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Original Research

Effect of Intra-operative multimodal cocktail on post-operative pain after Total Knee Arthroplasty

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ABSTRACT:
Background: Total Knee Arthroplasty is a common and successful surgery to relieve the pain in severe Osteoarthritis of knee. Post-operative pain after the surgery is an issue of concern as it influences the post operative recovery and rehabilitation. Several pain management strategies have been used in the past that include peripheral nerve blockade, patient-controlled analgesia and local infiltration analgesia, and oral opioid/nonopioid medications. Our study aimed at studying the effect of intra operative administration of multimodal cocktail on post operative pain after total knee arthroplasty. **Methods**: Periarticular injection of the multimodal cocktail consisting of cefuroxime, bupivacaine, ketorolac, adrenaline and normal saline was injected intraoperatively to the right knee (study knee) and same volume (40 ml) normal saline was injected in left knee (Control Knee) of the same patient undergoing bilateral total knee replacement. The comparison of mean VAS Scores of the patients for both the knees at 6, 12, 24 48, 72 and 96 hours was noted. Mean time taken to do active straight leg raise(ASLR) and active 90˚ flexion was also compared for both the knees. **Results:** Statistically significant decrease in pain score was observed in right knee (cocktail injected) as compared to the left knee (normal saline injected) during 6, 12, 24, 48 and 72 hours (p value < 0.05). Mean time taken to do active straight leg raise (ASLR) and to do active knee flexion to 90˚ of right (study) knee after surgery was significantly less as compared to the left (control) knee. **Conclusion:** The present observational study showed that intra-operative injection of multimodal cocktail significantly reduces post-operative pain in patients of total knee arthroplasty and promoted early recovery and rehabilitation.
Keywords: Total knee Arthroplasty, multimodal cocktail, pain, VAS Score, recovery, range of motion.

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INTRODUCTION

Total Knee Arthroplasty is most successful surgery to decrease the pain and improve the quality of life in patients of severe osteoarthritis of knee. The most important issues of perceived importance concerning patients is immediate postsurgical pain, pain after discharge from the hospital, chances that surgery would not alleviate pain, pain during surgery and various similar issues which often results in delays on the day of surgery or cancellations(1,2). Post-operative pain following TKA has been recognized as an important issue and a potential cause of delayed surgical recovery. Unrelieved postoperative pain has detrimental effects besides patients' discomfort following surgery (3,4). Various modalities commonly used for post-operative pain management after TKA include intravenous patient controlled analgesia (IV-PCA), epidural analgesia, femoral nerve blocks (peripheral nerve block), and local infiltration analgesia [5].Although Epidural analgesia is very commonly used for post-operative pain relief but

can result in complications like post-operative headache, hypotension and spinal infection(5-7) . Systemic opioids like morphine or fentanyl can cause headache, urinary retention, respiratory depression, nausea, vomiting, constipation and orthostatic hypotension [5]. Peripheral nerve block provides analgesic effect comparable to epidural analgesia but has lesser side effects than systemic opioids or epidural analgesia [6, 7]. However Peripheral nerve block can result in quadriceps muscle weakness which may interfere with early mobilization after TKA [8,9] . Therefore, good post-operative pain relief which facilitates rehabilitation is the need of the hour for better patient and surgeon satisfaction and a multimodal approach is preferred nowadays. Local infiltrative analgesia with a multimodal cocktail which when combined with an oral multimodal pain regimen, has led to increased patient satisfaction and a shorter length of hospital stay. Moreover, local infiltraton analgesia is easy to administer, does not require any special skills for administration, cost effective and has good efficacy. [10-13].

OBJECTIVE:

The objective of this study was to evaluate the effect of multimodal cocktail consisting of bupivacaine, Ketorlac, adrenaline, cefuroxime and normal saline on post operative pain in patients of bilateral Total Knee Arthroplasty (TKA). The time taken to achieve active straight leg raise and 90˚active flexion post-operatively was also studied.

