STUDY OF EFFICACY OF EXTRAOSSEOUS LOCAL INFILTRATION OF MULTIMODAL DRUG COCKTAIL FOR PAIN MANAGEMENT AFTER TOTAL JOINT ARTHROPLASTY IN LOWER LIMB – A STUDY PROTOCOL

Ankur Salwan¹, Gajanan L. Pisulkar²
¹Post Graduate Resident, Department of Orthopaedics, Jawaharlal Nehru Medical College, Datta Meghe Institute of Medical Sciences, Deemed to be University
²Professor, Department of Orthopaedics, Jawaharlal Nehru Medical College, Datta Meghe Institute of Medical Sciences, Deemed to be University

Corresponding Author: Ankur Salwan,
Post Graduate Resident, Department of Orthopaedics, Jawaharlal Nehru Medical College, Datta Meghe Institute of Medical Sciences, Deemed to be University
Email id: ankursalwan106@gmail.com
Contact no.: +917887448436

Abstract
Background: Postoperative pain, through diminished patient satisfaction and prolonged rehabilitation, may have a significant impact on patient recovery. While pain is an inevitable part of post-operative period, it is relevant common to have insufficient pain control which can have profound consequences. Post-operative pain has been a continuous struggle for health care, despite guidance and recommendations from pain management societies. Total joint arthroplasty is currently a potential treatment for severe arthritis, although post-operative pain control remains a concern. This study will compare two analgesic techniques (epidural infiltration and extraosseous infiltration) in terms of analgesic impact (as measured by the VAS score), early motor activities, and pain relief period duration after total joint arthroplasty, as well as drug safety.
Aim: Study the effect of extraosseous local infiltration of multimodal drug for post-operative pain management after total joint arthroplasty in lower limb.

Objective:
1. To compare the effect of epidural analgesia versus multimodal drug cocktail for pain relief in post-operative period with help of VAS score
2. To study comfort of patients in terms of walking distance, hip and knee range of movements in post-operative period.

Material and methods:
• Adults coming to Department of Orthopedics with advanced osteoarthritis of hip, knee and who will undergo arthroplasty surgery will be divided into 2 groups. Out of these 2 groups: one group will be given multimodal cocktail infiltration locally and other group will receive epidural analgesia.

Expected Results:
This study will help us determine the efficacy of extraosseous local infiltration of multimodal medication cocktail for pain relief following total joint arthroplasty in the lower limb. After the study, final results will be determined

Keywords: Post-operative pain, arthroplasty, local infiltration analgesia.

INTRODUCTION
Although the term "osteoarthritis" is not a good one (especially the use of "itis"), it is still used today, and we are gradually learning that it is not entirely incorrect. A number of experts have suggested that instead of using the suffix "itis" to show inflammatory pathology, alternative terms such as osteoarthritis or degenerative joint disease be used to describe the age-related mechanical degeneration of joints. Although arthritis refers to inflammation of a diarthrodial (synovial membrane-lined) joint, there is no inflammation in osteoarthritis. However, as understanding progresses, a number of inflammatory mediators involved for the development of this illness are being identified, therefore osteoarthritis may not be entirely incorrect. Despite the fact that arthritis refers to inflammation of a diarthrodial (synovial membrane-lined) joint, osteoarthritis does not involve inflammation. However, as knowledge of the disease grows, a variety of inflammatory mediators associated in its development are being found, therefore osteoarthritis may not be wholly inaccurate.
As a degenerative condition, osteoarthritis causes chronic pain and functional disabilities that can lead to impairment and poor quality of life.(1). Osteoarthritis cause damage and destruction of the articular cartilage, it
also causes sub-articular bone remodeling, formation of osteophytes, ligaments to undergo laxity, peri articular muscle weakness alongside synovial inflammation.

Prevalence of osteoarthritis:
A recent systematic review attempted to uncover the reasons behind the disparities in prevalence. Regarding the prevalence of Osteoarthritis in the knee, hip, and hand and wrist joints, according to case definition. The greatest estimates were obtained using the radiographic case definition, but self-reported and symptomatic OA criteria yielded similar results.

Osteoarthritis Epidemiology:
The majority of adults over the age of 60 have signs of OA in at least one joint, with radiological evidence in 70% of hips and knees in those over the age of 65. The frequency is 10% among 60-year-olds and rises with age; by 2020, the overall number of people affected will have doubled. OA is the fourth greatest cause of non-fatal health problems, accounting for 3% of all years spent disabled. Knee osteoarthritis is one of the common and debilitating type of Osteoarthritis.

Because of the growing old population and the obesity epidemic, the prevalence of OA is rising.

