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KEY WORDS: TKA, Local Infiltration analgesia, Periarticular Injection, Epidural Analgesia, Postoperative Pain, periarticular multimodal drug injection.

THE ANALGESIC EFFICACY OF A STANDARDIZED LOCAL INFILTRATION ANALGESIA TECHNIQUE OVER EQUIVALENT EPIDURAL ANALGESIA IN TOTAL KNEE ARTHROPLASTY AND A COMPARATIVE ANALYSIS WITH MOST CITED RCTs

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ABSTRACT

Background: Managing postoperative pain in TKA is a challenge and needs an imperative strategy to bring maximal knee function early, with minimal side effects and less hospital stay. Though local infiltration analgesia emerged as a potent alternative, consensus on whether local infiltration analgesia offers clinically relevant pain relief is still lacking due to inconsistent studies and lack of standardization. The present study is an attempt to deduce the analgesic efficacy of a standardized single-shot local infiltration analgesia (LIA) with epidural analgesia with comparative analysis of previous most cited studies.

Study Design & Methods: This is a prospective, randomized clinical trial done in n=74 patients with moderate to severe arthritis (Mean OKS - 15.24, SD 6.153) undergoing unilateral primary TKA in the south Indian population in a single center. The choice of analgesia, surgical technique, postoperative medications, and rescue analgesia and rehabilitation protocol on both groups are kept identical. In the LIA group, the CPN area is carefully avoided. The primary outcome is postoperative pain at rest and at activity, knee flexion and mobilization time quantified for 72hrs postoperatively. The student t-test, the chi-square test is used for analysis.

Results: The LIA group had significantly lower mean VAS scores at rest (P = <0.001) and during activity (p= < 0.001) for 72 hrs postoperatively, and the mean difference in knee flexion angle is low (7.20 ± 1.07) yet higher in LIA on D0 and a significantly better knee flexion angle is noted at postoperative D1 & D2 (P=0.001, 0.005). The mobilization time is significantly lower in the LIA group (P = <0.001) with a mean difference of 14.50 ± 6.236 hrs.

Conclusions: The multimodal local infiltration analgesia offers better pain relief, ROM and earlier mobilization than epidural analgesia if consistently standartized, facilitating rehabilitation and early return to day to day activities with lesser side effects and no transient peroneal nerve palsy if used methodically.

BACKGROUND

Being total knee arthroplasty (TKA) one of the most successful operations performed worldwide and its increasing numbers continues due to increased life expectancy and quality of life[1], it becomes mandatory to provide a good knee function within a shorter duration at all cost if possible.[2,3] Most patients experience moderate to severe pain which leads to prolonged hospitalization and increased post-operative complications.

Managing pain in TKA is a challenge, as it causes a variety of complications involving pulmonary, cardiac, renal problems and thromboembolism, also reflex endocrine, metabolic and inflammatory responses can occur if the pain is not brought under control. [4-6]Epidural analgesia is of proven benefit but it is associated with side effects such as spinal headache, neurogenic bladder, hypotension, respiratory depression, pulmonary hypertension, cardiac decompensation, and risk of spinal infection. [7,8]

Use of opiods in any form deals with post-operative pain efficiently but is often associated with nausea, vomiting, respiratory depression, drowsiness, pruritus, reduced gut motility, and urinary retention. [9]

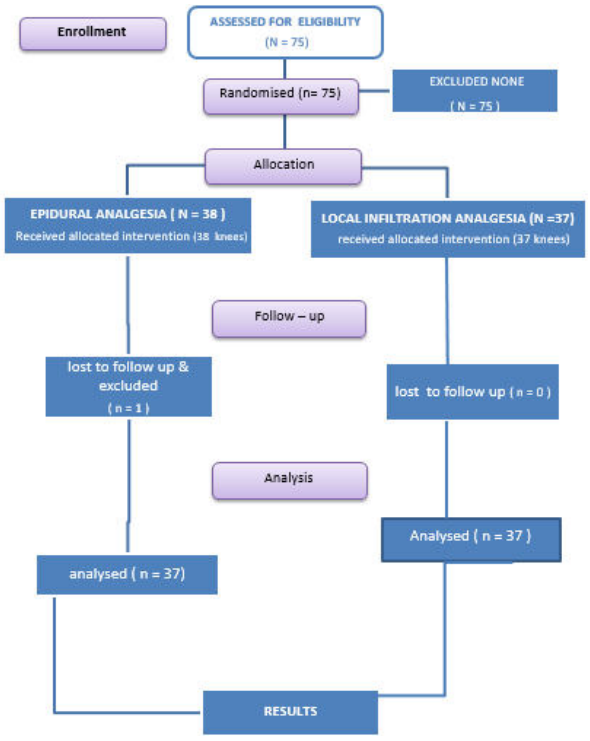
Thus in the process, to control postoperative pain efficiently with least side effects and with ensuring optimal muscle control for rehabilitation, various other methods have also been followed in which Local infiltration analgesia (LIA) has emerged as an alternative treatment[10] for postoperative pain, yet its efficacy remains inconclusive with inconsistent results from previous studies and meta- analyses. There is paucity of reports on the effects of LIA on functional capability & quality of life with many of the previous studies controlled poorly, with no standardization of analgesics. There is no agreement on which local anaesthetic agent and infiltration technique is most effective and well tolerated.

