

## Comparative evaluation of periarticular infiltration of two cocktail regimens for analgesia in post-operative patients of total knee replacement



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### ARTICLE INFO

#### Article history:

Received 30 April 2018

Received in revised form

28 October 2018

Accepted 9 November 2018

Available online 19 November 2018

#### Keywords:

Periarticular  
Multimodal approach  
Perioperative analgesia  
Corticosteroids  
VAS score

### ABSTRACT

**Purpose:** To compare the efficacy of two periarticular cocktail regimens for analgesia in postoperative patients of total knee replacement.

**Method:** This is a Randomized Control study done over the duration of 1.5 years. Twenty-five knees of either gender were selected with inclusion criteria (All osteoarthritis patients planned for TKA) and exclusion criteria (Inflammatory arthritis, patients allergic to local anaesthetic e.g. Ropivacaine, bupivacaine, known cardiac disorder patient having AV block, arrhythmia) & divided into 2 groups.

Group A was given a cocktail of Ropivacaine, adrenaline, clonidine & cefuroxime.

Group B was given a cocktail of bupivacaine, fentanyl, methylprednisolone & cefuroxime. The preoperative pain of the patient was assessed using VAS score. Combined spinal and epidural anaesthesia was given using 0.5% 2 ml of bupivacaine heavy in all patients. After taking bone cuts & before the placement of the implant, cocktail of the drug was infiltrated using sterile technique into 9 specific sites. The amount of drug infiltrated was calculated according to the weight of the patient.

The patients were assessed on: Pain relief postoperatively at specific duration using VAS score. The amount & frequency of epidural top-ups required. Knee ROM, Quadriceps strength, Extensor lag & Knee society score were assessed.

**Results:** Out of the total 25 knees included in the study, 12 belonged to Group A and 13 belonged to Group B. It was observed that 4 (33%) out of 12 Group A patient needed injection tramadol for 2–3 days and fentanyl patch 25mcg. In Group B, one (8%) out of 13 patients required injection tramadol and fentanyl dermal patch for 2–3 days. The difference in additionally required analgesic between patients of the two groups is statistically significant.

**VAS Score:** The VAS score of Group B was statistically lower than Group A patients till first 24 h postoperatively.

The extension lag was lower in group B compared to group A at 24 h after the surgery and up to 5 days. Overall after 6 weeks of follow-up, the extensor lag between the groups was not statistically significant. Average KSS in group A was 79.58 and in the group, B was 83.99 and the difference in KSS between patients of the two groups was statistically significant.

**Conclusion:** Both the cocktail regimens are effective in pain control postoperatively. The relief in pain with regimen B containing bupivacaine, fentanyl, methylprednisolone and cefuroxime was more striking in the first 24 h. By the end of two days, both regimens were found to be equally effective.

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## 1. Introduction

Total knee arthroplasty (TKA) is one of the very common surgeries performed now a day. It is associated with postoperative pain. Severe postoperative pain after TKA can add not only to patient suffering but also negatively affect postoperative recovery. If the severe postoperative pain is managed inadequately under these circumstances, the surgery-induced responses can be exacerbated, posing a serious danger to patients. Specifically, severe postoperative pain has been associated with serious complications including ischemic cardiac events and myocardial insufficiency that result from increased stress on the cardiovascular system.<sup>1</sup> In addition, immobilization caused by pain may increase the risk of decreased pulmonary function, gastrointestinal complications, such as ileus, and thrombus formation that are related to surgical stress.<sup>2,3</sup> An increase in stress hormone and sleep disorder due to severe pain can worsen the already decreased immunity, which leads to higher risk of infection. In particular, this may affect the mental status of elderly patients, causing delirium or anxiety disorder.<sup>4</sup>

LIA (Local Infiltration Analgesia) is a relatively simple technique that has shown early promise as a method of pain relief after TKA and it is simple, practical, safe, and effective for pain management after knee and hip surgery. Intraoperative periarticular multimodal drug injection using opioids and long-acting local anaesthetic agents is effective for postoperative pain management. Periarticular injection (PAI) significantly reduces pain without any complications, such as infection and produces additional pain-relieving effects when incorporated into multimodal pain control protocols.<sup>5,6</sup> However, the proper dosage and composition of injection cocktail and injection techniques have not been established and there is disagreement over its influence on reduced opioid consumption. Its efficacy is limited in time and patients should be informed on the occurrence of rebound pain after half-life of the treatment agents. The most commonly used drugs for periarticular injections include local anaesthetics, such as bupivacaine and ropivacaine, morphine, ketorolac, clonidine, and steroids.

