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How effective is periarticular drug infiltration in providing pain relief following Total Knee Replacement as compared to epidural analgesia?

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ABSTRACT

Introduction: The aim of the study was to compare the efficacy of pericapsular injection of analgesic drugs (PAI) with epidural analgesia (EA), in providing post-operative pain relief and early functional improvement of following Total Knee Arthroplasty.

Materials and methods: 50 patients were randomized to 2 arms of 25 patients each, receiving either pericapsular injection or epidural analgesia. The Visual Analogue Scale (VAS), functional outcomes and side effects related to the EA and PAI groups were assessed.

Results: The PAI group had significantly better pain relief on the first post-operative day with a mean VAS on 3.6 as opposed to 7 in the epidural group($p = 0.006$). Functional outcomes in the PAI group were significantly better in the early post-operative period with patients taking less time to achieve the same physiotherapy goals – straight leg raising, climb 14 steps and walking 50 m. Side effects like nausea, vomiting, pruritus and urinary retention were less with PAI. However, by the 5th postoperative day, functional independence and pain control were similar in both groups.

Conclusion: Pericapsular injection of analgesic drugs in total knee arthroplasty provides better pain control and functional recovery than epidural analgesia in the early post-operative period, and can be the choice method for analgesia following total knee replacement.

1. Introduction

The demand for Total Knee Replacement surgery has been on the rise and is predicted to grow even more significantly by the year 2030.[1] Post-operative pain associated with major operations like Total Knee Replacement (TKR) is quite considerable. More than half of these patients receive sub-optimal pain control and hence experience severe pain in the early postoperative period.[2] Adequate pain relief is essential for early mobilization and functional recovery.[3,4] Control of postoperative pain also reduces hospital stay and subsequent readmissions.[5–7]

Several therapeutic methods have been used to control pain and improve function in the post-operative period. These include patient controlled analgesia (PCA), femoral and adductor nerve blocks, epidural analgesia using a catheter and periarticular infiltration[6,8–10]. Though femoral nerve blocks are effective in pain control, the possible quadriceps weakness could delay the rehabilitation and ambulation.[11–13] While epidural analgesia is useful in postoperative pain control,[14,15] it is an invasive procedure and necessitates restricting the patient's mobility till the patient has recovered complete motor power. Epidural anaesthesia, like PCA, is associated with side effects that include nausea and vomiting, itching, in addition to urinary retention and motor deficits that may delay mobilization. The purpose of this study was to assess the efficacy of periarticular infiltration of an analgesic cocktail, in providing good pain control and aiding with early rehabilitation and mobilization following TKR. This was done by comparing the efficacy and complications with the current method of post-operative pain control at our institution i.e. epidural analgesia with bupivacaine.

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2. Methodology

Patients undergoing primary unilateral total knee replacement were recruited for the study. Exclusion criteria included patients with age >80 years, history of cardiac illnesses, or arrhythmias, patients undergoing complex primary or revision arthroplasty and severely painful opposite knee. Their functional status was measured preoperatively using the KSS (Knee Society Score) and the pain was assessed using the Visual analogue scale (VAS).

Patients were randomized into two arms by block randomization with concealed envelope method. In one arm, the patients received *epidural analgesia* with 0.1% Bupivacaine and 2mcg/ml of Fentanyl @ 4–6 ml per hour for 48 h postoperatively, and in the other, they received periarticular infiltration of an analgesic cocktail of drugs. The *analgesic cocktail* consisted of 50 ml of 0.2% Ropivacaine, 10 ml Normal saline, 0.3 ml Noradrenaline (0.6 mg), 40 mg Methylprednisolone acetate (Depomedrol), 10 mg Morphine, 30 mg Ketorolac, and 1gm Cefazolin. The first 30 ml of the cocktail was injected into the posterior knee capsule and soft tissues around the medial and lateral collateral ligaments before implantation of the actual prosthetic components. The quadriceps muscle, retinacular tissues, pes-anserinus, suprapatellar and infrapatellar fat pad were infiltrated with the remaining cocktail mixture.