STAGES OF PROGRESSION OF OSTEOARTHRITIS:
Stage 1: Changes in chondrocyte metabolism as a result of proteolytic destruction of the cartilaginous matrix. Catabolic enzymes (metalloproteinases like collagenase and stromelysin) are produced in greater quantities by chondrocytes, which degrade the cartilage matrix. Protease inhibitors (tissue inhibitors of metalloproteinases (TIMP) 1 and 2) are being produced in smaller quantities.

Stage 2: Fibrillation, erosion of cartilage results in the release of degraded and altered proteoglycan and collagen fragments into the synovial fluid, causing an inflammatory response.

Stage 3: Synovial inflammatory reaction that lasts for a long time. Synovial macrophages produce metalloproteinases, IL-1, and TNF-, which accelerate cartilage disintegration. Other proinflammatory chemicals, such as free radicals, may also play a role in Stage 3 inflammation.

Stage 4: The joint architecture changes as cartilage is lost, and compensatory bone expansion occurs to transfer pressure across a wider surface area. These modifications, on the other hand, irritate the synovium even more, setting in motion a vicious cycle.

Indications for Total Joint Arthroplasty:
Total Joint Arthroplasty is an safe and efficient surgical procedure for patients having grade-4 arthritis to alleviate discomfort, regain functions and improve the quality of life linked to health. Reduced joint pain, increased mobility and movement, correction of deformities, limb length equalization (not guaranteed), increased leg muscle strength, improved quality of life, and the ability to return to everyday activities are all benefits of arthroplasty.

It's for people who have pain, impairment, or reduced function due to osteoarthritis, RA, or any type of arthritic deformity around the knee / hip joint. Reduction of discomfort, return to daily activities, mechanical alignment, preservation of the joint line, and ligament balancing are all goals of total joint arthroplasty.

Pain management post Total Joint Arthroplasty:
However, regardless of the type of arthroplasty performed, extreme postoperative pain has generally been associated with this surgery. Total joint arthroplasty is a surgical procedure that is inherently painful. It's critical to manage pain after a knee replacement if you want to improve your function and heal faster. With this in mind, it's crucial to remember that everyone suffers varying levels of pain after surgery, and that even within that range, there's a wide range of outcomes. can be interpreted in a variety of ways by various people.

Up to 60 % of patients with complete joint arthroplasty have severe post-operative pain complaints and the another 30% have mild pain complaints. This can lead to excruciating pain, patient dissatisfaction contributes to poor surgery outcomes and a longer recovery period. Therefore, in today's result-based patient care, maximizing pain management for patients who will undergo complete joint arthroplasty is mandatory for patient well-being. For early recovery and improved functional performance, successful management of postoperative pain is important. Early post-operative pain management, however, is critical in shorter hospital stays, increasing patient satisfaction with enhanced recovery. To regulate pain, numerous procedures are used, including continuous epidural anesthesia, local infiltration anesthesia, peripheral nerve block.

Patient satisfaction suffers as a result of postoperative pain, and recuperation takes longer and longer rehabilitation period, may have a significant impact on patient recovery. While pain is an unavoidable aspect of the post-operative experience, it is common to have insufficient pain control which can have profound
consequences. Despite guidance and suggestions from pain management groups, post-operative pain is still seen as a serious health-care issue.

**Evolution of epidural and intra-articular injections:**

Cocaine was administered through the sacral gap to treat sciatica in the earliest epidural treatment publications published in 1901. The use of cocaine in lumbar intrathecal injections was demonstrated by De Pasquier and Leri, but the outcomes were unfortunately "toxic cocaine accidents." They claimed to have had more success with sacral epidural injections. In 1936, compound E (cortisone) was found. In 1950, Hench and colleagues used this chemical and saw a temporary relief from rheumatoid arthritis, rheumatic fever, and a variety of other ailments. At the same time, Hollander and colleagues published a study on the effects of a longer-acting corticosteroid, namely Compound F (hydrocortisone), given as intra-articular injection. Steroid injections became a standard treatment for a range of other diseases after the discovery of cortisone. Robecchi and Capra described the use of peri-articular hydrocortisone to treat lumbar disc herniation in 1952. It was the first ever epidural steroids have been used to increase concentrations in an irritated nerve root at a local level. In 1953, Lievre also gave an account that 5/20 of his patients improved after receiving caudal epidural hydrocortisone. When hydrocortisone, prednisone, or methylprednisolone acetate were added to the solution, Brown claimed "100% success" while treating patients with lower back pain or sciatic nerve root pain with use of caudal injections in 1960. Unfortunately, each of the 27 trials had flaws in the therapy, follow up, or both, making the results hard to repeat. For a brief time, steroid therapy (intrathecal) was popular, but high complication rates, such as arachnoiditis and, less frequently, meningitis, led to a return to epidural anesthesia therapy for sciatica in the 1970s. Steroids have traditionally been injected caudally and inter-laminarily into the posterior epidural space, although small amount peri-neural (transforaminal) epidural injections into the anterior or the lateral epidural space for steroid implantation have recently become more popular. There is no confirmation that systemic steroids can help with pain from the spine.