In this study, we have compared the efficacy of two periarticular cocktail regimens for postoperative analgesia in patients with TKA.

## 2. Materials and methods

This is a Randomized Control study done over the duration of 1.5 years in our institute.

Twenty-five knees of either gender were selected based on the criteria given below.

### 2.1. Inclusion criteria

1. All osteoarthritis grade 3 or 4 patients who failed conservative treatment for adequate duration and requiring TKA.
2. More than 60 years of age of either gender.
3. Patients who are fit for spinal/epidural anaesthesia.

### 2.2. Exclusion criteria

1. Inflammatory arthritis
2. Patients allergic to local anaesthetic (for e.g. Ropivacaine, bupivacaine)
3. Known cardiac disorder patient having AV block, arrhythmia.

### 2.3. Method

The study included 25 knees which were divided randomly into 2 groups based on a computerized lottery system.

The two groups were demographically matched including the age of the patients, grade of osteoarthritis, preoperative VAS score and Range of motion of the affected knee.

Group A was given a cocktail of Ropivacaine, adrenaline, clonidine & cefuroxime (Fig. 1(a and b)).

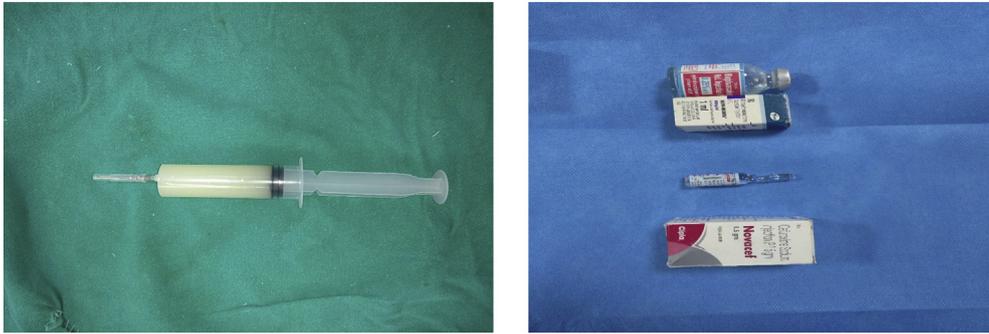
Group B was given a cocktail of Bupivacaine, fentanyl, methylprednisolone & cefuroxime (Fig. 2(a and b)).

The preoperative pain of the patient was assessed using VAS score and recorded. An epidural catheter was placed and combined spinal and epidural anaesthesia was given using 0.5% 2 ml of bupivacaine heavy in all patients. In perioperative period all patients were given tablet Gabapentine 300 mg HS. All the surgeries were done by a single surgeon using similar surgical technique in all the patients. The implant make and rehabilitation protocol was similar in all the patients.

