EFFICACY OF INTRAOPERATIVE PERIARTICULAR MEDICATION INJECTION USING LOCAL INFILTRATION ANALGESIA (LIA) IN TOTAL HIP ARTHROPLASTY.

Dr Sharman Joshi[1*], Dr Hardik labana[2], Dr Lavesh Agrawal[3], Dr Mustafa Johar[4]

Abstract

Background: Total Hip Arthroplasty (THA) have been recognized as a successful and long-lasting operative measure for the relief of significant morbidity caused by osteonecrosis or avascular necrosis of the hip joint. We conducted this study to determine the efficacy of perioperative periarticular medication injection using locally infiltrative analgesia (LIA) using a cocktail of Ketorolac, Clonidine, Ropivacaine, Adrenaline and distilled water in terms of postoperative pain management in patients undergoing THA.

Material and Methods: It was a prospective longitudinal study comprising of 50 patients (25 in study and control group each) conducted at a tertiary care centre of a metropolitan city in central India. Ethics approval was obtained from institutional ethics committee. Appropriate statistical tests were used. A *p value* < 0.05 was considered statistically significant.

Results: VAS score and McGill pain score were statistically significant at 8-hr postoperatively (**p < 0.01)**. However, at 16-hr postoperatively, only VAS score was found to be statistically significant in study group as compared to control group (**p < 0.01).**

Conclusion: The LIA cocktail mixture provided significant postoperative relief in pain as assessed by VAS and McGill pain scores.

Keywords: THA; LIA; VAS Score; McGill Pain Score

[1*]PG resident, Malwanchal University, Indore, E-mail: sharmanjoshi12@gmail.com
[2]PG resident, Malwanchal University, Indore
[3]Associate Professor, Devi Ahilya Vishwavidyalaya, Indore
[4]Prof & HOD, Barkatullah Vishwavidyalaya, Bhopal

***Corresponding Author:** Dr Sharman Joshi
*PG resident; Malwanchal University, Indore, E-mail: sharmanjoshi12@gmail.com

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Introduction:

Total Hip Arthroplasty (THA) has been recognized as a successful and long-lasting operative measure for the relief of significant morbidity caused by osteonecrosis or avascular necrosis of the hip joint. However, it is a painful surgery, therefore, successful rehabilitation of an individual mainly depends on management of pain and comfort level. Earlier mobilization, ambulation and return of normal gait are achieved better with pain control. In recent times, increased emphasis has been made on optimizing pain management after THA as a prerequisite for early recovery and rehabilitation. Presently, postoperative analgesia is delivered through different methods which includes continuous epidural infiltration, patient-controlled analgesia (PCA), peripheral nerve block, and continuous intraarticular infusion of analgesics. As far as relief from pain is concerned, continuous epidural infiltration and peripheral nerve blocks generally provide good postoperative pain relief; though, they are often associated with epidural bleeding, urinary retention, nausea, diminished muscle control, and damage to nerves.[1] Providing analgesia locally in the area of surgical manipulation with minimal systemic side effects is an attractive option.[2] Periarticular injection (PAI) (also known as local infiltration analgesia or periarticular multimodal drug injection) is a novel, alternative regional analgesic that involves administering analgesics into the surrounding tissue in the surgical field. This method usually consists of a local anesthetics of amide derivatives (e.g., bupivacaine, ropivacaine, levobupivacaine) and/or corticosteroids, opioids, epinephrine, nonsteroidal anti-inflammatory drugs and dilution with normal saline.[3] Locally infiltrative analgesia[4,5,6] included perioperative intraarticular infiltration of a "cocktail" of ketorolac, ropivacaine, and adrenaline into the perioperative tissues in patients undergoing total hip replacement surgeries. We conducted this study to determine the efficacy of perioperative periarticular medication injection using locally infiltrative analgesia (LIA) using a cocktail of Ketorolac, Clonidine, Ropivacaine, Adrenaline and distilled water in terms of postoperative pain management in patients undergoing THA.

Material and Methods:

The study was a prospective longitudinal study conducted for a duration of one year from March 2021 to February 2022 on patients admitted for elective hip surgery in the Department of Orthopedics at a tertiary care centre of a metropolitan city in central India. On the basis of a previous study conducted by Sreedharan et al,[7] and to detect a mean difference of 1.04 for Visual Analog Scale (VAS) score, the sample size at 95% confidence interval and 80% power of the study, came out to be 28 (14 in each group) using WIN PEPI software. Considering a non-response rate of 20% and to ensure power of the study, the final sample size was taken at 50 (25 individuals in each group).

