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Uma Maheswara Reddy
Surendra Multi Specialty
Hospital, Tirupati,
Andhra Pradesh, India

A study of cocktail injection: Pain control and knee motion recovery after total knee replacement

Uma Maheswara Reddy

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Abstract

Pain control after total knee replacement (TKR) is pivotal in postoperative rehabilitation. Usage of epidural analgesia or parenteral opioids can cause undesirable side effects hampering early recovery and rehabilitation. These side effects can be avoided by infiltration of an analgesic cocktail locally. Our study was performed to evaluate the benefits of a particular cocktail combination in patients undergoing TKR with respect to pain and knee motion recovery. Fifty consecutive patients who underwent simultaneous bilateral TKR were enrolled and received an intraoperative periarticular cocktail injection in the right knee (intervention) and normal saline in the left knee (control). Postoperative pain was recorded using the visual analog scale for each knee, and the time taken to achieve 90 degree of knee flexion was noted for each side. The cocktail injected knee had significantly less pain when compared with the control knee during the first 2 days and significantly shorter period to achieve 90 degree of knee flexion. The use of intraoperative periarticular cocktail injection significantly reduces early postoperative pain and provides better early knee motion.

Keywords: Total knee replacement, knee injury, intraarticular injection, pain, range of motion

1. Introduction

In patients with advanced knee arthritis, total knee replacement (TKR) has been found to be the most successful surgical procedure. However, early postoperative pain control is pivotal in reducing the hospital stay, increasing patient satisfaction, and for better rehabilitation. It also reduces the potential for postoperative complications such as pneumonia or deep vein thrombosis^[1-4]. Severe postoperative pain is experienced in approximately 60% of the patients and moderate pain in approximately 30% of patients undergoing TKR^[5-8]. Control of pain is achievable through multiple ways, and each has its own risks and benefits^[9-12]. Epidural anesthesia is a common modality for providing effective pain relief during the postoperative period, but it hinders early mobilization and leads to complications such as hypotension, postoperative headache, and spinal infection^[13-15]. Regional nerve blocks pose the risk of injuring neurovascular structures, hematoma formation, and infection^[16, 17]. Systemic opioids such as morphine or fentanyl can cause nausea, vomiting, drowsiness, respiratory depression, urinary retention, and constipation^[18]. An innovative approach to pain management is to aim at controlling local pain pathways and receptors within the knee^[19]. This has been possible through local intraarticular or periarticular injection of analgesic combinations which has good efficacy, is cost-effective, and is easy to administer without causing motor blockade. Also, it does not require any special technical skill for administration^[5]. Various studies about periarticular injection have reported promising results from various combinations of drugs such as ketorolac, ropivacaine, bupivacaine, morphine sulfate, epimorphine, methylprednisolone, cefuroxime, epinephrine, and normal saline^[20]. The patients experienced a prolonged narcotic-free postoperative period and also a reduced parenteral analgesia postoperatively^[21].

2. Materials and Methods

We included patients who underwent simultaneous bilateral TKR from Jan 2016 to Jul 2018 in our organization. For uniformity, we included only the patients for whom spinal anesthesia was the mode of anesthesia.

Corresponding Author:
Uma Maheswara Reddy
Surendra Multi Specialty
Hospital, Tirupati,
Andhra Pradesh, India

Fifty consecutive 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). 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.

2.1. Design of the study

Our study was a prospective, double-blinded, placebo controlled trial. All included patients signed an informed consent form, and the methods of this trial were approved by the institutional ethics committee of our institute.

2.2. Intervention

For all the patients, intraoperative periarticular cocktail injection was given to the right knee and the left knee was the control that received a same volume of normal saline (110 mL). The patients were blinded about which knee received the cocktail injection. All the patients received spinal anesthesia with a combination of 0.5% bupivacaine and 0.5 mL (25 mg) fentanyl. The antibiotic prophylaxis given was 1.5 g of injection cefuroxime 30 to 40 minutes before incision.

All the operations and the cocktail injections were performed by a single surgeon (first author) using a medial parapatellar arthrotomy approach. 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^[14] as depicted in Figures 1:

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

Injection at zones 2, 3, and 4 were administered after making the tibial and femoral cuts and ligament balancing. At zones 1, 5, 6, and 7, the injection was administered after implant placement. 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. No drains were used.

During the postoperative period, systemic analgesics used were intravenous injection of diclofenac (75 mg) and inj. tramadol (100 mg) along with inj. ondansetron (4 mg) every 12 hours for the first 2 days followed by tablet naproxen 500 mg and tablet tramadol hydrochloride (37.5 mg) with paracetamol (325 mg) for the next 10 days. Buprenorphine patch (10 mg) or oral pregabalin (75 mg) were used in patients for whom the aforementioned medications were insufficient in controlling pain or could not be tolerated.

Apart from mechanical deep vein thrombosis (DVT) prophylaxis such as DVT stockings, inj. fondaparinux 2.5 mg on the first day followed by oral aspirin 150 mg daily for 6 weeks were given. Patients were mobilized using a walker

after 3 to 4 hours of surgery on the same day, and range of motion (ROM) and isometric exercises were started. All the patients were observed till discharge and are being followed up regularly.

2.3. Outcome from the measurement

Postoperative pain over both the knees were separately recorded by the nurse, who was blinded about the study, using a 10 point VAS at 3,6,9,12,24 and 48 hours postoperatively, and then, at once-daily intervals till the fourth postoperative day. The VAS consists of a 10-cm line, in which 0 indicates no pain and 10 indicates the worst imaginable pain^[13-15].

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.