Thus here we conducted a prospective randomized control trial in which a single shot administration of local infiltration analgesia containing Ropivacaine, Ketorolac, Morphine, and epinephrine are compared with equivalent epidural analgesia dose postoperatively for 72hrs after TKA and the results are compared with previous most cited RCT's. We hypothesized that the postoperative pain score and the frequency of Opioid consumption and its related adverse effects must be comparable in both the groups (null Hypothesis).

PATIENTS AND METHODS

We conducted a single center, double blind, randomized control trial in which patients with a diagnosis of osteoarthritis, rheumatoid arthritis, post-traumatic osteoarthritis undergoing total knee arthroplasty (TKA) were randomly assigned to receive a periarticular injection or epidural analgesia.

The sample size was determined using Two Means - Hypothesis (equal variances), and a total of 75 patients were included in the study (with power 95% & Alpha Error 5.0%) and they were divided into two groups with n=37 each (as one lost followup & excluded, evident in the flow of patients through the study shown in flowchart.1)



Flowchart.1: CONSORT Flow Diagram Showing Flow Of Patients Through The Study

The **inclusion criteria** were, 1.all patients undergoing primary unilateral total knee arthroplasty. 2. Patients aged less than 80 years. 3. Patients with weight 50 – 100 kgs. 4. Patients with the ability to provide informed consent and to co-operate with the study. **Exclusion criteria** were, 1.Patients who were allergic to any of the ingredients of the injection in LIA. 2. Patients with major psychological problems. 3. Patients with renal insufficiency. 4. Patients with abnormal liver enzymes. 5. Patients with a major neurological deficit. All patients who were included in the study were operated in the Department of Orthopaedics, Medical Trust Hospital, Ernakulam, Kerala from October 2016 to December 2018. The study was approved by Institutional Ethical committee and written consent was obtained from all the patients before inclusion in the study.

RANDOMIZATION AND BLINDING

Patients were randomized using the numbers generated in the range from 0 to 99 by a computer software program (Microsoft Excel), each time when a patient is enrolled in the trial, a generated random number was allotted, such that patients with even numbers were taken for Epidural Analgesia Group (EPI) and odd numbers were taken for Local Infiltration Analgesia Group (LIA). The patient, the person who collected data and all other personnel involved in patient's care were kept blind throughout the study.

SURGERY AND PAIN MANAGEMENT

Detailed history of the patients including their comorbidities, pre-operative radiographs (standing AP, LAT, and patellar views) were recorded and evaluated. Total Knee Arthroplasty (TKA) was done by medial parapatellar approach, a tourniquet was used for all patients, drain was not used, and other perioperative interventions such as spinal anesthesia, prophylactic antibiotics, knee prostheses, and thromboprophylaxis were similar in all patients. Post-operatively all patients were started with the same standardized rehabilitation plan.

For EPI group an epidural catheter was placed at the L_2-L_3 or L_3-L_4 level at the time of administration of spinal anesthesia. The catheter was connected to an infusion pump delivering continuous infusion (at a flow rate of 4 ml/hr for 48 hrs) of 200ml of 1.85mg/ml (total 50ml) 0.75%Ropivacaine (at 7.5mg/hr), 2.5mics/ml (total 500mics) fentanyl hydrochloride (at 10µgm/hr) and 145ml Normal saline. The flow rate of the infusion pump was kept constant. The epidural infusion was started after wound closure, and the epidural catheters were routinely removed 72hrs after starting the epidural infusion.

For LIA group a drug mixture (cocktail) of 60ml volume was made with the following contents shown in table.1 below.

Table 1: Shows The Components Of Drugs Used For Local Infiltration Analgesia

Medication amount (in ml)	Strength/ dose	The total dose in a cocktail
Ropivacaine Hydrochloride (40ml)	0.75% (7.5mg/ml)	300mg
Morphine Sulphate (0.5ml)	15 mg	7.5mg
Adrenaline 0.5ml (1:1000)	1mg/ml	0.5mg
Ketorolac 2ml	30mg/ml	60mg
Normal saline 17ml		
Total of 60 ml solution		

The **injection technique** followed was systematic, given by the operating surgeon, and includes injection into all tissues involved during surgery. The injection was given in three stages using 20-ml syringes. The **first aliquot** of 20 ml of the mixture was injected, just prior to the implantation of the component, into the posterior aspect of the capsule and the medial and lateral collateral ligaments (as shown in figure.1), with 3 mm depth in the surrounding tissues (especially in the posterior capsule from one side to the other in a circular form) with the knee in flexion. We deliberately avoided injecting the mixture from 10'o clock to 12'o clock position in the right knee and 12'o clock to 2'o clock position in the left knee to avoid the peroneal nerve territory. Then, the **second aliquot** was given after placing the tibial and femoral components while the cement was curing (as shown in figure.2), the quadriceps mechanism and the retinacular tissues were infiltrated with an additional 20 ml of the mixture. Finally, the **third aliquot** (20ml) was used to infiltrate the fat and subcuticular tissues (figure.3). Lastly, a compression bandage was applied to reduce degradation and slow the diffusion of the local anesthetic into the bloodstream.