Before the study was initiated, approval was obtained from the institutional ethics committee. Written and informed consent was obtained from each patient before their participation in the study.

Inclusion criteria*:* All adults patients undergoing elective surgery for total hip replacement for osteonecrosis or avascular necrosis of hip joint.

Exclusion criteria*:*

- Any adult patient with local hip infection or patient having any remote (extraarticular), active/ongoing infection or bacteremia.
- Revision cases of total hip arthroplasty
- Known allergy or intolerance to one of the drugs used in the study.
- Inability to comprehend subjective pain scales such as Visual Analogue Scale (VAS)

Procedure: All patients diagnosed with osteonecrosis or avascular necrosis of hip joint resulting in severe debilitating pain were counselled for THR. After obtaining verbal and written informed consent from patient, the patients posted for surgery were randomized using sealed envelope into either of the two group – one which received the intraoperative drug cocktail (hereinafter referred as the study group) and another which did not receive any intraoperative drug cocktail (control group). It was made sure that patients were not aware about to which group they belonged to.

Patients received Inj. Clexane (Enoxaparin) 0.6 mg S/C for the first three days and then switched to Tab. Xarelto (Rivaroxaban) 10 mg OD for 21 days, as deep venous thrombosis (DVT) prophylaxis.

Anesthesia: Prior to the induction of anesthesia, oxygen saturation was monitored, electrocardiogram (ECG) was undertaken, and blood pressure was recorded. Surgical procedure (Total hip Arthroplasty) was conducted under spinal anesthesia. The anesthesia was administered at the L2-L3 or the L3-L4 level. Inj. Bupivacaine 5 mg/mL (Isobaric) was taken, and 3 ml was injected with the patient sitting on the operation table with

the back hunched backwards. The patients were subsequently sedated with Propofol 10-30mg IV or Inj. Midazolam 1-2mg IV.

Intervention:

LIA Cocktail Mixture: Before starting the surgical procedure, a "cocktail" of adrenaline, ketorolac, ropivacaine and clonidine along with distilled Water was prepared on table by the scrub nurse in appropriate concentration and amount, while taking sterile precaution and were mixed well. (**Figure 1**)

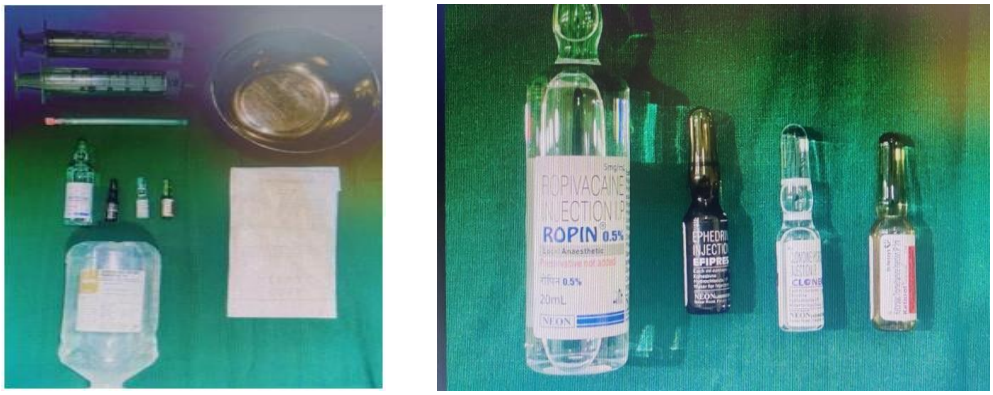

Figure 1: Depicting the components of the local infiltrative analgesia cocktail. [From left to right: Inj. Ropivacaine(5mg/ml), Inj. Epinephrine (1mg/ml), Inj. Clonidine 0.1mg/ml, Inj. Ketorolac (30mg/ml)]

Following preparation of LIA cocktail mixture, routine preoperative protocol was followed which included standardized painting and draping. Patient was positioned in a lateral decubitus position and total hip arthroplasty was performed using modified Hardinge approach to the hip.

