



MULTIMODAL PAIN MANAGEMENT PROTOCOL IN TOTAL KNEE ARTHROPLASTY

Orthopaedics

Dr. N.K. Vaishnav	MBBS MS ORTHO, Head of Dept. Orthopedics, Department of Orthopedics and joint Replacement surgery, Shri Ram Hospital, Jodhpur, India.
Dr. Jayesh Chouhan	MS Ortho, Department of Orthopedics and joint Replacement surgery, Shri Ram Hospital, Jodhpur, India.
Dr. Om Prakash Chaudhary	MS Ortho, Department of Orthopedics and joint Replacement surgery, Shri Ram Hospital, Jodhpur, India.
Dr. Nitesh Arora	MD Anesthesia, Department of Orthopedics and joint Replacement surgery, Shri Ram Hospital, Jodhpur, India.

ABSTRACT

Background: Total knee replacement surgery is associated with severe post operative pain. It is estimated that 50% of patient undergoing total knee replacement receive suboptimal postoperative pain management. Various methods of post operative pain management has been used by different surgeons, but still no any method is perfect. There is a need of effective pain management regime which gives good pain control and early mobility in post operative period with minimal side effects. **Methods:** Around 200 patients with 312 knee replacements has been observed, who has operated at our center, during a period of last 3 years. All types of patients are included in this study, like male and females, single and bilateral knee, all age groups, with different BMI, with or without comorbidities. Mostly all the operated patients were given spinal anesthesia. All the operated patients were observed for post operative pain using visual analogue score at 6 hr, 12hr, 24hr, 36hr and 48 hrs. and 72hrs. Use of opioid quantity, need of rescue dose, active SLR, first day flexion of knee, walking distance, nausea and vomiting are noted. Continuous epidural analgesia, femoral nerve block and infusion, adductor canal block and infusion, periarticular local infiltration with multimodal cocktail, sustained release transdermal opioid patch and combination of various methods are used in this study. **Results:** Epidural infusion is best analgesia in post operative period but it has drawbacks like, epidural hematoma after LMW, Patchy effect in some patients, decrease in motor power which delays in mobilization of patient. Femoral nerve block and infusion have a good pain control but quadriceps power decreases hence physiotherapy is delayed. Adductor canal block with continuous infusion needs expertise and USG machine, this needs opioids in post op period and rescue dose of analgesic. Multimodal periarticular intraoperative cocktail gives good pain control in post operative period without delay in walking, this needs very less training and equipment. it is cost effective and has least side effects. Opioid patches like fentanyl and buprenorphine has side effect like nausea, vomiting, altered sensorium, these alone are not effective in pain management. **Conclusions:** Multimodal intraoperative periarticular cocktail infiltration in combination with sustained release transdermal Buprenorphine skin patch preoperatively, with tapering dose of tramadol and diclofenac injections give best pain relief in TKR patients. It has less side effects, easy to use, cost effective and provides early post operative recovery.

KEYWORDS

Arthroplasty, Multimodal, Cocktail, Epidural, Infusion

INTRODUCTION:

For the patients of advanced arthritis, total knee replacement has been found to be the most effective surgical procedure. TKR can improve the quality of life of an individual by restoring the mobility and relieving the disabling pain. (1). Postoperatively severe pain is experienced in 60% of patients and moderate pain in 30% of patient undergoing knee replacement. (2).

Effective pain control in post operative period provide early ambulation of patient and decrease complications like DVT, Pneumonia, constipation, embolism. (3). Different surgeons use different techniques at their centers for pain relief. Still there is a need of effective pain control regime which will be, cost effective, needs less equipment and minimal side effects.

Table 1. Various pain control methods in TKR patients
Epidural infusions
Continuous femoral nerve infusions
Adductor canal blocks and infusions
Periarticular intraoperative cocktail infusions
Infiltration between popliteal artery and posterior capsule of knee (IPACK)
Genicular nerve block
Patient controlled epidural analgesia (Fentanyl + Ropivacaine)
Transdermal opioid patches (Fentanyl and Buprenorphine)
Injections of tramadol, diclofenac, piroxicam, butorphanol
Tapentadol nasal spray
Oral medications like opioids, NSAIDS
Continuous Intra articular infusion of Bupivacaine
Patient controlled analgesia (Morphine)
Combination of various methods has been used by different surgeons.

