower in the subperiosteal group. The values were 0.98±0.27 in periarticular group and 0.86±0.60 in subperiosteal group. The 12hour postoperative VAS in present study also showed similar trends with the values being 2±0.53 and 0.87±0.35 respectively.

The present study also had assessed the postoperative pain on various times, that is 12 hours, 24 hours, 48 hours, and 72 hours after the procedure. The subperiosteal injection group showed low values of VAS till first 24 hrs postoperatively, but a gradual weaning off of the analgesic effect was observed during the next 24 hrs. The periarticular group also had shown a similar pattern, but the mean pain scores were always higher than those in the subperiosteal injection group. As Wang et al had not taken the pain scores at all the 4-time intervals as in present study, an elaborate comparison on this will not be possible. There is difference in the composition of the cocktail used in the present study and that by Wang et al. Their cocktail consisted of tranexamic acid, epinephrine, methyl prednisolone, and ropivacaine, diluted to a total volume of 100 ml with normal saline. In the present study, the cocktail used contained bupivacaine, morphine sulphate, epinephrine (1:1000), cefuroxime and sodium chloride diluted to a total volume of 100 ml.[5] There are many proposed reasons why a subperiosteal cocktail injection would result in a better pain control following a TKA procedure. There are a lot of nerves and blood vessels present in the periosteum and bone marrow. Dense fibrous membrane that is found to be covering the periosteal surface may be interfering with the effects of cocktail injections that are given periarticularly.

The subperiosteal route will help bypassing this interference and provide a better analgesic and hemostatic efforts following the procedure. This effect might be as a result of the direct action of the cocktail in the subperiosteal nerves. Many studies have revealed the effectiveness of local infiltration analgesia (LIA) in postoperative pain management in TKA. Improved pain scores and better satisfaction levels were reported with LIA by patients after TKA compared to the placebo group.[8] In a meta-analysis of 10 studies by Zhang LK et al showed that LIA was as effective as a femoral nerve block.[9] Wall et al in a randomized controlled trial, found out that the LIA group were consuming less amount of morphine for pain relief after TKA, compared to the group with femoral nerve block.[10] Pain relief superior to that of peripheral nerve block and epidural analgesia has been reported by Hu et al among those with local infiltration.[11] These results are consistent with the findings of present study with respect to the improvements in pain score with the local infiltration of cocktails, though these previous studies had not compared the effectiveness of different routes of local infiltration, that is subpeirosteal or periarticular routes. The mean VAS in periarticular injection group 12 hours postoperatively in the present study is much lower when compared to the mean VAS 6 hours postoperatively in Altay et al study.[12] They had done a prospective randomized double blinded comparative study among three groups. The groups were those with no injection, with periarticular injection alone and those with combined periarticular and incisional injections. The subsperiosteal cocktail injection was not considered in their study.

Similarly, Seangleulur et al in a systematic review and meta-analysis of 38 randomized control trials, had shown that the group with intraoperative periarticular injection of local analgesics had lower pain scores, opioid consumption and postoperative nausea and vomiting, higher range of motion at 24 hrs and shorter length of hospital stay when compared to the no injection or placebo group.[13] In present study, the range of movements were

compared in both subperiosteal and periarticular injection groups. It was found that the extension lag was found to be gradually decreasing in both the groups with better recovery in subperiosteal group. Vijayaraja et al in their prospective cohort study at Sri Ramachandra medical centre in 40 patients undergoing total knee arthroplasty also had shown a similar result with respect to the improvement in pain in those receiving a periarticular cocktail injection.[14] The study had concluded that intraoperative periarticular injection with multimodal drugs can significantly reduce the pain and limits requirements for patient-controlled analgesia with no apparent risks, following total knee arthroplasty. When considering the improvements in the range of flexion, the present study findings go in agreement with that of another systematic review and meta-analysis of randomized control trials by Li et al in 2018.[15] Though their aim was to evaluate the efficacy and safety of local infiltration anaesthesia versus epidural analgesia (EPA) for postoperative pain control in total knee arthroplasty, and had not taken into account the subperiosteal route, the study had shown that LIA has equivalent efficacy as EPA for pain control after TKA and shows an increase of the range of motion.

A reduction of the occurrence of nausea and length of hospital stay were also shown as the advantages of local infiltration analgesia. But, as the present study had not studied these aspects like the adverse effects and duration of hospital stay, it cannot be compared. In Nair et al prospective, double blinded, placebo-controlled trial also, similar results were obtained with respect to the periarticular injection of cocktail.[16] The trial was designed such that the patients received an intraoperative periarticular cocktail injection in the right knee (intervention) and normal saline in the left knee (control).

The cocktail injected knee had significantly less pain when compared with the control knee in the first 48 hours and significantly shorter period to achieve 90^0 of knee flexion. This point towards the effective pain control with locally injected cocktails, though the generalizability of their study findings is limited as knees of the same patients were taken as controls. All the operations were performed by medial parapatellar arthrotomy approach in present study. We could only include a small number of cases and there was a lack of long-term follow-up because this study was a time limited study. Also, if we had included a blank control group as well, the comparison of effectiveness of the two cocktail injections could have been better explained. The analysis of the molecular mechanisms underlying the effects of these cocktail injections is also a necessity for the better explanation and understanding of the topic. This opens up scope for future research on the topic.

CONCLUSION

This study compared the effectiveness of intraoperative local analgesic cocktail injection given through subperiosteal and periarticular routes for analgesia in total knee arthroplasty. From our study we found that the subperiosteal route is superior to periarticular route for analgesic cocktail injection and it resulted in better pain control than the periarticular route. The local analgesic injection helps in early mobilization of the patients, resulted in better speed of recovery of range of movements and helps in preventing the complications associated with prolonged periods of immobilization. There is no significant difference in the 6 months postoperative functional score among the two study groups. Further investigation with different cocktail compositions, including steroids and a larger study population are required to establish the superiority of any method.

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