About anesthetic options available for intraoperative and post-operative pain control Spinal/epidural anesthesia tends to be less of a systemic risk than the general one. Although continuous epidural analgesia has been found to be helpful, it is accompanied with adverse effects such as post puncture headaches, neurogenic bladder, intra operative hypotension, respiratory depression, pulmonary hypertension, cardiac decompensation, the risk of spinal infection, nausea, and vomiting. Compared with systemic approaches to pain management, the combination of intraarticular penetration and Local Anesthetic injection or infusion in the surgical area is more effective.

Peripheral nerve blocking with continuous infusions of opioids and bupivacaine into the femoral nerve has been linked to protracted wound drainage and neurovascular bundle damage. Whatever the treatment, with or without the use of NSAIDS, opioids or corticosteroids, and which may cause post-operative complications such as pneumonia or deep vein thrombosis, cardiovascular complications may be decreased by reducing the function of opioids and by utilizing local analgesic cocktail infiltration. There are less systemic side effects of local anesthetic and periarticular injections and local infiltrations than epidural anesthetic injections. Most recently, Kerr and Kohn created multimodal drug infiltration / injection in 1993 to avoid the possible risks of conventional techniques. Intraoperative infiltration of Extraosseous Multimodal medications achieved adequate pain management, early mobilisation and short hospital stay. This pain control strategy is aimed at controlling local pain pathways. Infiltration of multimodal medications enhances pain ratings, increases patient satisfaction and increases early recovery. In addition, due to sufficient pain management, it assists in outpatient complete joint arthroplasty and same-day discharge. For this reason, perioperative pain management strategies are still under intense examination. Adequate pain management has been linked to quicker recovery and better patient satisfaction measures. There is a decreased chance of readmission, a shorter length of stay, and a lower risk of complications such as cardiac arrest, myocardial infarction, respiratory pneumonia, venous thromboembolic disease, and chronic pain syndromes. Both of these advantages work together to reduce treatment costs and raise the grade of care. A multidisciplinary approach to multimodal analgesia To optimize the adequate analgesic result and mitigate the medicinal side effects of pain control.

The ideal care regimen for pre-operative, intra-operative and post-operative pain remains uncertain, and an individual personalized approach to post-operative pain management is suggested. The basic lesson is that...
any pain management program must be pain-free from the start, and the anesthetic agent chosen should help to prevent rebound pain, which is typical when 24-hour epidurals are stopped.

Epidural analgesia:
The use of epidural anesthesia as a supplement to general anesthesia is common. This is most typically utilized when both knees are replaced at the same time, though it is becoming less common as anesthesiologists improve their adductor canal blocks. An epidural anesthetic has the advantage of leaving a catheter in place, which makes it easy to top up and can be used for up to three days after surgery. The disadvantages stem from the difficulty of insertion and the lack of consistency. Epidural anesthesia gives excellent pain relief when used properly. Epidural anesthesia, on the other hand, has a reputation for being unreliable. It usually affects one leg more than the other, and spreading it to the side where it is needed can be challenging. To try to remedy the spread and get the anesthetic to where it's needed, you might have to roll to the side for a moment to allow the anesthetic to go across the space.

Periarticular injection:
Periarticular injection with long-acting liposomal bupivacaine is an efficient way to reduce preoperative discomfort after total hip/knee arthroplasty while reducing opiate intake and side effects. It has the potential to improve muscle control during recovery while avoiding the side effects of opiates and peripheral nerve blocking. To avoid leaking from the soft tissues, the infiltration method must be carefully monitored, and intravascular injection should be avoided. To get the most out of periarticular injection, concentrate the Periarticular injection on areas of the knee and hip with more innervation. This can help with postoperative pain control after total joint arthroplasty.

AIM AND OBJECTIVES
AIM:
Study the effect of extrascinous local infiltration of multimodal drug for postoperative pain management after total joint arthroplasty in lower limb.
OBJECTIVES:
The objectives of the study include:
- To compare the effect of epidural analgesia versus multimodal drug cocktail for pain relief in postoperative period with help of VAS score.
- To study comfort of patients in terms of walking distance, hip and knee range of movements in post-operative period.