Control of pain is achievable via multiple ways and each has its own risk and benefits. Epidural infusion is a common modality for pain management during the post operative period but it prevents early mobilization and has side effects like hypotension, headache, epidural hematoma formation. Regional nerve blocks like femoral nerve blocks has side effects like injury to neurovascular structure, infections (4). systemic opioids can cause nausea vomiting, constipation, drowsiness, respiratory depression. (5).

The best modality in pain management is blocking the local pain pathway and pain receptors in knee. Multimodal combination of drug cocktail local infiltration during surgery at different sites has good efficacy, cost effective, and does not need any special instruments and training. (6). Providing local analgesia in the area of surgical trauma with minimal side effects is an attractive option. This provides less use of opioid consumption, early discharge from hospital. Various studies have reported promising results of periarticular injections (7).

MATERIAL AND METHODS:

In our study we have observed 200 patients with their 312 total knee replacements. All patients are operated at our center. We have included all categories of patients in our study male and females, all age groups, all BMI Pts., with or without comorbidities, all deformities of knee, unilateral and bilateral knees, osteoarthritis, inflammatory arthritis. This is a cumulative type of study design. Primary and revision cases both are included.

Prosthetic joint infection cases are excluded from this study. All patients has been observed for post operative pain at different time from surgery, mobilization, DVT, pulmonary embolism, side effects like nausea, vomiting, constipation and wound discharge. VAS score is used for pain observation. 1 to 10 scale is used for pain monitoring. Table no. 2 shows demographic data of study.

Table 2: Demographic Data

Average age	60 ± 5 Years	
Gender	107 females, 93 Male	
Average BMI	30 ± 2	
Average hospital stay	4 ± 1 day	
DVT	19	
Wound complication	08	
Oxford Knee Score: (60)	Pre op: 18	Post op: 48 (3 Month)
Womac Score (96)	Pre op: 34	Post op: 08 (3 Months)
VAS Score (10)	Pre op: 7 to 8	Post op: 1 to 2 (3Months)

Our aim is to control post operative pain to a minimal level, by opting any kind of pain control technique so that we can provide maximum comfort to the patient with early walking and minimal side effects. Pain is an unpleasant experience observed by the patient. Pain hinders the post operative physiotherapy protocol of the patient and delay in mobilization creates DVT, constipation, muscle weakness, chest infection and delayed recovery.

In the starting phase we used opioid patches like fentanyl (25mcg) and Buprenorphine (10mcg) with injectable tramadol and diclofenac. Using fentanyl transdermal patch 25mcg provides pain relief for 72 hrs. but dose related side effects like drowsiness, constipation, nausea, vomiting are there. More so ever other drugs has to be added with patches.

Epidural anesthesia and infusion was used in many patients for TKR pain management. fentanyl + Ropivacaine continuous infusion was given in post operative period @ 3ml per hr on first day, 2ml per hr. on second day, 1ml per hr. on 3rd post op day. Patients were very happy with epidural analgesia but in some patients where we have to give L.M.W./Heparin for symptomatic pulmonary embolism or fat embolism, we have to wait for 12 hrs. after removal of catheter to avoid epidural hematoma formation which can cause catastrophic complication like paraplegia. In operated TKR patients there is risk of embolism and this has to be deal quickly and aggressively so we have stopped using epidurals.

Femoral nerve block with continuous infusion is better than intravenous opioids and patches; gives good analgesic with less side effects. 0.75% Ropivacaine and 2mcg/ml fentanyl is used as infusion in epidural, femoral nerve block and adductor canal block.

Ropivacaine 7.5mg/ml x20ml+fentanyl 50mcg/mlx2ml+normal saline 0.9% x28ml =50ml

Adductor canal block (ACB) is used with the help of sonographic guide, the saphenous nerve which is considered the terminal sensory branch of femoral nerve is blocked at mid thigh level. Continuous infusion of fentanyl + bupivacaine is used for three days for post operative pain relief.

After using epidurals, femoral nerve blocks and adductor canal block we have started using periarticular cocktail infiltrations as various studies have shown very good results of this. (8)

Dr. Ranawat has published an article in clinical orthopedics and related research in march 2009. (9) we are using a modified version of Ranawat cocktail. A combination of ropivacaine, fentanyl, methylprednisolone, antibiotic, adrenalin, clonidine, tranexamic acid and normal saline is used as cocktail. Total 110ml volume is made for a single knee. *Table no. 3* represents the combination of cocktail. Two syringes of 55ml each filled and applied two times during surgery, one after completion of bone cutting, second after putting final implants. Small needle of size 18G(1.20)x1.5" (38mm) is used to infiltrate the tissue at different sites like post capsule, more on medial and less on lateral side, medial and lateral collateral ligaments, subperiosteal tissues of femur and tibia. Before wound closure quadriceps tendon, patellar tendon, subcutaneous tissue, fat, lateral patellar retinaculum is infiltrated. Care must be taken to avoid injury to peroneal nerve and avoid deep infiltration in lateral side of post capsule. We prepare our cocktail at the time of surgery, we do not store this. Some literature say that this can be prepared before surgery and can be stored for 48 hrs. In the starting we use long needle but after one case of peroneal nerve palsy we starts using small length needle 18G(1.20)X1.5"(38mm)