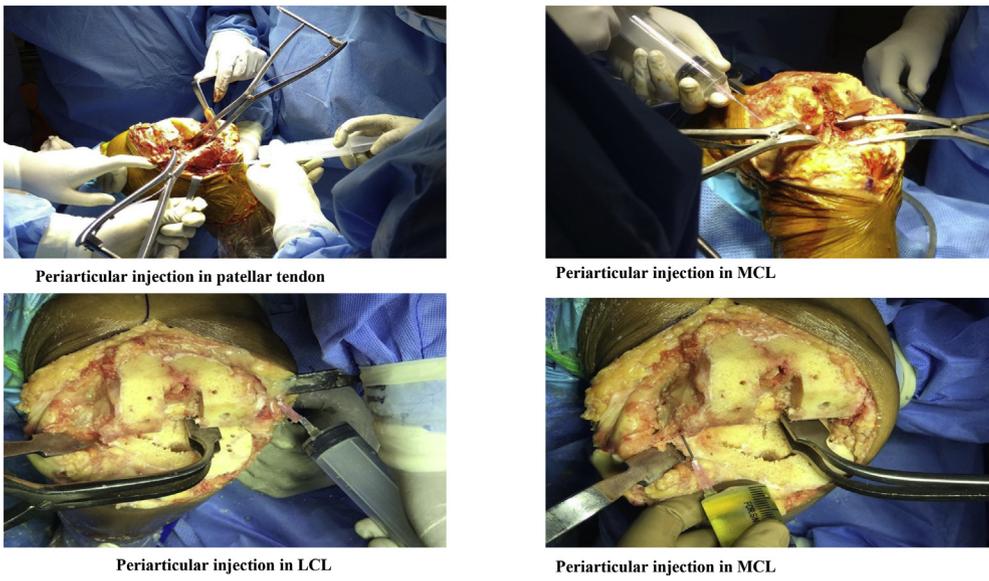
After taking appropriate femur and tibia bone cuts, a lamina spreader was introduced to visualize the surrounding soft tissues. Before the placement of implant, cocktail of drug was infiltrated using sterile technique into 9 specific sites: ACL femoral attachment, PCL attachment, posteromedial capsule along the residual posterior meniscal rim and posterior capsule attachment and into the residual middle and anterior residual rim of medial meniscus, postero-lateral capsule along the residual posterior rim of the lateral meniscus and posterior capsule attachment and in middle and anterior portion of the lateral meniscus according to the study group of the patient (Figs. 3 and 4).



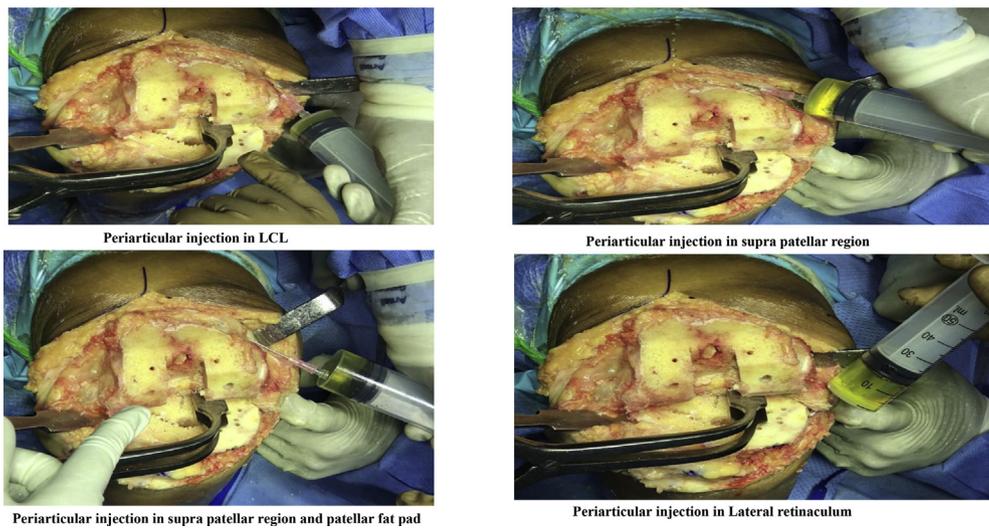
**Fig. 1.** (a,b)Photos showing periarticular injection and drugs Regimen A (Ropivacaine, clonidine, adrenaline and cefuroxime).



**Fig. 2.** (a,b) Photos showing periarticular injection and drugs Regimen B (Bupivacaine, methylprednisolone, fentanyl and cefuroxime).



**Fig. 3.** (a,b,c,d) Photos showing infiltration of periarticular injections.



**Fig. 4.** (a,b,c,d). Photos depicting injection sites in suprapatellar region and lateral aspect of the knee.

The amount of drug infiltrated was calculated according to the weight of the patient.