In the study group, after taking the appropriate femoral cut and reaming for the acetabulum and the femoral canal, 50mL of the LIA cocktail solution was injected into the periosteum, the central ligamentum teres and in and around the labral base, just prior to cementation. Remaining LIA cocktail solution (50mL) was injected into the hip joint capsule, substance of the gluteus maximus, the short external rotators and close to the incision line after giving a post-operative saline wash and just prior to subcutaneous closure. (**Figure 2**)

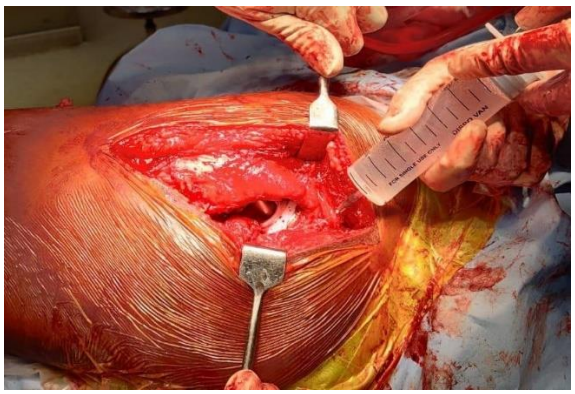

Figure 2: Injecting the LIA cocktail mixture into the hip joint capsule after implantation and prior to subcutaneous closure.

Post-operative management:

In the recovery room, all patients were administered aqueous formulations of Inj. Paracetamol (100ml IV infusion) and Inj. Diclofenac (100ml IV infusion). The patients were instructed preoperatively regarding pain assessment which would be undertaken on a 10-point rating scale, wherein the grading ranged from no pain = 0, and worst imaginable/bearable pain =10. The rating of pain intensity was recorded on the VAS at 8 hours, 16 hours, and 24 hours post operatively.

Evaluation: The patients were evaluated post operatively for pain using the VAS and the McGill pain questionnaire postoperatively at 8 hours, 16 hours, and 24 hours respectively and the findings were charted accordingly.

Adverse Event and Discharge from Hospital: During the first 10 days after surgery, there were no major adverse effects or complications reported that may be linked to the LIA cocktail. Concerns related to Ropivacaine toxicity were also quelled as we did not find any side effects attributable to ropivacaine use, including cardiotoxicity (determined by abnormal QRS complexes on the ECG and prolonged Q-T interval) cardiac arrest, seizures, major bleeding, or renal failure. All patients were discharged from the hospital by 12th post-operative day and subsequently followed up in outpatient department of the hospital. None of the patients reported with any side effects related to the use of LIA cocktail in the outpatient department.

Statistical Analysis: The data was collected and entered in Microsoft Excel 2016 and was analyzed using Statistical Package for the Social Sciences (SPSS for Windows, Version 25.0, IBM Corporation, Armonk, New York, United States). Continuous and categorical variables were expressed as the mean ± standard deviation, and frequency and percentage, respectively. Appropriate statistical tests were used to compare continuous and categorical variables between groups. A *p*-value of <0.05 was considered statistically significant.

Results: Table 1 shows the distribution of study participants in study and control group according to gender. Gender distribution was comparable across both the groups with males accounting for 64% of patients while 36% patients were females.

Table 1 Distribution of study participants according to gender

	Study group, n (%)	Control group, n (%)
Males	16 (64)	16 (64)
Females	9 (36)	9 (36)
Total	25 (100)	25 (100)

Table 2 shows distribution of study participants among groups according to age. They were comparable across both groups. Highest proportion belonged to less than 50 years as they comprised of around 66% (33) patients out of total study participants.

Table 2 Distribution of study participants according to age

Age (in years)	Study group, n (%)	Control group, n (%)
<50	15 (60)	18 (72)
51 – 60	5 (20)	5 (20)
> 60	5 (20)	2 (8)
Mean ± SD	45.84 ± 16.51	41.96 ± 12.12

Table 3 represents the comparison between VAS score between study and control group postoperatively at 8 and 16 hours respectively. Mann Whitney U test was used as data distribution was non-parametric. The difference between two groups was found to be statistically significant at 8 and 16 hours respectively (**p = < 0.01).** It was found that mean VAS Score at 8 hours was lesser among study group than control group. Similarly, at 16 hours post-operatively, the mean VAS Score was again found to be lesser in the study group when compared to the control group which did not receive the cocktail.