As the nerve supply of knee is more from medial side, around 60% of infiltration is done on medial side and rest on lateral side of knee. *Table no 3*. Shows cocktail combination used in our study.

Most of the patients are given spinal anesthesia for surgery. vital monitoring like Blood pressure, Spo2, ECG, pulse are monitored. Any sign of change in pulse, B.P. are noted at the moment of femoral canal opening, cement application, cocktail infiltration, and removal of tourniquet. suction of femoral canal is done with a wide bore suction catheter after opening of femoral canal to prevent embolism. Our tourniquet time is around 45 to 60 min., pressure is around 250 to 300 mm. (100 mm more than systolic pressure and also depends on thigh circumference). we use post op drains in all the patient to avoid post op hematoma and to prevent infection. We apply sterile betadine dressing and a compression bandage from ankle to mid thigh in all patient.

Post operative patients are monitored for vitals like pulse, blood pressure, Spo2 level, pain monitoring using visual analogue score 1 to 10. At times 6 hrs., 12 hrs., 24 hrs., 36 hrs., 48 hrs. and 72 hrs. Distal pulse of foot, foot movement, drain amount, nausea and vomiting are monitored.

Mobilization of patients started after 24 hrs. in single knee and at 48 hrs. in both knee surgery. Mechanical DVT pumps are used in all patients in post op period, ankle pumps and quadriceps exercises are started at 3 to 4 hrs. after surgery. Knee bending 30° started after 6 hrs. of surgery and 90° knee flexion is started at 24 hrs. after drain removal and removal of compression bandage. Patients with single knee are discharged at 3rd day and bilateral on 4th day. With instruction to contact immediately if they have fever, wound discharge and increase in pain.

RESULTS:

Around 200 patients were observed in our study with 312 TKRs. Epidural analgesia is the best effective pain control regime which requires minimal use of concomitant opioids, other medicine. But due to its limitations we have shifted to other methods. Femoral nerve block and adductor canal block are good modalities but they need training and sonography machine. Intraoperative multimodal cocktail infiltration is best regime in our observation. It is cost effective needs no any training, and control pain up to a good extent.

But we cannot rely on periarticular infiltration alone to control post operative pain. For a better pain relief we have to add some agents with this. we used to apply Buprenorphine transdermal patch 10 mcg in all patients preoperatively. Its blood level is achieved after 12 hrs. of application and effect last up to 7 days post application. Intraoperative infiltration of cocktail with pre op buprenorphine transdermal patch and post operatively injection of tramadol and diclofenac gives best pain relief in all the operative patient. Diclofenac can be used as transdermal 200mg patch or sos injection mode. VAS score is noted in patients at 6,12,24,36, 48,72 hrs. of surgery, while at rest and while walking. VAS score is less in all the patients as compared to other methods. There is no any need of rescue dose in any patients after using this protocol. If timely analgesic dose is given before the pain trigger starts, there is no pain to the patients.

It has been observed that if the operated patients are pain free for first 72 hrs. post surgery, the chances of pain in later days are very less.

OXFORD knee score and WOMAC score are better in patients who have good pain control post operatively. Post operative pain causes, decrease range of motion, decrease range of motion causes stiffness and arthrobrosis.

Side effect of opioids are still a challenge in our regime like nausea, vomiting, constipation, gastritis. There is no drowsiness, no spinal headache. *Table no 4*. Shows pain management protocol.

TABLE 4. PAIN MANAGEMENT PROTOCOL IN OUR SET UP	
Preoperatively:	Buprenorphine 10mcg patch on left side of chest.
	Tab alprazolam 0.5 mg HS
	Antibiotic cefuroxime 750/1500 mg HS
Operative period :	Intraarticular Local cocktail 110mg
Operative Day 0 :	Diclofenac patch 200 mg x every day for 3 days
	Inj. Tranexamic acid 1.0 g iv after 30 min in 100cc N.S.
	Inj. Tramadol 100 mg 6 hrly in 100 CC N.S.