Figure.1 & 2: showing first and second aliquot infiltration of LIA.

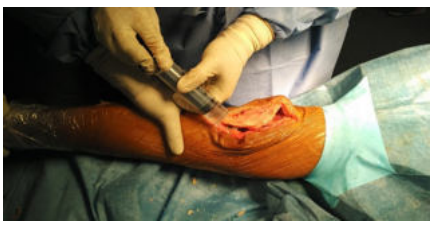


Figure.3: Shows Infiltration Of LIA in fat and subcuticular tissues.

In both the treatment groups, Oral tablet Diclofenac 75mg 12 hourly and capsule Omeprazole 20mg once a day was given. Opioid (tramadol hydrochloride 50mg) with centrally acting antiemetic Ondansetron 4mg SOS was used as rescue analgesia. A first-generation cephalosporin (Cefuroxime 1.2g) was used as the prophylactic antibiotic, intravenous perioperatively and for every 12 hrs for the first 48hrs after surgery. For thromboprophylaxis, injection Dalteparin 2500 IU subcutaneously once each evening was given for 10 days from post-op day 1. It is taken care that dalteparin was administered 12 hrs preoperatively and postoperatively.

OUTCOME MEASUREMENTS

The **primary outcome** was pain at rest and at activity, measured using numerical visual analog scale (VAS). The numerical VAS score ranges from 0 (indicating no pain) to 10 (indicates the extreme pain experienced in life) in 1cm increments. Pain scores at Rest(VAS-R) was recorded 6 hourly for a period of 72 hrs on POD-0,POD-1,POD-2 and pain scores at Activity(VAS-A) was recorded as the maximal pain experienced in 24hrs at activity(knee flexion) on POD-0,POD-1 & POD-2.

The **secondary outcomes** measured were Knee flexion angle(in degrees) on POD-0,POD-1,POD-2 & 1 month postoperatively, Mobilization time, Rescue analgesia (frequency on POD-0,POD-1,POD-2), Complications/Side effects if any and Duration of hospital stay.

Oxford Knee Scores(OKS) was used to assess TKA and is recorded preoperatively & 1 month post-operatively. It is concluded that the minimal clinically important difference (MCID) in OKS can be expected to be between 3 and 5 points (Murray et al [11], 2007) and can be used to power the studies and to ensure a statistical difference.

Statistical Analyses:

Data was entered in the Microsoft Excel datasheet and was analyzed using SPSS 22 version software. **Chi-square test:** (Comparison of) Gender, diagnosis, frequency of rescue analgesia, frequency of complications (P-value <0.05 was considered as statistically significant). **Unpaired t-test:** (comparison of) Age, Oxford knee scores, VAS pain scores, Knee flexion angle, Mobilization time, Duration of hospital stay (P-value <0.05 was considered as statistically significant).

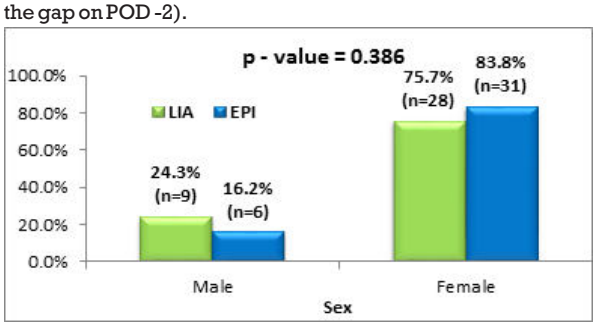
RESULTS

The mean age of patients in the local infiltration analgesia (LIA) group was 64.30 years and the epidural analgesia (EPI) group was 62.14 years. The difference between the two groups was not statistically significant (P = 0.238). The Mean preoperative Oxford knee score shown in the LIA group was 14.89 and in the EPI group was 15.59 and the difference between the two groups was not statistically significant (P = 0.625), table 2. The sex distribution among LIA group & EPI group was comparable and there was no significant difference (P = 0.386) as shown in Graph 1.

Table 2: Mean age distribution and preoperative Oxford Knee scores between the groups

Group	Mean	± SD	P-value
Age (in years)			
LIA	64.30	8.882	0.238
EPI	62.14	6.672	
Preoperative Oxford knee score			
LIA	14.89	6.411	0.625
EPI	15.59	5.895	

On comparing the Mean pain scores at Rest (VAS-R), LIA group showed a statistically significant difference (p = <0.001) in pain reduction at 6hrs, 12hrs & 18hrs on POD-0, POD-1, POD-2 (as shown in table 3) with a decrease in difference between the two groups in POD-2 (evident on figure.4,line diagram, with a larger gap opening between blue line & redline on POD-0 and the progressive closing of the gap on POD -2).