Table 3 Comparison of VAS scores postoperatively at 8 and 16 hours in Study and control groups

	Study Group			Control Group			Mann Whitney U*, p value **
VAS Score	**Mean**	**Median**	**Standard Deviation**	**Mean**	**Median**	**Standard Deviation**	
At 8 hours	3.44	4.00	1.00	6.12	6.00	1.13	24.50, <**0.01**
At 16 hours	5.12	5.00	0.83	5.96	6.00	0.93	164.50, <**0.01**

- Mann Whitney U Test used as non-parametric distribution - p value < 0.05 significant*

In the present study, the McGill Pain Score was compared at 8 and 16 hours postoperatively among the study and control group. Since the data was distributed non-normally, Mann Whitney U test was used. At 8 hours postoperatively, the mean McGill pain score was 2.28 in the study group and 3.56 in the control group. The difference was found to be statistically significant (**p = <0.01).** However, the McGill pain score at 16 hours postoperatively between the study and control group was not statistically significant (p = 0.09). (Table 4)

Table 4 Comparison of McGill Pain score postoperatively at 8 and 16 hours in Study and control groups

	Study Group			Control Group			Mann Whitney U*, p value **
McGill Pain Score	**Mean**	**Median**	**Standard Deviation**	**Mean**	**Median**	**Standard Deviation**	
At 8 hours	2.28	2.00	0.46	3.56	4.00	0.51	38.50, <**0.01**
At 16 hours	2.96	3.00	0.73	3.28	3.00	0.46	237.00, 0.09

- Mann Whitney U Test used as non-parametric distribution - p value < 0.05 significant*

Discussion:

Pain after THA is not well tolerated; it is severe in 60% and moderate in 30% of patients.[8] Postoperative pain management is important from point of early recovery and rehabilitation. In our study, we compared postoperative pain in patients those who received periarticular local infiltrative

analgesia (LIA) cocktail injection as compared to those who do not receive it after THA.

Busch et al conducted a study that involved randomizing 64 patients to receive either intraoperative periarticular injection containing ketorolac, epimorphine and epinephrine, or no injection. Those who received the injection had lower VAS score for pain during activity in the post-anaesthetic care unit and at 4 hours postoperatively and there was no cardiac or central nervous system toxicity observed.[2]

Dalury conducted the study for patients undergoing total knee arthroplasty and added Clonidine to the mixture of ropivacaine, ketorolac and epinephrine and used this cocktail mixture for perioperative intraarticular analgesic injection. In this study, he reported that the trial group which received the LIA cocktail perioperatively had significantly lower VAS pain scores (p value < .001) than the control group which received no cocktail (p value = .113).[9] These results are similar to our study.

Liu et al conducted a randomized clinical trial by using local and intraarticular cocktail analgesic injection in patients undergoing elective THA and they reported that VAS score at rest were lower for group receiving cocktail mixture as compared to the control group postoperatively at 6,10, and 24 hours (**$p < 0.05$**).[1]

As different designs have been used by different investigators, it becomes difficult to compare studies. Apart from this, previous studies conducted on LIA cocktail were mainly carried out in patients who underwent TKA; therefore, there were limited studies which have been carried out on THA. Parvataneni,et al randomized patients undergoing THA or TKA either to a study group receiving PIA or a control group receiving PCA with or without femoral nerve block (TKA patients only). THA patients demonstrated significantly lower average pain scores and higher overall satisfaction, lower opioid use and side effects, and improved early functional recovery when compared with controls.[10]

In another study carried out by Karen et al in which he randomized 80 patients undergoing THA into two groups. The trial group received an infiltration at the hip joint combined with a single-shot intraarticular injection, while control group received epidural infusion. The trial group had lower pain scores at rest and mobilization as compared to control group.

Sreedharan et al conducted a study to evaluate effectiveness of intraoperative periarticular cocktail injection for pain control and knee motion recovery after total knee replacement and they found that VAS scores (used to assess pain) postoperatively were lower than in the control group.[7] These results are similar to study results we reported in our study.

Negative or no effect on postoperative pain have also been reported. Lunn et al conducted a randomized, double-blind trial to assess postoperative pain after administrative of intraoperative local infiltration analgesia in patients undergoing THA. They found that pain was lower in the trial group who received the LIA as compared to the control group but was not statistically significant.[12] Similar results have also been reported by Reeves et al who administered continuous intraarticular ropivacaine in patients during TKA sutgery.[13]

One of the limitations of our study was as the number of patients included in the study were limited, therefore we cannot definitively confirm the safety of LIA. Another limitation of our study was that we did not attempt to evaluate the long-term clinical outcomes of our patients. There was no assessment of functional outcome after THA.

Conclusion:

The LIA cocktail mixture provided significant postoperative relief in pain as assessed by VAS and McGill pain scores. Apart from this, administration of intraoperative periarticular injection with multimodal drugs (as used in the cocktail) can significantly reduce the postoperative pain and may help in quicker recovery and rehabilitation and thus, improving patient satisfaction after total hip arthroplasty.

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