Tab Alprazolam 0.5 mg HS	
Post op day 1	Inj. Tramadol 100 mg i.v 8 hrly in 100 cc N.S.
(After 24 hrs)	Diclofenac 200mg patch
	Inj. Pantoprazole , inj. Ondansetron i.v.
Post op day 2 :	Inj. Tramadol 100 mg mg i.v. BD
(After 48 hrs.)	Diclofenac patch 200 mg
Post op day 3	Inj. Tramadol 100 mg according to pain
(After 72 hrs.) discharge day	Oral tablets Tramadol, NSAIDS, pregabalin. Clonazepam, antacids. Tapentadol nasal spray
Rescue dose :	Inj. Tramadol 100 mg i.v. in 100cc N.S.+ inj diclofenac 100 mg I.M.

DISCUSSION:

Post operative pain in total knee replacement may be a result of trauma to the bone and soft tissue, hyper perfusion following tourniquet release (10). The active ingredient of cocktail work in different ways. Steroid act as anti inflammatory, Ropivacaine act as to block the afferent pathways, epinephrin reduces the toxicity of Ropin by keeping it localized to the injectable tissue(11). Fentanyl act as pain reducing agent, antibiotic reduce infection, clonidine prolongs the action of local anesthetic and the effect of cocktail

The bupivacaine level was measured in systemic circulation after 4 hrs. of surgery and found to be 60 ng/ml which is 2.5 times less than its toxicity level, reported by Knudsen et al (150ng/ml). (13).

Acc to Badner et al (14) addition of opioid in the cocktail like morphine did not provide any significant advantage. we have no any experience of this. A to Christensen et al (15) addition of steroid to cocktail did not help in pain relief but causes risk of infection, so we used to avoid steroid in diabetic patients (16). There can be rupture of patellar tendon by using steroid in cocktail ,so we avoid infiltration in patellar tendon.(17).

The results of immediate post op pain control by local infiltration by various authors are promising, Mula ji. et al. (18).

Some authors reported itching in patients using epidural infusions, we have no any such complain in our patients. Buprenorphine patch have not been tolerated in few patients due to severe vomiting within 6 to 8 hrs. of application and has to be removed.

Some patient which have cardiac history can have arrhythmias due to adrenalin in the cocktail mixture, while applying during surgery. So adrenalin should be used cautiously in cardiac patients. Applying a pressure bandage post operatively after surgery aid to extent the effect of local infiltration cocktail. (19)

Still we are using preop and post op opioids in combination of periarticular infiltration and we are not able to eliminate pain completely. Unfortunately we are still searching an ideal technique of pain relief which eliminate pain completely with minimal side effects.

CONCLUSION:

Multimodal, intraoperative periarticular cocktail infiltration in combination with preoperative 10mcg buprenorphine transdermal patch and postoperatively tapering dose of tramadol and diclofenac patch is the best combination in pain control. This is the most effective pain control regime with very less side effects, cost effective, no need of any expertise, and allows early mobilization.

Disclosure:

We have no any experience of patient control analgesic (PCA), patient control epidural analgesia (PCEA). In some patients due to Intolerability of buprenorphine patch , it has to be removed after 6 to 8 hrs. of application. we have not measured the level of ropivacaine in blood after infiltration to judge its systemic toxicity. Due to PNDT rules (*Prenatal diagnostic techniques Act ,1994*) it is difficult to shift

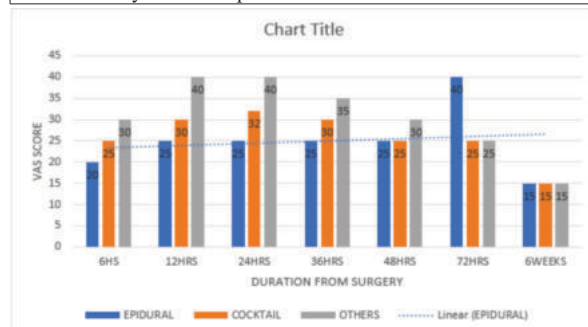
the sonography machine in operating room , so adductor canal block and femoral nerve blocks are difficult to apply. All author declare that we have not received any financial support for this study.

TABLE 3.

COCKTAIL COMBINATION FOR SINGLE KNEE

Drugs	volume
Ropivacaine 0.75%	40 ml
Fentanyl 50mcg/ml	2 ml
Adrenalin 1.1000	0.3 ml
Cefuroxime 1.5 g	10 ml
Methyl pred. 40mg	2ml
Clonidine 150mcg/ml	1ml
Tranexamic acid 1000mg	10 ml
Normal Saline 0.9%	45 ml
Total	110.3ml

Methyl prednisolone is not used in diabetic patients, adrenaline is used cautiously in cardiac patients.