Graph 1: Showing The Sex Distribution Between The Groups

Table 3: Comparison of Mean VAS - R between LIA & EPI for 72hrs postop

VAS - R	LIA	EPI	p - value
POD 0			
6 Hours	1.622 ± 1.460	3.351 ± 0.889	<0.001*
12 Hours	1.622 ± 1.320	3.622 ± 1.233	
18 Hours	1.892 ± 0.966	3.892 ± 1.308	
POD 1			
8:00 AM	2.108 ± 1.286	3.297 ± 0.909	<0.001*
2:00 PM	1.892 ± 1.712	3.243 ± 0.796	
8:00 PM	2.135 ± 1.494	3.811 ± 0.967	
POD 2			
8:00 AM	2.324 ± 1.107	3.514 ± 0.607	<0.001*
2:00 PM	1.865 ± 1.032	3.270 ± 0.871	
8:00 PM	2.000 ± 1.225	2.919 ± 0.862	

*significant

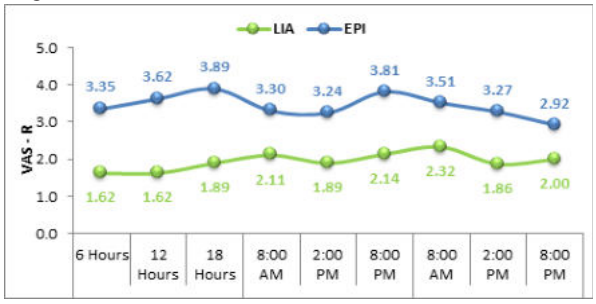


Figure 4: Line Diagram Showing Patterns Of Mean VAS - R for 72hrs Postop.

The Mean VAS–A scores in the LIA group showed significantly lower values than the EPI groups on POD-0, POD-1, POD-2 respectively (shown in table 4 & figure 5)

Table 4: Comparison Of The Mean VAS-A Between The LIA Group And EPI Groups

Group	Mean	SD	p-values
POD 0			
LIA	3.027	1.040	<0.001*
EPI	5.108	1.075	
POD 1			
LIA	3.297	1.077	<0.001*
EPI	4.757	0.925	
POD 2			
LIA	3.676	0.709	<0.001*
EPI	4.595	0.644	

* Significant

The comparison of Knee flexion angle (the angle of maximal flexion of knee in a day were taken as knee flexion angle of that day and was recorded and analysed) on postoperative days 0, 1 and 2 between LIA group & EPI group showed significantly better knee flexion in the LIA group on POD 1

and POD 2, however it was not significant on postoperative day 0 (on the day of surgery), given in table 5.

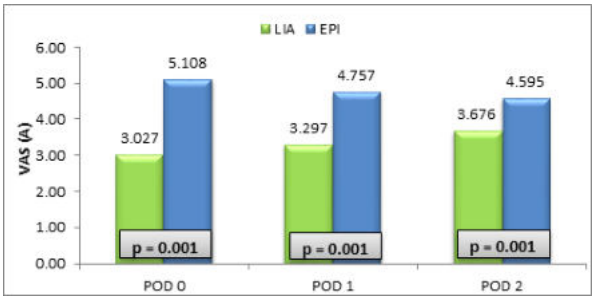


Figure 5: Bar diagram showing patterns of Mean VAS – A between LIA & EPI groups

Table 5: Comparison Of Knee Flexion Angle Between LIA and EPI

Group	Mean (in degrees)	SD	p-value
POD 0			
LIA	68.78	14.64	0.065
EPI	62.97	11.93	
POD 1			
LIA	83.51	14.43	<0.001*
EPI	70.54	12.40	
POD 2			
LIA	90.27	12.74	0.005*
EPI	81.22	13.81	

* Significant

On comparing the mobilization time (was recorded as the time from the end of surgery to the time at which the subject was first made to stand with or without support for > 30 sec's after active SLR > 45 deg) between the two groups, the readings were recorded and is shown in table 6, the difference in mobilization time between LIA and EPI was statistically significant (P = <0.001).The Mean mobilization time was significantly lower in LIA group (18.84 ± 7.844) when compared to the EPI group (32.89 ± 14.08).

Table 6: Comparison Of Mobilization Time Between LIA and EPI

Group	Mean	SD	p-value
LIA	18.84	7.844	0.001*
EPI	32.89	14.08	

* Significant

The number of patients who have taken Rescue analgesia was almost similar in both the groups and the difference is not statistically significant (as shown in table 7 & Figure 6).

Table 7: Comparison Of Rescue Analgesia Consumption Between LIA & EPI Groups

Rescue Analgesia	LIA (N=37)	EPI (N=37)	p - value
POD 0	5 (12.0%)	8 (20.0%)	0.359
POD 1	7 (20.0%)	6 (16.0%)	0.760
POD 2	5 (16.0%)	5 (16.0%)	1.000

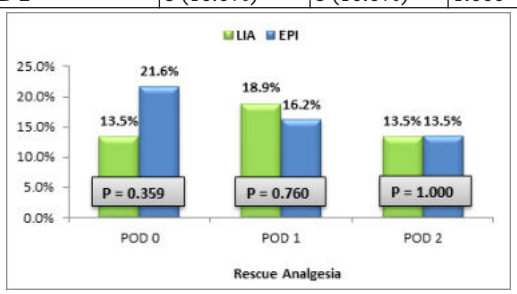


Figure 6: Comparison Of Rescue Analgesia Consumption Between LIA & EPI Groups.