MATERIAL AND METHODS
Type of study: Interventional study
Study design: Prospective study
Study area: Acharya Vinoba Bhave Rural Hospital, Sawangi (Meghe)
Study subjects: Adults from any age group coming to Orthopedic IPD with advanced osteoarthritis of hip, knee, who is admitted in AVBRH for arthroplasty surgery with postoperative pain management
Sample size:
The sample size for this study will be 30.
Duration of data collections and follow up: November 2020 to November 2022
Data analysis: NOVEMBER 2020 to NOVEMBER 2022
Inclusion criteria:
- All Patients who will undergo Total hip joint Arthroplasty
- All Patients who will undergo Total knee joint Arthroplasty
Exclusion criteria:
- Patient is allergic to any of the drug to be given in the multimodal cocktail
- Patients with deformities of spine
Research methodology:
Sample size 30
Group A (15 joints) – study group
Group B (15 joints) – control group
Drug sensitivity test for the drugs constituting the cocktail
Out of these 2 groups one group will be given multimodal cocktail infiltration locally and epidural analgesia with no infiltration in the other group of individuals
Pre-operative Workup:
Detailed history of all patients (medical co-morbidities, previous surgery, drug reactions) will be taken in consideration.
All patients are evaluated medically prior to surgery including evaluation and clearance /fitness by a physician and a cardiologist will be done to avert potential complications.
All patients will be randomized and selected for the technique Operative and post-operative period.
After a complete pre-op evaluation, all patients were scheduled for surgery under spinal anesthesia with standard surgical technique.

Operative and post-operative period:
After a complete pre-op evaluation, all patients were scheduled for surgery under spinal anesthesia with standard surgical technique.

Epidural infiltration:
Group A will receive epidural anesthesia with Epidural catheter no. 18 passed under aseptic precautions, in supine position after proper ascertaining of epidural space with loss of resistance technique.
Bupivacaine 0.125%, 5 ml/hour by infusion was administered epidurally during intraoperative period and with the help of infusion pump post operatively Epidural top up.

Cocktail preparation:
Group B to receive extraosseous multimodal drug cocktail

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dosage</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bupivacaine</td>
<td>0.5% (200-400mg)</td>
<td>24cc</td>
</tr>
<tr>
<td>Clonidine</td>
<td>0.08mg</td>
<td>0.8cc</td>
</tr>
<tr>
<td>Tramadol</td>
<td>30mg</td>
<td>10cc</td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>750mg</td>
<td>10cc</td>
</tr>
<tr>
<td>Adrenaline</td>
<td>300µg</td>
<td>0.3cc</td>
</tr>
<tr>
<td>Normal saline</td>
<td>0.9%</td>
<td>55cc</td>
</tr>
</tbody>
</table>

SITE OF THA INFILTRATION
Before the final reduction:
Anterior capsule, Iliopsoas tendon and insertion site
After final reduction (after irrigation and before the final closure)
Abductors
Fascia lata, Gluteus maximus and its insertion, Posterior capsule and short external rotators

SITES OF INFILTRATION IN TOTAL KNEE ARTHROPLASTY
Before insertion of liner and reduction
Posterior capsule
Posteromedial and posterolateral structures

After reduction
Extensor (quadriceps) mechanism
Synovium
Pes anserinus, anteromedial capsule, and periosteum
Iliotibial band Collateral ligaments and origins

EXPECTED OUTCOME
Use of multimodal drugs locally has gained widespread popularity because of its low risk of complications and shorter hospital stay and better post-operative pain management. This study will help us determine the efficacy of extraosseous local infiltration of a multimodal medication cocktail for pain relief following total joint arthroplasty in the lower limb. After the study, final results will be determined.

LIMITATION:
Long term effect of cocktail couldn’t be assessed due to short duration of study
In this study, we focused on the pain score, degree of movement shortly after arthroplasty surgery
A longer follow-up period would be preferable to assess the outcomes, particularly in terms of long-term knee motion and comorbidities. A study about the long-term outcome of peri-articular infiltration is needed to confirm the advantage of local infiltration.
Sampling procedure being purposive, the selection of representative sample and generalizability becomes a limitation. Hence, the study needs to be conducted in a larger sample and in a community-based setting to generalize the obtained results.

**DISCUSSION**

Although total joint arthroplasties are well-known for their success, they are frequently linked with lengthy and painful recovery periods. In recent years, significant progress has been achieved in reducing patient suffering and improving recovery. Less invasive surgical techniques, more selective soft tissue balance, increased patient education, and maybe enhanced tool and implant design have all contributed to a patient's overall rehabilitation after Total joint Arthroplasty. Improvements in pain control, on the other hand, deserve the most credit for the more speedy recoveries that are currently being observed.

Periarticular injections of long-acting liposomal bupivacaine are an excellent way to reduce postoperative pain following Total joint arthroplasty and while also reducing opiate intake and side effects. It has the potential to be beneficial in the following ways:

- With therapy, you'll get more muscular control while avoiding difficulties.
- Opiates and peripheral nerve inhibition are linked.
- To prevent leaching from soft tissues, an infiltration approach is required, as well as care. To avoid intravascular injection, precautions should be followed. Focusing on the periarticular infiltration. To maximize results, injections in areas of the joint with greater innervation are required.
- Periarticular injection has a number of advantages.

**REFERENCES**