All patients had perioperative analgesia with other drugs, which included Tab. Aceclofenac 100 mg twice daily, Cap. Omeprazole 20 mg twice daily, Cap. Pregabalin 75 mg twice daily - all started 36 h before the surgery and postoperatively with Inj. Paracetamol (Perfalgan – M/S Bristol Myers Squibb) 1gm IV once every 6 h for 48 h followed by Tab. Paracetamol 1gm once every 6 h for 7days. Injection Morphine 5 mg (subcutaneous) was given as required for breakthrough pain in the immediate postoperative period. Patients on epidural infusion had either bolus doses or an increase in the infusion rate for breakthrough pain. Inj. Ondansetron was used intravenously for postoperative nausea and vomiting.

Surgery was performed under general anaesthesia/spinal anaesthesia using a standard medial para-patellar arthrotomy using a pneumatic tourniquet by surgeons who were specialized in knee surgery. Prostheses used were Genesis II (Smith & Nephew, Memphis, TN, USA) and HP Sigma (DePuy, Johnson & Johnson, Warsaw, IN, USA). The implants were fixed with cement and patellae were resurfaced as required. A closed suction drain was placed inside the knee joint capsule before wound closure and removed 48 h later. Inj. Tranexamic[16] acid (10–15 mg/kg) was injected intravenously 15 min before tourniquet was released, and top up doses were given 3 and 6 h later. Anticoagulation was initiated postoperatively as per institutional guidelines.

Patients underwent a standard physiotherapy program that involved ankle pump exercises in bed, and SLR (Straight leg raise) from the first postoperative day – initially with a knee brace and subsequently without. They were encouraged to walk from the second postoperative day. A brace for the knee was used till the patient could do an active SLR. Number of days taken to walk 50 m without the brace and to climb a flight of 14 steps was documented. The distance walked in 6 min with a walker was recorded on the 10th postoperative day.

Pain experienced by the patient postoperatively was assessed using the Visual Analogue Scale by the primary investigator on a daily basis. It was also noted every 4 h by the hospital pain team for the first 72 h. The maximum VAS score for each day, as recorded by the primary investigator or the pain team, was noted. Additional medication used for breakthrough pain was noted.

Side effects including nausea, vomiting, pruritus, headache, urinary retention, cardiovascular complications, infection/postoperative wound ooze, ICU stay, nerve palsy and mortality were noted.

Institutional ethics committee clearance was given for the study; after which patients who consented for the study were recruited.

2.1. Statistical analysis

Setting the mean (SD) of the pain scale on a 10 point Likert scale, at about 4 (±1.5), and keeping the non-inferiority margin at 1.5, with alpha and beta errors at 5% and 20% respectively, the sample size required was 12 subjects in each arm. We have analysed the results of 25 in each arm. SPSS version 20 was used for analysis.

3. Results

50 patients were recruited for the study; of which 25 were randomized to receive the periarticular infiltration cocktail (PAI) and 25 received epidural analgesia (EA). Both the groups were demographically comparable. The demographic details of these patients are described in Table 1.

In the EA group, there were 19 cruciate retaining (CR) knees, and 6 posterior stabilized (PS) knees; where as in the PAI group, there were 20 CR knees and 5 PS knees. Five patients in the EA group and 4 in the PAI group had their patella replaced.

In terms of postoperative pain relief, the PAI group had significantly better relief of pain on the first post operative day (Fig. 1) ($p = 0.006$). The mean VAS on day 1 for the PAI group was 3.6 (±3.2), whereas it was 7(±2.8) for the EA group. Six out of the 25 patients who received EA had a pain score of 10 on the first day, while only 1 patient who received PAI had a score of 9. For the remaining postoperative duration, the PAI group consistently had better pain relief than the EA group till the 10th postoperative day – though the differences were not statistically significant (Fig. 1).

50% of the patients who had PAI required top up Morphine for postoperative pain control, while 72% (18 of 25 patients) on EA required either bolus doses of epidural infusion or a hike in the infusion rate or subcutaneous morphine to control pain postoperatively.

On assessment of functional outcome, the PAI group had significant early functional recovery, but by the 5th day, though the PAI group was functionally slightly better, the difference was not statistically significant (Table 2). All patients could climb a flight of 14 steps prior to discharge.

The EA group had a significantly higher percentage of side effects - probably due to the Fentanyl used in the epidural infiltration. 64% (16/25) of patients had postoperative nausea/vomiting, 36% (9/25) had pruritus and 36% (9/25) had a feeling of urinary retention. None had to be catheterized.

Table 1
Demographic profile.