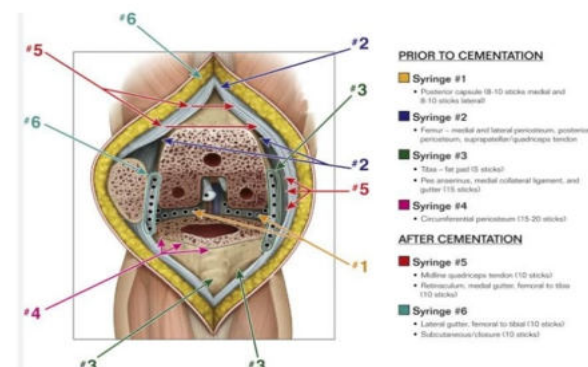
Comparison Of Pain In Epidural, Cocktail And Other Methods Bar Chart

Blue (1st BAR) Epidural analgesia

Orange (2nd BAR) Cocktail infiltration

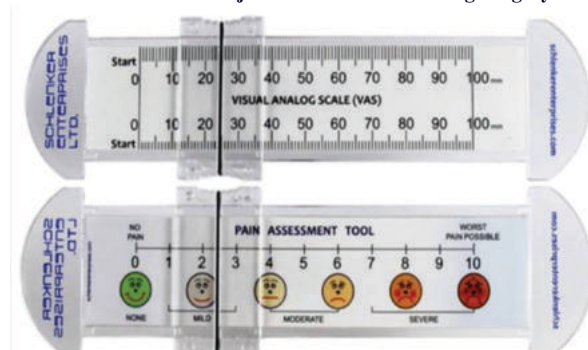
Black (3rd BAR) Other methods FNB,ACB.

Other methods includes femoral nerve infusion, adductor canal infusions.

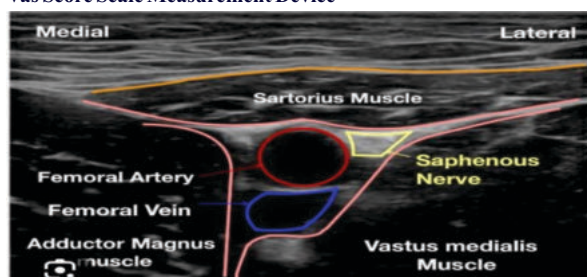


SITES OF INTRA ARTICULAR INJECTION OF COCKTAIL DURING SURGERY

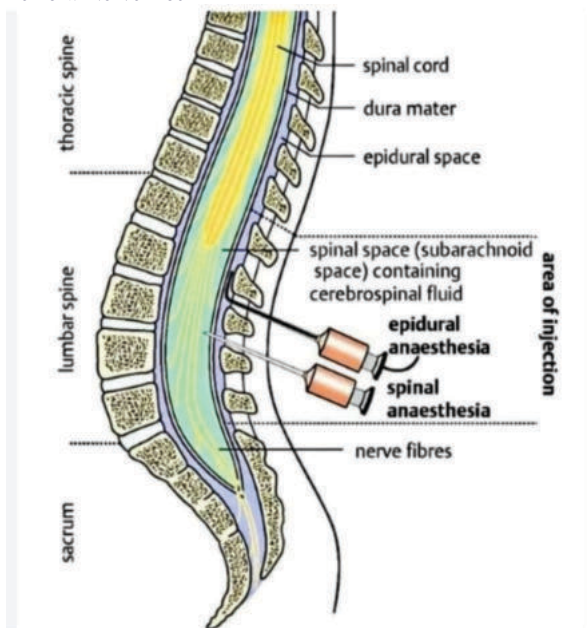
Sites Of Intra Articular Injection Of Cocktail During Surgery



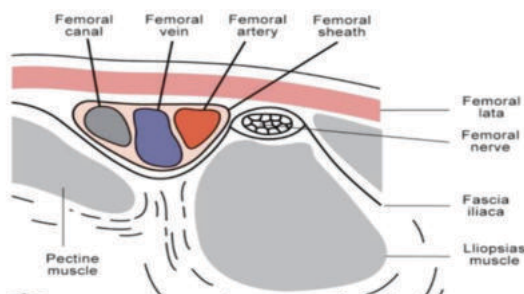
Vas Score Scale Measurement Device



Femoral Nerve Block



Epidural Application



Adductor Canal Block

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