The difference in all complications noted between LIA and EPI was not statistically significant. The distribution of complications was almost the same in both the LIA group and EPI group, yet nausea was noted more (45.9%) in the EPI group and edema was noted more (16.2%) in the LIA group. Hypotension was noted in 2.7% (n = 1) of patients in the EPI group given in table 8.

Table 8: Comparison Of Complications Between LIA And EPI Groups.

Complications	LIA (N=37)	EPI (N=37)	p – value
Surgical Site Infection	1 (2.7%)	0 (0.0%)	0.990
Edema	6 (16.2%)	1 (2.7%)	0.107
Nausea	11 (29.7%)	17 (45.9%)	0.150
Pruritis	0 (0.0%)	0 (0.0%)	--
Respiratory Depression	0 (0.0%)	0 (0.0%)	--
Hypotension	0 (0.0%)	1 (4.0%)	0.990
Transient Peroneal Palsy	0 (0.0%)	0 (0.0%)	--

The duration of hospital stay in subjects was recorded from the time of admission to the day of discharge, where subjects were considered for discharge if a: they have an Uncomplicated wound healing, b: Hb > 9mg/dl, c: No evidence of DVT, d: At least 90 degree of knee flexion, e: able to get out of bed & onto a chair independently, e: able to walk 10 meters with or without support and f: climb one or more flights of stairs with or without support.

The duration of hospital stay was almost similar in both groups and was not statistically significant, with LIA group (6.946 ± 2.041 days) and EPI group (7.486 ± 1.304 days) readings shown in table 9.

Table 9: Comparison Of Duration Of Hospital Stay Between LIA And EPI

Group	Mean (days)	SD	p - value
LIA	6.946	2.041	0.179
EPI	7.486	1.304	

The readings of Knee flexion angle and Oxford knee score (OKS) recorded postoperatively on follow up review after 1 month showed no statistically significant difference in post-op knee flexion between LIA and EPI group (P = 0.568). The Mean knee flexion was almost the same in LIA (115.3 ± 11.60) and the EPI group (113.6 ± 12.67). The difference in Oxford Knee scores between the groups was not found to be statistically significant (Table 10).

Table 10: Knee Flexion Angle And OKS In LIA And EPI Groups On 1 Month Followup Review.

Group	Mean	SD	p-value
Postoperative Knee Flexion Angle			
LIA	115.3	11.60	0.568
EPI	113.6	12.67	
Postoperative Oxford Knee Score			
LIA	44.32	3.489	0.129
EPI	45.27	1.367	

DISCUSSION

In this randomized clinical trial, we evaluated and compared the efficacies of single-shot local infiltration analgesia (LIA) with epidural analgesia (EPI) for postoperative pain control after total knee arthroplasty (TKA). We found that LIA Group was associated with significantly lower early postoperative pain at rest (VAS-R) in POD-0, POD-1, POD-2 than EPI Group (P = <0.001) and significantly lower pain scores at activity (VAS-A) in POD-0,POD-1,POD-2 than EPI Group (P = <0.001). The finding of our study was in agreement with Busch CA et al; [9] who stated that there was a statistically significant improvement in VAS pain scores (P = 0.007) in patients receiving LIA. Also,

Jiang J et al; [12] who demonstrated lower VAS scores in the LIA group at 6h, 24h and 48h postoperatively. Similarly, Mika Niemeläinen et al; [13] demonstrated that a median level of < 3 in the VAS score was considered to be an adequate level of pain management, and this was achieved in both groups in his study until 48h postoperatively. A study by Tsukada S et al; [14] in 2014 showed that periarticular injection group had significantly lower VAS pain scores postoperatively in 72hrs, however, there was no significant difference in VAS pain scores during activity.

Also, knee flexion angle was better in LIA group than EPI group for 72hrs postoperatively, and was statistically significant in POD-1 and POD-2 (P = <0.001, 0.005 respectively), though the flexion angle in POD-0 was statistically not significant the Mean flexion angle in LIA group (68.78 ± 14.64) was characteristically greater than EPI group (62.97 ± 11.93). Jiang J et al; [12] and Tsukada S et al; [14] showed similar results with significantly better knee flexion on POD-1 & POD-2 (P = 0.0072,0.021 respectively). A recent systematic review and meta-analysis of 38 RCTs done by Alisa seangleulur et al; [15] found that the LIA group had significantly lower pain scores and better ROM in the early postoperative period in 6hrs (P-value of <0.001) and 24hrs respectively.