2.4. Statistical analysis

The obtained data were tabulated, coded, and analyzed using SPSS, version 17, for Microsoft Windows. Descriptive statistics was reported as mean and standard deviation. Unpaired t test was used to test the statistical association between the intervention arm and control arm. For analyzing the change in pain scores over the same knee during the 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.

3. Results and Discussions

A total of 50 patients (50 pairs of knees) were included in the study. Osteoarthritis was the underlying condition in 47 patients, while the rest of them had rheumatoid arthritis.

The mean pain scores (VAS) at 3,6,9,12,24 and 48 hours, and at third and fourth days in both knees are enumerated in Table 1 and Figure 2. When compared with the control knee, a statistically significant reduction in pain score was noted in the cocktail injected knee at 6,9,12,24 and 48 hours ($P < .001$ in all cases). However, the difference in the mean pain scores between both knees at the third ($P = .684$) and fourth ($P = .251$) days were not significant.

The mean time taken for achieving 90 degree 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 (3, 6, 9, 12 and 24 hours) after surgery. However, a statistically significant difference in the pain scores was noted at 48 hours ($P < .001$), 72 hours ($P < .010$), and 96 hours ($P < .001$), compared with the 24-hour score. Within the control group, there was a significant difference in pain scores over different time points (Table 2). However, a post hoc analysis showed that there was no significant difference within various time points on the first day (3, 6, 9, 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.

3.1. Discussions

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 [11]. 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.

Table 1: VAS Comparisons between groups

S. No	Post-operative Duration	Group	Mean	Standard Deviation	Standard Error Mean	P Value
1	3h	Control	3.75	1.939	0.194	<.001 *
		Intervention	1.99	1.419	0.142	
2	6h	Control	3.54	1.927	0.193	<.001 *
		Intervention	1.9	1.406	0.141	
3	9h	Control	3.34	1.778	0.178	<.001 *
		Intervention	1.87	1.376	0.138	
4	12h	Control	3.16	1.77	0.177	<.001 *
		Intervention	1.84	1.375	0.138	
5	24h	Control	2.64	1.365	0.137	<.001 *
		Intervention	1.6	0.656	0.066	
6	48h	Control	2.3	1.056	0.106	<.001 *
		Intervention	1.17	0.825	0.083	
7	3d	Control	1.2	1.056	0.106	0.685
		Intervention	1.18	1.036	0.104	
8	4d	Control	1.11	1.026	0.102	0.252
		Intervention	0.96	0.825	0.083	

* Significant at P< .05

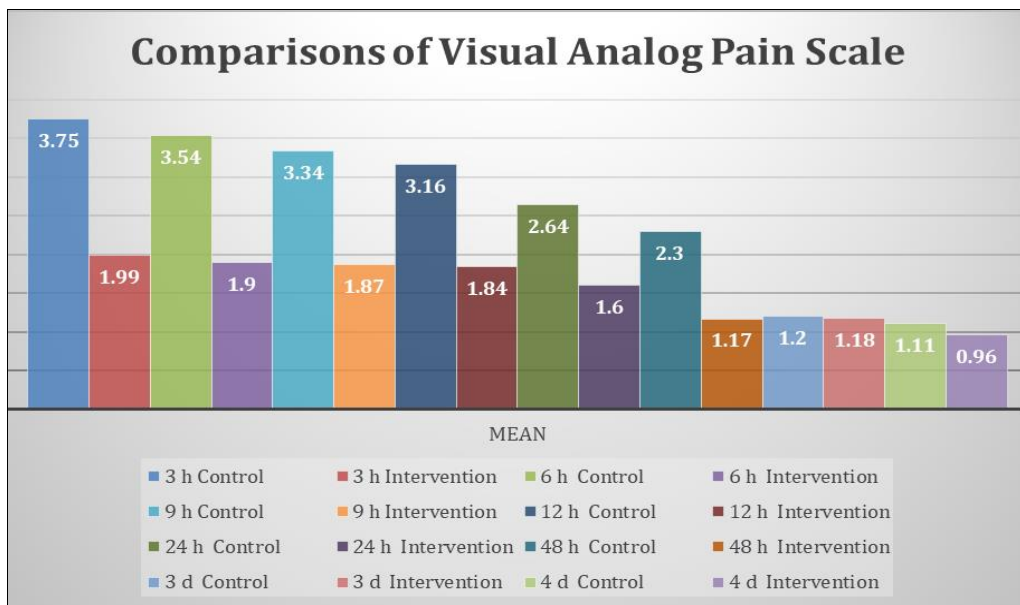


Fig 2: Comparisons of VAS

Table 2: Postoperative duration

N= Sample Size	Group	Postoperative duration	Mean	Standard Deviation	P Value
200	Control	3 h	3.75	1.939	<.001
		6 h	3.54	1.927	
		9 h	3.34	1.778	
		12 h	3.16	1.77	
		24 h	2.64	1.365	
		48 h	2.3	1.056	
		3 d	1.2	1.056	
		4 d	1.11	1.026	
	Intervention	3 h	1.99	1.419	<.001
		6 h	1.9	1.406	
		9 h	1.87	1.376	
		12 h	1.84	1.375	
		24 h	1.6	0.656	
		48 h	1.17	0.825	
		3 d	1.18	1.036	
		4 d	0.96	0.825	

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 opposite side at 3, 6, 9, 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^[2, 8]. 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^[1-4]. Nair *et al.* also comparing the 2 groups of 40 knees each, reported that the cocktail injected patients reported significantly less PCA and postoperative pain recordings at 3, 6, 9, 12, 24, 48, and 72 hours after TKR.

4. Conclusion

In this study concludes that periarticular cocktail injection in TKR not only helps in relieving the pain but also aids in early recovery and rehabilitation. Because, 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.

5. Acknowledgements

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6. References

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