	Epidural Analgesia (EA)	Periarticular Infiltration (PAI)
Number	25	25
Mean age (Years)	55	59
Preop functional score, KSS (0–100)	43	59
Sex		
Male	12	11
Female	13	14
Side		
Right	10	8
Left	15	17
Diagnosis		
Osteoarthritis	15	18
Rheumatoid Arthritis	8	7
Gout	2	0

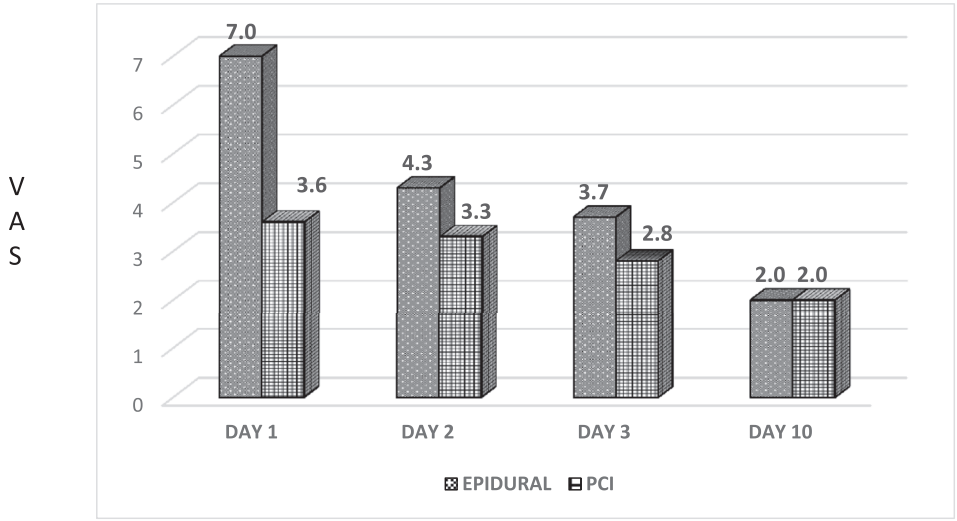

Fig. 1. Postoperative VAS scores.
Legend Figure 1 – Visual analogue scores (VAS) for pain following epidural analgesia (EA) and Periarticular injection (PAI).

Table 2
Functional outcome.

	Epidural Analgesia (EA)	Periarticular Infiltration (PAI)	P value
Time taken to do SLR while supine (without a brace)	3.9 days (1–7)	2.4 days (1–4)	0.032
Time taken to walk 50 m	3.5 days (2–7)	2.7 days (2–4)	0.050
Time taken to climb 14 steps	5.2 days (3–9)	4.95 days (4–7)	0.455
Distance walked in 6 min on Day 10	142 m	138 m	0.786
Knee flexion on 10th POD (mean)	97°	93°	0.889

In the PAI group, 32% (8/25) of patients had postoperative nausea/vomiting, 16% (4/25) had pruritus and 16% (4/25) had a feeling of urinary retention.

One patient who received PAI had a transient rise in blood pressure with bradycardia when the tourniquet was released. She required ICU observation for 1 day. This was probably because of the Noradrenaline in the cocktail mixture. None of the other patients required HDU/ICU admission. None of the patients had postoperative headache, backache, infections, meningitis, nerve palsies or wound related complications postoperatively.

4. Discussion

Postoperative pain after TKR is a significant concern to patients and a focus of several recent research papers. Several techniques such as patient controlled analgesia, femoral and adductor nerve blocks, epidural analgesia and periarticular injection of medications have been reported.

In this study, we have studied the efficacy of periarticular infiltration of a cocktail of drugs in controlling pain and enabling early functional recovery. The study shows that the periarticular infiltration is significantly better than the epidural injection in the first 24 h after the surgery. Even after the first 24–48 h, when we would have expected the analgesic effect of the injection to wear out, the pain scores were consistently less in the PAI group than in the epidural group. Functional ability in the first 24 h was also significantly better in the PAI group.

An additional advantage of the PAI over the EA is the reduced incidence of side effects like nausea, vomiting and pruritus. Additionally, mobilization is easier, as there are no catheters restricting the patient.

Arun Mullaji[17] in 2009 reviewed the effectiveness of a mixture of opioid, corticosteroid and a local anesthetic for periarticular injection in patients undergoing bilateral TKR. They injected one of the two knees with the drug cocktail. They reported significantly lower pain scores and better quadriceps recovery on the side that had periarticular injection of the anesthetic cocktail, as compared to the side that did not have the injection.