In our study comparing the mobilization time, LIA group had significantly lower time for mobilization (P = <0.001) with a Mean duration of 18.84 ± 7.844 (EPI group 32.89 ± 14.08) hours following the end of surgery. The results of this study are contrary to Mehdi Moghtadaei et al; [16] who found that, there was no significant difference between the two groups and a median of almost 12 hours was reached by each patient to walk first, however in this study Mobilization time is recorded as the time taken by the subject to be able to walk at least 3 meters (with or without the help of a physiotherapist) after the operation, which may be a possible explanation for the contrasting findings. Our results were in agreement with Parvataneni HK et al; [17] in 2007 (prospective, non-blinded, RCT) who found that LIA group had an improved ability to perform straight leg raise on day 1 (63% Vs 21%), and similarly Spangehl MJ et al; [18] in 2015 (prospective, non-blinded, RCT) found that the subjects of LIA group were able to do straight leg raise on POD 1 (79% Vs 24%). The significant reduction in early postoperative pain of patients in our study aided us to control pain at a later stage also and gave us the confidence to mobilize, make subjects bear weight and start rehabilitation much earlier, thus producing a significant difference in knee flexion and mobilization time despite local edema at the surgical wound.

There was no statistically significant difference in taking rescue analgesia and the distribution was almost the same between the two groups [LIA (16%) versus EPI (17.3%)]. The study of Tsukada S et al; [15] in 2014 was consistent with us, while Mika Niemeläinen et al; [13] in 2014 reports a contrasting result with statistically significant (P = <0.001) reduction in consumption of rescue analgesia (oxycodone) within 24 hrs. Spangehl MJ et al; [18] in 2015 (LIA Vs CFNB + SNB) showed a conflict of interest with LIA group had higher narcotic(morphine) consumption on the day of surgery and equivalent thereafter. The inconsistency surrounding this topic is evident in multiple studies(shown in table 11). Where some RCTs used bupivacaine, while others used ropivacaine in varying doses lacking standardization and arrived at varying conclusions regarding effectiveness. Some studies also used corticosteroids in conjuction, which is still debatable if generalized.

We observed surgical site infection (of 2.7%, n=1) in the LIA group, empirical antibiotic (Inj.Cefeperazone sulbactum 1g/1g IV infusion after test dose 12 hourly) was started and a swab taken from the surgical site was sent for routine culture and sensitivity, showed no growth and antibiotics (Tab.Cefuroxime 500mg BD) were continued for 3 weeks. Until recent follow up after 3 months the patient had no signs of recurrence of infection. We also noted hypotension in 4% (n=1) in the EPI group. Studies in the larger population may be necessary to validate the precise incidence of hypotension between LIA & EPI groups. A meta-analysis of eight RCTs studied by Fowler SJ et al; [19] in 2008 in evaluating the use of epidural analgesia in postoperative pain control, showed a higher incidence of hypotension and urinary retention in EPI group.

In our data, we have not noted a single case of transient peroneal nerve palsy, this may be explained by the fact that we voluntarily avoided injecting the cocktail from 10'clock position to 12'o clock position on the right knee and 12'oclock to 2'o clock position in left knee both before and after the placement of implants (further studies and larger sample size are needed to validate the finding). The overall distribution of complications is almost the same in both groups.

We have not observed a significant difference in duration of hospital stay on comparing both groups (P = 0.179, with Mean difference between the two groups being 0.54 ± 0.737). It is imperative to note the systematic review of 27 RCTs done by Anderson & kehlet;[20] in 2014, which asserts, the length of stay stated in different RCTs reported variable data and potential reasons for the difference cannot be found and it was not related to the type of analgesic technique in the trials. Out of 27 RCTs only 12 studies described a welldefined discharge criteria yet length of stay dependency on pain was not reported in any study.

The follow up review at one month interval showed no significant difference in knee ROM (LIA – 115.3 ± 11.60 and EPI – 113 ± 12.67) and Oxford knee score (OKS) (LIA – 44.32 ± 3.489 and EPI – 45.27 ± 1.367 points) which concurs with the studies of Essving et al [21] in 2010 and Mika Niemeläinen et al; [13] in 2014. Though adequately powered, our study did not find any evidence of reasonable effect size as we found that the mean difference in OKS (MCID) after 1 month is 0.95 ± 2.122 points, is too low to ensure a statistical difference (P = 0.129) in a typical patient.

Table 11: Trial Charecteristics Of Studies Comparing LIA With Other Modalities Of Pain Control For Patients Undergoing Athroplasty Reffered In Our Study

Reference	TYPE OF STUDY	Procedure	Groups compared	LIA components Used*	Primary outcome	conclusion
Busch et al [9] 2006	Prospective single blind RCT	Unilateral TKA	LIA & Without LIA	Ropivacaine*,Ketorolac Epimorphine epinephrine	Overall analgesic consumption of both groups.	LIA provided better post op pain control.
Jiang J et al [12] 2013	Meta analysis of 21 RCTs	TKA or THA	Peri articular multimodal drug injection (PMDI) & placebo	Ropivacaine*** (except 5 studies, they used bupivacaine) Epinephrine,Ketorolac, Morphine. (9 studies used corticosteroids in conjunction)	Pain score by VAS at Rest & Activity.	PMDI is superior to placebo for pain relief.