REGIMEN A	Weight <70 kg	Weight >70 kg
Ropivacaine (0.75%)	300 mg (40 cc)	400 mg (53.3 cc)
Adrenaline(1:1000)	0.3 cc	0.3 cc
Clonidine(500µg/ml)	0.6 cc	0.8 cc
Cefuroxime (750 mg)	750 mg	750 mg
Normal Saline	4.1 cc	5.6 cc
Total volume	45 cc	60 cc
REGIMEN B	Weight <70 kg	Weight >70 kg
Bupivacaine (0.25%)	100 mg (40 cc)	133 mg (53.3 cc)
Methyl prednisolone acetate (40 mg/ml)	40 mg (1 cc)	40 mg (1 cc)
Fentanyl (50µg/ml)	100µg (2 cc)	100µg (2 cc)
Cefuroxime (750 mg)	750 mg	750 mg
Normal saline	2 cc	3.7 cc
Total volume	45 cc	60 cc

The patients were assessed on:

1. Pain relief postoperatively at the immediate postoperative period, at 3 h, at 6 h, at 12 h, at 24 h of the surgery, alternate day, weekly up to 3 weeks, day of discharge & at 6 weeks using VAS scoring.
2. The amount & frequency of epidural top-ups required for adequate analgesia was compared.
3. Knee ROM was assessed by goniometer at 24 h after the surgery, alternate day till the day of discharge, at 3 weeks & at 6 weeks.
4. Quadriceps strength was assessed by MRC grading at 24 h after the surgery, alternate day till the day of discharge, at 3 weeks & at 6 weeks.
5. Extensor lag was assessed by goniometer at 24 h after the surgery, alternate day till the day of discharge, at 3 weeks & at 6 weeks.
6. Knee society score was assessed at 6 weeks.

### 3. Results

Out of the total 25 knees included in the study, 12 belonged to Group A and 13 belonged to Group B. The difference in the distribution of gender and age between the two groups was not statistically significant as per the Chi-square test (P value 0.673).

**Post-operative additional analgesic requirement:** Injection tramadol, Fentanyl dermal patch, Buprenorphine dermal patch and bupivacaine top up were kept for rescue analgesia. Injection tramadol and fentanyl patch 25mcg for 2 days was used as first line of additional analgesic in patients with VAS Score more than or equal to 5 on postoperative day 1. Buprenorphine dermal patch and bupivacaine top up were considered as second line of additional analgesic, if VAS score is still more than or equal to 5 after administering injection tramadol and fentanyl patch for 1 day. It was observed that 4 (33%) out of 12 Group A patient needed injection tramadol and fentanyl patch 25mcg for 2 days. In Group B, one (8%) out of 13 patients required injection tramadol and fentanyl dermal patch 25mcg for 2 days. No patients in both groups required additional buprenorphine dermal patch and bupivacaine top up. The difference in additionally required analgesic between patients of the two groups is statistically significant as per the Chi-Square Tests. (P value 0.036).

**VAS Score:** The average pre-operative VAS score was noted in both group. The score was lower in group A (1.9) than group B (2.3). The difference pre-operative VAS between the patients of the two groups is statistically not significant.

At 0 h: Average VAS score in group B (2.84) was lower as

compared to group A (3.5). The difference in VAS score between patients of the two groups was statistically significant. (p-value 0.037).

At 3 h: Average VAS score in group B (2.6) was lower as compared to group A (3.6). The difference in VAS score between patients of the two groups was statistically significant. (P value 0.028).

At 6 h: Average VAS score in group B (2.4) was lower as compared to group A (3.5). The difference in VAS score between patients of the two groups was statistically significant. (P value 0.018).

At 12 h: Average VAS score in group B (2.1) was lower as compared to group A (2.9). The difference in VAS score between patients of the two groups was statistically significant. (P value 0.04).

At 24 h: Average VAS score in group B (1.9) was lower as compared to group A (2.8). The difference in VAS score between patients of the two groups is statistically significant. (P value 0.035).

After 24 h of surgery, VAS score between the patients of both groups was almost equal and statistically not significant.

Average VAS score after 24 h of surgery between the patients of both groups.

GROUP	Day 3	Day 5	Day 7	Day 9	Day 11	Day 13	3 weeks	6 weeks
A	2.2	1.6	1.5	1.16	1	1	1	1
B	2	1.8	1.3	1.2	1	1	1	0.8

After 24 h of surgery, VAS score between the patients of both groups was almost equal and statistically not significant.