Thorsell et al.[18] in his comparative study on total knee arthroplasty patients using local infiltration anaesthesia technique with Ropivacaine, Ketorolac and Adrenaline to epidural anaesthesia reported earlier mobilization in the group treated with local infiltration technique. They concluded that this technique also offered better patient satisfaction and hence was better for postoperative pain relief than epidural anaesthesia.

Nattapol Tammachote et al.[19] compared the pain control effect of intrathecal morphine and multimodal drug injections in patients undergoing total knee arthroplasty. They found that though initially there was no difference between the two modalities, 12–16 h postoperatively, the intrathecal group consumed significantly more Ketorolac and that the side effects of nausea and vomiting was also more in this group compared to the group treated with multimodal drug injections.

Gudmundsdottir et al.[20] showed in a randomized double controlled study in 69 patients that there was no additional advantage of giving continuous adductor canal block on pain control or on early mobilization following knee replacement. Hence there is probably no need for additional nerve blocks for postoperative analgesia.

Spreng et al.[21] compared the efficacy of periarticular infiltration anaesthesia and epidural anaesthesia in total knee arthroplasty patients and reported that epidural anaesthesia provided better

pain relief in the immediate postoperative period, where as local infiltration anaesthesia provided better pain relief after the initial 24 h.

The above observations are contrary to what was found in our study, where we found better relief of pain with periarticular injection in the first 24 h. The level of analgesia was better for the remaining hospital stay as well, though the difference was not statistically significant. Early functional recovery was possible with PAI, though most patients in both groups were able to climb 14 steps by the 5th postoperative day. The reason for the prolonged beneficial effect of the PAI has not been fully explained by other investigators. Several theories have been postulated. It is possible that the excellent pain relief in the immediate postoperative period minimized the central neural sensitization, thereby reducing the pain thereafter. The steroid in the cocktail could also have a role in reducing the inflammatory pain postoperatively.

One of the major limitations in this study is that the epidural catheters were introduced by anaesthesiologists with varied skill and seniority. This could potentially have an effect on the efficacy of the infiltration. It is also possible that the infusion pump may occasionally have been turned off in the postoperative ward due to episodes of hypotension, and then restarted later by the surgical team. This could result in difficulties in titration of drugs to achieve the desired level, and an increased pain score in the immediate postoperative period.

While several surgeons use epidural anaesthesia to provide adequate analgesia and hypotension during the surgery, the necessity to continue the use of the epidural infusion[22] postoperatively should be questioned. This could potentially lead to issues with postoperative pain control and delayed functional improvement. Postoperative hypotension has not been a significant issue with PAI. This study demonstrates that better analgesia and pain control is provided by PAI, and the use of postoperative EA may not be required.

It has been reported that liposomal bupivacaine provided a longer duration of analgesia, and hence is to be choice for pericapsular cocktails and nerve blocks. However a recent Cochrane review[23] did not support its superiority over bupivacaine hydrochloride. We have used Ropivacaine hydrochloride for the cocktail in this study, as it has reportedly less cardiac side toxicity, and hence was preferred for this population.[24]

The study does not assess the effect on hospital stay, as at our center, most patients opt to stay till suture removal, which is very unusual in the current health care scenario. This is due to the fact that most patients come from long distances, and find it difficult to get safe lodging outside the hospital. However, it is assumed that early functional improvement will translate to early discharge in a different environment. In both groups, adequate control of pain provided the patient an opportunity to participate in the physiotherapy program at an early stage and attain functional independence within 4–5 days.

5. Conclusion

Both epidural analgesia and periarticular infiltration of analgesic cocktail are effective in controlling pain after total knee replacement. In this study we have shown that periarticular infiltration provides significantly better pain control and functional recovery in the first 24 h following surgery. Side effects like nausea, vomiting, pruritus and urinary retention are also less with periarticular infiltration of the analgesic cocktail. By the 5th postoperative day, functional independence and pain control are similar in both groups. We therefore conclude that periarticular injection of a cocktail of drugs is more effective than epidural analgesia, especially in the first 24 h, and can be the choice method for analgesia following total knee replacement.

Conflicts of interest

Nil.

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Appendix A. Supplementary data

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