Mika niemelainen Et al [13] 2014	Double blind RCT	Unilateral TKA	LIA & Placebo	Levo bupivacaine, ketorolac & adrenaline	Oxycodone consumption over 48 hrs post op.	Cumulative consumption of oxycodone is low in LIA group. LIA has no effect on functional outcome after 1 year.
Tsakuda S et al [14] 2014	Prospective single centre RCT	Unilateral TKA	Peri articular injection (PAI) & Epidural Analgesia	Ropivacaine**, morphine hydrochloride, epinephrine, ketoprofen, Methyl prednisolone	Pain scores by VAS at Rest for 22hrs post op	PAI had better post op pain relief than epidural analgesia with improved knee flexion.
Alias seangleulur Et al [15] 2016	Systematic review & meta analysis of 38 RCTs	Unilateral TKA	LIA & Placebo	Bupivacaine (18 studies) Ropivacaine*** (17 studies) Morphine (2 studies) Ketamine (1 study) Ketorolac, epinephrine Morphine (6 trials used corticosteroids & 3 trials used antibiotics in conjunction)	Pain intensity by VAS & morphine consumption over 48hrs.	LIA Provides better pain relief , improves ROM & shortens duration of hospital stay.
Mehdi moghtadaei Et al [16] 2014	Prospective double blind RCT	Unilateral TKA	LIA & single femoral nerve block (SFNB)	Ropivacaine**, ketorolac, epinephrine	Pain intensity by VAS & morphine consumption 24 to 48 hrs, patient satisfaction	LIA showed low pain scores (in first 6 hrs) & less morphine consumption (in first 24 hrs), yet no statistically significant difference.
Parvataneni HK et al [17] 2007	*Prospective non-blinded RCT*	*TKA & THA*	Peri articular injection (PAI) & patient controlled analgesia	Bupivacaine, morphine, epinephrine, methyl prednisolone, cefuroxime.	Pain scores by VAS , patient satisfaction scores & narcotic usage.	PAI shown to safely provide excellent pain control & functional recovery.
Spangehl MJ et al [18] 2015	*Prospective non-blinded RCT*	Unilateral TKA	Peri articular injections & continuous femoral block + single shot sciatic block (PNB)	Ropivacaine***, morphine, epinephrine, ketorolac.	Pain scores by VAS	PAI provides comparable pain relief to PNB & is simple to administer & slightly reduces length of stay.
Anderson & kehlet [20] 2014	Systematic review of 27 RCTs	TKA (17 studies) & THA (10 studies)	LIA & Placebo/peripher al nerve blocks (PNB)/ Continuos epidural analgesia / Intra thecal morphine	Ropivacaine ***(15 studies), epimorphine, ketorolac & And epimorphine , bupivacaine (2 studies).	Pain scores by VAS	LIA provides improved pain relief than placebo/ PNB/ continuous epidural analgesia
Essving et al [21] 2010	Randomised double blind study	TKA	LIA & Placebo	Ropivacaine* , ketorolac , epinephrine	Total opiod consumption (morphine & oral tramadol)	LIA is effective and safe esp' in early postoperative period for 4hrs

*ropivacaine 400mg, **ropivacaine 300mg, ***ropivacaine used in varied doses (like 150,200,225,300,350,400 mg)

Limitations of the study:

The first author who carried out the data collection and analysis was not blinded. Visual Analog pain score at rest (VAS-R) calculated at the day of surgery (DOS) was recorded every 6 hourly, more frequent measurement (Two hourly) can demonstrate the peak & plateau of distribution in the first 24 hours.

This would give more accurate readings as far as results are concerned. However, even 6 hourly is fairly acceptable in terms of results for analysis. The Formulated Discharge criteria was not validated and is not directly related with pain, thus it needs further studies to validate the relation between pain and length of hospital stay.

CONCLUSION

The use of a single shot standartized local infiltration analgesia protocol in total knee arthroplasty offers a better pain relief both in rest and in activity up to 72 hours postoperatively with better knee flexion and earlier mobilization time than epidural analgesia, facilitating rehabilitation and early return to day to day activities with

lesser side effects and no transient peroneal nerve palsy if used methodically and offers no long term benefit.