MATERIAL AND METHODS:

In this study, 60 patients of bilateral osteoarthritis knee admitted in Orthopaedics Department of Adesh Institute of Medical Sciences and Research (AIMSR), Bathinda, Punjab from October 2019 to March 2020 for uncomplicated primary bilateral TKA were selected. Informed consent from the patient was taken. The protocol of our observational study was approved by the Institutional ethical committee of our Institute. Periarticular injection of the multimodal cocktail consisting of 1.5 gram cefuroxime mixed in 20 ml normal saline, 17.5 ml of bupivacaine (bupivacaine hydrochloride 0.5%), 2 ml inj. Ketorlac 30 mg, 0.5 ml adrenaline was injected intraoperatively to the right knee(study knee).. Same volume (40 ml) normal saline was injected in left knee (Control Knee). The right and left knee of the same patient undergoing the total knee Arthroplasty surgery were considered as study and control knee to avoid the confounding factors like variation of patients' toleration to pain and effects of spinal anaesthesia. All the patients were made to understand the 10 point VAS Score. All the surgeries were done by the same surgical team under spinal anaesthesia.

Inclusion Criteria: - All patients of either sex with grade III or IV osteoarthritis knees (Kellgren and Lawrence system (14) scheduled for a primary uncomplicated bilateral TKA are included.

Exclusion Criteria: - Patients with following conditions are excluded: Active connective tissue or inflammatory diseases like SLE and Rheumatoid Arthritis, patients having dearranged renal or liver function, history of sensitivity or allergy to medications used in the study, history of Coagulopathies or other hematological/neurological disorders, patients in whom spinal anaesthesia could not be given.

Procedure:

All demographic data and associated conditions were noted pre-operatively. All patients selected for study were operated by single surgical team under spinal anaesthesia. Tourniquet was inflated to pressure 320mm of Hg before giving skin incision. Midline vertical skin incision was used. Arthrotomy was done through medial para-patellar approach. Standard bony cuts and releases were made. Trialing with trial implants was done to assess sizes of actual implant components. In right knee cocktail was injected before cemented implantation at 8 points (4-5 ml at each site) i.e. supra patellar pouch and synovium around quadriceps tendon, infra patellar fat, medial meniscus capsular attachment, lateral meniscus capsular attachment, postero-medial capsule, postero-lateral capsule, medial retinaculum and lateral retinaculum. Same volume of normal saline was injected in left knee. Tourniquet was released after putting implant. Meticulous haemostasis was achieved before closing wound. Wound was stitched in layers. No drain was used. Standard Post operative pain management protocol was followed. Systemic Analgesia during the post-operative period consisted of intravenous injection of diclofenac (75 mg) and injection ondansteron 4mg for the first day followed by tablet piroxicam 30 mg and paracetamol 325 mg for the next 10 days. Rescue analgesia (Tramadol 50 mg i.v.) was used for patients complaining of unbearable pain (VAS $\geq$5). VAS score was noted for both knees at 6 hours, 12 hours, 24 hours, 48 hours, 72 hours and 96 hours. Time taken for active straight leg raise (ASLR) and to achieve 90 degree active flexion was noted for both the knees.

Data Analysis: Unpaired t test using the OpenEpi software was used for analysis of data. For all comparisons 5% significance level was adopted. Mean and standard deviations were calculated for VAS Score, time taken for ASLR and for 90˚knee flexion.

RESULTS:

Mean age of the patient was 59.48±7.32 years. Male to female ratio was 26:34. Deformity (varus/valgus) right (study) knee was 16.52±1.29 and left (control) knee was 17.13±1.36. Mean pre operative flexion right (study) knee was 111.56±1.25 and left (control) knee was 112.09±1.56. (Table I).

The comparison of mean VAS Scores of the patients for both the knees at 6, 12, 24 48, 72 and 96 hours have been tabulated in Table II. Statistically significant decrease in pain score was observed in right knee (cocktail injected) as compared to the left knee (normal saline injected) during 6, 12, 24, 48 and 72 hours (p value < 0.05). However, the difference in mean pain scores between both the knees became insignificant at 96 hours (p>0.05).