In group A, flexion ranged from 66.2° to 103.7° and in group B flexion ranged from 72° to 105° in the post-operative period.

Mean flexion in group A after 24 h of surgery was 66.2° and in the group, B was 72°.

At 3 days, the mean flexion 78.2° and 77.5°, at 5 days 83° in both group, at 7 days 84.3° and 88°, at 9 days 88.3°, at 11 days 90° and 93.8°, at 13 days 90° and 93.8°, at 3 weeks 97° and 97.3°, at 6 weeks 103° and 105° in respective group A and B.

The extension lag was lower in group B compared to group A at 24 h after the surgery and up to 5 days. After which, the average extensor lag was not much different. Overall after 6 weeks of follow-up the extensor lag between the groups was not statistically significant (p-value 0.355).

Average KSS in group A was 79.58 and in the group, B was 83.99 and the difference in KSS between patients of the two groups was statistically significant using Mann Whitney test (p-value 0.006).

The quadriceps strength after 24 h surgery are almost equal (3+) in both group up to 3 days of post-operative period. After 3 days of surgery, quadriceps strength were better in group B patient up to 10 days after the surgery. After 2 weeks, quadriceps strength (4+) were almost equal in both group. The quadriceps strength between the groups was not statistically significant as per the Chi square test.

**Other Complications:** In group A, one of the patients had persistent low blood pressure postoperatively. It was treated with intravenous fluid.

In group B, one of the patients complains of suture site soakage at post-operative day 5. His culture was sterile and wound healed normally.

### 4. Discussion

The usefulness of a multimodal approach to pain control after TKA has been reported.<sup>7</sup> The concepts of pre-emptive analgesia and

multimodal pain protocols are commonly used. Periarticular injection of a combination of agents is the most important component of the multimodal approach<sup>8</sup> and also a key component.<sup>9,10</sup>

We found that the level of post-operative pain and the use of rescue analgesia in the early postoperative period in the first 24 h was less in the group B than group A. The relief in pain with regimen B containing bupivacaine, fentanyl, methylprednisolone and cefuroxime was more striking in the first 24 h. There have been two RCTs which do not support the efficacy of corticosteroid (methylprednisolone) in periarticular injection<sup>11,12</sup> and four RCTs which do.<sup>13–15</sup> We have found that patients who were administered group B regimen infiltration obtained a better range of motion in the operated knee at 24 h and 7 days after the surgery as compared to group B regimen. Most of the subjects from B group obtained less extensor lag as compared to group A. Dexamethasone is a long-acting glucocorticoid with potent anti-inflammatory properties. Its anti-inflammatory effects, both locally and systemically, were confirmed in this study by evaluating IL-6 in drain fluid and serum CRP. Regarding the duration of the analgesic effects, our results were consistent with the physiological effects of dexamethasone remaining for 36–72 h in the human body. Chia et al. have advised against injecting the extensor mechanism because of the risk of delayed tendon rupture.<sup>12</sup> Transient peroneal nerve palsy may occur, because of infiltration into the area of the common peroneal nerve. Cautious infiltration in the posterior aspect of the capsule is done. In our study, there is no such complication.

**Limitations:** This study was conducted in a single centre and only one surgeon was involved. Second, the sample size was underpowered to make definitive conclusions about the ratio of complications, including surgical site soakage and wound complication. Several studies have reported patients developing a surgical site infection after periarticular injection which contained corticosteroid.<sup>16</sup> To analyze the impact of corticosteroid on surgical site infection, a larger sample size is needed.

## 5. Conclusion

Both the cocktail regimens are effective in pain control post-operatively. The relief in pain with regimen B containing bupivacaine, fentanyl, methylprednisolone and cefuroxime was more striking in the first 24 h. By the end of two days, both regimens were found to be equally effective. This initial pain relief by regimen B improved the patient's satisfaction and early participation in post-operative rehabilitation.

## Conflicts of interest

The authors & co-authors declare that they have no conflict of interest.

## Funding

There is no funding source.

## Ethical approval

Ethical Approval taken from the Ethics Committee of the Institute.

## Informed consent

Informed consent was obtained from all individual participants included in the study.

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