REFERENCES

1. Paul JE, Arya A, Hurlburt L, Cheng J, Thabane L, Tidy A, et al. Femoral nerve block improves analgesia outcomes after total knee arthroplasty: a meta-analysis of randomized controlled trials. Anesthesiology. 2010; 113(5):1144–62. PMID: 20966667 DOI: 10.1097/ALN.0b013e3181f4b18
2. Ryu J, Saito S, Yamamoto K, Sano S. Factors influencing the postoperative range of motion in total knee arthroplasty. Bulletin Hosp Jt Dis 1993;53:35-40. PubMed PMID:8012266
3. Shoji H, Solomonow M, Yoshino S, D'Ambrosia R, Dabezies E. Factors affectingpostoperative flexion in total knee arthroplasty. Orthopedics 1990 Jun;13(6):643-49. PubMed PMID:2367246
4. Bonica John J. Postoperative pain. In: Bonica JJ, editor. The management of pain. 2nd ed. Philadelphia: Lea and Febiger; 1990;461:80-82. [ISBN 10: 0812111222]
5. Allen HW, Liu SS, Ware PD, Nairn CS, Owens BD. Peripheral nerve blocks improve analgesia after total knee replacement surgery. Anesth Analg 1998; 87:93-97. DOI: 10.1097/00000539-199807000-00020 PubMed PMID: 9661553
6. Kehlet H. Surgical stress: the role of pain and analgesia. Br J Anaesth 1989;63:189-89. DOI:10.1093/bja/63.2.189 PubMed PMID:2669908
7. Pettine KA, Wedel DJ, Cabanela ME, Weeks JL. The use of epidural bupivacaine following total knee arthroplasty. Orthop Rev. 1989;18:894-01. PMID:2771438
8. Mahoney OM, Noble PC, Davidson J, Tullos HS. The effect of continuous epidural analgesia on postoperative pain, rehabilitation, and duration ofhospitalization in total knee arthroplasty. Clin Orthop Relat Res. 1990; 260:30-7.59. PMID:1977542.
9. Busch CA, shore BJ, Bhandari R, Ganapathy S, Mac Donald SJ, Bourne RB, Rorabeck CH, Mc Calden RW. Efficacy of periarticular multimodal drug injectionin total knee arthroplasty. A Randomised trial. J Bone Joint Surg Am.2006 may;88-A(5):959-63. PMID:16651569 DOI:10.2106/JBJS.E.00344
10. Vendittoli PA, Makinen P, Drolet P, Lavigne M, Fallaha M, Guertin MC, Varin F. A multimodal analgesia protocol for total knee arthroplasty: a randomized controlled study. J Bone Joint Surg Am. 2006; 88:282–89. PMID:16452738 DOI: 10.2106/JBJS.E.00173
11. Murray DW, Fitzpatrick R, Rogers K, Pandit H, Beard D J, Carr A J, Dawson J. The use of the oxford hip and knee scores. J Bone Joint Surg (Br) 2007; 89-B: 1010-14 DOI:10.1302/0301-620X.89B8.19424 PMID:17785736
12. Jiang J, Teng Y, Fan Z, Khan MS, Cui Z, Xia Y. The efficacy of periarticular multimodal drug injection for postoperative pain management in total knee or hip arthroplasty. J Arthroplasty 2013;28(10):1882-87. PMID:23910819 DOI: 10.1016/j.arth.2013.06.031
13. Niemeläinen M, Kalliovalkama J, Aho AJ, Moilanen T, Eskelinen A.Single periarticular local infiltration analgesia reduces opiate consumption until 48 hours after total knee arthroplasty. A randomized placebo-controlled trial involving 56 patients. Acta Orthop. 2014 Dec;85(6):614-19. PMID: 25238439 PMCID:PMC4259019 DOI:10.3109/17453674.2014.961399
14. Tsukada S, Wakui M, Hoshino A. Postoperative epidural analgesia compared with intraoperative periarticular injection for pain control following total knee arthroplasty under spinal anesthesia: a randomized controlled trial. J Bone Joint Surg Am. 2014 Sep 3;96(17):1433-8. PMID: 25187581 DOI:10.2106/JBJS.M.01098
15. Alisa Seangleulur, Pramook Vanasbodeekul, sunisa prapaitrakool. The efficacy of local infiltration analgesia in the early postoperative period after total knee arthroplasty: a systematic review and Meta-analysis. European journal of anaesthesiology 2016; 33(11): 816-831. PMID: 27428259 DOI: 10.1097/EJA.0000000000000516
16. Moghtadaei M, Farahani H, Faiz S H, Mokarami F, Safari S. Pain Management for Total Knee Arthroplasty: Single-Injection Femoral Nerve Block versus Local Infiltration Analgesia, Iran Red Crescent Med J. 2014; 16(1):e13247. DOI: 10.5812/ircmj.13247.
17. Parvataneni HK, Shah VP, Howard H, Cole N, Ranawat AS, Ranawat CS, Controlling pain after total hip and knee arthroplasty using a multimodal protocol with local periarticular injections. A prospective randomized study. J arthroplasty 2007;22(6,suppl 2): 33-38. PMID:17823012 DOI:10.1016/ j.arth.2007.03.034
18. Spangehl MJ, Clarke HD, Hentz JG, Misra L, Blocher JL, Seamans DP. The Chittaranjan ranawat award: Periarticular injections and femoral and sciatic blocks provide similar pain relief after TKA: A randomized control trial. Clin Orthop Relat res 2015;473(1):45-53. PMID: 24706022 PMCID:PMC4390909 DOI: 10.1007/s11999-014-3603-0
19. Fowler SJ, Symons J, Sabato S, Myles PS. Epidural analgesia compared with peripheral nerve blockade after major knee surgery: a systematic review and meta-analysis of randomized trials. Br J Anaesth. 2008;100(2):154–64.10. PMID: 18211990 DOI:10.1093/bja/aem373
20. Andersen LO, Kehlet H. Analgesic efficacy of local infiltration analgesia in hip and knee arthroplasty: a systematic review. British journal of anaesthesia (2014); 113(3):360–74. DOI:10.1093/bja/aeu155
21. Essving P, Axelsson K, Kjellberg J, Wallgren O, Gupta A, Lundin A. Reduced morphine consumption and pain intensity with local infiltration analgesia (LIA) following total knee arthroplasty. Acta Orthop 2010; 81 (3): 354-60. DOI: 10.3109/17453674.2010.487241