Mean time taken to do active straight leg raise (ASLR) of right (study) knee after surgery was 20.35±2.33 (hours) and that of left (control) knee after surgery was 22.24±2.51 (hours). The difference between two knees was statistically significant (p =0.00003902).Mean time taken to do active knee flexion to 90˚ of right (study) knee after surgery was 51.35±7.68 hours and that of left (control) knee after surgery was 58.09±9.83 hours. The difference between two knees was statistically significant (p=0.00005512). (Table III)

DISCUSSION:

The results of our study are consistent with studies conducted by various other authors. In study conducted by Busch CA et al, it was concluded that intraoperative periarticular injection with multimodal drugs can significantly reduce the requirements for patient controlled analgesia and improve patient satisfaction with no increased risks following total knee arthroplasty (13). Sreedharan Nair V et al observed that the cocktail injected knee had significantly less pain when compared with the control knee during the first 48 hours and significantly shorter period to achieve 90° of knee flexion and the use of intraoperative periarticular cocktail injection significantly reduces early postoperative pain and provides better early knee motion(15). Mullaji et al used bupivacaine, fentanyl, methylprednisolone and cefuroxime in their intra articular cocktail and found that in comparison to the non-infiltrated side, the infiltrated knee showed significantly lower pain scores, significantly greater active flexion up to 4 weeks, and superior quadriceps recovery up to 2 weeks after surgery(16). Badner et al used combination of bupivacaine and epinephrine and concluded that intra-articular injection of these medications decreases the need for narcotics and increases the range of motion after an elective knee replacement (17).

Table I: Demographic and clinical parameters of patients

Characteristics		
Age	59.48±7.32 (years)	
Sex (Male:Female)	26:34	
Deformity (varus/valgus)	16.52±1.29 **(**Right knee)	17.13±1.36 (Left knee)
Pre operative flexion	111.56±1.25 (Right knee)	112.09±1.56 (Left knee)

Table II: Comparison of Mean VAS Score in two groups

	VAS Score				
	Control		**Study**		**P Value**
Post operative time	**Mean**	**SD**	**Mean**	**SD**	
6 hours	3.63	1.83	1.84	1.22	<0.000001*
12 hours	3.03	1.31	1.76	1.42	=0.000001141*
24 hours	2.59	1.41	1.67	1.01	=0.00007374*
48 hours	2.21	1.11	1.41	0.98	=0.00005516*
72 hours	1.68	1.05	1.26	1.06	=0.03121*
96 hours	1.12	0.86	1.01	0.75	0.4567**

***p- Value is significant **p-Value is insignificant**

Table III: Post Operative time for Active Straight Leg Raise (ASLR) and 90˚flexion

	Time in Hours (Mean ±SD)		
	Left Knee (control)	**Right Knee (Study)**	**P value**
ASLR	22.24±2.51	20.35±2.33	0.00003902
90˚Flexion	58.09±9.83	51.35±7.68	0.00005512

Anderson et al (18) used subcutaneous ropivacaine and observed that intraoperative subcutaneous infiltration with ropivacaine in bilateral total knee arthroplasty effectively reduces early post-operative pain, while a post-operative subcutaneous bolus administration through a multiholed catheter did not show improved analgesia compared with the administration of saline. Vaishya et al (19) used bupivacaine, adrenaline, morphine, ketorlac and gentamycin. According to the meta-analysis conducted by Zhang Z and Shen B, the efficacy of local infiltration analgesia in improving short-term postoperative pain relief and reducing total narcotic consumption has been confirmed but no consensus has been reached regarding the best infiltration sites, volumes, or timings of LIA.(20) Results of study by Cheng KY et al demonstrated that peri-articular injection provides superior analgesic benefit to intra-articular injection in patients of total Knee Arthroplasty during first 48 hours while Range of Motion was continuously better in peri-articular group than intra-articular group during the first 3 days after the surgery. In addition, it took less time for Peri-articular group to perform straight leg raise postoperatively (21).

CONCLUSION:

The results of our observational study show that intra-operative injection of multimodal cocktail significantly reduces post-operative pain in patients of total knee Arthroplasty as compared to the placebo group. It also helps to achieve the range of motion earlier and therefore promotes early recovery.

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